Does Low Socioeconomic Status Potentiate the Effects of Heightened Cardiovascular Responses to Stress on the Progression of Carotid Atherosclerosis?

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ABSTRACT

Objectives. This study examined whether heightened cardiovascular reactivity and low socioeconomic status had synergistic effects on the progression of carotid atherosclerosis in a population of eastern Finnish men.

Methods. Data from the Kuopio Ischemic Heart Disease Risk Factor Study were used to measure 4-year progression of intima-media thickness in 882 men according to cardiovascular reactivity and socioeconomic status. Associations were examined in relation to risk factors and were stratified by baseline levels of atherosclerosis and prevalent ischemic heart disease.

Results. The effect of reactivity on atherosclerotic progression depended on socioeconomic status. Men who had heightened cardiovascular responsiveness to stress and were born into poor families, received little education, or had low incomes had the greatest atherosclerotic progression.

Conclusions. An understanding of associations between individual risk factors and disease should be based on etiologic hypotheses that are conceived at the population level and involve fundamental social and economic causes of disease. This study demonstrates how examining the interaction of an individual biological predisposition with low socioeconomic status over the life course is etiologically informative for understanding the progression of atherosclerotic vascular disease. (*Am J Public Health.* 1998;88:389–394)

Introduction

A large body of evidence shows that lower socioeconomic status groups and certain racial and ethnic minorities experience a disproportionate cumulative burden of stressful life conditions.[1–7] Greater exposure to difficult life circumstances may set the stage for the expression of individual differences in susceptibility to cardiovascular disease. When faced with psychological stress, some individuals exhibit exaggerated increases in heart rate and blood pressure that are mediated by the sympathetic nervous system.[8] These differences in cardiovascular reactivity have been identified in children, are reported to be relatively stable individual characteristics generalizable across a variety of stressful situations, and are thought, at least in part, to reflect an underlying biological and genetic predisposition.[9–11] While studies have demonstrated associations between exaggerated reactivity and cardiovascular disease, there remains some controversy over the etiological significance of heightened reactivity.[12–15]

Manuck proposed that the pathological effects of heightened cardiovascular reactivity may be evident only in conditions of chronically elevated stress, where this biological predisposition is expressed.[16] Studies of cynomolgus monkeys have demonstrated that more reactive animals evidence greater atherosclerosis in unstable and stressful social environments.[17] This model of how genetic predispositions might interact with social circumstances in producing disease has intuitive appeal and suggests that the health effects of a biologic/genetic predisposition toward cardiovascular hyperresponsiveness may be contingent on the nature of the social environment in which individuals act out their daily lives.

It seems plausible, then, to examine whether heightened cardiovascular reactivity and greater lifetime exposure to stressful environments have synergistic effects on cardiovascular disease. We used 3 measures of socioeconomic status, representing temporally distinct stages of the life course, as proxies for cumulative exposure to stressful life circumstances and investigated their interaction with cardiovascular reactivity in the progression of carotid atherosclerosis.

Cardiovascular disease events such as myocardial infarction and cardiovascular mortality occur late in the natural history of the disease and are a combination of underlying atherosclerotic processes and various triggering factors.[18,19] Ultrasonographic assessment of the carotid arteries has provided opportunities to noninvasively study the development of atherosclerosis within human populations[20–22] and has been shown to be reliable, to relate to the extent of coronary artery disease, and to have predictive validity for risk of coronary events.[20,23–26]

To our knowledge, this is the first study to examine the interaction of socioeconomic status and cardiovascular reactivity in 4-year progression of carotid atherosclerosis. Extensive baseline information on atherosclerotic risk factors and prevalent ischemic heart disease enabled us to examine associations between socioeconomic status and cardiovascular reactivity and ath-

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eroslerotic progression, with adjustment for known risk factors and stratification by both prevalent disease and the extent of atherosclerosis at baseline.

