Bulletin of the World Health Organization, 62 (1): 121-132 (1984)

International collaborative study on juvenile hypertension. 2. First follow-up report

INTERNATIONAL COLLABORATIVE GROUP [1]

From 17 634 children born in 1964 and screened in 1977 two sample groups were selected: 10% of children from the upper 5% of the systolic and diastolic blood pressure distribution curves (95th percentile and above) were taken to form an "upper" group, and 10% from the remainder as a "lower" group. These children were re-examined in 1978. There was an 89% response rate (3640 children), with no difference in this rate between sexes or between the two groups. Data from the parents' responses to a questionnaire on themselves and the children were compared for differences between the two groups.

The parents' ages, smoking habits and marital status, and the children's order of birth, number of siblings, and proportion of twins did not differ significantly between the upper and lower groups.

The prevalence of hypertension and diabetes among the children, and the prevalence of hypertension, stroke and diabetes in the medical history of the parents were significantly higher in the upper than in the lower group. Signs of left ventricular hypertrophy and symptoms of a hyperkinetic heart syndrome (based on heart rate, innocent systolic murmurs, the magnitude of R and S waves on the ECG, and mean values of cardiothoracic and heart volume indices) occurred more frequently in the upper than in the lower group.

Children in the upper group were sexually more developed, taller, more obese (higher Quetelet's index and skinfold thickness), and less active physically.

Average values of blood sugar and serum uric acid were also higher in the upper than in the lower group. No significant difference was found between the two groups in the proportion of smokers among the children or in mean cholesterol values.

These differences between the upper and lower groups were strengthened by the comparison of children who showed repeatedly a low arterial pressure below the 30th percentile of the systolic and diastolic blood pressure distribution curves.

As reported earlier in an account of the procedures for the international collaborative study on juvenile hypertension (*1*), 17 634 children born in 1964 were screened in 1977. From these children two sample groups were selected: children whose systolic or diastolic blood pressures reached or exceeded the 95th percentile of the respective systolic and diastolic blood pressure distribution curves, who were designated as the "upper" group (about 10% of the screened population); and a 10% random sample from those with blood pressures below this level, here described as the "lower" group. A total of 3640 children were thus followed up in 1978.

On the assumption that a detailed study of these groups might give basic information on the preclinical phase of essential hypertension, data from questionnaires answered by the parents and from detailed medical examinations of the children in the two groups were collected and compared. Comparison was also made among groups of children whose blood pressures at the initial screening and during the follow-up examination were below the 30th percentile and at or higher than the 70th, 90th and 95th percentiles of the distribution curves.

The present paper reports the results of the first follow-up examination and shows considerable differences between the two groups in a number of variables.

METHODS

The questionnaire sent to the parents inquired into the following: birth order of the child and number of siblings, whether the child is a twin, and the child's

[1] The names of the research centres and investigators involved in this study are listed in Annex 1 on page 132. This article was prepared on behalf of the International Collaborative Group on Juvenile Hypertension by E. Török, I. Gyárfás, and M. Csukás. Requests for reprints should be addressed to Dr E. Török, Department of Cardiology, Hungarian Institute of Cardiology, H-1450 Budapest, P.O.B. 88, Hungary.

medical history (hypertension, heart disease, diabetes, renal disease, concussion of the brain, and admissions to hospital due to these diseases), and the parents' ages, smoking habits, and any history of cardiovascular disease or diabetes.

Children in both groups were investigated in detail; the physical examination included three blood pressure readings (same methods as during screening), assessment of sexual maturity, anthropometric measurements (height, weight, brachial and subscapular skinfold thickness, and left upper arm circumference), resting electrocardiogram with 12 leads (evaluated according to the Minnesota Code and standardized by the WHO ECG Reference Centre in Budapest, and measurement of the R, S, and T waves in some leads), chest X-ray for determining the heart volume index and cardiothoracic index, measurements of serum cholesterol (standardized by the WHO Reference Laboratory in Prague), serum uric acid, and blood glucose (one hour after an oral load), typing of ABO and Rh blood groups, and ophthalmoscopic examination of the fundus. The children were questioned about their smoking habits (5 or more cigarettes weekly), physical activity ("active" meant 7 hours or more of sports activity every week), and any drug treatment. These examinations were performed by physicians who were not aware of which group the child belonged to, and they took place 6–9 months after the initial screening in 7 out of the 8 centres. In one centre (Berlin-Köpenick) this examination was carried out 18 months after screening. The results from the two groups were compared by sexes and centres.

To account for any rapid blood pressure changes in these children it had to be checked whether the subjects in the upper and lower groups still remained in the same percentile range of the blood pressure distribution after 6–9 months during the follow-up examination. Therefore new blood pressure distribution curves were constructed by weighting the lower and upper group values in order to adjust for their different sizes; the blood pressure values in the lower group were multiplied by their sampling rates, and the values in the upper group were added. Comparison was also made among groups of children with readings below the 30th percentile, and those with values at or higher than the 70th, 90th and 95th percentiles in both the screening and the first follow-up distribution curves.

Statistical evaluation

Significance tests were calculated for each of the 8 centres. To compare upper and lower groups and the repeatedly low (below the 30th percentile) and high blood pressure groups (at 70th, 90th and 95th percentiles or above) during the screening and first follow-up examinations, t and u tests were used.

Probability values (P_i) for each centre were pooled by using the following formula:

$$\chi^2_{(2K)} = 2K \sum_{i=1}^{K} Pi$$

where K = number of centres.

Multiple regression coefficients were computed by adding one variable after another in sequence. The statistical significance of the change in R^2 (R being the multiple correlation coefficient) was tested by F-statistics.

RESULTS

Parents' questionnaire

The response rate to the questionnaire was 76.1% (Table 1). Data relating to children in the upper group and lower group (figures given below in parentheses are, respectively, for these two groups) showed no significant difference between the two groups in the ages of the fathers (29.7 ± 6.3 vs. 29.5 ± 6.3 years) and of the mothers (26.8 ± 5.3 vs. 26.4 ± 5.3 years) at the time of the child's birth. The age of the fathers varied from 28.6 ± 6.0 (Berlin-Köpenick) to 31.7 ± 7.6 years (Havana), and that of the mothers from 25.4 ± 5.3 (Budapest) to 27.8 ± 5.0 years (Moscow 3). The proportion of fathers over 40 years (6.6% vs. 6.7%) and of mothers over 35 years (7.5% vs. 7.8%) also did not differ significantly between the upper and lower groups.

The proportion of parents divorced was higher in the lower than in the upper group ($P < 0.05$). The proportion divorced was highest in Kaunas (34.4% vs. 34.1%) and lowest in Moscow 3 (16.9% vs. 9.7%).

