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Current topics

Cardiovascular risk factors in childhood

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It is regrettable that although the incidence of fatal coronary heart disease on the other side of the Atlantic and in Australia is falling, the toll here, even if not increasing at the great pace of the 'fifties and 'sixties, is only just beginning to level off. Few of us can afford to be complacent, and we as paediatricians have a duty to sow the seeds of longevity in our patients. For these reasons it seems timely to review cardiovascular risk factors in children, not least with the admonitions of the Reith lecturer ringing in our ears about our lack of concern for preventive medicine.

Atherosclerotic disease begins early in life. Indeed already at birth there is a difference between the aorta of boys and that of girls which might suggest that testosterone is actually atherogenic.[1] Perhaps we have to settle for these sex ratios of susceptibility but numerous studies have shown the importance of risk factors in adult populations and now is the time to look to an age group in which the disease is not already far advanced.

The way that cholesterol forces itself into the arterial wall is ultimately the crucial point to consider. Here the interactions of endothelial injury, platelet stickiness, and a leaky endothelium lead to invasion of the vessel wall by lipoproteins and other foreign substances. Repair then takes place and it seems that these repeated brief insults become cumulative over the years and bad luck or bad management leads to the final event of an infarct, by which time the individual needs not just a routine service to repair major damage but a whole new set of plumbing.

The liability of an individual's arteries to undergo atherosclerotic change varies with age, sex, geographical location, and race. Lesions seem to be related to serum cholesterol and to dietary fat and salt intakes when comparing populations but the data are insufficient (and hence the advocacy of extreme stances) to confirm these associations on an individual basis within a population. Hypertensive subjects, diabetics, and smokers fare badly, but obesity and exercise on their own seem to be receding in importance; they may exacerbate other factors but it is the interaction of the risk factors that counts.

The definition of what constitutes significant hypertension, hyperlipidaemia, or obesity is vital. Are minor degrees important? Simple measurement in the population is not adequate: this gives the situation as it is and not necessarily as it should be. What is the contribution of time to this; does it interact with a small degree of risk to increase its force? Most important of all, what is the genetic liability to suffering the consequences of the various risk factors? The same quantity of factor manifestly does not carry the same risk in different families so it is best to choose healthy parents. Whether this is to get good genes or a good family environment is hard to say but to have maximum impact a paediatrician could be justified in first pursuing the yet-healthy children of risk-loaded parents with a poor family history. The increasing fashion in the private sector for medical checks on husbands and wives could be the beginning of an important contribution: contact tracing has, after all, a pretty good record in the case of the infectious diseases.

Blood pressure

Hypertension is an important risk factor and leads to more deaths from heart attacks and heart failure than from strokes. The earlier that a tendency to hypertension is detected, the better, but which of us can truthfully say that it is measured routinely in every single patient for whom we are responsible? Centile charts for blood pressure are available[2] and should be used by paediatricians, especially by those working in community child health, just as we use centile charts for height and weight.

Blood pressure values run in families but they do so also in adopted children,[3] so much the same arguments can be used for the contribution of genes and environment for blood pressure as for obesity.[4] However, the balance of evidence favours a more

substantial genetic contribution to the determination of blood pressure,[5] even though environmental factors are manifestly very important. Much more fascinating than the actual levels however, are the differing cardiovascular responses of the non-hypertensive offspring of hypertensive and non-hypertensive parents.[6 7] Here is a real clue to a programme of action.

Hypertension and salt. Interest in salt and its effect on blood pressure is waxing again, although the subject is becoming more complex because of the interaction between salt and potassium. This is not made easier to understand by the fact that hormones we used to regard as salt conserving (for example aldosterone) may have a primarily kaliuretic role and be regulated by serum potassium concentration rather than by sodium concentration.

In our society, blood pressure levels increase with age and it is the exaggeration of this increase that we call essential hypertension. In 'no salt' cultures this fails to occur[8] but the move of a saltless person to a salty land restores the liability to hypertension.[9] Salt therefore, seems to be a pressor agent in everybody although mildly hypertensive subjects seem to be more reactive than non-hypertensive ones.[10] The intriguing possibility that potassium may be a depressor agent[10] offers distinct possibilities for intervention, and more studies are needed. The mechanism by which it might be effective is far from clear since it seems that potassium alone can both raise the aldosterone levels and lower the blood pressure. This depressor effect of potassium has been found in the non-hypertensive sons of hypertensive parents but is absent in the sons of normotensive parents.[7] Perhaps a lack of potassium is important to children with a familial predisposition to hypertension.

