Artículo de revisión

Diet and public health: the rise and fall of coronary heart disease

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Resumen

Estudios epidemiológicos y experimentales sugieren que la nutrición deficiente durante periodos tempranos del desarrollo (vida fetal y niñez), aunque se corrija poco después, aumenta la vulnerabilidad y respuesta grave a enfermedades infecciosas y acorta la expectativa de vida. Las enfermedades coronarias (EC) y otras crónicas y latentes (accidentes vasculares cerebrales, AVC) parecen tener su origen en la infancia, influida por el estado de salud del organismo en desarrollo. Los padecimientos infecciosos y la liberación concomitante de mediadores inflamatorios durante la vida adulta tienen un efecto adverso en las arterias coronarias en personas mal nutridas durante las etapas tempranas del desarrollo. El descenso más notorio de la frecuencia de enfermedades cardiacas después de 1950 y durante los años 70, se debió principalmente a la introducción de una alimentación adecuada, sana y equilibrada, al control de infecciones (vacunación) y a otras medidas de salud pública (programas contra el tabaquismo) y no al uso de antibióticos o de medicamentos que disminuyen los niveles de lípidos. Irónicamente, en la actualidad los programas de salud pública deben enfocarse a disminuir el ascenso de los problemas de "sobrenutrición", de obesidad en los jóvenes, factor de alto riesgo de padecer enfermedades cardiovasculares en la edad adulta.

"La niñez muestra al hombre como la mañana muestra al día" John Milton (1608-1674) Bk. IV Paraíso Recuperado

Abstract

Epidemiological and experimental studies suggest that malnutrition during early rapid developmental periods (i.e., fetal life and early childhood), albeit corrected shortly thereafter, results in an increased vulnerability and a more severe response to infectious diseases and a shortened life expectancy. Cardio-vascular disease particularly coronary heart disease (CHD), and perhaps other chronic and latent disease (i.e., cerebral vascular accidents CVA) appears to have its origin in early life, the progression of which is influenced by the health status of the rapidly developing organism. Chronic infectious diseases, and the concomitant release of inflammatory mediators, experienced during adult life may result in a more adverse effect on the coronary vascular system in those poorly nourished during very early developmental periods. The most marked and steady fall in the incidence of heart disease after 1950 and well into the 1970s was essentially due to the establishment of an abundant, safe and adequate food supply, the control of infectious disease (e.g., vaccinations) and other public health measures (e.g., anti-smoking programs) and not to antibiotics nor to the use of lipid lowering drugs. Ironically, major public health initiatives should presently take aim at mitigating the increasing incidence of "over-nutrition", obesity in our young, a major risk factor for CHD in later life.

The Childood Shews the Man as the Morning Shews the Day John Milton (1608-1674) Bk. IV Paradise Regained

Introduction

It has been stated, "We have cause to celebrate the steep reductions in mortality from CHD (coronary heart disease) that have occurred over the past 30 years. These declines are best explained by joint contributions from primary and secondary prevention". The purpose of this paper is to suggest that reductions in total cardio-vascular disease

(CVD) (i.e., CHD and cerebral vascular accident or CVA) as well as in mortality, particularly in CHD, are best explained by the correction of nutritional deficiencies, an adequate food supply, an abundance of food choices, and public health measures (i.e., the control of infectious diseases without the use of antibiotics), all improvements that began in the early 1900. These measures, in addition to the use of more recent technological advances (e.g., angioplasty) in the acute care of coronary events, have contributed far more than any drug-elicited change in serum cholesterol levels or primary or secondary prevention initiatives to the steady decline in CHD mortality from the peak (late 1940s to mid-1950s) to the present [1-4]. In essence, the major decline in CHD deaths occurred long before the use of lipid lowering drugs and low-fat diets, including the more recent use of