The proportion of smokers among the fathers was slightly higher in the lower (55.8%) than in the upper group (54.7%); this difference was not significant. The proportion of smokers among mothers was, however, significantly higher in the lower than in the upper group ($P < 0.01$). The proportion of smoking fathers was lowest in Berlin-Köpenick (46.3% vs. 38.6%) and highest in Havana (66.3% vs. 66.7%). The proportion of smoking mothers was lowest in Moscow 3 (0% vs. 1.4%) and highest in Budapest (29.4% vs. 32.0%). The mean blood pressure values of the children showed no significant association with the smoking habits of either parent.

The proportion of first-born children and of twins showed no difference between the two groups. The mean blood pressure values of first-born children and

Table 1. Data from the questionnaire indicating percentage responses in the population and in the upper and lower groups concerning the parents and the child

Variables	Population (n = 13 035)	Children followed-up		P values
		Upper group (n = 1342)	Lower group (n = 1362)	
Response rate	76.1	68.1	65.4	< 0.001
Parents divorced	23.3	21.4	23.7	< 0.05
Father smokes	55.8	54.7	55.8	N.S.[a]
Mother smokes	21.2	19.0	21.6	< 0.01
Child:				
a twin	1.8	1.4	1.3	N.S.
first born	57.7	57.8	56.5	N.S.
no siblings	27.6	30.1	27.0	< 0.001
Child's history:				
Heart disease	2.5	2.6	2.4	N.S.
Renal disease	3.7	3.2	3.7	N.S.
Hypertension	1.9	5.7	1.6	< 0.001
Diabetes	0.2	0.5	0.08	< 0.001
Concussion of the brain	6.2	4.7	6.1	< 0.05
Admission to hospital	9.3	9.1	8.9	N.S.
Parents' history:				
Hypertension				
father	11.6	14.5	10.3	< 0.001
mother	13.3	16.3	12.8	< 0.001
Myocardial infarction				
father	1.8	2.0	1.8	N.S.
mother	0.4	0.5	0.4	N.S.
Stroke				
father	0.7	0.8	0.6	N.S.
mother	0.2	0.3	0.08	< 0.01
Diabetes				
father	1.5	1.5	1.4	N.S.
mother	1.1	2.1	0.9	< 0.001

[a] N.S. = not significant.

of twins did not differ from those of other children. The proportion of children without siblings was significantly higher in the upper than in the lower group ($P < 0.01$).

Medical history of the children

There was no significant difference in reported heart disease and renal disease in children between the upper and the lower groups (Table 1). A history of hypertension was, however, significantly more common in the upper than in the lower group ($P < 0.001$); this trend was noted in all the centres and in both sexes. Diabetes was reported in 26 (0.21%) children; 7 of the children with diabetes were in the upper group and 1 in the lower group ($P < 0.001$). Concussion of the brain was reported more often in the lower than in the upper group ($P < 0.05$) in 6 of the centres and in both sexes. The admissions to hospital due to these diseases showed no significant difference between the two groups (Table 1).

Medical history of the parents

A history of hypertension in both fathers and mothers was reported significantly more often in the upper than in the lower group ($P < 0.001$). This was found in all centres and in parents of children of both sexes.

Children with a positive history of hypertension in either parent showed higher mean systolic and (to a lesser extent) diastolic blood pressures than children both of whose parents had a negative history; these differences were significant for only the systolic blood pressures (Fig. 1).

In the case of mothers only, a history of stroke and diabetes was significantly more common in the upper than in the lower group ($P < 0.01$ and $P < 0.001$). No difference in parental history of myocardial infarction was found between the two groups (Table 1).

First follow-up examination of the children

Out of the 4054 children selected for the first follow-up medical examination, 3640 (89.8%) were examined. The response rate varied from 83% (Budapest) to 99% (Kaunas). There was no significant difference between the upper and lower groups by centres and sexes. Of the 3640 children examined, 1846 (50.7%) were boys and 1794 (49.3%) were girls. There were 1775 (48.8%) children in the upper and 1865 (51.2%) in the lower group.

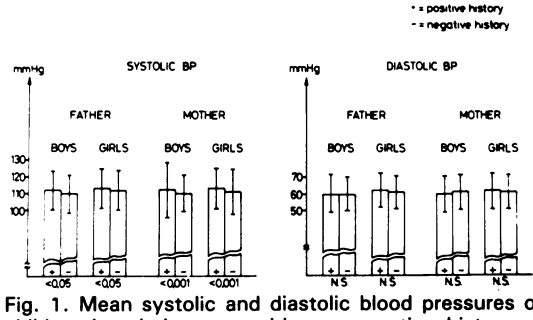


Fig. 1. Mean systolic and diastolic blood pressures of children in relation to positive or negative history of hypertension in parents.

The ages of the children at the first follow-up examination showed no difference in the two groups; the mean age was between 160 and 165 months in 7 of the centres, while in Berlin-Köpenick the average age was 175 months (Table 2).

The blood pressure values at the first follow-up examination, compared to those at screening, showed that the difference in blood pressures between the upper and lower groups decreased (regression towards the mean). Nevertheless, a highly significant difference remained in blood pressures between the two groups ($P < 0.001$). Mean values of the blood pressure of the population were significantly higher at the first follow-up examination than at screening (Fig. 2).

The heart rates of the girls and boys were higher in the upper groups from all centres ($P < 0.001$). Both in the upper and in the lower groups, girls showed higher heart rates than boys in all the centres ($P < 0.001$) (Fig. 3). Sinus tachycardia—a heart rate of $\geqslant 100$/min (Minnesota Code 8-7)—was observed more often in the upper than in the lower group in both sexes ($P < 0.001$). Among the boys, left ventricular hypertrophy (Minnesota Code 3-1) was seen more frequently in the upper than in the lower group ($P < 0.001$); there was no such difference among the girls. Left axis deviation on the ECG (Minnesota Code 2-1) varied from 0% to 6.1% in boys and from 0% to 9.3% in girls between centres, and was not significantly different between the upper and lower groups (Fig. 4).

In both sexes, the R waves in the ECG were greater in the upper than in the lower group ($P < 0.01$). Only girls showed greater S and T waves in the upper groups ($P < 0.05$) (Fig. 3). The cardiothoracic and heart volume indices were examined in Budapest and Havana. The heart volume index was higher in the upper than in the lower groups both in boys ($P < 0.05$) and in girls ($P < 0.01$); only girls showed a higher cardiothoracic index in the upper group ($P < 0.01$) (Fig. 3).

