Special Article

PRIMARY PREVENTION OF ATHEROSCLEROSIS: RESPONSIBILITY OF THE PEDIATRICIAN?

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Coronary artery disease (CAD) is now emerging as one of the most important cardiovascular disease. Unchecked, the epidemic is threatening to engulf the whole society. At this rate of demographic transition, with the expected life expectancy in the vicinity of 64 years for an average Indian, by the turn of century, CAD in India could assume an alarming public health dimension. It is feared that if present conditions persist, every second person born alive will die of CAD(1).

The development of atherosclerosis and coronary lesions above the surface of clinical recognition, is a long drawn out process, dependent on time. However, in view of the increased incidence of precocious ischemic heart disease (IHD)(2) for the last few years, this duration appears to be on the decline. Also it is becoming increasingly clear that atherosclerosis is not an unavoidable product of aging process. There is a growing convictions(3) that the only way to substantially reduce the toll from atherosclerotic disease is to attack its constitutional and environmental precursors, long before overt symptoms start. Epidemiologic and pathologic studies(4) suggest that only early intervention is likely to have a major impact on the evolution of the disease. There are many reviews(5-7) available, which deal with the complex interaction of various genetic and environmental factors in the development of atherosclerosis. The possible relationship has been summarized in the *Figure*.

The best way to approach the problem of atherosclerosis is to formulate the risk-factor approach. It must, however, be pointed out that the role of genetic factors has been fully elucidated. It must also be understood that the environmental risk factors do not operate with a genetic vacuum–rather, they produce damage in individuals with hereditary predisposition to respond adversely. The important concert, therefore, is not so much as the specific factor but an overview of the interaction between heredity and environment.

Broadly speaking, atherosclerosis can be termed a product of an unhealthy life style(8). The various factors influencing its development can be categorized as non-modifiable, *viz.*, family history, genetics, gender and age; partially correctable, *viz.*, hypercholesterolemia, hypertension and hyperglycemia and totally correctable, *viz.*, smoking, obesity and physical inactivity.

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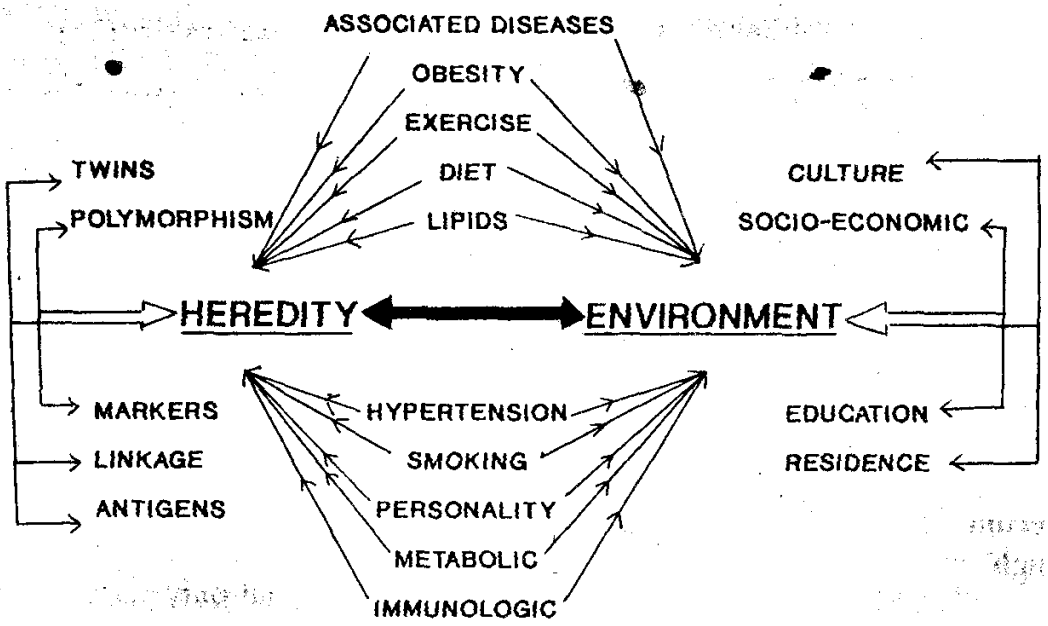

Fig. 1. Postulated relationship for development of atherosclerosis.

