DOES SOCIAL MEDICINE STILL MATTER IN AN ERA OF MOLECULAR MEDICINE?

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ABSTRACT To ask whether social medicine still matters may seem to be in poor taste at a symposium to honor Martin Cherkasky, but social medicine has always had the courage to take on difficult questions. There is all the more reason to do so when its legitimacy is challenged. The extraordinary findings emerging from the human genome project will revolutionize diagnostic and therapeutic methods in medicine. The power of medical interventions, for good and for harm, will increase enormously. However, in the next millennium, as in this one, social factors will continue to be decisive for health status. The distribution of health and disease in human populations reflects where people live, what they eat, the work they do, the air and the water they consume, their activity, their interconnectedness with others, and the status they occupy in the social order. Virchow's aphorism is as true today as it was in 1848: "If disease is an expression of individual life under unfavorable conditions, then epidemics must be indicative of mass disturbances of mass life." Increasing longevity resulting from major economic transformations has made ours the age of chronic disease. Changes in diet and behavior transform genes that once conferred selective biologic advantage into health hazards. Although disease risk varies with social status, medical care makes an important difference for health outcomes. Access to care and the quality of care received are functions of social organization, the way care is financed, and political beliefs about the "deserving" and the "undeserving" poor. It is a moral indictment of the US that ours is the only industrialized society without universal health care coverage. In educating the American public about the social determinants of health, a goal Martin Cherkasky championed, the very power of the new molecular biology will help make our case. Social medicine is alive and well.

The accomplishments of molecular biology are prodigious. Not a week passes without the discovery of a new gene locus for this or that disease or trait. Virtuosos at DNA mapping already have provided the complete genome of a number of microorganisms. Within 3 to 5 years, the human genome will have

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been deciphered. Designer drugs and anti-idiotype antibodies are already in use. The first antisense drug has been approved by the Food and Drug Administration, and another half-dozen are in the pipeline. Gene therapy still may be a promise rather than a fact, but there is no reason to doubt the technical barriers will be overcome.

Bedazzled by biomedicine's technical virtuosity, shall we inter social medicine, giving it a proper burial for its glorious past, but acknowledging that it is brain dead? Not at all! The developments in molecular biology highlight the salience of the social environment and underscore the urgency of rectifying inequity and injustice. All medicine is inescapably social medicine. Let me try to make the case for this outrageous proposition by taking on instances at the margin, that is, by examining the role of social forces in infectious diseases, on the one hand, and diabetes mellitus on the other, diseases that are commonly thought to be explained fully by the standard reductionistic biomedical paradigm.

THE "ANTHROPOLOGY" OF INFECTIOUS DISEASE

If there is a case to be made for the proposition that the causes of disease are biological, infectious diseases would appear to be prime instances. By definition, an infectious agent is a *necessary* cause of the disease. Further, eliminating the agent eliminates the disease. Yet, if an infectious agent is the necessary cause by Koch's postulates, is it a *sufficient* cause? The fact is that not every person exposed to the agent develops clinical disease. The resistance of the host is as decisive as the virulence of the agent.[1]

Moreover, the characteristics of the agents alone do not account for the epidemiology of infectious diseases. Human social organization creates the conditions necessary for infectious diseases to exert selective evolutionary pressure on human biology.[2] Diseases that are infectious only in the acute phase, such as measles or poliomyelitis, could not become endemic in Neolithic populations. The penetration of such a virus into a small hunter-gatherer community of several hundred happens today as it did 100,000 years ago; it rapidly kills or immunizes so high a proportion of the population that the virus is no longer able to propagate itself, and it disappears until the next encounter with strangers.[3] Part of the reason for the high mortality is the restricted gene pool among inbred aborigines. A virus that infects the first tribesperson is "preadapted" to genetically similar fellows and gains in virulence in subsequent encounters. With limited polymorphism among isolated peoples, especially those who are endogamous, exposure to mutable pathogens wreaks havoc.[4] Only when the agrarian revolution generated

resources sufficient to permit the large-scale aggregation of human groups did such infectious agents have a host reservoir large enough to maintain the chain of transmission.