Methods

Subjects were participants in the Kuopio Ischemic Heart Disease Risk Factor Study, which was designed to investigate unestablished risk factors for ischemic heart disease, carotid atherosclerosis, and other related outcomes in a population-based sample of eastern Finnish men.[27] Details of the study sample have been published elsewhere.[28,29] Baseline examinations were conducted between 1984 and 1989 on 2682 men. Follow-up examinations were conducted on men who underwent ultrasonographic scans at baseline. Mean follow-up time was 4.1 years (range: 3.9 to 5.2 years). Of the 1229 participants who were eligible for the follow-up exams, 52 had died, were suffering severe illness, or had migrated away from the area and 139 could not be contacted or refused to participate. Information on blood pressure reactivity to stress, progression of carotid atherosclerosis, covariates, childhood socioeconomic status, and education was available for 882 men; information on income was available for 866 men. A small percentage of the sample had imputed age-specific values for high-density lipoprotein 2 (6%), serum apolipoprotein B (3%), and serum triglycerides (1%) so as to maximize the sample size. Use of imputed values did not alter the results. The participants included 221, 213, 235, and 213 men aged 42, 48, 54, and 60 years, respectively. In this sample, 122 men participated in an unrelated clinical trial of pravastatin.[30] Inclusion of these men did not alter the findings.

Assessment of Carotid Atherosclerotic Progression

Atherosclerotic progression was assessed with high resolution B-mode ultrasonographic scanning that involved, on average, 100 measures of intima-media thickness over a 1.0- to 1.5-cm section of the left and right common carotid arteries below the carotid bulb. Details of the scanning protocol, technical aspects of the measurement, and their reliability have been described elsewhere.[19–21,31]

The present study involved 3 measures of intima-media thickness. Maximum thickness was defined as the average of the maximum in the right and left carotid arteries. Plaque height was defined as the difference between the maximum and minimum recordings, and mean thickness was defined as the mean of the approximately 100 readings from each artery. These measures were conceptualized to represent potentially different aspects of atherosclerotic progression. Maximum thickness provided an assessment of how far thickening intruded into the lumen; plaque height was sensitive to the roughness of the arterial wall; and mean thickness was an overall measure of atherosclerosis. Atherosclerotic progression was calculated as the arithmetic difference between the baseline and 4-year follow-up values for each of the 3 measures.

Baseline recordings were classified by a physician (R.S.) into 4 categories: (1) no atherosclerotic lesion, (2) intima-media thickening, (3) nonstenotic plaque, and (4) large, stenotic plaque. Intima-media thickening was defined as more than 1 mm between the lumen-intima and media-adventitia interfaces. Nonstenotic plaque was defined as a distinct area of mineralization or focal protrusion into the lumen. Plaque was defined as stenotic if it obstructed more than 20% of the lumen diameter.[20]

Assessment of Socioeconomic Status

This paper reports results using childhood socioeconomic status, educational attainment, and current income. An index of childhood conditions was based on the following items: father's and mother's education and occupation, whether the family lived on a farm, the size of that farm, and the degree to which the family was perceived as wealthy.[32] The childhood index was dichotomized so that the bottom tertile was considered low (n = 273; 31.0%). Educational attainment was dichotomized so that those with primary education or less were categorized as the low education group (n = 268; 30.4%). Income was dichotomized so that the bottom quintile was considered low (n = 182; 21.0%). Details of these measures have been published elsewhere.[1,19,29,31,33]

Assessment of Cardiovascular Reactivity

Cardiovascular reactivity was measured as systolic blood pressure response in anticipation of a maximal exercise stress test, calculated as the difference between seated resting systolic pressure and pressure taken while seated on a bicycle ergometer 5 minutes prior to the start of the exercise test. Differences between blood pressure at rest and in anticipation of the exercise test reflected psychological and emotional arousal in response to the impending exhaustive physical challenge. The top quartile of men whose systolic response was greater than 30 mm Hg were classified as the high reactivity group (n = 214; 24.3%). This measure has been associated with incident hypertension in this population.[12]

Assessment of Covariates

Lipoproteins were separated from unfrozen plasma by means of ultracentrifugation and precipitation within 3 days of sampling. The cholesterol content of all lipoprotein fractions was measured enzymatically. Serum apolipoprotein B was determined with an immunoturbidimetric method using an antiserum.[34] Blood pressure was measured with a random-zero sphygmomanometer both supine and sitting, after 5-minute rests in each position. Two systolic and diastolic pressures were taken in each position and averaged. Average systolic pressure was used in this analysis. Body mass index was calculated by dividing the subject's weight by the square of his height (kg/m^2). Alcohol consumption was assessed via instructed dietary recording for a 4-day period, as well as for the previous 12 months, by self-administered questionnaire.[35] Smoking status was classified as "never smoked," "former smoker," and "current smoker" (measured in pack-years). Treatment for hypertension or hyperlipidemia was assessed by a review of medications.

