Invited Commentary: Height-Cardiovascular Disease Relation: Where to Go from Here?

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Since a report by Gertler and White in 1954 (1), many studies have found that short stature in adulthood is associated with increased risk of total cardiovascular disease, coronary heart disease, and stroke (2). Short stature has also been related to higher risk from respiratory diseases (3). The current issue of the American Journal of Epidemiology contains a further contribution on this topic. McCarron et al. (4) found, in a cohort of 8,361 male Glasgow University students followed for a median of 41 years, that adult height was inversely related to mortality from cardiovascular disease, particularly coronary heart disease, corroborating findings of most prior studies on this issue. Strengths include the large cohort size and its impressively lengthy follow-up. Weaknesses of the study, acknowledged by the authors, are the limited generalizability of findings based on men only, absence of non-Whites, and unavailability of certain possible confounding variables, especially blood lipids. McCarron et al. (4) clearly show a correlation between membership in one of the higher social classes and adult height. Following multivariate adjustment for several potential confounders, including systolic blood pressure, body mass index, cigarette smoking, father’s social class, and year of birth quintile, significant inverse relations between height and total cardiovascular disease, as well as coronary heart disease, remained. Accordingly, the results, as the authors point out, reduce but do not completely eliminate the possible confounding role of socioeconomic status on the relation between adult height and cardiovascular disease. While not diminishing the importance of any currently accepted cardiovascular disease risk factors, these findings can direct attention toward research on factors related to growth and development in early life that may influence both adult height and long-term cardiovascular disease. Such factors would include those not related, as well as those clearly related, to socioeconomic status, including nutritional habits, physical activity, alcohol consumption, and other lifestyle behaviors that were not measured in this study.

The study of prenatal and early life exposures is difficult. Measurement of possibly relevant exposures is complex, such as nutrition in early life, prenatal nourishment, and other prenatal exposures. In addition, long-term follow-up is tedious and costly. Accordingly, surrogate markers, such as adult height, have been commonly used instead of measuring early life exposures directly. Prenatal exposures may influence both adult height and eventual risk of cardiovascular disease (5). Birth weight (6) has been used as a surrogate for prenatal nutrition, but specific elements of the prenatal environment have not yet been clearly identified. An additional marker of early life exposures is childhood leg length. In a recent study, childhood leg length was found to be the component of childhood height most strongly associated with diet and living conditions in childhood, particularly between the ages of 2 and 8 years. Shorter leg length was also related to increased risk of coronary heart disease in adulthood (7). Another marker of childhood environment is the rate of height increase in childhood. In an earlier report in the American Journal of Epidemiology, Miura et al. (8) found that height increase, especially from age 3 years to age 20 years, was inversely related to blood pressure and serum cholesterol in young adults independent of birth weight as a marker of intrauterine environment. Thus, surrogate measures of prenatal and early childhood exposures have raised awareness that cardiovascular disease in adulthood has origins in childhood as well as in utero. This concept is corroborated by anatomic studies that demonstrate the onset of lumen-narrowing coronary atherosclerosis as early as the teenage years (9).

Many of the traditional “adult” risk factors for atherosclerosis have been associated with the presence of atherosclerosis in children and adolescents. Specifically, cigarette smoking, atherogenic lipoproteins, obesity, and hypertension in childhood are known risk factors for early development of atherosclerosis (10, 11). These same risk factors, measured in young adult males aged 18–39 years, have been linked to long-term risk of coronary and total cardiovascular mortality in later adulthood (12, 13). It is therefore beyond reasonable doubt that early life exposure to many already known factors can cause early atherosclerosis as well as eventual clinical events in later adulthood.

McCarron et al. state, “understanding of the mechanisms underlying these associations” between early life exposures and cardiorespiratory disease risk “could usefully inform primary prevention strategies” (4, p. 687). However, as stated above, considerable information is already at hand that has enabled formulation of a primary preventive strategy begin-
ning in childhood. What other research questions should be asked to refine or augment the preventive strategy? To return to the link between adult height and subsequent cardiovascular disease, is it possible that distinct nutritional behaviors during infancy and childhood are jointly responsible for future height and subsequent risk of cardiovascular diseases? Specifically, are there links between childhood intakes of protein, calcium, meats, dairy products, fruits, vegetables, whole grains, legumes, or other specific foods or nutrients and adult height and cardiovascular disease risk? What about childhood aerobic physical activity? Is it linked to one’s final adult height and, if so, could this be a link to adult cardiovascular disease? Is there a link between passive smoking during childhood and eventual adult height that could partially account for the height-cardiovascular disease relation? Moreover, could there be a link among childhood infections, adult height, and subsequent cardiovascular disease? Several biologic indices of inflammation and/or some types of viral and bacterial infection in adults are apparently associated with increased cardiovascular risk (14, 15). As children with a history of frequent infections are known to have diminished adult height (16) and childhood respiratory infection probably reduces adult lung function, it may be useful to determine whether certain types of childhood infection can increase future cardiovascular risk. Studies such as those suggested here will not be easy, but the new information could be of considerable value.

Although fruitful new research, in areas such as these, can enhance and refine knowledge of the etiology and can expand preventive strategies, it is a fact that young adult and middle-aged people with favorable status in regard to known major coronary heart disease-cardiovascular disease risk factors (serum cholesterol, blood pressure, cigarette use) do not experience epidemic rates of cardiovascular disease as shown by long-term follow-up of large cohorts (17). At present, less than 10 percent of such cohorts are in this low-risk population. These and related facts are the firm foundation for current worldwide efforts to achieve primary prevention of cardiovascular diseases, especially coronary heart disease, from the earliest stages of life. These include, foremost, concerted efforts to prevent the known major risk exposures of cigarette smoking, adverse dietary patterns, and physical inactivity leading to obesity, glucose intolerance (18), unfavorable blood lipids, and high blood pressure. With increasing recognition of the importance of this strategic emphasis, it is likely that research on intrauterine and early life factors will be expanded, yielding new knowledge that contributes to the primumal prevention effort.

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REFERENCES