In hunter-gatherer societies, risk for disease was distributed uniformly; there were no privileged social positions. Beginning with the agricultural revolution and accelerating with subsequent economic transformations, disease epidemiology began to correspond to social stratification. One hundred fifty years ago, Virchow, a founder of social medicine, identified the synergy between poverty and disease.[5] Upper Silesia was in the grips of an epidemic of "famine fever" (now known as relapsing fever) in the summer of 1847. The central government in Berlin was obliged to appoint a Commission of Investigation; Virchow was an active member. In a scathing report, he insisted that the causes of the epidemic were more social than medical. The deplorable overcrowded housing and the endemic malnutrition afflicting the workers made them vulnerable. Nothing but prosperity, culture, and freedom, he declared, could bring about an improvement, and these could only be achieved by "complete and unrestricted democracy." In Virchow's words: "If disease is an expression of individual life under unfavorable conditions, then epidemics must be indicative of mass disturbances of mass life."[6(p680)]

That statement is as true today as it was then. In August 1998, Raoult et al.[7(p357)] reported a devastating epidemic of typhus in Burundi; like relapsing fever, it reflects "a mass disturbance of mass life." As the authors comment:

> Wide-spread epidemic typhus can not occur unless social conditions also provoke wide-spread body-louse infection . . . among the displaced population. . . . Fifty thousand typhus cases have been clinically diagnosed. . . . Louse-associated disease remains a major health threat in this and other war torn regions of the world.

The same can be said for human immunodeficiency virus (HIV) infection and multiple-drug-resistant tuberculosis: Social chaos is a culture medium in which they thrive.

If poverty and war propagate disease, improved living conditions inhibit its growth. Well before the introduction of chemotherapy, mortality from infectious diseases in industrialized countries fell markedly because of the reduced exposure to infectious agents through provision of pure water, sewage disposal, better personal hygiene, and less crowded housing and because of greater host resistance secondary to better nutrition and improved general health.[8,9]

THE SOCIAL CONSTRUCTION OF DIABETES AS A CHRONIC DISEASE

If social forces play a decisive role in acute infectious disease, do they have any salience for chronic disease? The evolution of diabetes as a clinical disease

graphically illustrates the interaction among mode of life, means of care, and the biology of the disease process itself, transforming a once acute and fatal disease into a chronic, debilitating disorder.

Diabetes mellitus is characterized by defective regulation of glucose metabolism. Since the work of Himsworth,[10] we have distinguished two principal forms of diabetes mellitus: insulin-dependent diabetes mellitus (IDDM or type 1) and non-insulin-dependent diabetes mellitus (NIDDM or type 2). The first is relatively uncommon, affecting about 4 per 1,000 in the US; the latter is far more common at a prevalence of 60–70 per 1,000. Persons with type 1 diabetes mellitus have an absolute deficiency of insulin secretion associated with pancreatic islet atrophy, whereas patients with type 2 diabetes mellitus suffer from tissue resistance to relatively normal amounts of secreted insulin.

Although IDDM occurs among all populations studied, its incidence varies almost 60-fold between countries.[11] For example, within Italy alone, rates are 30.2 per 100,000 in Sardinia (the second highest incidence in the world) versus 6.5 per 100,000 in the Lazio region of the Italian mainland, a region lying opposite Sardinia across the Tyrrhenian Sea. Mutoni et al.[12] compared the incidence of IDDM in children born in Lazio to parents of Sardinian origin. Sardinians are a relatively homogeneous population, genetically distinct from other Italians.[13] Historically, there had been little exchange between Sardinia and Lazio until 1950, when many Sardinians began to settle in Lazio as the result of postwar economic opportunity. The incidence of IDDM among children born in Lazio of two Sardinian parents is four times as high, and among children of mixed marriages is two times as high, as the rate among the indigenous children. Genetic differences, however, account for only part of the story. There has been a steady increase in the incidence of IDDM in Sardinia over the past several decades, pointing to as yet unidentified environmental agents; the increase in its prevalence reflects the remarkable success in treating diabetes and delaying the onset of its complications.[13] Higher prevalence, reflecting greater survival of children and adolescents with the disease, leads to further increase in incidence as more people with type 1 diabetes mellitus survive to produce viable offspring.

