Coronary risks: its origin in childhood nutrition
บทบาทของการรักษาในวัยเด็กต่อโรคหัวใจขาดเลือด

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Coronary heart disease (CHD) due to atherosclerosis is a leading cause of disability and death in industrialised and developing countries including Thailand. CHD ranks first in terms of social security cost, direct health care costs and lost wages. It has been estimated that in the U.S., 1 in 5 boys are likely to develop CHD before the age of 60 years.\(^1\) Thai children who adopt a life-style (nutrition, physical activity, smoking, alcohol consumption, etc.) similar to western countries would predictably have a similar chance of developing CHD in later life. Since 1968 there has been a marked decline in CHD mortality for all major sex and race groups in Australia\(^2\)\(^-\)\(^5\) and the U.S.\(^6\)\(^,\)\(^7\) It has been estimated that from 1969 - 1977, the CHD mortality among men aged 35 - 74 years declined 19% in Australia and 22.6% in the U.S.\(^7\) Unfortunately, comparable data from Thailand are not available. The reason for the decline in Australia and in the U.S. has been variously ascribed to changes in life-style, improved medical care, increased knowledge about the disease and the identification of specific cardiovascular risk factors\(^2\)\(^,\)\(^7\)\(^,\)\(^8\) but has not yet been clearly determined.

Epidemiological studies have established several factors related to the Western style of living which may play an important role in the prevalence and incidence of CHD in the adult. These risk factors are listed below.

1. Cigarette smoking
2. Hypertension
3. Hypercholesterolaemia
4. Hypertriglyceridaemia
5. A positive family history of CHD
6. Obesity
7. Physical inactivity
8. High alcohol consumption

Of these factors smoking, elevated diastolic blood pressure and hypercholesterolaemia are considered to be the most important. Despite the fact that the clinical symptoms of CHD do not become apparent until
much later in life, it is now recognised that CHD is a disease that often has its origin in childhood nutrition. Several observations have led to this recognition.

1. Animal studies

It may never be possible to determine with certainty the specific events that lead to atherosclerosis in humans. Therefore, systematic examination of the sequence of events occurring in animals most like humans is particularly useful. The animal models believed to be most similar to humans in relation to their lipid metabolism are non-human primates, swine and the WHHL rabbit (Watanabe Heritable Hyperlipidaemic).\(^{10}\) These models have been used to describe the sequential changes which occur in the arterial wall in response to dietary induced hypercholesterolaemia and to show the progression of experimentally induced fatty plaques by dietary means.\(^{11-13}\)

2. Autopsy studies

These studies have shown that aortic and coronary atherosclerosis begin early in life, however, at the present time, it is still not clear whether the fatty streaks found in the arterial blood vessels of young children are directly related to future atherosclerotic plaque.\(^{10}\) Katz et al.\(^{14}\) by demonstrating intermediate lesions between fatty streaks and advanced plaques provided support for the concept of a progression from coronary fatty streaks to fibrous plaques. Fatty streaks are found in the aortas of many children less than 3 years of age and in almost all children over the age of 3 years.\(^{15}\) The presence of fatty streaks in the coronary arteries, however, is rare prior to age 10 years, but after this time fatty streaks in the coronary arteries of children occur in increasing numbers. By age 20 years, most people in Europe and North America have evidence of fatty streaks in the coronary arteries.\(^{15-17}\)

In the Bogalusa Heart Study, subjects aged 5 - 24 years who died of accidents, were found to have aortic fatty streaks which strongly related to ante-mortem levels of both serum total cholesterol (TC) and low density lipoprotein cholesterol (LDLC) independently of race, sex and age (r = 0.67 ; P < 0.0001).\(^{20}\) Coronary fatty streaks, on the other hand were correlated strongly with very low density lipoprotein cholesterol (VLDLC) (r = 0.41 ; P < 0.05). Mean systolic blood pressure (SBP) was also higher in the subjects with coronary fibrous plaques than in those without them (112 mmHg vs 104 mmHg). These findings document elevations of serum lipoprotein cholesterol levels and of systolic blood pressure (SBP) in childhood which are related to the subsequent development of early atherosclerotic changes in the aorta and/or coronary vasculature.\(^{18}\)