This type of classification is, however, artificial and as already pointed out, many of these conditions are inter-related and frequently co-exist. It is interesting to note that with the exception of smoking, diet seems to be related with almost all correctable risk factors.

Lipids and Lipoproteins

Lesions of atherosclerosis progress because of a derangement in the cellular metabolism of cholesterol; hence any discussion on atherosclerosis and preventive programme must include lipids and lipoproteins as its main plank. Are lipid and lipoprotein abnormalities recognizable in children? Studies(9) have suggested that LDL or total cholesterol (TC) levels in cord blood might be useful indicators of familial hypercholesterolemia. LDL in particular has been found to be a reliable predictor of cholesterol abnormalities, to be found at the age of 1-2 years in children having one parent with hypercholesterolemia. Other studies have shown(10) that there is a comparability of TC levels from the middle of first year of life through childhood and adolescence. After initial variability, the levels 'track' reliably by one year of age. Children of CAD parents have been demonstrated to exhibit hypercholesterolemia significantly higher than age and sex matched controls(11,12).

Many studies(13,14) have attempted to define the 'normal' range of cholesterol for children and the results can be summed up as follows–the cholesterol concentration in the neonate is about 65 mg/dl. The level tends to rise during first few months so that by 2 years of age, a mean value of 165 mg/dl is reached. There is no further significant variation in cholesterol level with age, sex, rate of growth or level of sexual maturation, until approximately 20 years of age. At that time, slow progressive rise begins, which continues till the age of 60 years.

In spite of their detailed description in literature(15), the inherited hyperlipoproteinemias comprise only a small percentage of cases of hypercholesterolemia. The majority are affected by environmental and less obvious genetic influences; of the envi-

ronmental factors, dietary cholesterol intake has gained the major attention and interest, because it can be potentially controlled. Experimental studies(16) have clearly demonstrated dietary cholesterol and saturated fats as the key factors in the development of atherosclerosis.

Hypertension

Hypertension has also emerged as one of the most common and potent elements, predisposing to atherosclerosis. Normal values for childhood blood pressure have been established by many investigations(17-19) with minor variations for race and geographic location. Blood pressure exhibits wide variability and 'tracks' poorly throughout childhood(20). However, when a blood pressure elevation is identified and it does track, considerable confidence can be placed on this finding.

Findings of Zinner *et al.*(21) suggest that the process of essential hypertension and ultimately its influence on the rate of atherogenesis has its roots very early in life. Prospective studies(22) of adults also reveal that most cases of essential hypertension originate before the age of 30.

Hypertension has shown a familial aggregation, suggesting a genetic basis for the same; environmental factors, however, play no less a role, as suggested by studies of spouses married for over 15 years(23). Therefore, children with hypertension should be treated vigorously so as not to let them grow up as adults with hypertension and thus have an increased risk for atherosclerosis.

Sodium intake has been shown to play a crucial role in the development of primary hypertension(24). The apparent link between salt intake and hypertension becomes tenuous in intra-population studies(25) but it does not negate the observation that many hypertensives do benefit from salt restriction(26).

Other Risk Factors

Existing epidemiological data suggests a weak association between obesity *per se* and atherosclerosis risk. It is thought that the risk largely attributable to propensity of the obese individual to have hypercholesterolemia to be sedentary, to have impaired carbohydrate tolerance and hypertension. That there are powerful family influences is demonstrated by studies of Garn *et al.*(27), which have shown that in families containing both biological and adopted children, the relationship in fat fold thickness between parents and their children is similar.

It is suggested by existing data(28) that individuals with a positive family history of premature CAD (before 50 years of age) are at an increased risk of developing atherosclerosis. The risk appears to be greatest for individuals, who have a first degree relative with CAD. The exact cause of this familial aggregation remains unclear(29) but may represent the overall influence of the familial pattern of other risk factors in addition to the metabolism of coronary arteries themselves(30).

The association of diabetes and atherosclerosis has been well documented in literature; risk has also been associated with asymptomatic hyperglycemia(31). In addition, diabetes is also associated with hypertension, obesity and abnormal serum lipids. It has been postulated that adult onset, keto-resistant, obesity related diabetes may be a late sequelae of childhood obesity(32). At the present time, control of hyperglycemia alone does not appear to reduce the risk of atherosclerosis, suggesting that elimination of other risk factors may be more important.