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inhibitors of hydroxy-methylglutaryl coenzyme A (i.e., statins) in the late 1970s and early 1980s.
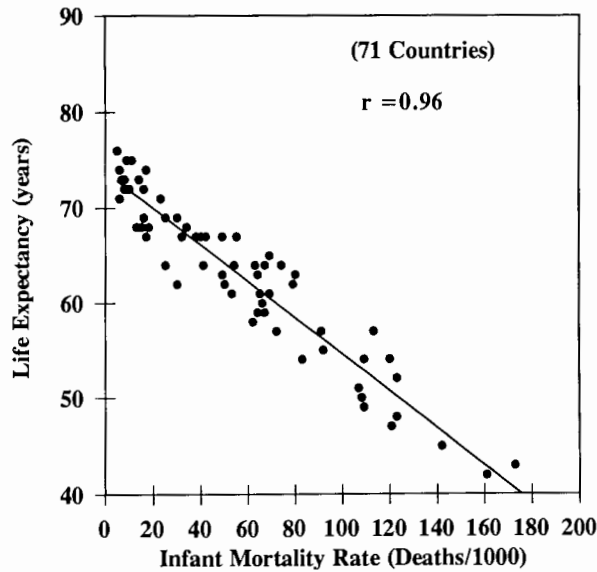

Figure 1. Data from seventy-one countries: Relation between infant mortality (IM) (deaths per 1000 live births) and life expectancy at birth.

Figure one illustrates the significant correlation between infant mortality rates and life expectancy suggesting the obvious. Those who survive in such areas of the world where infant mortality is high are at risk of a shortened life expectancy. The major causes of infant mortality at the beginning of the 20th century were infectious diseases, combined with malnutrition. In the early 1900s due to an improved agricultural system, an established food supply and the institution of appropriate health measures, infant mortality rates fell dramatically, from approximately 18 per 1000 live births in 1900, to 7 in 1950, to 2 in 1980 [3-5]. Those who survived in such hostile environments lived long enough to die of CHD or other adult onset diseases in their 40s and 50s, the average life expectancy in 1900. CVD deaths peaked between sometime after 1940 (Figure 2) and declined rapidly thereafter with essentially no change in the rate after the mid-eighties, some 12 to 15 years ago with the most rapid rate of decline in CVD deaths occurring between 1950 and 1977 [1-7]. The constancy of deaths due to CVD during the past several years suggest that death is inevitable and that more and more of the population are reaching their life expectancy. The plateau in deaths from CVD, particularly

from CHD, or simply a delayed death from some other cause, can hardly be attributed to the use of lipid or cholesterol lowering drugs. Clearly, early recognition of CHD and acute care of myocardial infarction have also played an important role in the decline in deaths due to CVD.
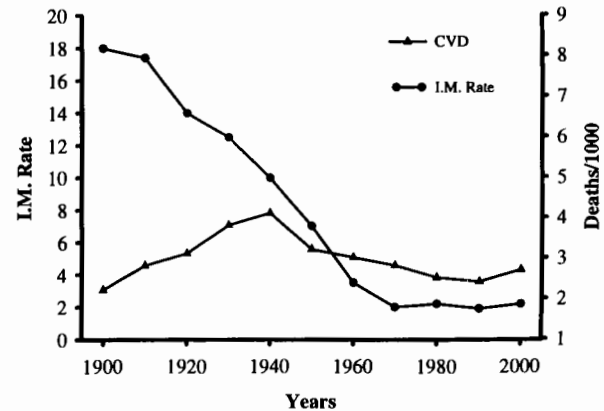

Figure 2. Changes in the United States in infant mortality (IM), rates, deaths per 1000 live births, relative to age-adjusted cardiovascular deaths (CVD) from 1900 to 1998.