Assessment of Prevalent Ischemic Heart Disease

Subjects were considered to have prevalent ischemic heart disease at baseline if they (1) had any history of prior myocardial infarction or angina pectoris, (2) currently used anti-angina medication, or (3) had positive indications of angina according to the London School of Hygiene Cardiovascular Questionnaire.[36]

Statistical Methods

Associations between socioeconomic status and cardiovascular reactivity and the progression of atherosclerosis were assessed by estimating mean change in plaque height, maximum thickness, and mean thickness for each combination of socioeconomic status and reactivity. Socioeconomic status and reactivity were modeled dichotomously, and a multiplicative interaction term was included. The overall F statistics reported in Tables 1 through 3 tested the interactive effects of

TABLE 1—Childhood Socioeconomic Status (SES), Education, Income, Reactivity Status, and Mean 4-Year Progression of Maximum Intima-Media Thickness (IMT), Plaque Height, and Mean IMT Adjusted for Age and Baseline IMT: 882 Middle-Aged Men

		Maximum IMT			Plaque Height			Mean IMT		
	Reactivity	Change, mm	SE	P^a	Change, mm	SE	P^a	Change, mm	SE	P^a
Childhood SES										
Low	High (n = 71)	0.33	0.02	.003	0.34	0.02	.009	0.15	0.02	.03
High	High (n = 143)	0.28	0.02	.30	0.27	0.15	>.50	0.12	0.01	.42
Low	Low (n = 202)	0.25	0.01	>.50	0.26	0.01	>.50	0.11	0.01	>.50
High	Low (n = 466)	0.25	0.01	Reference	0.26	0.01	Reference	0.11	0.01	Reference
Interaction Term (F)		2.74		.10	4.72		.03	1.26		.26
Education										
Low	High (n = 88)	0.34	0.02	.006	0.33	0.02	.003	0.16	0.01	.01
High	High (n = 126)	0.27	0.02	.24	0.27	0.02	.27	0.12	0.01	.40
Low	Low (n = 180)	0.26	0.01	>.50	0.26	0.01	>.50	0.11	0.01	>.50
High	Low (n = 488)	0.25	0.01	Reference	0.25	0.01	Reference	0.11	0.01	Reference
Interaction Term (F)		3.23		.07	2.28		.13	2.67		.10
Income										
Low	High (n = 50)	0.34	0.03	.01	0.31	0.03	.15	0.18	0.02	.001
High	High (n = 161)	0.28	0.02	.12	0.29	0.01	.08	0.12	0.01	.23
Low	Low (n = 132)	0.27	0.02	.42	0.27	0.02	>.50	0.12	0.01	.44
High	Low (n = 523)	0.25	0.01	Reference	0.26	0.01	Reference	0.11	0.01	Reference
Interaction Term (F)		1.19		.28	0.05		.83	2.49		.11

[a]Refers to pairwise comparison with the particular high-SES/low-reactivity reference group, adjusted for multiple comparisons.

cardiovascular reactivity and socioeconomic status on atherosclerotic progression. The analyses were conducted with the general linear model procedure from SAS version 6.09 on a Sun Sparc station II.[37] This procedure allowed for age-adjusted least square mean values of intima-media thickness to be estimated and contrasted for the combinations of socioeconomic status and reactivity while simultaneously controlling for baseline covariates.

We also compared progression between the high socioeconomic–low reactivity group (reference) and all other socioeconomic–reactivity categories to determine the magnitude of the differences. Pairwise contrasts were adjusted for multiple comparisons.[38] In addition to age, baseline thickness, and covariates, all estimates were adjusted for participation in the clinical trial, zooming depth of the scan, and ultrasonographic technician.[20]

Results

Table 1 presents age- and baseline-adjusted 4-year increases in maximum thickness, plaque height, and mean thickness according to childhood socioeconomic status, education, income, and reactivity status. For each measure of socioeconomic status, there was evidence of an interaction with blood pressure reactivity such that the effect of reactivity on atherosclerotic progression depended on the level of socioeconomic status. In the case of the interaction of childhood conditions and reactivity, the F values were 2.74 (P = .10) for progression of maximum thickness, 4.72 (P = .03), for plaque height, and 1.26 (P = .26) for mean progression. When education was used as the measure of socioeconomic status, the F values for the interactions with reactivity were 3.23 (P = .07) for maximum thickness, 2.28 (P = .13) for plaque height, and 2.67 (P = .10) for mean change.