Hypertension and stress. There remains much of interest for the researcher, since the hormones of stress are legion and the mechanisms by which they could promote atherosclerotic change are many. It is true that the normotensive offspring of hypertensive parents have a higher neuradrenergic sympathetic activity but whether they would react differently, say, to an infusion of adrenocorticotrophic hormone or to other hormones of stress is unknown. I do not know what advice could be offered by a physician, given our present state of ignorance.

Hypertension and obesity. In 1978 the *New England Journal of Medicine* published an important paper which showed that weight loss alone (without salt restriction) reduced the blood pressure of overweight hypertensive patients.[11] The relationship between blood pressure and weight is as true for children as it is for adults, and overweight subjects have an increased incidence of stroke and coronary heart disease. On the other hand the obese person with a normal blood pressure appears not to have much of an increased risk for cardiovascular disease. These findings suggest a principle of management which may have practical use. While I have considerable doubts and reservations about how worthwhile is the active involvement of physicians in the management of 'simple' obesity, particularly in childhood, the situation is very different when the obese child is aggregating other risk factors. I propose that physicians be active in the management of obesity in childhood if the blood pressure (carefully measured with an appropriately sized cuff) is at least 90th centile for age. Since the active management of obesity also necessarily means the restriction of carbohydrate, fat, and sodium intakes (and perhaps even the increase of dietary potassium), the dietary management of the obese hypertensive child can only be a step in the right direction. Apart from this I think that doctors have a duty to set an example, just as they have done in smoking, that weight penalties[12] are severe and that effort is well spent avoiding them.

Lipids

Considerable advances have been made in understanding serum lipids in the last two decades, particularly in adults. There has been a great difficulty in terminology and at least three systems of classification are widely used. For the purposes of this discussion low density lipoproteins (LDL, which migrate as the β band on electrophoresis) predominantly carry cholesterol and very low density lipoproteins (VLDL, which migrate on paper electrophoresis between the β and α zones and are called pre-β lipoproteins) are rich in triglycerides. LDL and VLDL are considered atherogenic; VLDL is not actually found in atheromatous plaques but endothelial lipases may contribute to intimal invasion by LDL cholesterol. High density lipoprotein (HDL, which migrates as the α band on electrophoresis), although it carries an appreciable amount of cholesterol, has been shown in some studies but not in others to be antiatherogenic, a negative risk factor.[13]

Cholesterol, unlike fatty acids derived from adipose tissue which owe their origins to dietary carbohydrate and its conversion to triglyceride in the liver, is not an energy-producing lipid and less is known about its metabolism than about triglycerides. The measurement of total serum cholesterol

includes the cholesterol carried on the LDL and HDL so a measurement of total serum cholesterol is akin to the measurement of total bilirubin concentration in a jaundiced neonate. Ideally one would have access to HDL cholesterol and total cholesterol measurements, but total cholesterol is generally a practical and effective means of assessing the individual risk of cardiovascular disease associated with blood lipids. The preventive practice of lowering total cholesterol levels is generally appropriate and has been shown to be effective.[14]

No studies have yet looked at the influence of genetics and environment on lipid levels in normal populations to establish the contributions made by genes and the environment, most attention having been focused on the genetic aberrations in lipid metabolism which lead to very high or low levels. Lipid levels change with age and vary with geographical location, season, diet, body weight, and other factors—such as smoking and the use of contraceptive pills. A recent study in adolescence[15] has shown that girls have higher HDL cholesterol concentrations than boys, and that smoking was associated with lower HDL cholesterol concentrations. In girls the use of oral contraceptives was associated with lower HDL cholesterol concentrations. The favourable effects of raising HDL levels are also associated with lower total cholesterol levels and these findings carry some clear messages about losing weight, not being sedentary, not smoking, and not drinking alcohol excessively.[16]

Smoking

Cigarette smoking causes many of the 40 000 deaths from coronary heart disease in men and women of working age in this country. Reduction of cigarette smoking quite rapidly leads to a fall in the number of deaths from coronary heart disease.[17] The relationship between cigarette smoking and heart disease is poorly recognised by the public compared with awareness of the risks of lung cancer. Paediatricians, especially school medical officers, could and should be aware of these facts; the popular Superman versus Nick O'Teen campaign by the Health Educational Council is likely to be much more effective than school health education lectures.

