Association of Childhood Socioeconomic Status With Subsequent Coronary Heart Disease in Physicians

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Background: Adult socioeconomic status (SES) is an independent risk factor for the development of coronary heart disease (CHD), but whether low childhood SES has an effect in adults who have achieved high SES is unknown.

Methods: We examined the risk of CHD and mortality associated with low childhood SES in 1131 male medical students from The Johns Hopkins Precursors Study, a prospective cohort of graduates of The Johns Hopkins University School of Medicine from 1948 to 1964 with a median follow-up of 40 years.

Results: Of 1131 subjects, 216 (19.1%) were from low-SES families. Medical students from low-SES families were slightly older at graduation (26.8 vs 26.2 years; \( P = .004 \)) and gained more weight over time (\( P = .01 \)). Low childhood SES conferred a 2.40-fold increased hazard of developing CHD on or before age 50 years (95% confidence interval, 1.21-4.74) but not at older ages. The impact of low SES on early CHD was not reduced by adjusting for other CHD risk factors, including body mass index, cholesterol level, amount of exercise, depression, coffee drinking, smoking, hypertension, diabetes mellitus, and parental CHD history. Low childhood SES did not confer an increased risk of all-cause mortality.

Conclusions: Low childhood SES is associated with an increased incidence of CHD before age 50 years among men with high adulthood SES. This risk is not mediated by traditional risk factors for CHD. These findings highlight the importance of childhood events on the development of CHD early in adulthood and the persistent effects of low SES.

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Despite advances in medical and surgical care, coronary heart disease (CHD) remains the primary cause of morbidity and mortality in the United States.1 In addition to traditional risk factors such as older age, male sex, cigarette smoking, hypertension, diabetes mellitus, and hypercholesterolemia, low socioeconomic status (SES) is a consistent, moderately strong predictor of CHD risk.2-7 Individuals with low SES have poorer health outcomes compared with high-SES populations,2-10 and the health care community has been challenged to eliminate this disparity.11

Most studies of the effect of childhood SES on CHD in adulthood have focused on middle-aged or older populations; in these studies, no distinction was made between early vs late onset of CHD.12-20 Because most cardiovascular risk factors are more prevalent at older ages, the effects of childhood SES may play less of a role in the development of CHD at older ages.

The Johns Hopkins Precursors Study measures physicians’ health outcomes over their lifetime and provides a unique opportunity to prospectively examine the effects of childhood SES on the development of CHD before and after middle age and to adjust for traditional risk factors measured throughout adult life. It also provides the results of a natural experiment: do physicians who are born into low-SES families but who have high levels of adulthood SES, medical knowledge, and access to high-quality health care have optimal health care outcomes? We hypothesized that the risk of poor health outcomes, particularly CHD presenting at a young age, would be greater in physicians with low childhood SES compared with those who grew up in a high-SES family.

Methods

The Johns Hopkins Precursors Study was designed and initiated by Caroline Bedell Thomas, MD, in 1947 to identify precursors for cardiovascular disease. It is an ongoing,
longitudinal cohort study of 1337 former medical students at The Johns Hopkins University School of Medicine in the classes of 1948 to 1964. Excluded from this analysis were the small number of women (n = 121), men of non-European ancestry (n = 36), those who did not answer the questions about parental occupation (n = 56), and those who were unavailable for follow-up (n = 15), leaving 1131 white male medical students for analysis of incident CHD (some individuals met >1 exclusion criterion).

DATA COLLECTION
At baseline during medical school, each participant provided a detailed medical history and underwent physical examination, including measurement of blood pressure, height, and weight. After medical school, follow-up data were collected using annual mailed questionnaires. In general, yearly response rates exceeded 70% and, during any 5-year interval, at least 85% of participants responded at least once. In addition, ongoing mortality surveillance is conducted by review of alumni records and obituaries and by periodic National Death Index searches. A committee of internists (including M.J.K. and D.E.F.) reviews copies of the death certificates, medical records, and self-reports to assign disease outcomes and assess cause of death.

