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Cholesterol screening in childhood: Results of a 9-year follow-up study in Swiss and Italian children in Switzerland

Summary

Mass screening for blood cholesterol as part of routine preventive health care of children continues to be discussed in several countries. Results of longitudinal studies underline the importance of the predictive value of cholesterol levels assessed during childhood. Some countries have changed their recommendations during the past years to blood cholesterol screening for obese children only or for children of high risk families. In the Kindergarten-study Basel, a follow-up study on somatic, psychic and social development of Swiss and immigrant schoolchildren, cardiovascular risk factors were assessed at the ages of 5, 10 and 14 years. The age-specific levels of total and LDL-cholesterol found in our study were slightly higher and HDL-cholesterol lower than, for example, those found in the Bogalusa Heart Study. For total cholesterol no significant tracking correlations over the 5 and 9 year periods were found. Tracking of LDL- and HDL-cholesterol differed between nationalities and sexes. The total cholesterol/HDL-cholesterol index tracked slightly better. Italian girls showed the best 9-year tracking for HDL-cholesterol ($r = 0.56$). The differences between this and other studies can only partially be explained by different sampling and laboratory methods. Individual changes in cholesterol levels between the ages of 5 and 14 were marked. Sexual maturation was found to be of minor influence. Body mass index was the most consistent risk factor in our population. Changes of sex or growth hormone levels during puberty, but also changes of nutritional habits or physical activity might influence the individual cholesterol levels. Before recommendations on mass screening of cholesterol in children are made, the different longitudinal patterns of changes in cholesterol levels, and subpopulation-specific changes of nutritional habits and physical activity, should be discussed. The results of the Kindergarten-study Basel suggest that attention should be paid to screening for obesity and to health education regarding nutrition and physical activity.

In industrialised countries cardiovascular diseases are still the most important cause of premature death, and unfavorable serum lipids, high blood-pressure and smoking are their most important risk factors. It is known that, although these diseases lead to increased mortality and morbidity after the third or fourth decade of life, precursors are found much earlier. Atherosclerotic lesions (fatty streaks) are found even in young children, as autopsy studies have reported¹. These lesions could be shown to be related to cholesterol levels, blood pressure and overweight². This knowledge and the fact that elevated blood cholesterol levels are observed in childhood and adolescence have been the motive for including the screening for cardiovascular risk factors, mainly for hypercholesterolaemia, not only in preventive programmes for children with a positive family history of cardiovascular disease, but also in routine preventive health care of children. Thus, cholesterol percentiles by age based on cross-sectional studies have been used for identifying risk or therapy groups in the population screened^{3,4}. It is well known that not only in adults but also in children the blood cholesterol levels are influenced by nationality,

race, and sex^{3,5-9}. Only a few studies have followed up cohorts of children until adolescence or adulthood. The Bogalusa Heart Study and the Muscatine Study reported important tracking of cholesterol levels during childhood and adolescence¹⁰ and between childhood and adulthood^{11,12}. These results supported the claim that mass screening for cholesterol levels in populations of children should be started^{6,13}. Some authors even proposed to start these screening programs as early as at the age of 3 years¹⁴. In many industrial countries mass screening for cholesterol in populations of children has been discussed^{13,15} and a series of pilot programmes have been established^{6,16,17}. Recent recommendations of paediatric academies include cholesterol screening for children with a positive family history of dyslipidaemia or early myocardial infarction in a first degree relative only, because the disadvantages and limitations of a mass screening of children outweigh the advantages^{18,19}. The reported limitations include poor standardisation of equipment, important fluctuations in cholesterol levels, and the possibility of inappropriate drug therapy being based on a single sporadically elevated cholesterol level. Despite the fact that recommendations have been made in several countries the discussion on the need for mass screening of cholesterol in general populations of children is continuing²⁰. The results of screening programs of practising paediatricians, who reported the detection of an important number of cases of hyperlipidaemia, have revived this discussion^{14,21,22}. The assessment of cardiovascular risk factors was part of the Kindergarten-study Basel, a follow-up study on the somatic, mental and social development of a representative cohort of children at the ages of 5, 10 and 14 years^{23,24}. The Kindergarten-study Basel looked for longitudinal results concerning

serum cholesterol levels and blood pressure. The degree of tracking of these risk factors and comparisons between Italian immigrant children and Swiss children were the special focus of interest.