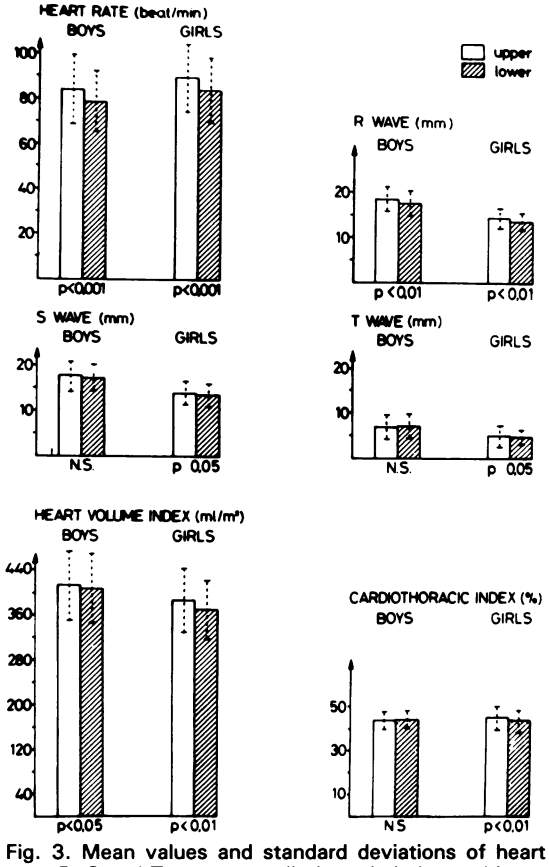
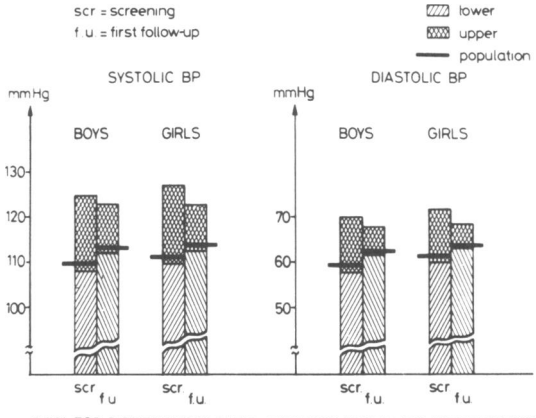


Fig. 3. Mean values and standard deviations of heart rate, R, S and T waves, cardiothoracic index and heart volume in the upper and lower groups, by sexes.



p < 0,001 FOR DIFFERENCES IN BPs BETWEEN UPPER AND LOWER GROUPS AT FIRST FOLLOW-UP

p < 0,001 FOR CHANGES IN BPs OF THE POPULATION AND OF UPPER AND LOWER GROUPS MEASURED AT SCREENING AND AT FIRST FOLLOW-UP

Fig. 2. Blood pressures of the population and of upper and lower groups at screening and at first follow-up examination.

Eleven (0.3%) children had obvious heart disease; 9 (0.25%) of these were of congenital and 2 (0.05%) of rheumatic origin. Of the 9 children with congenital heart disease, 4 had coarctation of the aorta, with no significant difference between boys and girls. Among the boys from all centres and the girls from 5 centres, innocent systolic murmurs were more frequent in the upper group ($P < 0.01$) (Fig. 4).

Eyegrounds were examined in Budapest and Kaunas, where hypertensive signs were more often seen in both girls and boys in the upper groups (for boys, $P < 0.001$; for girls, $P < 0.01$) (Fig. 4).

In all the centres and in children of both sexes the weight, height, Quetelet's index, skinfold thickness, and arm circumference measurements were signifi-

Table 2. Number of children in the upper and lower groups who were selected and the number who were examined, with their mean ages and sex, in the 8 centres

Centres	No. of children selected			No. of children examined							Age in months (mean ± S.D.)			
				Total	Boys			Girls			Boys		Girls	
	Total	Upper group	Lower group		Total	Upper group	Lower group	Total	Upper group	Lower group	Upper group	Lower group	Upper group	Lower group
Berlin-Köpenick	370	180	190	317	166	80	86	151	76	75	174.9 ± 4.7	175.8 ± 3.4	174.6 ± 4.6	175.2 ± 4.1
Berlin-Pankow	477	231	246	431	220	108	112	211	107	104	164.8 ± 3.6	164.7 ± 3.6	164.6 ± 3.8	164.0 ± 3.3
Budapest	1119	554	565	924	469	240	229	455	215	240	162.8 ± 4.2	162.6 ± 4.2	162.8 ± 3.9	162.4 ± 4.2
Havana	382	190	192	359	180	94	86	179	89	90	160.2 ± 3.6	160.1 ± 3.7	160.5 ± 3.3	159.9 ± 3.6
Kaunas	416	203	213	411	202	104	98	209	98	111	162.8 ± 3.2	162.7 ± 3.0	162.9 ± 3.4	163.0 ± 3.4
Moscow 1	481	244	237	428	220	106	114	208	110	98	162.2 ± 3.4	162.4 ± 3.5	161.9 ± 3.8	162.0 ± 3.7
Moscow 2	431	198	233	400	208	99	109	192	85	107	162.2 ± 3.7	162.3 ± 3.4	161.9 ± 3.6	162.4 ± 3.5
Moscow 3	378	171	207	370	181	83	98	189	81	108	161.7 ± 3.2	161.0 ± 3.6	164.4 ± 3.6	161.3 ± 3.7
Total	4054	1971	2083	3640	1846	914	932	1794	861	933	163.6 ± 5.3	163.6 ± 5.4	163.5 ± 5.2	163.3 ± 5.2

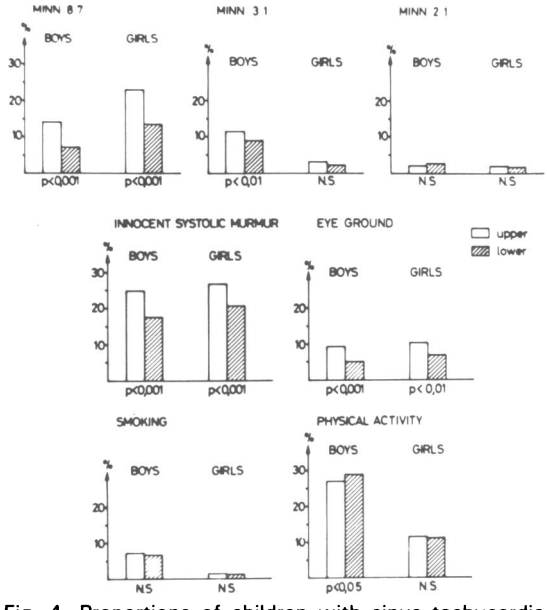


Fig. 4. Proportions of children with sinus tachycardia (Minnesota Code 8-7), left ventricular hypertrophy (Code 3-1), and left axis deviation (Code 2-1), and with innocent systolic murmurs, eyeground changes, smoking, and physical activity in the upper and lower groups, by sexes.

cantly greater in the upper group than in the lower group (Fig. 5). Weight and height were lowest in Havana as they were during screening. Quetelet's index was also lowest in Havana among both boys and girls from the lower groups.