Recent reports warning of an "Epidemic of CHD in Developing Countries" in the year 2020 should be viewed as relatively good news in those countries [8]. These reports should suggest that the transformations that occurred in the early part of the twentieth century in the U.S. are now beginning to occur there. As malnutrition and infectious diseases are being mitigated early in life (e.g. by vaccination programs), the survivors of these populations are getting old enough to develop the diseases of more affluent societies. The strong negative correlation between infant mortality rates and life expectancy supports the concept, proposed by many, that malnutrition and/or infectious diseases in early life significantly promotes the progression of chronic latent diseases, including CHD, in those who survive [9-14].

In the United States, the decline in the CHD mortality rate has continued since the 1950s while there has been little, if any, significant change in the consumption of dietary fat, red meats, butter and eggs [15]. Nor is there evidence of any significant changes in serum cholesterol or lipid levels during this period [15-18]. Furthermore, in 1900, 1950 and 1998 life expectancy increased from 47.3 years to 68.2 and 76.7 years, respectively [3-5]. The greatest gains in life expectancy and the health of the older population began in the mid-

1990s and continued through the 1950s with no help from lipid lowering drugs or antibiotics. The gains came from available food choices, meeting the nutritional requirements of mothers and infants, public health measures and control of infectious diseases. Those who should be celebrated for the current state of cardiovascular health are those in the agricultural business, the *bona fide* nutritionists and public health professionals.

Cholesterol reduction. CVD deaths and life expectancy

Powerful economic forces in the health related foundations and pharmaceuticals continue to promote the idea that lowering blood lipid levels will prevent CHD deaths. Intervening late in the disease process with very expensive drugs that are aimed principally at reducing "undesirable blood lipid levels" has resulted in a decrease in the absolute risk of a CHD death by an average of two per cent (range: 0-4%) [6,19-24]. Many physicians believe that approximately 66 million individuals in the United States aged 50 and older should be given, for life, one of the lipid lowering drugs, preferably one of the inhibitors of hydroxy-methyl-glutaryl-co-enzime A reductase (statins) to mitigate the risk of having a coronary event or prevent death from CHD [5]. Using only a third of this figure, a most conservative estimate of 22 million Americans taking a statin, at a minimum of one U.S. dollar per day, the total drug cost would be slightly over eight billion dollars per year. In 1999, approximately 900,000 individuals died from cardiovascular disease (approximately 750,000 from CHD and 150,000 from CVA) or about 0.3% of the population of 270 million [3-5,25]. Generously assuming a two per cent reduction in total deaths due to the use of lipid-lowering drugs, some 18,000 lives would have been saved (900,000 x 0.02) at a cost of over eight billion dollars. This words out to over 400,000 dollars per life saved. How many more years of life have been added as a result of lowering blood lipid levels? Based on available data taken from some earlier studies, the answer is in the range of weeks to several months or a few years [19,20,26]. Additionally, the added time to life in many studies may well be attributed to controlling and treating diseases associated with the progression of CHD and mortality; e.g., hypertension, diabetes, familial hyperlipidemias and the more serious growing problem of obesity. There are no unequivocal demonstrations that hypercholesterolemia, per se, in of itself induces CHD/mortality and/or myocardial infarction or death in humans or in animal models. Indeed, a serum cholesterol level is of little, if any, value in predicting a coronary event.

Perhaps an exception are those individuals with familial hypercholesterolemia (FHC), especially in those who are heterozygotes for the disease but who may have concomitant underlying disease. There is no convincing data that fatty streaks or atherosclerotic changes induced in rats or sub-human primates by simply inducing hypercholesterolemia have resulted in sudden-death due to an arrhythmia or a plaque rupture or to a myocardial infarction [27-29].

Nevertheless, those who maintain that hypercholesterolemia is an independent risk factor for CHD mortality, need to respond to two questions: 1) for whom is hypercholesterolemia an independent risk factor, and 2) how would individuals with hypercholesterolemia be indentified as candidates for lipid lowering interventions? One reasonable answer to the first might be to target only those individuals with clearly defined multiple risk factors and second, not simply on the basis of a blood cholesterol level, particularly in the elderly. The results of the Heart Prevention Study (Oxford, England) comprising approximately 20,000 subjects followed over a five-year period, were reported at the recent Heart Association meeting (November 14, 2001). The difference in the absolute risk reduction in CHD mortality and total mortality between those given simvastatin and those given a placebo was 2.3% and 1.6% respectively. Further, the reported effects of simvastatin were unrelated to initial cholesterol levels; those with high or low cholesterol faired equally well.