Methods

Between 1976 and 1978 a 10% random sample was drawn from 5 year old Swiss and Italian children in the kindergartens of Basel (n = 375). The children of the Italian immigrant families were born in Switzerland. The study population was followed up to age 10 and 14. Between the three visits 126 children (34%) were lost to follow up, mainly Italian children who returned with their families to Italy. Longitudinal results of a 9 year period are available for 249 children (66%), 218 of Swiss and of 31 of Italian nationality. Because of the drop-out rate an oversampling of 147 children was added at the age of 10 to increase the numbers for cross-sectional results, as illustrated by Figure 1.

The examination took place during the routine examination of the city school health service and included physical examination, assessment of motoric skills, social indicators and psychological testing. Cardiovascular risk factors like height and weight (Quetelet index) and blood pressure – using a random zero sphyngo-manometer²⁵ – were measured at each examination. Most parents agreed to capillary blood samples being taken from their child at each visit (97% of all children). The children had not been fasting before blood samples were taken, but all samples were obtained at the same time in the morning. Because the study started in the 1970s, the laboratory methods consistently applied during the study differed from those used in more recent studies. Total cholesterol was analysed enzymatically following the SMAC-Method (Boeringer); VLDL-, LDL- and HDL-cholesterol were measured using electrophoresis. In order to estimate the VLDL, LDL and HDL cholesterol concentrations the lipo-

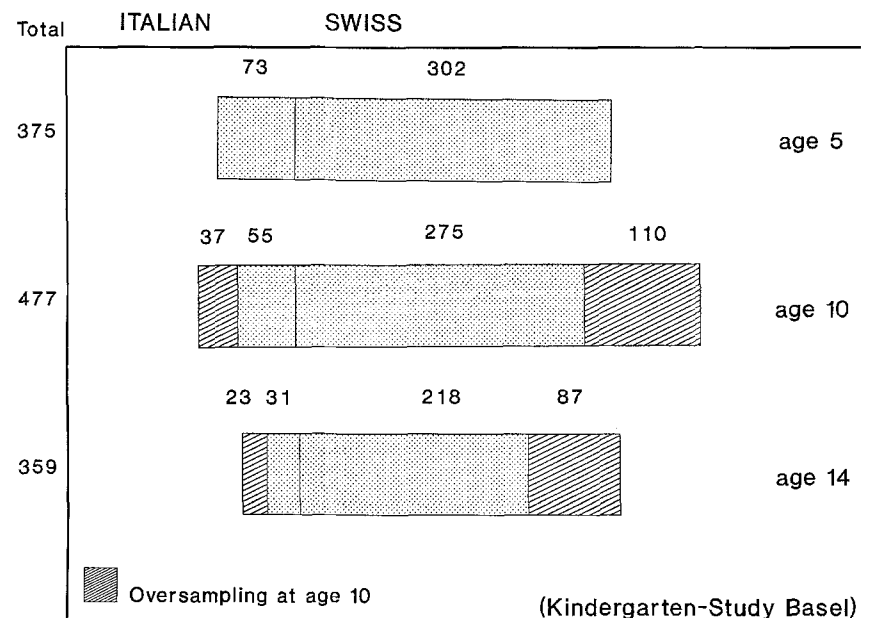


Figure 1. Study population.

proteins were separated electrophoretically. The lipoprotein electrophoresis on agarose was stained and the relative distribution of cholesterol to the lipoprotein classes was estimated by measuring the area under the densitometrically obtained curve. Cholesterol content was calculated assuming identical staining intensities for cholesterol in cholesterol ester, triglycerides and phospholipids. The area under the curve was weighted according to the cholesterol concentration in the lipoproteins LDL (47%), VLDL (20%) and HDL (33%). Cross-sectional and longitudinal results are reported separately because they relate to slightly different populations (drop-outs and the oversampling at the age of 10). Data for drop-outs and oversampling children were included in the cross-sectional results, as no differences in the mean cholesterol levels were found compared to the 249 children who participated in all three visits.