Higher scores for sexual maturation were found in both sexes in the upper group (for boys, $P < 0.01$; for girls, $P < 0.01$) (Fig. 5). The proportion of girls after menarche was higher in the upper group (87%) than in the lower group (76%) in all centres ($P < 0.001$).

Serum cholesterol was examined in 4 centres (Berlin-Köpenick, Berlin-Pankow, Budapest, and Moscow 1). There were no significant differences between the upper and lower groups either in girls or in boys. The postload blood sugar was examined in Berlin-Köpenick, Berlin-Pankow, and Budapest and was found to be higher in the upper groups among boys ($P < 0.05$). Serum uric acid was measured in Berlin-Pankow and Budapest; boys and girls in the upper groups had higher values in both centres. These differences were significant in Budapest both for boys ($P < 0.05$) and for girls ($P < 0.01$), and in Berlin-Pankow for girls only ($P < 0.01$) (Fig. 6). Blood groups were typed in Berlin-Pankow, Budapest, and Moscow 1; no characteristic blood group type for upper or lower groups was found. Only 15 children (0.4%), 9 boys and 6 girls, were being treated with antihypertensive drugs; all the boys and 4 of the girls were in the upper group.

There was no significant difference in smoking habit between the upper and lower groups (Fig. 4). More boys than girls smoked; there was also a considerable difference between centres, varying from 2.0% (Kaunas) to 20.2% (Moscow 1) in boys, and from 0% (the four Soviet centres) to 7.7% (Berlin-Pankow) in girls.

The physical activity of boys was higher in the lower than in the upper group ($P < 0.05$). The pooled data for girls showed no difference between upper and lower groups (Fig. 4).

Multivariate regression analysis

Multivariate regression analysis was performed in which the systolic blood pressure (SBP) and diastolic blood pressure (DBP) were related to the other variables examined. Height, weight, and heart rate were the most powerful independent variables, together

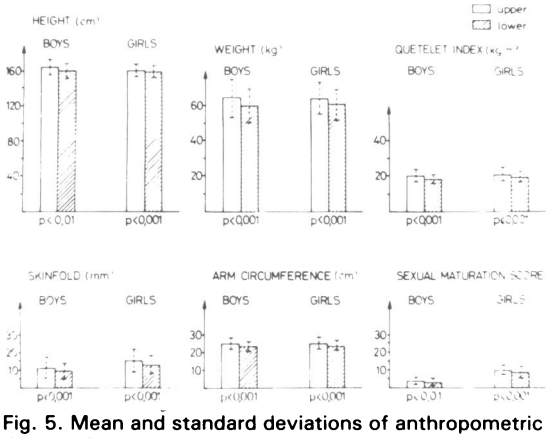


Fig. 5. Mean and standard deviations of anthropometric data and sexual maturation in the upper and lower groups, by sexes.

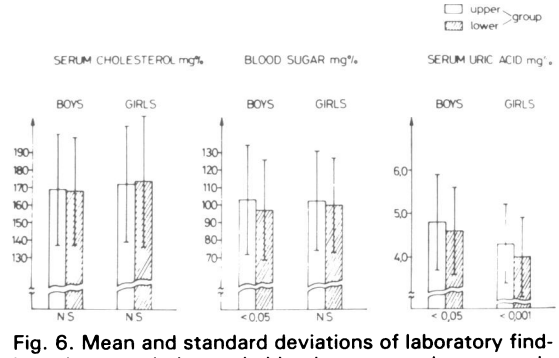


Fig. 6. Mean and standard deviations of laboratory findings (serum cholesterol, blood sugar, and serum uric acid) in the upper and lower groups, by sexes.

contributing about 20% to the SBP in both girls and boys. This contribution was less in boys from Budapest and Moscow 3 and in girls from Havana and Moscow 2 and 3. Sexual maturation contributed a further 2%. Age did not contribute to the SBP, within the narrow age range of the present study. R and S waves of the ECG made a 2–3% independent contribution. All these variables together contributed up to 36% to the SBP in both girls and boys (Berlin-Köpenick and Moscow 1). In Budapest the serum uric acid, blood sugar, serum cholesterol, heart volume index, and cardiothoracic index were also measured and taken into consideration; they contributed a further 4%.

Height, weight, and heart rate contributed about 10% to the DBP in both boys and girls. This contribution was less in boys from Kaunas and Moscow 1, and in girls from Moscow 2. Sexual maturation contributed 1%, and R and S waves of the ECG a further 1–2% to DBP. In boys the total contribution from all measured variables was 25% (Berlin-Pankow) and in girls, 42% (Berlin-Köpenick). Allowing for serum uric acid, blood sugar, serum cholesterol, heart volume index and cardiothoracic index, a further 1% contribution to DBP was seen in Budapest (Table 3).

Table 3. Regression coefficients (R^2) resulting from multivariate regression analysis of data from the Budapest centres

Independent variables	Dependent variables			
	Systolic blood pressure		Diastolic blood pressure	
	Boys	Girls	Boys	Girls
Number of children	194	189	194	189
Height (H)	0.01	0.03	0.03	0.02
H + Weight (W)	0.03	0.17	0.06	0.10
H + W + Heart rate (HR)	0.07	0.22	0.08	0.13
H + W + HR + Sexual maturation (SM)	0.07	0.22	0.11	0.13
H + W + HR + SM + Age	0.07	0.22	0.12	0.14
H + W + HR + SM + Age + R wave	0.08	0.22	0.12	0.15
H + W + HR + SM + Age + R wave + S wave	0.09	0.24	0.12	0.15
H + W + HR + SM + Age + R wave + S wave + serum uric acid	0.11	0.24	0.16	0.15
H + W + HR + SM + Age + R wave + S wave + serum uric acid + blood sugar	0.14	0.27	0.18	0.16
H + W + HR + SM + Age + R wave + S wave + serum uric acid + blood sugar + serum cholesterol	0.14	0.27	0.18	0.16
H + W + HR + SM + Age + R wave + S wave + serum uric acid + blood sugar + serum cholesterol + heart volume index (HVI)	0.16	0.28	0.18	0.16
H + W + HR + SM + Age + R wave + S wave + serum uric acid + blood sugar + serum cholesterol + HVI + cardiothoracic index (CTI)	0.16	0.28	0.23	0.16

Association of continuous variables and repeatedly high and low blood pressure

We also compared children with repeatedly low and with repeatedly raised blood pressure values on the basis of the distribution curves during screening and at the first follow-up medical examination. The children were classified into four groups on the basis of each SBP and DBP distribution curve: those who showed repeatedly low blood pressure values (below the 30th percentile) and those with raised values (at the 70th, 90th, and 95th percentiles or higher) on the basis of sex-specific distributions both during screening and at the first follow-up examination.