The role of physical activity or lack thereof, in the development of atherosclerosis remains controversial though, detrimental effect of sedentary living has been demonstrated(33). There is paucity of evidence relating physical inactivity to atherosclerosis risk in children. The recent TV and Video boom may be having a great influence, by not only promoting sedentary living but also indirectly contributing to obesity by increased consumption of "in-between the meal" snacks.

Qualification of Risk

These factors can be used as guides to devise suitable preventive approaches. If a child has a father, who sustained a myocardial infarction before the age of 50, the approach should be aggressive and aim at eliminating all risk factors, other than a positive family history.

The scoring system proposed by Nora(34) deserves a mention (*Table I*). Most questions can be updated on follow-ups, once an initial information has been obtained. A maximum score of 10 is allotted and risk factors are accordingly calculated. If a child has a first degree relative with premature CAD, he may be burdened with 3 points and an irreducible two fold risk of atherosclerosis. But how to keep the risk lowest is suggested by the index. Avoiding any additional points from smoking, sedentary life or hyperlipidemia reduce the risk to minimum achievable levels.

Intervention

That even children with extreme risk factors benefit from intervention, has been shown by improved survival of patients with homozygous familial hyperlipoproteinemia treated with plasma exchange(35). In most children, however, any risk factor may be present to only a minor degree. Are these children likely to benefit?

This question cannot be answered with certainty since necessary studies have not been carried out. All that is possible is to extrapolate the results from adult studies to children. Few would disagree that children should be discouraged from smoking, becoming obese or sedentary but what about modification of other risk factors? Most will investigate and treat hypertension. Same is true of diabetes. Due emphasis should be laid on diet also.

Diet is important in reducing cholesterol levels. Published dietary recommendations differ but have many things in common. These include lowering energy intake, reducing total fat and saturated fatty acid intake and increasing the consumption of complex carbohydrates and dietary fibres(36). Degree of compliance with diet is important and is less likely with more draconian measures. Lowering of elevated cholesterol can not only reduce the rate of development of atherosclerosis but may also promote the regression of existing lesions. In view of these, it would be reasonable to attempt to lower the serum cholesterol levels in children, by dietary modifications.

It may be argued at this point that would a diet that provides decreased cholesterol and fat intake and an increased P/S ratio be safe for adolescents and children? Reducing the amount of fat energy to below 35% and increasing fibre are accepted(37) but the timing is debated.

All essential fatty acids in man are poly-unsaturated. There is no theoretical reason, why a decrease in saturated fats and cholesterol should, *per se,* be deleterious. Growth and development have been

TABLE I—*Scoring System for Rick of Atherosclarosis*

Risk index	
* Family history (Max score 3)	
– CAD in 1st degree relative before 55	3
– CAD in 1st degree relative before 65	2.5
– CAD in 2nd degree relative before 65	1
– Stroke in 1st degree relative before 55	1
– Stroke in 2nd degree relative before 65	0.5
* Cholesterol and triglycerides (Max score) 2	
– Cholesterol >200 mg/dl	2
– Cholesterol >190 mg/dl	1
– Triglycerides >120 mg/dl	0.5
* Other risks (Add all values)	
– Smoking	1.5
– Diabetes in child	1
– No regular exercise	1
– BP >95th percentile	0.5
– Relative weight 1.20	0.5
– Type A behavior	0.5

Prediction of Risk

Risk score	Increased risk
3.0	× 2
3.5	× 3
4.0	× 5
4.5	× 6
5.0	× 15
5.5	Not calculable

Adapted from Nora(34)

normal at 3 years in a group of children fed on low-cholesterol low saturated fats diet(38). However, dietary modification is not entirely without risk-diarrhea, gall stones and reduction is HDL levels have been reported(39). It may be noted, however, that these diets were very artificial and it may be possible to advise a 'safe' diet with only minor modifications of the usual diet.

Role of a Pediatrician

Two avenues of intervention are currently available–the first is the direct physician-patient interaction and the other is through public health education. In the first system, clinician would try to alter the disease process by modifying the individual at risk. The second method may be implemented through the environmental engineering technique via public education. For either system to be effective, the first step should necessarily be directed towards motivation of primary care physician, whose responsibility it would be to identify the children at high risk, institute general preventive measures and to provide community education and intervention.