MEASURE OF CHILDHOOD SES
Childhood SES was defined on the basis of the subject’s father’s occupation as reported from a 10-item checklist on a medical school questionnaire, derived from the occupations listed on the 1930 census of the population. A subject was classified as having a low childhood SES if he reported that his father was a farmer, laborer, service worker, clerical worker, sales worker, machine operator, or craftsman. A subject was classified as having a high childhood SES if he reported that his father was a professional (such as an accountant, banker, scientist, engineer, or lawyer), manager, or physician. In sensitivity analyses, alternate definitions of childhood SES were based on the mother’s, as well as the father’s, occupation. Socioeconomic status was also categorized as a 3-level variable: low (farmer, laborer, service worker, clerical worker, sales worker, machine operator, or craftsman), middle (clerical workers, sales workers, and craftsmen), and high (professionals, physicians, and managers).

COVARIATES
Information about other risk factors for CHD was also collected at baseline and during follow-up using annual questionnaires and medical records. Starting with the class of 1949, nonfasting serum cholesterol level was measured during medical school. Physical activity was assessed during medical school and follow-up using the question, “How much physical training have you had in the past month?” Possible responses were “none,” “little,” “moderate,” and “much.” Parental history of premature CHD was defined as development of CHD before age 55 years in a participant’s father or before age 65 years in his mother. Prevalence of CHD in parents was assessed at baseline and throughout follow-up.

Body mass index (BMI) was defined as weight in kilograms divided by the square of height in meters. Number of cigarettes smoked per day was categorized as follows: 0, 1 to 10, 11 to 20, 21 to 39, and 40 or more. Participants indicated their current coffee intake based on 8 possible responses ranging from 0 to 7 or more cups a day.

Hypertension was defined as a blood pressure of 160/105 mm Hg or greater on 1 annual questionnaire, 140/90 mm Hg on at least 2 readings at least 1 week apart, or pharmacologic treatment of hypertension. Type 2 diabetes mellitus was defined as report of pharmacologically treated diabetes on a single questionnaire, report of nonpharmacologically treated diabetes on 2 or more questionnaires, physician diagnosis of diabetes in medical records, or report of a fasting plasma glucose level of at least 140 mg/dL (7.8 mmol/L) or a nonfasting plasma glucose level of at least 200 mg/dL (11.1 mmol/L). Incidence of clinical depression was measured on the mailed surveys with direct questions concerning the occurrence of depression and associated treatment.

OUTCOME MEASURES
The primary dependent variable for this analysis was the incidence of CHD occurring on or before age 50 years. Secondary dependent variables were all CHD (incident events, fatal and nonfatal) occurring at any age, CHD mortality, and total mortality. Coronary heart disease was defined as myocardial infarction, sudden death, angina pectoris, chronic ischemic heart disease, and other coronary disease requiring coronary bypass surgery or percutaneous coronary intervention.

STATISTICAL ANALYSIS
Follow-up began at graduation from medical school and continued through December 31, 2001. Baseline characteristics for physicians from low- and high-SES families were summarized and compared using means and t tests for continuous variables and percentages and χ² tests for categorical variables. Kaplan-Meier methods and the log-rank test were used to compare the time to event for incident CHD and mortality between physicians with low and high childhood SES. Proportional hazards models were used to assess the impact of possible CHD risk factors on the relationship between childhood SES and CHD. These factors were serum cholesterol level and exercise during medical school and the presence of parental history of premature CHD and of hypertension, diabetes mellitus, depression, smoking, coffee drinking, and BMI as time-dependent covariates. Follow-up was truncated at age 50 years in models used to assess the effects of covariates on incidence at or before age 50 years. The relatively few CHD events at and before age 50 years limited our ability to adjust for multiple variables simultaneously. Thus, bivariate models were used to determine whether the effect of childhood SES on CHD was mediated through other CHD risk factors. The proportionality of hazards was confirmed with log-log plots and by examining the Schoenfeld residuals. A 2-tailed P <.05 was considered statistically significant. All statistical analyses were carried out with commercially available software (Stata Release 8.0; StataCorp, College Station, Tex).