Tracking coefficients were calculated using Spearman's coefficients using absolute values of cholesterol or other risk factors.

Results

Cross-sectional

Table 1 shows the means of total cholesterol levels by nationality, age and sex. For total cholesterol an increase was found between the ages of 5 and 10 years, followed by lower levels at the age of 14. The LDL-cholesterol levels did not show any significant changes over the described 9-year period. HDL-cholesterol levels increased slightly between the ages of 5 and 14 years. The Italian boys had significantly lower total cholesterol levels at the ages of 5 and 10. The same was found for LDL- and HDL-cholesterol (only at age 5). For total cholesterol, LDL- and HDL-cholesterol no difference between girls

Age	Swiss girls	Italian girls	Swiss boys	Italian boys
5	4.30 mmol/l (SD 0.98) n = 124	4.28 mmol/l (SD 1.12) n = 25	4.28 mmol/l (SD 0.82) n = 143	3.62 mmol/l (SD 0.75) n = 36
10	4.47 mmol/l (SD 0.97) n = 174	4.51 mmol/l (SD 1.03) n = 47	4.55 mmol/l (SD 0.88) n = 204	4.11 mmol/l (SD 0.96) n = 44
14	4.32 mmol/l (SD 0.86) n = 120	4.36 mmol/l (SD 0.79) n = 30	4.18 mmol/l (SD 0.78) n = 151	4.00 mmol/l (SD 0.88) n = 21

Table 1. Total cholesterol: Means by nationality, sex and age.

	Age 5–10	Age 10–14	Age 5–14
Total cholesterol	0.07 (286) p = 0.11	0.20 (316) **	0.09 (200) p = 0.09
LDL-cholesterol	0.20 (276) **	0.29 (310) **	0.19 (194) **
HDL-cholesterol	0.19 (275) **	0.21 (310) **	0.16 (194) **
Total cholesterol/ HDL-cholesterol-index	0.34 (275) **	0.40 (310) **	0.27 (194) **

Spearman-Correlation r (n) p; ** p < 0.01.

Table 2. Cholesterol: Tracking correlations (all children).

and boys was found in the Swiss population. All differences in the mean cholesterol levels between the population subgroups disappeared at the age of 14.

Tracking (longitudinal results)

To analyse the predictive value of cholesterol levels at the age of 5 years tracking correlation over 5 and 9 year periods are used. Table 2 shows the results for all children. In the whole population, a significant correlation for total cholesterol was found over the 10 to 14 year period only. LDL- and HDL-cholesterol showed low tracking, the correlations over the whole period were less than $r = 0.2$ and the best tracking for LDL levels for the 10 to 14 year period was $r = 0.29$. Only the total cholesterol-HDL-

cholesterol index (TC/HDL-index) showed slightly better results. The best tracking was found in the 10 to 14 year period with a correlation coefficient of $r = 0.4$.

When analysing the 5- and 9-year tracking stratified by nationality and sex some marked differences were detected. Table 3 shows the tracking correlations of LDL-, HDL-cholesterol and TC/HDL-index according to sex and nationality. The groups of the Italian children became small (n between 10 and 30), therefore only a few correlations are statistically significant. For LDL-cholesterol a difference between the sex groups during the 5 to 10 year period was found, but was only significant for the girls. The subgroups differed only slightly in the 5 to 14 year period with tracking correlations