NIDDM also has a hereditary basis, as evident from (1) greater concordance in identical twins, (2) aggregation in families, and (3) marked differences between geographically and ethnically separate populations. Children of parents with NIDDM, later to become diabetic, exhibit hyperinsulinemia on oral glucose tolerance testing a decade or more before hyperglycemia appears.[14] At the same time, an environmental contribution is evident from the higher risk for clinical disease with (1) lower activity level, (2) higher caloric intake, and (3) greater extent of

obesity. The Harvard Nurses' Health Study, based on a longitudinal study of 65,000 nurse volunteers, found that a diet containing "a high glycemic load and a low cereal fibre content" increases the risk for diabetes in women.[15]

Of particular interest for the sociobiology of disease are the "epidemics" of diabetes that have appeared among Polynesians, American Indians, and Aboriginal Australians as their lifestyles have been "modernized." A striking recent example occurred on Nauru, a small Pacific island inhabited by about 5,000 Micronesians. Until World War II, high energy expenditure was required for sheer survival via fishing and subsistence farming. After the war, the introduction of phosphate mining by foreign companies yielded rental income for the Nauruans that rapidly transformed them into one of the world's wealthiest and most sedentary peoples. Today, virtually all foodstuffs are imported, and most have a high calorie content; obesity is ubiquitous. NIDDM, previously minimal, began to reach epidemic proportions in the 1950s and now afflicts almost two-thirds of 55-to 64-year-old adults. Paradoxically, wealthy Nauru now has one of the world's shortest life spans because of diabetes and its complications.[16]

The distribution of the disease among Nauruans has continued to change during the past 50 years. Health surveys in recent decades reveal that the age-standardized prevalence of impaired glucose tolerance rose to 21% in the mid-1970s and then declined to half that value by the late 1980s; yet, the risk factors persisted. The most parsimonious explanation for the rise and subsequent fall is that NIDDM resulting from the affluent lifestyle has already afflicted most of the genetically susceptible Nauruans, leaving a residual population of relatively resistant individuals. The Nauru epidemic has ominous implications for Southeast Asia. Rates of diabetes among Chinese and Indian expatriates living in the West (in contrast to low rates in China and India) make it virtually certain that the improved living standards anticipated for India and China in the next century will lead to epidemics of NIDDM.

How did the NIDDM genotype become widespread? Higher mortality and shorter longevity should lead to adverse genetic selection. Neel[17] has proposed the "thrifty genotype" hypothesis. During most of our history as a species, life has been characterized by a fluctuating food supply and frequent famines. A quick insulin trigger reduces calorie loss and permits more fat storage during periods of relative plenty; insulin resistance in muscle may also contribute to the thrifty genotype by blunting the hypoglycemia associated with fasting.[18] Individuals with thrifty adaptations (i.e., those able to release insulin rapidly when a temporary food glut becomes available) can convert most of their ingested

calories into fat. Greater fat stores would make them better able to survive subsequent periods of starvation. The very same genotype becomes a handicap in the presence of abundant high-calorie foodstuffs and reduced physical activity.

Until World War II, the population on Nauru was under intense pressure for selection of the thrifty genotype: their ancestors had reached the island only after long sea voyages; crop failures on the island were common (indeed, many Nauruans suffered from starvation during the Japanese occupation). The sudden change in economic circumstances on Nauru created the conditions for an "epidemic." The cresting and recession of the epidemic display in heightened fashion what occurred over a century in the West on a more gradual course with a longer period of accommodation. What is the biological moral of this story? It was put succinctly by Neel[17]: "Genes and combinations of genes, which were at one time an asset may in the face of environmental change, become a liability."