RESULTS

BASELINE CHARACTERISTICS
The baseline characteristics of the 1131 men in this study assessed during medical school are given in Table 1. Of 1131 subjects, 216 (19.1%) were from low-SES families. Medical students from low-SES families were slightly older at graduation (26.8 vs 26.2 years; P = .004), and there was no difference in other CHD risk factors at the time of medical school graduation, including BMI, serum cholesterol levels, cigarette smoking, amount of exercise, or family history of premature CHD.
Changes in cardiovascular disease risk factors over time

Body mass index increased over time in physicians from both low-SES and high-SES families (Table 2). Physicians from low-SES families, however, had a significantly higher mean BMI at ages 40 to 49, 50 to 59, and 60 to 69 years. While the rates of cigarette smoking decreased in both groups over time, physicians from low-SES families had higher smoking rates in each decade, although the differences were not statistically significant.

The mean age of developing hypertension and diabetes mellitus was similar in the 2 groups. Physicians from low-SES families developed hypertension 1 year earlier than did physicians from high-SES families, with a mean (SD) age at onset of 54.1 (13.3) vs 55.0 (13.0) years, although this difference was not significant. There was no difference in the age at onset of diabetes mellitus, with a mean age of 57 years in both groups.

Childhood SES and risk of CHD

Median follow-up time in this analysis was 40 years, yielding 43 160 person-years of observation. During this period, 217 men experienced CHD events. The incidence of CHD from age 40 to age 75 years was consistently greater in men from lower childhood SES backgrounds than in those from higher SES families (Figure). During the entire follow-up, differences in incidence between the groups did not achieve a conventional level of statistical significance (P=.11; Figure), but the incidence of CHD on or before age 50 years was significantly greater in physicians with low compared with high childhood SES (P=.01). Incidence of CHD, fatal CHD, and total mortality by 50 and 70 years are given in Table 3.
during medical school, amount of exercise during medical school, amount of cigarette smoking or coffee drinking during follow-up, BMI during follow-up, parental history of premature CHD, or development of diabetes mellitus, hypertension, or depression during follow-up (Table 4).

CHILDHOOD SES AND MORTALITY

During a median follow-up of 40 years, 52 deaths related to CHD and 224 total deaths occurred. When the entire follow-up was considered, participants with low childhood SES demonstrated a trend toward increased CHD mortality (hazard ratio [HR], 2.0; 95% CI, 0.99-3.90) compared with physicians with high childhood SES, but no such association was seen for all-cause mortality (HR, 1.08; 95% CI, 0.78-1.48). There were few events by age 50 years (6 deaths due to CHD and 42 total deaths). When only these events were considered, there was the suggestion of an association of low SES with CHD death (HR, 4.27; 95% CI, 0.86-21.17), but not with all-cause mortality (HR, 0.99; 95% CI, 0.46-2.14).

SENSITIVITY ANALYSIS

When information on the mother’s occupation was used to reclassify 19 of the participants with low childhood SES as high-SES subjects, our results were unchanged. In addition, analyses using 3 levels of childhood SES also showed a higher risk of premature CHD in the lowest SES group (data not shown).

COMMENT

The present study found that low childhood SES is a risk factor for incident CHD before age 50 years in men with uniformly high adulthood SES. We noted a trend toward increased CHD mortality in physicians of low childhood SES, but no difference in all-cause mortality. This increased risk exists despite physicians’ high level of SES as adults, their medical knowledge, and their access to high-quality health care. The higher risk of early CHD was not mediated by BMI, cholesterol level, exercise, depression, coffee drinking, smoking, hypertension, diabetes mellitus, or parental history of CHD.

Several conceptual models have been proposed to explain how lower childhood and adulthood SES may lead to increased risk for cardiovascular disease.7 The latent effects model proposes that adverse early life experiences permanently affect the individual in a way that is not influenced by adult experiences. The pathway model suggests that early life experiences affect adult health by influencing adult behavior and risk factors. The cumulative model hypothesizes that health is determined by the cumulative number of years that an individual spends in either a low- or high-SES category. Individuals with low childhood SES in our study did have higher BMI and were more likely to smoke cigarettes than were individuals with high childhood SES, supporting the pathway model. Low childhood SES was associated with higher CHD risk only before the age of 50 years. After that age, individuals with low SES in childhood in this cohort had spent proportionately more of their lifetime at a high SES than at a low SES.