The greatest progression of atherosclerosis was observed in the group with high levels of blood pressure reactivity and low socioeconomic status. In terms of absolute differences between socioeconomic and reactivity groups, men who had been born into poor families and who were highly reactive had significantly greater 4-year progression of maximum thickness (0.33 vs 0.25 mm; P = .003), plaque height (0.34 vs 0.26 mm; P = .009), and mean thickness (0.15 vs 0.11 mm; P = .03) than men born into more advantaged childhood circumstances and who had low reactivity. This same pattern of relationships was confirmed when education and income were used as the measures of socioeconomic status. Men with less than a primary school education and who were highly reactive had significantly greater progression of maximum thickness (0.34 vs 0.25 mm; P = .006), plaque height (0.33 vs 0.25 mm; P = .003), and mean thickness (0.16 vs 0.11 mm; P = .01) than more educated men who were less reactive.

Table 2 presents 4-year increases in carotid wall thickness according to childhood socioeconomic conditions, education, income, and reactivity status as in Table 1, but with additional adjustments for covariates. Table 2 shows that the pattern and magnitude of associations were essentially unchanged by adjustment for atherosclerotic risk factors.

Table 3 presents 4-year increases in carotid wall thickness by socioeconomic and reactivity status in men who were free from ischemic heart disease at baseline. The pattern of associations was unchanged in this subsample. Highly reactive men of low socioeconomic status had greater 4-year progressions of atherosclerosis, regardless of which measure was used. Similar analyses (not shown) that excluded men with advanced atherosclerosis at baseline demonstrated the same pattern as in the whole sample, but the magnitude of the associations was somewhat reduced.

Discussion

Our results show that men who had heightened cardiovascular responsiveness to stress—and who had been born into poor families, received little education, or had low incomes—experienced the greatest 4-year progression of carotid atherosclerosis. These

TABLE 2—Childhood Socioeconomic Status (SES), Education, Income, Reactivity Status, and Mean 4-Year Progression of Maximum Intima-Media Thickness (IMT), Plaque Height, and Mean IMT Adjusted for Age, Baseline IMT, and Covariates

		Maximum IMT			Plaque Height			Mean IMT		
	Reactivity	Change, mm	SE	P^a	Change, mm	SE	P^a	Change, mm	SE	P^a
Childhood SES										
Low	High (n = 71)	0.33	0.02	.003	0.34	0.02	.002	0.15	0.02	.03
High	High (n = 143)	0.28	0.02	.40	0.27	0.01	>.50	0.12	0.01	.46
Low	Low (n = 202)	0.25	0.01	>.50	0.26	0.01	>.50	0.11	0.01	>.50
High	Low (n = 466)	0.25	0.01	Reference	0.26	0.01	Reference	0.11	0.01	Reference
Interaction Term (F)		3.19		.07	5.16		.02	1.49		.22
Education										
Low	High (n = 88)	0.34	0.02	.001	0.32	0.02	.009	0.16	0.01	.01
High	High (n = 126)	0.27	0.02	.33	0.27	0.02	.42	0.12	0.01	.49
Low	Low (n = 180)	0.25	0.01	>.50	0.26	0.01	>.50	0.11	0.01	>.50
High	Low (n = 488)	0.25	0.01	Reference	0.25	0.01	Reference	0.11	0.01	Reference
Interaction Term (F)		4.18		.04	2.76		.10	3.38		.07
Income										
Low	High (n = 50)	0.34	0.03	.01	0.30	0.03	.26	0.18	0.02	.001
High	High (n = 161)	0.28	0.02	.14	0.29	0.01	.21	0.12	0.01	>.50
Low	Low (n = 132)	0.26	0.02	>.50	0.26	0.02	>.50	0.12	0.01	.28
High	Low (n = 523)	0.25	0.01	Reference	0.26	0.01	Reference	0.11	0.01	Reference
Interaction Term (F)		1.37		.24	0.05		.82	2.89		.09

Note. Covariates were high-density lipoprotein 2, apolipoprotein B, triglycerides, systolic blood pressure, body mass index, smoking, alcohol, and treatment for hypertension or hyperlipidemia.
[a]See Table 1 for description.

associations were evident in a subsample of men free from ischemic heart disease at baseline and in men who did not have advanced atherosclerosis at baseline, and these associations were virtually unchanged by adjustment for atherosclerotic risk factors.