It may be pointed out here, even at the cost of repetition, that atherosclerosis has its origin in early childhood and it has a long drawn out asymptomatic period, becoming clinically apparent only during adulthood. The earlier in life the risk factors are identified and modified, better are the chances of success. Pediatricians have long been instrumental in health maintenance and their participation is critical to the success of any long term intervention. Living habits and factors that influence atherosclerosis are generally established during childhood. Only by controlling or altering child's environment early in life, will long lasting beneficial changes be made. The prevention of atherosclerosis can best be accomplished by avoiding or altering poor habits, before they are firmly ingrained. The key areas, where intervention is desired are nutritional counselling, encouragement of proper exercise and avoidance of smoking.

Nutritional forms of intervention can have wide spread effects on several risk factors. Because eating habits established in early infancy and childhood persist into adult life, it seems prudent to teach infants and children to eat in moderation with proper nutritional content.

Which children should have dietary modifications? Certainly, those with elevated cholesterol levels deserve intervention. Although, the distribution of cholesterol is unimodal, with 95th percentile being in range of 200-220 mg/dl, this figure is considered too high. More realistic would be to consider the upper limit of normal as that observed in population of children with less potential for developing atherosclerosis, *i.e.,* around 165 mg/dl, with values between 165-200 mg/dl being considered suspect(40). The diet should be low in cholesterol, saturated fats and simple sugars, yet adequate in calories to allow optimal growth. Argument exists that because of the need for fatty acids in the myelinisation of CNS and for the integrity of integument, low cholesterol diets should be avoided prior to first birthday(41). It is, however, important to realize that absolute reduction of serum cholesterol levels is probably not as important in childhood, as the nutritional patterns established at that age.

Whenever nutritional advice is given, cultural and social differences in eating practices should be respected. Meals should be spaced throughout the day and excess consumption of carbohydrates, especially sweets, biscuits and proprietary drinks should be avoided. Use of sweets as reward for food behavior need to be discouraged. Salt control should actually be initiated in infancy, before the infant acquires a taste for salt. Parents should discourage adding salt at the table and addition of salt to cooking should be reduced.

Many may question the wisdom of identifying individuals at risk of disease, 30-40 years later. It may be argued that

perhaps more psychological harm may be done than health advantages accrued. However, screening and identification may be possible on a low key basis, so as not to create a fear psychosis. If initial evaluation at school entry is normal, it might not be necessary to screen again till adolescene.

The published data lead one to believe that it is possible to identify with considerable confidence, the child, who is a candidate for CAD as an adult. Incorporation of risk factor analysis and a programme for atherosclerosis prevention into pediatric practice requires a new orientation and may initially be disruptive. However, once this initial obstacle is hurdled, the benefits to the community and individual in particular are potentially great.

The concern about instituting changes is another issue. However, it is difficult to fault advocacy of a life style that embraces exercise, normal weight, prudent diet, stress control and abrogation of smoking. It is also difficult to resist the temptation of deliberately identifying children at high risk to assure that they are given every opportunity to reduce their risk through a preventive programme.

REFERENCES

1. Parmeshwara V. Ischaemic heart disease—an overview. J Ass Phys India 1988, 36: 485-496.
2. Manoria PC, Misra NP. Value of predisposing factors in atherosclerosis. *In:* Progress in Cardiology. Misra NP New Delhi, Arnold Heinman, 1981; pp 31-38.
3. Falkner F. Prevention in childhood of health problems in adult life. Geneva, WHO, 1980, pp 71-86.
4. Holman RL, McGill HC, Strong JP *et al.* The natural history of atherosclerosis. Am J Pathol 1958, 34: 209-235.
5. World Health Organization. Prevention of Coronary Heart Disease. Tech Rep Srs No. 678, 1982, pp 1-45.
6. Ball MJ. The etiology of atherosclerosis and CAD. J Appl Med 1988, 4: 463-469.
7. Roy CC, Galcano N. Childhood antecedants of adult degenerative diseases. Pediatr Clin North Am 1985, 32: 517-533.
8. Kaplan NM. Importance of CAD risk factors in the management of hypertension. Am J Med 1989, 86 B: 1-4.
9. Evans GR, Taylor KG. Pediatric Origin of atherosclerosis. J Appl Med 1988, 4: 453-469.
10. Glueck CJ. Pediatric primary prevention of atherosclerosis. New Engl J Med 1986; 31: 175-177.
11. Mirza K, Ahmed P, Bilgrami NL, Salahuddin A. Serum lipids and lipoprotein values in children of CAD parents. Indian Pediatr 1984, 21: 235-240.
12. Kumar K, Anand NK, Janah S. Serum lipids profile in children of parents with CAD. Indian Pediatr 1979, 16: 1107-1114.
13. Mathur PP, Prasad R, Jain SK, Pandey DN, Singh SP. Cord blood cholesterol. Indian Pediatr 1986, 23: 103-106.
14. Mirza K, Ahmed P, Bilgrami NL, Ullah MS. Lipid and lipo protein values in normal children. Indian Pediatr 1984, 21: 313-317.
15. Mahajan MN, Sainani GS. Physiology and pathophysiology of hyperlipidemias. J Appl Med 1989, 15: 303-305.
16. Vega GL, Denke MA, Grundy SM. Metabolic basis of hyper-choles- terolemia. Circulation 1991, 84: 118-128.
17. Aggarwal VK, Sharan R, Srivastava AK, *et al.* Blood pressure profile in children. Indian Pediatr 1983, 20: 921-925.