Diet

It has been difficult to get any clear consensus about what we should be recommending our patients about diet. The more fat and cholesterol one eats, the higher are the LDL and total serum cholesterol concentrations likely to be. The lipid composition of the diet is reflected in the level of serum cholesterol which is related (but not necessarily causally) to the long-term risk of death from coronary heart disease in middle-aged American men.[14] There can therefore, be no objection to the suggestion that a reduction in cholesterol intake is good. Maintaining roughly equal proportions of saturated, monounsaturated, and polyunsaturated fatty acids, and taking increased roughage and less-refined carbohydrates would be a contribution to gastronomy and should help to reduce the number of large-bowel diseases and the risk of coronary heart disease.

What this means in practice is using olive oil (monounsaturated) or polyunsaturated oils (corn oil, sunflower seed oil etc) instead of dripping. It means grilling rather than frying and probably limiting egg yolks to about 3 a week. In a good French restaurant one does not see huge quantities of cream and butter on the table so an antiatherogenic diet does not have to be a penance. Furthermore, those of us who like such things cannot of course fail to be delighted by the 'strong and specific negative associations between ischaemic heart disease, death, and wine consumption'.[18] In fact the risk effect of alcohol is J-shaped and much alcohol increases blood pressure. Consumption seems to be inversely related to the incidence of coronary heart disease morbidity and mortality, but not to the risk of dying from stroke, accidents, or violence,[19] so moderation pays in all things.

Exercise

Those who take regular vigorous exercise are less likely to develop heart attacks[20] but such people have all sorts of other characteristics that contribute to such a desirable state. No study has shown that coronary heart disease can be prevented by exercise *alone*. Manipulation of diet and exercise can certainly change profiles of lipids, weight, and blood pressure favourably but exercise *per se* does not seem to be particularly effective.[21] It is positively dangerous suddenly to send an overweight middle-aged man jogging or on to a squash court. It is better generally either to take vigorous exercise regularly, or persistently to look after one's body, which probably comes to much the same thing in the end.

Conclusion

The understanding of the risk factors and the assumption of a life style that may influence the early natural history of atherosclerosis is critical to the prevention of cardiovascular disease. If today's children follow their parents, 20–30% of them will have hypertension as adults, 90% will develop

significant atherosclerotic lesions, and more than half will die from the cardiovascular complications.[22] Against the background of such statistics what can the physician do? Firstly, he can encourage government, government agencies, and charitable foundations to recognise their responsibilities. Education of teachers might be a good place to start and it is impressive that the American Heart Association has made heart health education in the young a top priority.

If a doctor finds this too political and too large a topic, at an individual level, he should look at his child patients to see how many risk factors each is accumulating. This means looking at family history, family dietary and smoking habits, blood pressure, and perhaps estimation of lipid levels of the most at-risk subjects. Physicians in hospital should seek out the children of adult hypertensive patients and of patients with advanced atherosclerotic disease to prevent the aggregation of risk factors which seems to be so dangerous. In doing so they are likely to meet a receptive audience and one that is grateful that something can be done not only not to 'become like Dad' but also actually to help Dad after his coronary not to get another one.[23]

General advice needs to be practical. The number of cookery books bears witness to the general interest in food, and a diet which is moderate in fat and refined carbohydrate and low in salt (?high in potassium) cannot be exceptionable, particularly if it is reasonably generous in garlic, onions, and wine.

Chiefly we should avoid being a bind to our patients. Life should be fun and happiness must be a protective factor, even if it does not influence HDL concentrations (and who can say it does not?). Maybe the physician's personal example that the good life does not necessarily require monastic discipline is the best preventive medicine we could practice.

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