Low childhood SES may confer an increased risk of CHD on or before age 50 years but not later in life for several reasons. First, other CHD risk factors are more prevalent later in life; thus, the proportionate effect of low childhood SES may be reduced. A similar relationship has been noted in The Johns Hopkins Precursors Study cohort with other risk factors.6 Second, the current study may have been underpowered to detect a small risk of CHD at older ages. For example, in the Nurses’ Health Study of 117,006 participants, the age-adjusted risk of total cardiovascular disease events was 1.13 (95% CI, 1.02-1.24) for nurses with low vs high childhood SES,17 similar to the risk seen in the present study for incident CHD over the lifespan, 1.29. Likewise, the lack of statistical significance for the 2-fold increase in the risk of CHD mortality associated with low childhood SES likely reflects lack of statistical power.

Three other studies have examined the risks of CHD in individuals who have moved from lower SES to higher SES. Two of them, a case-control study of former Harvard University students17 and the Nurses’ Health Study,17 found a higher risk in persons with low childhood SES. A study of Finnish men born in the late 1950s found that adulthood SES had a greater effect on mortality than did childhood SES, although childhood SES had a persistent effect on mortality from cardiovascular disease.18

Besides these studies, which specifically examined the move from low childhood SES to high adulthood SES, many other studies have investigated the relationship between childhood SES and cardiovascular events.12-20 However, most of these studies were conducted outside the United States,12-16,18,19,21-29 or, if a prospective design was used, started follow-up in midlife, assessing only for

Table 4. Risk of CHD Associated With Low Childhood SES at Different Age Thresholds in 1131 White Male Medical School Graduates in the Johns Hopkins Precursors Study*

<table>
<thead>
<tr>
<th>Covariate</th>
<th>Age ≤50 y</th>
<th>All Ages</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of events, low SES/high SES</td>
<td>13/23</td>
<td>31/166</td>
</tr>
<tr>
<td>Unadjusted</td>
<td>2.40 (1.21-4.74)</td>
<td>1.29 (0.94-1.77)</td>
</tr>
<tr>
<td>Adjusted for</td>
<td></td>
<td></td>
</tr>
<tr>
<td>BMI†</td>
<td>2.39 (1.21-4.73)</td>
<td>1.27 (0.93-1.74)</td>
</tr>
<tr>
<td>Cholesterol level‡</td>
<td>2.31 (1.14-4.66)</td>
<td>1.28 (0.91-1.80)</td>
</tr>
<tr>
<td>Exercise†</td>
<td>3.21 (1.53-6.71)</td>
<td>1.46 (1.03-2.08)</td>
</tr>
<tr>
<td>Depression‡</td>
<td>2.41 (1.22-4.75)</td>
<td>1.30 (0.95-1.77)</td>
</tr>
<tr>
<td>Coffee drinking†</td>
<td>2.38 (1.12-4.70)</td>
<td>1.29 (0.94-1.76)</td>
</tr>
<tr>
<td>Smoking‡</td>
<td>2.24 (1.11-4.51)</td>
<td>1.25 (0.91-1.72)</td>
</tr>
<tr>
<td>Hypertension‡</td>
<td>2.39 (1.21-4.72)</td>
<td>1.26 (0.92-1.72)</td>
</tr>
<tr>
<td>Diabetes mellitus‡</td>
<td>2.43 (1.23-4.80)</td>
<td>1.29 (0.94-1.76)</td>
</tr>
<tr>
<td>Parental premature CHD</td>
<td>2.41 (1.22-4.76)</td>
<td>1.31 (0.96-1.79)</td>
</tr>
<tr>
<td>Adjusted for all variables</td>
<td>2.62 (1.18-5.85)</td>
<td>1.27 (0.89-1.84)</td>
</tr>
</tbody>
</table>

Abbreviations: BMI, body mass index; CHD, coronary heart disease; SES, socioeconomic status.
*Data are presented as hazard ratio (95% confidence interval) unless otherwise indicated.
†Assessed during medical school.
‡Assessed during follow-up.