	Age 5–10		Age 10–14		Age 5–14	
<i>Swiss girls</i>						
LDL Cholesterol	0.24 (108)	**	0.29 (116)	**	0.17 (74)	p = 0.08
HDL -Cholesterol	–		0.16 (116)	*	–	
Chol./HDL-index	0.34 (108)	**	0.35 (116)	**	0.26 (74)	**
<i>Italian Girls</i>						
LDL Cholesterol	0.29 (17)	p = 0.13	0.17 (30)	p = 0.18	0.16 (10)	p = 0.33
HDL Cholesterol	–		0.46 (30)	**	0.56 (10)	*
Chol./HDL-index	0.21 (18)	p = 0.21	0.49 (30)	**	0.38 (10)	p = 0.14
<i>Swiss boys</i>						
LDL Cholesterol	–		0.31 (143)	**	0.27 (95)	**
HDL Cholesterol	0.29 (123)	**	0.25 (143)	**	0.25 (95)	**
Chol./HDL-index	0.38 (123)	**	0.37 (143)	**	0.23 (95)	**
<i>Italian boys</i>						
LDL Cholesterol	–	**	0.22 (21)	p = 0.12	0.13 (15)	p = 0.32
HDL Cholesterol	0.32 (37)	*	–		–	
Chol./HDL-index	0.40 (27)	*	0.53 (21)	**	0.56 (15)	**

Spearman Correlation r (n) p; * p < 0.05; ** p < 0.001.

Table 3. Cholesterol: Tracking correlations.

	Age 5–10	Age 10–14	Age 5–14
Total cholesterol	–	0.30 (136) **	0.11 (79) **
LDL-cholesterol	0.23 (36) *	0.46 (133) **	0.23 (76) *
HDL-cholesterol	–	0.26 (133) **	0.27 (76) **
Total cholesterol/HDL-cholesterol-index	0.334 (76) **	0.56 (133) **	0.34 (95) **

Spearman Correlation r (n) p, * p < 0.05; ** p < 0.01.

Table 4. Cholesterol: Tracking correlations (Tanner >= 4 at age 14).

less than $r = 0.3$. In contrast to LDL-cholesterol, for HDL-cholesterol only the levels of the boys had a significant tracking up to the age of 10. For the 9 year period the Italian girls showed the most important tracking for HDL-cholesterol with $r = 0.56$. The levels of the Swiss girls and the Italian boys tracked only a little and for the Swiss girls and the Italian boys no significant tracking was found between the age of 5 and 14. Again the best results were found for the TC/HDL-index. The most impor-

tant tracking correlation can be reported for the Italian boys, with $r = 0.56$ for the 9-year period. Sexual maturation is well known to have an influence on blood cholesterol levels^{26,27}. Changes of sex- and growth-hormone levels are expected to influence the blood cholesterol levels and to cause a decrease in cholesterol during puberty. To reduce this influence on our 9 year results we analysed the group of children with the most advanced sexual maturation at the age of 14 separately (children who

passed the decrease of the cholesterol levels). Sexual maturation was assessed by Tanner stages at age 14. Table 4 shows the tracking correlations of cholesterol on children with most advanced sexual maturation at age 14 (Tanner >=4). Only a tendency towards consistently higher r-values was found in this group. Other cardiovascular risk factors showed a more constant longitudinal pattern than the blood cholesterol levels. The systolic blood pressure tracked slightly better

	Age 5–10	Age 10–14	Age 5–14
Body mass index	0.75 (341) **	0.78 (399) **	0.62 (277) **
Systolic blood pressure	0.26 (104) **	0.26 (390) **	0.33 (90) **

Spearman-Correlation r (n) p , ** $p < 0.01$.

Table 5. Body mass index and systolic blood pressure: Tracking correlations (all children).

than the blood cholesterol levels. The most constant cardiovascular risk factor was the body mass index (kg/m^2), indicated in Table 5. A correlation coefficient of $r = 0.62$ was found for the analysis of the children over the 9 year period. All nationality-sex specific subgroups showed important tracking correlations on this index. The most important correlations were found in the group of the Italian girls. These children had the highest rate of obesity and reported the lowest physical activity (sports) in the interview.