Among centres the mean SBP of the groups with values below the 30th percentile was in the range of 88–108 mmHg (11.7–14.4 kPa) (lowest in Moscow 1 and highest in Berlin-Köpenick) in both sexes. The mean SBP of the groups with values at or above the 95th percentile was in the range of 135–151 mmHg (18.0–20.1 kPa) (lowest in Kaunas and Havana, highest in Berlin-Köpenick) in boys, and from 138 mmHg (18.4 kPa) to 147 mmHg (19.6 kPa) (lowest in Moscow 1 and Havana, highest in Budapest) in girls. The mean DBP of the groups with values at or above the 95th percentile varied from 78 mmHg (10.4 kPa) to 87 mmHg (11.6 kPa) (lowest in Havana, highest in Budapest) in boys, and in the range of 72–91 mmHg (9.6–12.1 kPa) (lowest in Moscow 2 and highest in Budapest) in girls (Fig. 7 and 8).

All the continuous variables studied were evaluated within each group for an association with blood pressure distributions.

Age. No significant difference was found in the ages of the children among the four groups established on the basis of systolic and diastolic blood pressure distributions (below the 30th percentile and at the 70th, 90th, and 95th percentiles or above) (Fig. 9).

Anthropometric data. Measurements of height, weight, Quetelet's index, skinfold thickness, and arm circumference were significantly higher in the upper groups (at or above the 70th, 90th, and 95th percen-

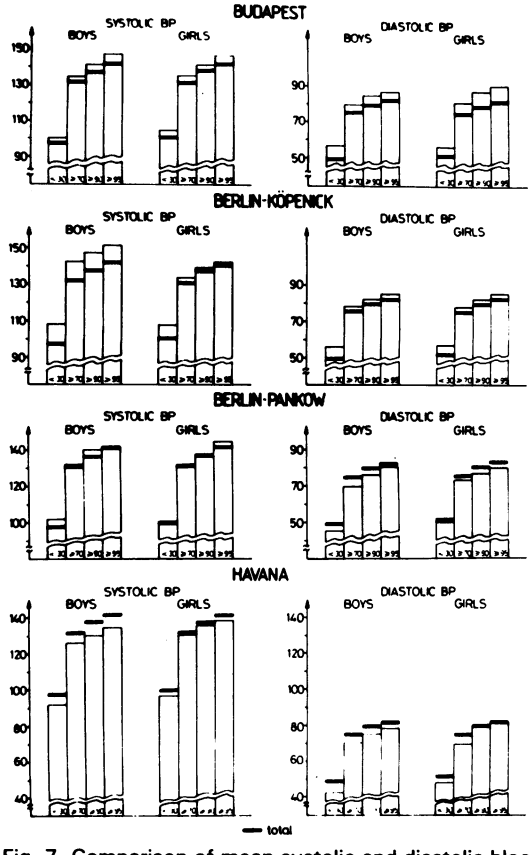


Fig. 7. Comparison of mean systolic and diastolic blood pressures of children with blood pressures below the 30th percentile and at or higher than the 70th, 90th and 95th percentiles of the distribution curves both at initial screening and at the follow-up examination in four centres (Budapest, Berlin-Köpenick, Berlin-Pankow, and Havana).

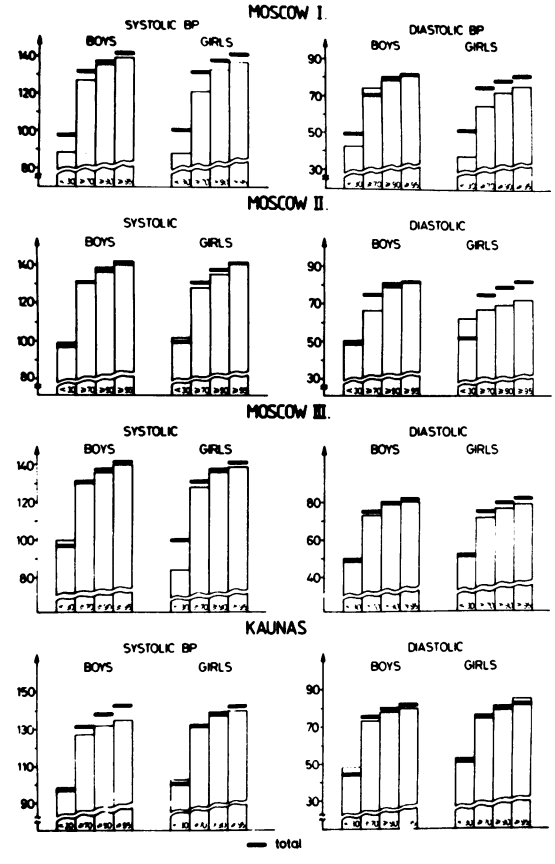


Fig. 8. Comparison of mean systolic and diastolic blood pressures of children with blood pressures below the 30th percentile and at or higher than the 70th, 90th and 95th percentiles of the distribution curves both at initial screening and at the follow-up examination in four centres (Moscow 1, 2 and 3, and Kaunas).

tiles) for both SBP and DBP in both sexes within each centre and in the pooled data (Fig. 9 and 10).

Sexual maturation. Scores of sexual maturation were significantly lower in the lower groups (below the 30th percentile) of SBP and DBP in both sexes (Fig. 10).

Blood pressure. The mean values of DBP in the lower SBP group (below the 30th percentile) was significantly lower than those in the upper groups (at the 70th, 90th, and 95th percentiles or over) in both sexes. The same association was observed for the mean values of SBP in the low DBP group (Fig. 11).

Heart rate. The heart rate was significantly lower in the lower groups (below the 30th percentile of SBP and DBP distributions) in both sexes than in the upper groups (at the 70th, 90th, and 95th percentiles or above (Fig. 12).