The World Health Organization (WHO) Five Cities Study\(^{19}\) demonstrated that 10 % of
boys and girls aged 10 - 11 years already had atherosclerotic plaques in their coronary arteries. Further, Enos et al.\(^{(20)}\) found that 77% of autopsied Korean War casualties in young men with a mean age of 22 years had obvious evidence of coronary arteriosclerosis i.e. fibrous thickening, streaking or plaques causing luminal narrowing. Later McNamara et al.\(^{(21)}\) reported that 45% of autopsied Vietnam War casualties had similar evidence of coronary atherosclerosis. These findings suggest that although the clinical symptoms of CHD manifest in adult life, the process underlying atherosclerotic lesions begins well before the age of 20 years. The difference between the two latter studies, with respect to the frequency of atherosclerosis, is difficult to explain since both related to young males and the presence or absence of atherosclerosis.\(^{(21)}\) If the difference is real, a logical explanation is that in the 18 years between the two studies, changes occurred which had a significant impact on the process of atherosclerosis during childhood and adolescence.

### 3. Cross-sectional epidemiological studies

The results of the autopsy studies CHD risk factors in children have now been conducted.\(^{(22-26)}\) These investigations demonstrate that risk factors for CHD could already be identified in children. The reported prevalence of at least one risk factor for CHD in American children aged 7 - 12 years ranges from 46% - 62%, and from 14% - 36% for two or more risk factors. These values are obviously dependent on the cut-off values used in each study and can only be interpreted in the light of this information. As a specific example in the Muscatine study in children in age 14 - 18 years using serum TC > 220 mg/dL; SBP > 140 mmHg or DBP > 90 mmHg; weight > 130% relative weight, it was found that 23% were positive for one CHD risk factor, 5% for two and 1% for three.\(^{(23)}\) On the basis of adult experience a child who has multiple CHD risk factors is at a considerably higher risk for CHD than one who has only one or no risk factors.

### 4. Longitudinal epidemiological studies

Longitudinal studies can provide more information than cross-sectional studies because they provide a better understanding of the pattern of disease over time. Many longitudinal studies in relation to CHD risk factors in children and adolescents have been performed such as the WHO Collaborative Study of Atherosclerosis Precursors in Children, International ‘Know Your Body Program’, the Bogalusa Heart Study, the Muscatine Study, the Zoetermeer and Zutphen Studies, the North Karelia Youth Project and the Oslo Youth Study. Longitudinal studies can relate past environmental and genetic factors to present CHD status. The notion that some of the most common CHD risk factors ‘track’ during childhood
has also been the subject of a number of investigations. (27–34) Tracking is a measure of the tendency of an individual to maintain a rank relative to their peers through time. (34) It has been shown that a high proportion of children who are at the extreme end of the distribution for elevated blood pressure (BP), lipid levels and obesity continue to exhibit these coronary risk factors as they grow. (27, 29, 33) For example, in the Muscatine study, 60% of children (5–18 years) whose SBP was in the upper quintile initially had a SBP in the upper two quintiles 6 years later. For cholesterol and triceps skinfold thickness, nearly 60% and 53% of the subjects initially in the highest quintile were still in the same quintile 6 years later. (35)

5. Family studies

Certain atherogenic serum lipid disorders are due to inborn errors of lipid metabolism while others are acquired or associated with various disease processes. For example, inherited hypercholesterolaemia with xanthomatosis or familial associated with premature and severe atherosclerosis. It is a genetically determined autosomal dominant disorder. (9) The majority of children with this type of disorder are heterozygous, with an incidence in the general population of 1:100 to 1:200 (36) and frequently asymptomatic during childhood. Individuals with this disorder have a 50% chance of developing of CHD by age 50 years and a mortality rate of 75% by the age of 60 years. (37) The homozygous form of the disease is extremely rare. Premature CHD is a uniform manifestation, with myocardial infarction usually occurring during children who are known to have problems of CHD with a specific genetic aetiology, there are other children who develop CHD in later adult life who may also have a genetic component of CHD risk factor transmission. Family studies of CHD risk factors in early life may be able to identify these children. Several investigators have focussed on family studies of individual risk factors e.g. blood pressure (38–41) and blood lipids. (38, 42, 43) Currently there are only few studies which have reported on clustering of CHD risk factors in families. However, there has been no such study in Thailand.

References


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