Discussion

The mean cholesterol levels in the Kindergarten-study Basel are similar to those found in other studies in Switzerland^{7,28} in each age group. Compared to American studies, for example the Bogalusa Heart Study, higher total and LDL-cholesterol levels and much lower HDL-cholesterol levels were found in the different age groups of our study². These differences could be caused by different sampling and laboratory methods. In the Kindergarten-study samples were taken from capillary blood, using a standardized method. The laboratory analyses were based only on the relative distribution of the cholesterol fraction among the lipoprotein classes. The tracking results are unlikely to be serious biased, because of the consistent use of the same laboratory methods during the study, but comparisons of age

specific cholesterol levels between studies using different methods have to be interpreted with caution. However, the trends shown by cholesterol levels (for example the increase of total cholesterol between age of 5 and 10 followed by lower levels at the age of 14) were similar to results from other studies in different countries^{3,4,5,29}. Most of these studies report a decrease of cholesterol levels in females at an average age of 12 and in males at a average age of 13, followed by an increase to adult cholesterol levels. In Basel only the Italian boys showed cholesterol levels different from the rest of the population; their total and LDL-cholesterol levels at the age of 5 and 10 and their HDL-cholesterol levels at the age of 5 were significantly below the levels of the other children. By the age of 14 differences between the subgroups disappeared. A comparable Swiss study in Geneva also reported lower total cholesterol levels in Italian children⁷.

Among the longitudinal results the low tracking correlations of the blood cholesterol levels were most important. For total cholesterol there was no significant tracking at all. Concerning LDL-, HDL-cholesterol and the TC/HDL-index marked differences between the population subgroups were found. Important tracking was only detected in HDL-cholesterol in Italian girls and in TC/HDL-index in Italian boys. The best tracking correlation coefficient between different periods and different sub-

groups was 0.56. These results differ from tracking correlations reported in other studies^{10–12,30}. The Bogalusa populations showed much better tracking^{10,12}. One reason for this difference could be found in the different methods of analysis in Bogalusa where combined age groups were used. Thus the age-dependence of the tracking, which is reported by the Muscatine Study^{11,26}, is diluted. Even taking this factor into account, there is much lower tracking in the Basel population than in comparable studies like Citadella or Muscatine^{11,30}. For these differences in the longitudinal results the different sampling and laboratory methods could be important. If non-tracking was mainly due to the measurement error of cholesterol fractions the best tracking would be expressed for total cholesterol and poorest for the TC/HDL-index, since the measurement error is included twice in this ratio. However, the opposite was found, which enhances confidence in the assessment technique. The constance of the laboratory methods in our study, the fact that comparable mean levels are reported in other studies in Switzerland, and the differences of the tracking between the nationality-sex subgroups with significant tracking in subgroups, strengthen our longitudinal results. Sexual maturation is known to influence cholesterol levels and tracking between childhood and adolescence^{26,27,29}. Results from our study show a less important influence of this factor during the

reported period between 5 and 14 years. In the group of children who had passed puberty by the age of 14 only slightly better tracking correlations of cholesterol levels were found.

Another cardiovascular risk factor, the body mass index (BMI), tracked much better than cholesterol levels. Thus overweight was a more constant risk over the reported school age period. Italian girls who had the highest BMI in all age groups reported low physical activity in the interview and showed the most important tracking correlation of HDL-cholesterol levels. This supports the well-known relationship between HDL-cholesterol levels and nutritive factors, overweight, and physical activity^{31–34}.

Intervention studies on children report significant relations between weight control by diet or physical activity and changes in

cholesterol levels^{32,35}. Thus, “natural” changes in nutritional habits and in physical activity during childhood and adolescence will be important factors influencing individual changes in cholesterol levels. The predictive value of a child’s cholesterol level does not only depend on known factors such as later smoking or contraceptive use²⁶, but also on changes in dietary habits and physical activity. Longitudinal patterns of blood cholesterol levels in childhood and adolescence are also a result of changing nutritional habits, and differences between parents and children might occur particularly different in immigrant populations. Longitudinal studies in Japan support this conclusion, as they show an increase in cardiovascular risk because of changes to western nutrition mainly in young people²⁹.