ECG. The magnitude of the R and S waves of the ECG were significantly smaller in the lower groups of SBP (below the 30th percentile) in both sexes. There was no such association for the DBP or between T wave magnitude and blood pressure values in these groups (Fig. 12).

Cardiothoracic and heart volume indices. No significant difference was observed in the cardiothoracic index between the groups. The heart volume index showed significantly higher values in the upper groups of SBP at the 70th, 90th, and 95th percentiles or above in both sexes. A weak association was found between the DBP values and the heart volume index (Fig. 11).

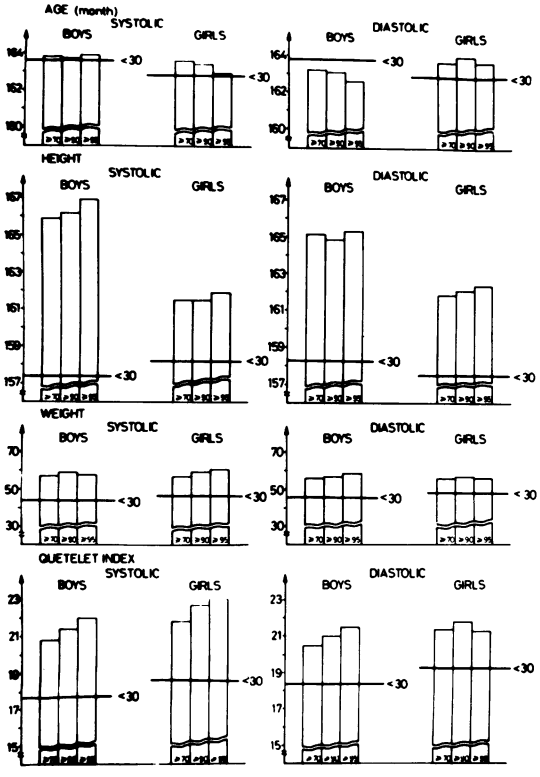


Fig. 9. Comparison of mean values of variables (age, height, weight, and Quetelet's index) in children with blood pressures below the 30th percentile and at or higher than the 70th, 90th and 95th percentiles of the distribution curves both at initial screening and at the follow-up examination.

Laboratory tests. Blood sugar and cholesterol levels did not differ significantly either in the SBP or in the DBP groups. Only boys showed significantly lower serum uric acid values in the low SBP and DBP groups (Fig. 13).

DISCUSSION

On the basis of three consecutive blood pressure measurements on a single occasion (during screening), two 10% samples of children were selected: an upper group ($n = 1775$) with systolic or diastolic blood pressures reaching or exceeding the 95th percentile of the distribution curve, and a lower group ($n = 1865$) randomly chosen from those below this level (*1–4*).[a]

[a] Papers presented by Glasunov, I. et al. and by Grabauskas, V. & Bojarskas, Y. L. at the WHO/ISFC Meeting on Precursors of Atherosclerosis in Children, Geneva, 1977.

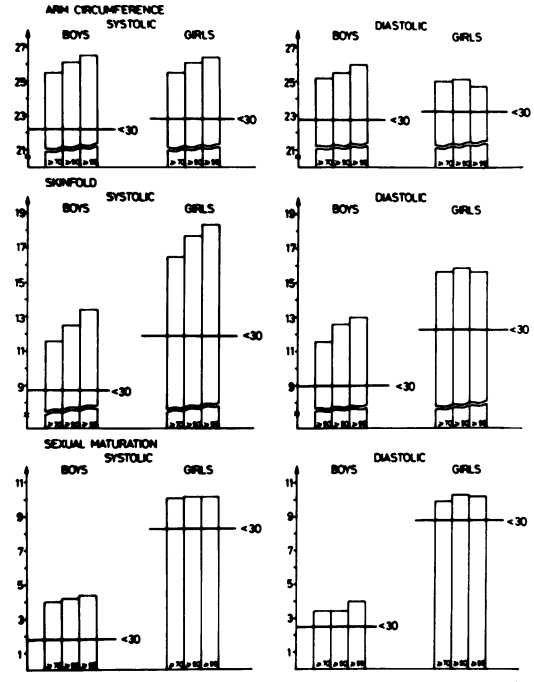


Fig. 10. Comparison of mean values of variables (arm circumference, skinfold thickness and sexual maturation) in children with blood pressures below the 30th percentile and at or higher than the 70th, 90th and 95th percentiles of the distribution curves both at initial screening and at the follow-up examination.

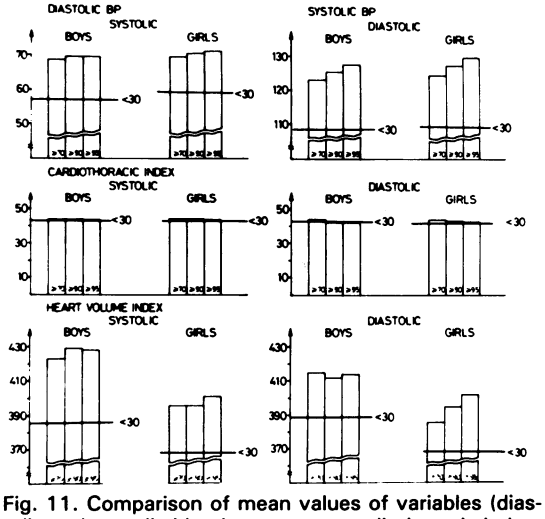


Fig. 11. Comparison of mean values of variables (diastolic and systolic blood pressures, cardiothoracic index, and heart volume index) in children with blood pressures below the 30th percentile and at or higher than the 70th, 90th and 95th percentiles of the distribution curves both at initial screening and at the follow-up examination.

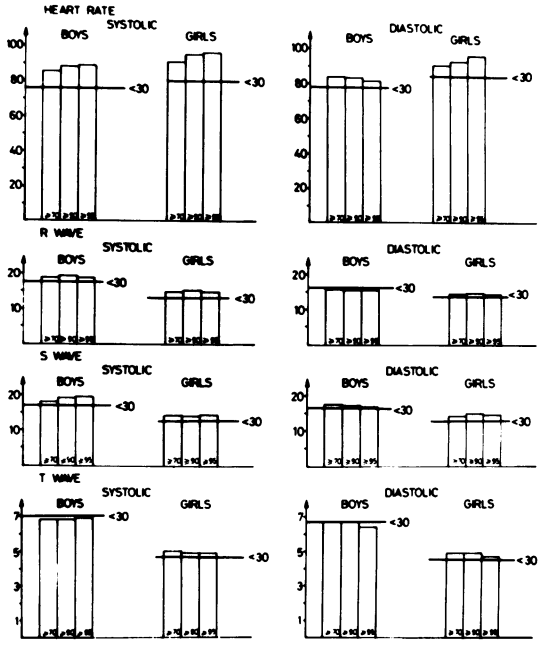


Fig. 12. Comparison of the mean values of variables (heart rate and R, S and T waves) in children with blood pressures below the 30th percentile and at or higher than the 70th, 90th and 95th percentiles of the distribution curves both at initial screening and at the follow-up examination.