The evolution of diabetes as a clinical disease (its changing prevalence as opposed to its changing incidence) reflects advances in patient care that have converted what was once an acute and uniformly fatal disease into a chronic ailment with secondary complications that now dominate the patient's life experience.[19] Joslin, who specialized in the care of diabetic patients before and after the introduction of insulin, summarized progress during the preinsulin era in his 1922 Shattuck lecture[20(p536)]: "The average known duration of the fatal cases of diabetes in the city of Boston between 1895 and 1913 was 3.3 years; during 1915, it was 4.3 years and 1920, it was 5.3 years."

Diabetics died of the acute complications of their disease: coma, gangrene, and infections. Scrupulous attention to hydration, diet, and personal hygiene partially controlled these complications. Nonetheless, in the preinsulin era, half of patients with IDDM died within 20 months of the diagnosis; less than 1 in 10 survived for 5 years.[14] When the discovery of insulin was announced, Joslin predicted that the treatment of diabetes would become as simple as that of myxedema: "The promised land is plain in view." Unfortunately, matters proved to be far more complex. Progress, yes; victory, no.

Thirty years after his view of the promised land, Joslin[21] reported that the average age at death had risen from 44 to 64 years. Diabetic coma as a cause of death had fallen from 64% to less than 2% of the total, whereas cardiovascular and renal deaths had risen from 17% to 70%. Insulin, antibiotics, antihypertensive treatment, renal dialysis, and vascular surgery have prolonged survival markedly, but at the cost of retinopathy, nephropathy, and vascular complications

(coronary heart disease, stroke, and peripheral vascular disease) among survivors.[14]

Progress in the clinical management of IDDM continues. For many years, a bitter battle was fought between protagonists for precise and close control of blood sugar levels and others who championed a "liberal" regime on the grounds that the goal of treatment should be a life as normal as possible, not sugar-free urine. Decisive evidence for the superiority of one or the other philosophy of management was not to be found until the completion of the recent Diabetes Control and Complications Trial,[22] which enrolled 1,400 patients with IDDM in a multicenter study to compare standard care with intensive care for insulin-dependent diabetics. Patients in the intensive therapy arm of the study were placed on one of two regimens: multiple daily insulin injections or continuous subcutaneous insulin infusion delivered by a pump. Treatment was initiated by 4 days in a hospital, followed by frequent individual outpatient visits, group meetings, and telephone calls to review progress to monitor hemoglobin A1c levels, adjust insulin dose, maintain diet and weight control, and regulate exercise patterns.

The results were unequivocal: the intensive management program significantly delayed the onset and slowed the progression of the microvascular and neurologic complications of diabetes; the only important side effect was a modest increase in the number of hypoglycemic episodes. The powerful benefit of close and continuous involvement with patients and active patient participation in managing chronic disease is evident from a startling statistic: 99% of the patients completed the trial. This is a tribute to the cooperative relationship between the research team and its patients; the treatment program demanded major lifestyle changes and strict adherence to a demanding protocol. Patients had to understand what they were doing and why; nurse clinicians were available for consultation when needed in addition to the regular phone and clinic visits they provided.

The annual cost of intensive treatment[23] was about three times greater than that for conventional treatment. If the approximately 120,000 diabetic patients in the US who meet the trial's eligibility criteria were placed on intensive rather than conventional therapy, the cost would be an additional $4 billion over the lifetime of this population; in return, each patient, on average, would gain an additional 7.7 years of sight, 5.8 years free from end-stage renal disease, and 5.6 years free from lower extremity amputation. The incremental health care costs would be just under $20,000 per quality-adjusted life-year gained, a cost-benefit ratio similar to that for other effective treatments.[24] Recent data indicate that

patients with type 2 diabetes also benefit from close control of blood glucose and blood pressure.[25-29]