Before recommendations on mass screening of cholesterol as part of

the routine health care of children are formulated, the pattern of development of cardiovascular risk factors other than diet factors and physical activity should be followed up in more detail in the populations to be screened. Depending on these population-specific results the target group for screening programs should be defined for different age groups. But even in selective screening further research is needed, for example cost-benefit-analysis³⁶. In the Swiss population with its mixture of nationalities and cultures, the influence of factors such as big changes of nutritional habits during childhood and adolescence is likely to be too important for mass screening programmes in childhood and adolescence to be recommended. The results of the Kindergarten-study Basel support more the importance of screening regarding obesity, and intervention programmes encouraging healthy nutrition and sport in school age children.

Zusammenfassung

Cholesterinscreening bei Kindern: Resultate einer neunjährigen Längsschnittuntersuchung von Schweizer- und Italienerkindern in der Schweiz

Screeninguntersuchungen des Blutcholesterins bei Kindern werden weiterhin diskutiert. Einige Länder schlossen in die Empfehlungen jedoch nur noch adipöse Kinder oder solche von Hochrisiko-Familien mit ein. In unserer Längsschnittstudie zur somatischen, psychischen und sozialen Entwicklung von Schweizer- und Immigrantenkinder wurden auch kardiovaskuläre Risikofaktoren im Alter von 5, 10 und 14 Jahren untersucht. Für das Gesamtcholesterin wurden keine signifikanten Tracking-Korrelationen über die Perioden von fünf oder neun Jahren gefunden. Die Tracking-Korrelationen des LDL- und HDL-Cholesterins sind abhängig von Geschlecht und Nationalität. Unterschiede zu anderen Studien können nur teilweise durch die Studienpopulation oder durch Labormethoden erklärt werden. Es fanden sich insgesamt deutliche individuelle Schwankungen im Cholesterinspiegel zwischen dem fünften und vierzehnten Lebensjahr. Der Body-Mass-Index war konstanter. Die Längsschnittverläufe deuten auf Unterschiede in Subpopulationen, welche auf eine Abhängigkeit von verschiedenen Faktoren u.a. auch von Veränderungen des Bewegungs- und Ernährungsverhaltens hinweisen. Die Resultate unterstreichen somit eher die Wichtigkeit von Adipositas-screening bei Kindern und die Bedeutung der Gesundheitsförderung in den Bereichen Ernährung und Sport.

Résumé

Les screening du cholestérol chez les enfants: Les résultats d'une étude longitudinale d'enfants suisses et immigrés en Suisse sur la période de 9 ans

On continue de discuter le screening du cholestérol chez les enfants. Différents pays ont changé au courant des dernières années leur attitude vis-à-vis du screening, en le limitant aux enfants obèses ou appartenant à des familles à haut risque. Dans notre étude longitudinale sur le développement somatique, psychique et social d'enfants suisses et immigrés en âge scolaire, les facteurs de risque cardiovasculaires ont été analysés à l'âge de 5, 10 et 14 ans. Pour le cholestérol total, aucune corrélation de tracking tout au long des périodes de 5 et 9 ans a été trouvée. La corrélation de tracking du cholestérol LDL et HDL par contre a montré des différences de niveau par nationalité et par sexe. Les différences trouvées par rapport à d'autres études ne s'expliquent qu'en partie par les différences dans les populations ou par les méthodes de laboratoire. L'étude a trouvé en outre des différences individuelles considérables dans le niveau de cholestérol entre l'âge de 5 et celui de 14 ans. Le body-mass-index était plus constant. Non seulement la puberté, mais également les changements des habitudes alimentaires ou de l'activité physique – spécifique dans les subpopulations – peuvent exercer une influence sur le niveau individuel de cholestérol. Les résultats de l'étude bâloise soulignent l'importance du screening d'obésité et de la promotion de la santé dans les domaines de l'alimentation et du sport.

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Acknowledgements

Support by grant from the Swiss National Research Found (Grant No 6.156-0.75, No 6.965.0.80 and No 3.807.0.84). In Gedenken an Prof. Dr. med. G. Ritzel unter dessen Leitung die vorliegende Studienarbeit am Schularztamt Basel-Stadt 1976 begonnen wurde, sowie in Gedenken an Prof. Dr. med. F. H. Epstein für seine fruchtbaren Anregungen zum vorliegenden Artikel.

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