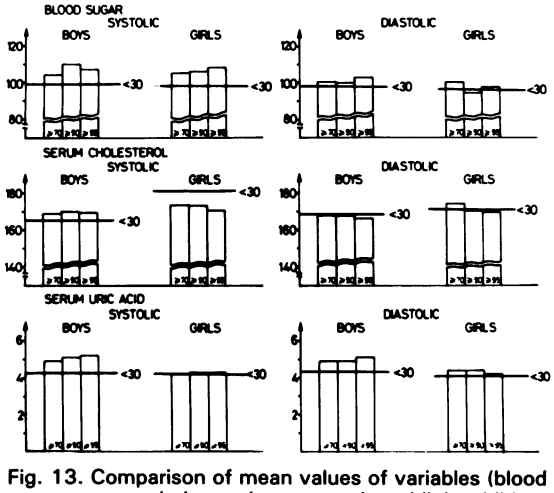


Fig. 13. Comparison of mean values of variables (blood sugar, serum cholesterol, serum uric acid) in children with blood pressures below the 30th percentile and at or higher than the 70th, 90th and 95th percentiles of the distribution curves both at initial screening and at the follow-up examination.

Detailed re-examination of these groups, which was carried out 6–9 months after the screening, showed marked differences in a number of variables. A history of hypertension both in parents and in children, and a history of stroke among mothers were significantly more common in the upper group, as was found by Londe and others (*5–7*).

Children in the upper group were taller, heavier, and sexually more developed. The higher average of Quetelet's index and skinfold thickness in the upper group suggests a relationship between obesity and elevated blood pressure. The fact that there was more physical activity in the lower group (among boys) than in the upper group, however, may reflect the reverse. Studies in children and adolescents have proved that obesity is appreciably more prevalent in hypertensives (*8, 9*).

Higher values of heart rate and symptoms of a hyperkinetic heart syndrome (innocent systolic murmurs, heart rate of $\geqslant$ 100/min (Minnesota Code 8-7)) were more frequent in the upper group than in the lower group. The hyperkinetic heart syndrome has been recognized as a predictor of hypertension in adolescents and young adults (*10–17*).

Cardiovascular signs of an elevated blood pressure also differed in the two groups. In the ECG, signs of left ventricular hypertrophy (Minnesota Code 3-1) were more frequent, and R waves in both sexes and S waves in girls were greater in the upper than in the lower groups. A higher prevalence of deep S waves in hypertensive adolescents has been reported (*18*). Based on the chest X-ray, the heart volume index in both sexes and the cardiothoracic index in girls were higher in the upper groups. Others have reported normal findings on chest X-ray in both normotensive and hypertensive subjects, although no quantitative measurements of the heart volume and cardiothoracic indices were done (*18*). The early stage of hypertension on eyeground examination was seen more frequently in the upper groups in both sexes.

The prevalence of diabetes was higher in the medical history of children in the upper group, and twice as many mothers also suffered from diabetes. A higher mean postload blood sugar concentration was found among boys in the upper group. Similar findings have been reported in other studies (*19, 20*).

Children of both sexes in the upper group had higher serum uric acid concentrations, which have been reported by others in children with essential hypertension (*21*).

No difference between the two groups was seen in the proportion of smokers or in the average serum cholesterol level. Other investigators have found a relationship between serum cholesterol and blood pressure in boys only (*14, 19*).

Multivariate regression analysis showed that

weight and heart rate were the most important independent variables contributing to SBP and DBP, the impact of other factors being less important. In agreement with our findings, others have reported that weight and heart rate were the most important contributors to SBP and DBP (*22*, *23*).

We also investigated the relationships between associated factors and blood pressure in children with blood pressure levels at or above the 95th, 90th, 70th percentiles, and below the 30th percentile in both the initial screening and at the first follow-up examination 6–9 months later. We compared the lower group (SBP and DBP below the 30th percentile) and the upper groups (SBP and DBP at 70th, 90th, and 95th percentiles or over) in order to see whether the factors (continuous variables) that were related to the blood pressure level would show the same pattern as was found in the previous comparison between the upper and lower groups selected on the basis of blood pressure measurements taken on a single occasion (during screening). In the upper groups, measurements of height, weight, Quetelet's index, arm circumference, skinfold thickness, sexual maturation, heart rate, R and S waves of ECG, heart volume index, and serum uric acid showed significantly higher values than in the lower group. There was no difference in serum cholesterol concentrations among children in the low and elevated blood pressure groups.

A comparison of the findings in children from the upper and lower groups shows that there is a significant relationship between the blood pressure level and a number of associated factors that could be predictors of hypertension before this is manifest. As no significant difference was found when these factors were related to blood pressures taken on one or two separate occasions, we should like to emphasize the importance of having casual blood pressure measurements in children.

RÉSUMÉ

ÉTUDE INTERNATIONALE CONCERTÉE SUR L'HYPERTENSION JUVÉNILE

Parmi 17 634 enfants nés en 1964 et ayant fait l'objet d'un dépistage en 1977, on a constiué deux groupes: un groupe «supérieur» formé des enfants (10% environ) ayant une tension artérielle, systolique ou diastolique, correspondant aux 5% supérieurs de la courbe de distribution (chiffres tensionnels égaux ou supérieurs au 95^{e} percentile), et un groupe «inférieur» comprenant 10% des enfants ayant une tension plus faible. Ces enfants ont de nouveau été examiné en 1978. Le taux de réponse a été de 89% en moyenne (3640 enfants), sans différence sensible ni selon le sexe ni selon le groupe. Les parents ont été interrogés par questionnaire à la fois sur eux-mêmes et sur leurs enfants et l'on a comparé les réponses en vue de faire apparaître d'éventuelles différences entre les deux groupes. Dans le groupe «supérieur» comme dans le groupe «inférieur», aucune différence significative n'a été constatée en ce qui concerne l'âge, les habitudes tabagiques et la situation matrimoniale des parents ni en ce qui concerne la parité des enfants, le nombre de frères et sœurs et la proportion de jumeaux.