The pattern of associations was generally consistent across measures of socioeconomic status and across 3 measures of atherosclerotic progression. The differential pathological importance of changes in maximum thickness, plaque height, and mean thickness remains to be clearly established. It seems reasonable to suggest, however, that the combination of low socioeconomic status and high reactivity is associated with progression of the overall atherosclerotic burden, as well as the development of focal lesions that protrude into the lumen, increase the surface roughness of the carotid artery, and raise the potential for plaque fissuring and possible rupture. The differences in progression seen in these data may have potentially important public health interpretations. While there is little information on the relationship between carotid atherosclerotic progression and clinical events, Salonen and Salonen have demonstrated cross sectionally that a 0.1-mm difference in maximum thickness significantly raises the risk of acute myocardial infarction by 11% (95% CI = 6%, 16%; $P < .001$).[20]

Several points should be mentioned before interpreting these findings. First, important conceptual and methodological issues have been raised in interpreting "interaction" in epidemiologic analyses, including variable categorization, sensitivity of the interaction to model specification, and low power.[39,40] While these issues remain unsettled, we believe it is a reasonable interpretation of the data presented here to conclude that heightened cardiovascular reactivity and low socioeconomic status have synergistic effects on atherosclerotic progression. This conclusion is supported by noting that, in all pairwise comparisons, the largest increases in atherosclerosis were observed in the high reactivity—low socioeconomic status group. The conclusion is further strengthened if the assessment of interaction is based on the synergy index (data not shown) derived from an additive model of interaction proposed by Rothman.[41]

Second, we found that the magnitude of the differences between reactivity and socioeconomic groups was virtually unchanged by adjustment for atherosclerotic risk factors. Lack of confounding from these risk factors should not necessarily be interpreted as evidence that greater progression of carotid atherosclerosis in the low socioeconomic–high reactivity group was "independent" of these risk factors. Socioeconomic status and reactivity are associated with baseline levels of atherogenic risk factors and changes in risk factors over time; thus, the analytic strategy of examining the association of socioeconomic status and reactivity with changes in atherosclerosis by adjusting for baseline levels of risk factors may be problematic. It is also possible that there are other atherosclerotic risk factors, such as hemostatic variables, that were not included in these analyses.

Third, it is possible that the associations between low socioeconomic status, heightened reactivity, and progression of carotid atherosclerosis reflected the fact that those of lower socioeconomic status and higher reactivity had increased prevalent heart disease at baseline. We repeated the analysis in a subsample that excluded all men who had any indication of prevalent heart disease at baseline and found the pattern and magnitude of the associations consistent with those obtained within the entire sample.

Fourth, while these results implicate low socioeconomic status and heightened reactivity in atherosclerotic progression, it is possible that heightened blood pressure responsiveness is a consequence of underlying atherosclerotic disease. We conducted a more stringent examination of these associations by excluding men who showed evidence of carotid stenosis or nonstenotic

TABLE 3—Childhood Socioeconomic Status (SES), Education, Income, Reactivity Status, and Mean 4-Year Progression of Maximum Intima-Media Thickness (IMT), Plaque Height, and Mean IMT Adjusted for Age and Baseline IMT: 694 Men Free of Prevalent Ischemic Heart Disease at Baseline

		Maximum IMT			Plaque Height			Mean IMT		
	Reactivity	Change, mm	SE	P^a	Change, mm	SE	P^a	Change, mm	SE	P^a
Childhood SES										
Low	High	0.31	0.02	.06	0.33	0.02	.006	0.14	0.02	.27
High	High	0.26	0.02	>.50	0.25	0.02	>.50	0.12	0.01	.46
Low	Low	0.26	0.01	>.50	0.26	0.01	>.50	0.12	0.01	>.50
High	Low	0.25	0.01	Reference	0.25	0.01	Reference	0.11	0.01	Reference
Interaction Term (F)		1.41		.23	5.14		.02	0.31		.58
Education										
Low	High	0.32	0.02	.03	0.31	0.02	.05	0.14	0.02	.24
High	High	0.25	0.02	>.50	0.26	0.02	>.50	0.11	0.01	>.50
Low	Low	0.26	0.032	>.50	0.26	0.02	>.50	0.11	0.01	>.50
High	Low	0.25	0.01	Reference	0.25	0.01	Reference	0.11	0.01	Reference
Interaction Term (F)		2.24		.08	1.92		.17	0.85		.36
Income										
Low	High	0.36	0.03	.004	0.30	0.03	.36	0.20	0.02	.001
High	High	0.26	0.02	>.50	0.27	0.02	>.50	0.12	0.01	>.50
Low	Low	0.26	0.02	>.50	0.27	0.02	.36	0.11	0.01	>.50
High	Low	0.25	0.01	Reference	0.25	0.01	Reference	0.11	0.01	Reference
Interaction Term (F)		4.62		.03	0.14		.71	7.36		.007