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possible confounders occurring later than age 40 years. 20,28 Nevertheless, low childhood SES was associated with a higher risk of cardiovascular events in all of the studies, although the effects of adjustment for established CHD risk factors and adulthood SES varied. 15,16,18 Thus, compared with all studies of childhood SES and CHD, the present study offers a unique perspective of early CHD in a well-defined cohort of medical school graduates.

The present study adds to the body of information on childhood SES and CHD in several ways. First, data on childhood SES were collected earlier in adulthood, before clinical events had occurred, minimizing possible recall bias. Second, all of the participants graduated from medical school and thus had uniformly high adulthood SES, thereby eliminating confounding by changes in adulthood SES. Finally, unlike the other studies, we examined the relationship between childhood SES and early CHD.

Although different life-course models help to conceptualize the relationship between childhood SES and the development of CHD in adulthood, the underlying biological factors are less clear. The association between lower SES in adulthood and CHD risk has been ascribed to a higher prevalence of CHD risk factors in adults with low SES, including hypertension, 39 the metabolic syndrome, 49 and unhealthy behaviors, including smoking, high-fat diets, and low levels of physical activity. 41 Evidence also suggests that adults with low SES have differential activation of biological pathways that are implicated in the development of CHD. Compared with adults of high SES, those with lower SES have higher levels of cortisol, 52 higher levels of C-reactive protein, 41 greater platelet activation, 53 and more atherogenic lipid profiles. 54 More data are needed on the persistence of the relationships between low SES and these biological variables.

Some limitations of our study deserve mention. Our exposure definition, parental occupation, is based on self-report, which can be subject to error. If persons with low childhood SES systematically reported higher levels, as defined by parental occupation, then the true association between low SES and CHD would most likely be diluted. In addition, these findings should be generalized with caution to groups other than male physicians of European ancestry. Furthermore, our conclusions are based on a relatively small number of events before age 50 years. Another limitation is the use of paternal occupation as a measure of childhood SES. Socioeconomic status is a multidimensional construct, and other studies have used parents' level of education, occupation, and/or income as measures. 46,47 Income may be the best marker of childhood SES, 56-50 but occupation is used in about a quarter of studies and is a reasonable surrogate for childhood SES. 6,65-60

Nevertheless, The Johns Hopkins Precursors Study cohort offers study strengths. The strengths of the present study include a long follow-up period and an excellent response rate from participants. The cohort design also allows for accurate measurement of confounders that vary over time and for precise measurement of exposure status before disease onset without the risk of recall bias or reverse causality. In addition, self-reports of CHD risk factors and clinical outcomes have been validated in this cohort. 51 In conclusion, these results indicate that, even for individuals with uniformly high SES in adulthood, the presence of low SES in childhood confers an increased risk of developing CHD before age 50 years. This increased risk is not mediated by established CHD risk factors. These findings highlight the importance of childhood events in the development of CHD in adulthood. More importantly, the data illustrate the difficulty in eliminating health status disparities between low-SES and high-SES populations: even an intervention that allowed low-SES individuals to assume the lifestyle of physicians did not totally eliminate disparities in early CHD outcomes.

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Author Contributions: All authors had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. Study concept and design: Kittleson, Wang, Ford, and Klag. Acquisition of data: Kittleson, Wang, Ford, and Klag. Analysis and interpretation of data: Kittleson, Meoni, Wang, Chu, Ford, and Klag. Drafting of the manuscript: Kittleson. Critical revision of the manuscript for important intellectual content: Kittleson, Meoni, Wang, Ford, and Klag. Statistical analysis: Kittleson, Meoni, Wang, Chu, Ford, and Klag. Obtained funding: Klag. Administrative, technical, and material support: Ford and Klag. Study supervision: Ford and Klag.

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