L'hypertension et le diabète chez les enfants, de même que les antécédents d'hypertension, d'accidents cérébro-vasculaires et de diabète chez les parents avaient une prévalence sensibilement plus élevé dans le groupe «supérieur» par rapport au groupe «inférieur». De même, on a constaté une plus grande fréquence, dans ce groupe «supérieur», des signes d'hypertrophie ventriculaire gauche et de symptômes de syndrome d'hyperkinésie cardiaque (fréquence cardiaque accrue, souffles systoliques sans signification pathologique plus fréquents, ampleur supérieure des ondes R et S à l'électrocardiogramme et valeurs moyennes supérieurs de l'index du volume cardiaque et de l'index cardiothoracique).

Les enfants du groupe «supérieur» étaient plus développés sur le plan sexuel, plus grands, plus gros (valeurs plus élevées de l'indice de Quetelet et de l'épaisseur du pli cutané) et moins enclins à l'exercice physique.

La glycémie et l'urémie également étaient plus élevées en moyenne dans le groupe «supérieur» que dans le groupe «inférieur». Aucune différence significative n'a été observée entre les deux groupes en ce qui concerne la proportion des fumeurs chez les enfants ou le taux moyen de cholestérol.

Ces différences entre les deux groupes sont apparues encore plus marquées quand le groupe «inférieur» était constitué d'enfants présentant de façon répétée une hypotension, avec des chiffres tensionnels inférieurs au 30^{e} percentile des courbes de distribution de la tension, systolique ou diastolique.

REFERENCES

1. INTERNATIONAL COLLABORATIVE GROUP. *Bulletin of the World Health Organization*, **59**: 295–304 (1981).
2. TÖRÖK, E. In: Gross, F. & Strasser, T., ed. *Mild hypertension: natural history and management*. London, Pitman, 1979, p. 67.
3. TÖRÖK, E. ET AL. In: Giovanelli, G. et al., ed. *Hypertension in children and adolescents*. New York, Raven Press, 1981, p. 301.
4. ALEXANDROV, A. ET AL. *IX World Congress of Cardiology, Moscow, 1982*. Abstracts, p. 589.

5. LONDE, S. & GOLDRING, D. *American journal of cardiology*, **37**: 650 (1976).
6. LONDE, S. In: Giovanelli, G. et al., ed. *Hypertension in children and adolescents.* New York, Raven Press, 1981, p. 1.
7. LOGGIE, J. M. H. In: Giovanelli, G. et al., ed. *Hypertension in children and adolescents.* New York, Raven Press, 1981, p. 2.
8. LONDE, S. ET AL. In: New, M. I. & Levine, L. S., ed. *Juvenile hypertension.* New York, Raven Press, 1977, p. 13.
9. RAMES, L. K. ET AL. *Pediatrics*, **61**: 245 (1978).
10. LEVY, R. L. ET AL. *Journal of the American Medical Association*, **129**: 585 (1945).
11. PAFFENBARGER, R. S. ET AL. *American journal of epidemiology*, **88**: 25 (1968).
12. JULIUS, S. ET AL. *Circulation*, **43**: 382 (1971).
13. JULIUS, S. *Pediatric clinics of North America*, **25**: 35 (1978).
14. STAMLER, J. ET AL. In: Paul, O., ed. *Epidemiology and control of hypertension.* New York, Stratton Intercontinental, 1975, p. 307.
15. MATOS, L. & TÖRÖK, E. *Acta Medica Academiae Scientiarum Hungaricae*, **26**: 207 (1969).
16. GOTTSEGEN, G. ET AL. *Magyar belorvosi archivum*, **17**: 281 (1964).
17. TÖRÖK, E. & MATOS, L. *Magyar belorvosi archivum*, **20**: 213 (1967).
18. GOLDRING, D. & HERNANDEZ, A. In: Giovanelli, G. et al., ed. *Hypertension in children and adolescents.* New York, Raven Press, 1981, p. 113.
19. FLOREY, C. DU V. ET AL. *British medical journal*, **1**: 1368 (1976).
20. VOORS, A.W. ET AL. *American journal of epidemiology*, **113**: 347 (1981).
21. PREBIS, J. W. ET AL. *Journal of pediatrics*, **98**: 702 (1981).
22. HOLLAND, W.W. & BERESFORD, A. A.: In: Paul, O., ed. *Epidemiology and control of hypertension.* New York, Stratton Intercontinental, 1975, p. 375.
23. KHOURY, P. ET AL. *Arteriosclerosis*, **1**: 280 (1981).

Annex 1

PARTICIPATING INSTITUTES AND INVESTIGATORS

City Hospital, Berlin-Köpenick, German Democratic Republic
S. Böthig,[a] S. Ulrich, I. Kunigk, R. Teichert, I. Helmer

Central Hospital for Cardiovascular Research, Berlin-Pankow, German Democratic Republic
I. Böthig,[a] D. Eisenblätter, M. Weiss, W. Briedigkeit, S. Cholnowski, I. Heuman, G. Fischer

Hungarian Institute of Cardiology, Budapest, Hungary
I. Gyárfás,[a] E. Török,[a] M. Csukás,[a] J. Duba, S. Rózsa, S. Tarján, P. Ofner, A. Zorándi

Institute of Hygiene of Children and Adolescents, Budapest, Hungary
I. Kamarás[a]

Steven Municipal Hospital, Budapest, Hungary
M. Domokos, P. Tar

National Institute of Cardiology, Havana, Cuba
P. Nordet,[a] J. Royo, R. Lirio, P. S. Fanjul, L. R. de la Vega, A. H. Canero

Medical Institute of Cardiology, Kaunas, USSR
J. Bojarskas,[a] A. Sackuté, R. Petkevicius, A. Zaborskis, O. Grinkevicene

All Union Cardiological Research Centre, Academy of Medical Sciences (Moscow 1), USSR
I. Glazunov,[a] A. A. Alexandrov,[a] V. M. Shamarin, A. D. Dejev, A. F. Likhov, V. I. Gromov, E. N. Shugaeva

Research Institute of Hygiene of Children and Adolescents, Ministry of Health (Moscow 2), USSR
L. Antonova,[a] A. N. Usolcev, G. R. Rzajev, I. K. Zvezdina, T. M. Mechtieva, L. P. Prilepko, I. G. Barodulina, L. V. Shatunova, B. M. Peltz

Institute of Paediatrics of the Academy of Medical Sciences (Moscow 3), USSR
E. A. Nadezdina,[a] I. S. Vintovkina, V. S. Kurbatov, K.Ju. Petrosian

Data processing was carried out at the Computer and Automation Institute of the Hungarian Academy of Sciences, Budapest, Hungary, by M. Ruda and J. Soltész.

[a] Principal investigators.