Note. Prevalent ischemic heart disease was defined as history of prior myocardial infarction or angina pectoris, current use of anti-angina medication, or positive indications of angina according to London School of Hygeine Cardiovascular Questionnaire.
[a]See Table 1 for description.

plaque at baseline. The results were unchanged, suggesting that the negative effects of low socioeconomic status and heightened reactivity are evident early in the natural history of carotid atherosclerosis.

This study investigated the pathological significance of the interaction between a biological predisposition and socioeconomic status. While cardiovascular reactivity to stress is no doubt influenced by underlying biological and genetic factors, the magnitude of the responses also reflects social experiences. Lewontin and others have argued that the interaction of genetic and environmental factors is the only sensible way to understand how genes affect health.[42,43] Individuals who are born with a genetic predisposition to heightened reactivity and who grow up in chronically stressful environments are more likely to show exaggerated cardiovascular reactivity as adults. Once established, this hyperresponsiveness becomes an "individual trait" that is elicited in stressful situations, and it may become pathologically significant under continuing exposure to stressful conditions. Anderson has argued that the distribution of a biological/genetic predisposition for elevated cardiovascular reactivity probably differs very little between different racial and ethnic groups.[44] The fact that African-American children and adults exhibit higher levels of reactivity may not be related to differences in the distribution of the underlying genetic predisposition; rather, it may be the result of different exposure and adaptation to chronically stressful environments.

We measured socioeconomic status as an individual characteristic, but it also represents exposure to a set of social circumstances.[33] For instance, in this population, 70% of the men born into poor families received less than a primary school education. These men were more likely to have lost their fathers during World War II; to report "more difficult" childhoods; to have poorer perceptions of their performance at school; to enter the workforce at an earlier age; to take up physically and psychologically demanding, low-paid blue-collar or farm work; to have greater financial insecurity, fewer material possessions, and higher rates of work injury, unemployment, and disability retirement; and to perceive their health as poor.[1] Such a cascade of undesirable social circumstances may have potentiated the negative effects of heightened cardiovascular reactivity on atherosclerotic progression.

We chose to explicitly examine the interaction between an individual biological predisposition and socioeconomic variables that represented exposure to chronic social stressors because the concept of atherosclerotic disease's being related to the interaction of biological predispositions and social circumstances was plausible and potentially informative. Much of modern epidemiology has been concerned with establishing the "independent" status of particular risk factors for disease by adjusting associations for confounding. Not only does this approach have methodological caveats; it may fail to do justice to the rich complexity of how multiple-level risk factors are actually related in vivo and may limit understanding of the processes that influence population health patterns.[29] While it is valuable to examine important independent risk factors, this process alone may not be ultimately informative in understanding the complexity of disease causation.

This study set out to examine complex relations between potentially important predictors of cardiovascular disease[45] and is consistent with comments made recently about conceptual frameworks and the future of epidemiology.[46] Pearce argued that epidemiology should reintegrate a population perspective because it is "first and foremost a branch of public health."[47] One way to achieve this is to understand associations between individual risk factors and disease in etiologic hypotheses that are conceived at the population level and involve the fundamental social, economic, and political causes of disease.[48] Susser and Susser went further and used the metaphor of "Chinese boxes" to describe a paradigm for the future of epidemiologic research in which understanding population health patterns relies on

concepts of interaction among systems at multiple levels.[49] Our study demonstrates how examining the interaction of an individual biological predisposition with a set of undesirable social circumstances is etiologically informative for understanding atherosclerotic progression and is consistent with efforts to reintegrate a public health perspective with epidemiology. □

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