18. Laroia D, Sharma M, Diwedi V, Belapurkar KM, Mathur PS. Profile of blood pressure in normal school children. Indian Pediatr 1989, 26: 531-536.

19. Mani S, Rao PPS. Blood pressure levels in South Indian adolescents. Indian Pediatr 1992, 29: 715-722.

20. Tondon R. Systemic hypertension and preventive pediatrics. Indian Pediatr 1982, 19: 735-737.

21. Zinner SH, Levy PS, Kass EH. Familial aggregation of blood pressure in children New Engl J Med 1971, 284: 401-406.

22. Oliver MF. Prevention of coronary heart disease: propaganda, problems, promises and prospects. Circulation 1986, 73: 1-8.

23. Winkelsteum W, Kantor S, Ibraham M. Familial aggregation of blood pressure. JAMA 1965, 195: 818-820.

24. Freis ED. Salt volume and prevention of hypertension. Circulation 1976, 53: 589-595.

25. Hemt JC. Sodium intake and hypertension–A cause for concern. Ann Intern Med 1983, 98: 724-728.

26. McCarron DA, Henry HJ, Morru CD. Human nutrition and blood pressure regulation. Hypertension 1982, 4S: 2-13.

27. Garn SM, Clarke DC. Trends in fatness and origin of obesity. Pediatrics 1976, 57: 443.

28. Schrott HC, Clarke WR, Lauer RM, Conner WE, Weibe DA. Increased coronary mortality in relatives of hypercholesterolemia children. Circulation 1979, 59: 320-324.

29. Jullin DG, Humphires JO. Preventive Cardiology. 1st edn. London Butterworths & Co, 1983, pp 123-144.

30. Samuelson O, Whilhemsen L, Elmfeldt D, *et al.* Predictors of cardiovascular morbidity. J Hypertens 1985, 3: 167-176.

31. Kannel WB, McGee DL. Diabetes and cardiovascular disease. JAMA 1979, 241: 2035-2058.

32. Lees R, Wilson DE. The treatment of hyperlipidemia New Engl J Med 1971, 284: 186-189.

33. Krause RM. Exercise, lipiproteins and coronary artery disease. Circulation 1989, 79: 1143-1146.

34. Nora JJ. Identifying the child at risk for coronary artery disease as an adult. J Pediatr 1980, 97: 706-714.

35. Thomson GR, Miller JP, Breslow JL. Improved survival of patients with homozygous familial hypercholesterolemia treated with plasma exchange. Brit Med J 1985, 291: 1071-1073.

36. Report of Canadian Consensus on Cholesterol, Rapport 1988, 3: 1-3.

37. Taits IS. Diet of young children and cardiovascular disease. Brit Med J 1987, 294: 920-921.

38. Friedman J, Goldberg SJ. An evaluation of the safety of low saturated fat, low cholesterol diet in infancy. Pediatrics 1976, 58: 655-657.

39. Shephard J, Packard CJ, Patsch JR, *et al.* Effect of dietary polyunsaturated fat on the properties of HDL and metabolism of apolipoproteins. J Clin Invest 1978, 61: 1582-1592.

40. Liyod JK, West RJ. Childhood prevention of coronary heart disease. Postgrad Med J 1986, 62: 97-100.

41. Tsang RC, Glueck CJ. Perinatal cholesterol metabolism. Clin Perinatol 1975, 2: 275-279.