Nutritional and infectious components of CHD

Almost 100 or more years ago, Frothingham [30] and Ophus in 1921 [31] and more recently, others suggested that chronic infectious diseases might have a causative role in the progression, and perhaps initiation, of atherosclerosis and CHD [32-43]. One of the most convincing early arguments for a prominent role of an infectious process in the pathogenesis of CHD was the demonstration by Fabricant in 1978 that it was difficult to induce atherosclerotic lesions in specific pathogen-free animals. However, atherosclerotic lesions, similar to those seen in humans, were easily produced after inducing a viral infection (Marek's herpesvirus) [35]. During recent years, the evidence supporting these earlier observations has become compelling: 1) infectious diseases have a role in the pathogenesis, and perhaps in the initiation

of CHD and 2) markers of inflammation, particularly C-reactive protein, may be as or more valid predictive indicators of CHD morbidity and mortality than serum lipid levels [44-50].

There is general agreement that CHD is a chronic inflammatory disease and that the chronic, intermittent release of inflammatory mediators, acute phase proteins (APP) as a result of years of intermittent chronic infections, may play a prominent role in its progression and possibly plaque rupture [50]. Albeit retrospective in nature, the reports of the inverse relation between past use of anti-inflammatory agents (i.e., aspirin and antibiotics) and CHD mortality and morbidity support this view [51-55]. Screening and monitoring of inflammatory mediators, particularly in the young adult population or those at risk, and reviewing past medical records may prove more useful and less expensive than screening for hypercholesterolemia in establishing interventions that may prevent or delay CHD mortality. If antibiotics and aspirin reduce the risk of CHD mortality by acting as anti-inflammatory agents, as it has been suggested for statins [54-58], the cost of reducing the risk of CHD with their use would be immensely less. The long-term use of antibiotics to reduce the risk of CHD mortality is unlikely but an 81 milligram aspirin a day may will keep CHD at bay.

That inflammatory mediators play a role in the initiation or progression of CHD by causing endothelial injury seem reasonable; CHD is a chronic inflammatory disease. Whether they have a primary or secondary role (i.e., modulating an already "dysfunctional" endothelium) in CHD morbidity and mortality is moot. It also seems reasonable to assume that the more frequent and severe the episodes of infection resulting in inflammation, the more frequent the exposure of endothelial cells to inflammatory mediators. Family history, hypercholesterolemia, hypertension, smoking, diabetes, obesity, genetic predispositon, etc. may well be risk factors, albeit weak, in the initiation and rapid progression of CHD; inflammatory mediators may act to accelerate the process. Nonetheless, these putative risk factors, independently, are of little predictive value in assessing an individual's absolute risk of dying prematurely from CHD.

The major cause of morbidity and mortality in children, world wide, is due to the interactions between malnutrition and infectious diseases. Malnutrition, in even a single nutrient (vitamin, mineral, fat, amino acid) or in calories (marasmus), compromises one or more components of host defenses, leading to a more severe response to the infectious process. In experimental animals, malnutrition experienced

early in life, though corrected before adulthood, results in an increased vulnerability and a more severe response to infectious diseases throughout life [59-64]. Those who survive may be permanently and adversely affected and at increased risk not only to a death from CHD but from certain cancers as well. The recent report of a significant relationship between infant mortality rates and cancer, as well as CHD, supports this view [65].

Conversely, infectious diseases further exacerbate malnutrition as every infection through fever and anorexia enhances the loss and shortage of nutrients. Pregnant mothers, infants, and growing children are far more vulnerable to nutritional deficits than adults since developing organisms require nutrients for growth and development as well as for maintenance. The many prospective and retrospective human studies linking low birth weight, intra-uterine growth retardation, income inequities, inequality in health care and childhood obesity to an increased risk of CHD in the adult are totally in keeping with observations made in experimental animals [14,66-69]. Elevated levels of inflammatory markers and depressed immunoglobulin levels with defective phagocytosis are seen in the malnourished child as they are in the adult [70,71]. It is reasonable to assume that the more frequent, severe and chronic the infection, as a result of malnutrition during developmental periods, the more frequent the exposure of the cardiovascular system to inflammatory mediators. The effects of early malnutrition and the catabolic effect of infectious diseases on nutrients and nutritional status during growth and development have long-term consequences.

The contrast of the high cost of lipid lowering drugs, with their low degree of efficacy in reducing CHD mortality has promoted several questions. They include: 1) "Is it possible to develop better markers for those at risk of a CHD death"; 2) "From what will we die in 2020", and perhaps most important, 3) "When should heart disease prevention begin" [72-75]. The answer to the first may be the monitoring of acute phase proteins or markers of chronic infection which may be better predictors of an impending coronary event or death, rather than blood lipid levels. The answer to the second question would be, hopefully, by sudden death due to CHD, as in a coronary event, rather than from a debilitating neurodegenerative disease or cancer. From a nutritional and public health perspective, the anwer to the third question is obvious; prevention should begin *in utero* and continue especially during active, rapid growth. It should also include

the control of infectious diseases and obesity, particularly the latter since increased levels of C-reactive protein have been reported in young obese adults [47]. The incidence of obesity, a major risk factor for CHD is increasing, particularly in children, despite the exorbitant amount of money expended yearly on fad diets and weight control drugs [76,77]. The increase in obesity, perhaps to some extent, maybe related to maternal malnutrition, particularly under-nutrition or starvation during critical periods of gestation affecting fat cell cellularity and centers regulating food intake and growth [78,79]. The increase in childhood obesity is of serious concern leading some to predict an increase in CHD deaths and a shortened life expectancy in the coming years. The most serious nutritional problem in developing countries is allegedly one of excessive caloric intake.

Conclusion

The majority of deaths due to CHD occur late in life [25]. The age-adjusted death rate due to CHD has been constant for the past several years in the United States with essentially no contribution to this constancy, or in the decline in CHD deaths over the last fifty years, from lipid/cholesterol-lowering drugs. Clearly, the control of hypertension, of diabetes, of obesity and surgical interventions, among others, also has contributed greatly to the observed increase in life expectancy during the last few decades. Nonetheless, significant and major contributions to the decrease in CHD deaths and increase in life expectancy since 1950 and to the present day, have come from preventing malnutrition and controlling infectious and other catabolic diseases during pregnancy and in the young. Funding public health programs (e.g., vaccinations, access to health care services, control of pathogen vectors, safe food and water supplies) aimed at preventing malnutrition and infectious diseases during fetal and early periods of rapid development are far more cost-effective than the indiscriminate prescribing of expensive lipid lowering drugs to those with the only questionable risk factor of "hypercholesterolemia", particularly for those in their seventh and eighth decade of life.

While CHD is the leading and major cause of death in most developed countries, most of these deaths occur in the seventh and eighth decade of life; a death that may be preferred over many others. *"Modern medicine, at least in its research aspirations, seems to have made death public enemy number one. It is not –at least not any longer- in developed countries with the average life expectancy approaching 80 years. The enemies now are serious chronic illness and an inability to function well"* [80].

If you are interested in having the References, please contact the Servicio de Publicaciones Médicas. Instituto Nacional de Pediatría. Insurgentes Sur 3700-C. Col. Insurgentes Cuicuilco. México 04530 D.F. Tel: 56 06 00 02 ext. 112 and 489 Fax: 56 06 00 02 ext. 112 (ask for tone)

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