MORTALITY, MORBIDITY, AND SOCIOECONOMIC STATUS

If endocrinology and infectious disease are but thinly disguised subspecialties of social medicine, the rest of medicine is self-evidently social. Comparisons of morbidity and mortality with income and education between countries and within countries show remarkably consistent inverse correlations the world over. The decline in life expectancy in Russia since 1990, unprecedented in an industrialized country, is a result of the social chaos in the wake of the collapse of central government; deaths of adults between ages 30 and 60 from accidents, alcohol-related causes, and cardiovascular disease account for the largest part of the drop.[30] The greatest declines in life expectancy occurred in predominantly urban regions, with higher rates of labor turnover, larger increases in crime, and a higher average, but unequal, distribution of household income.

Not only are absolute income levels important to health, but disparities in income distribution also matter. In an examination of the associations between income inequality and mortality in 282 US metropolitan areas, those areas with the greatest income inequalities had death rates far higher than those with narrower extremes. Excess mortality ranged from 64.7 to 95.8 per 100,000. Effects were most evident for infant mortality and mortality in the adult years from 15 to 64. To put the magnitude of this mortality difference into perspective, it is comparable to the combined loss of life from lung cancer, diabetes, motor vehicle crashes, HIV infection, suicide, and homicide.[31] Socioeconomic (SES) circumstances in fetal life and early childhood have a major impact on the prevalence of chronic disease in adulthood.[32-34] Of increasing interest is the relationship between individual socioeconomic trajectories and health outcomes[35,36]; that is, what are the effects of upward or downward social mobility? How do poor health and social disadvantage interact over a lifetime?

What intervening mechanisms account for the relationship between SES and health? Although behaviors that put health at risk (smoking, alcohol consumption, sedentary lifestyle, and obesity) are more common among lower-income groups, they account for no more than a fraction of the mortality differential.[37] Systematic research to clarify the economic, behavioral, social, psychological, and community dynamics that underlie inequalities in health must be high on the social medicine agenda.[38] Understanding dynamics may identify interventions powerful enough to mitigate class effects.

What of access to care? The US, alone among industrialized countries, tolerates large numbers of people with no health insurance (about 45 million) or inadequate insurance (29 million). Of the uninsured, 11 million are children.[39,40] They are twice as likely to have no regular physician and are four times more likely to go without needed care than children with insurance.[41] To make the scandal worse, almost 5 million of these children are eligible technically for Medicaid, but are not enrolled, perhaps because their parents do not know they are eligible or perhaps because they fear the stigma associated with services for the poor.[42] In the words of the Princeton economist Uwe Reinhardt[43(p1447)]:

> The United States . . . countenances the practice of rationing healthcare for millions of American children . . . by their parents' willingness and ability to procure charity care in their role as health care beggars.

Minority patients are doubly disadvantaged. Not only are they more likely to be uninsured and underinsured, but they receive less care, even when they are eligible for Medicare or treatment at Veterans Administration facilities. This is true for access to HIV therapy,[44] treatment for acute chest pain,[45] access to recombinant erythropoietin during dialysis,[46] breast cancer treatment,[47] coronary revascularization,[48] or analgesia in emergency departments.[49]

As if all of this were not injustice enough, the abysmal failure of the Clinton effort at health reform has enshrined competition as the governor of the "medical marketplace"; the ethos of health policy has become cost control and profitability.[50] The uninsured and the underinsured have disappeared from the radar screen. In the absence of federal regulation, the ability of the uninsured to obtain care varies from area to area dependent upon the vagaries of local and state health policy.[51] Market-driven medical care is forcing doctors to choose between the best interests of their patients and their own economic survival.[52] Will any patient be able to trust any doctor when doctors are at risk for the costs of the care they prescribe?

SOCIAL MEDICINE AND SOCIAL ACTION

In the very first issue of his journal, *The Medical Reform*, published on July 10, 1848, Virchow announced that "the physician is the natural attorney of the poor." Medicine must be reformed for the sake of patients, not doctors.[53] Because social and economic conditions have an important effect on health and disease, the measures taken to combat disease must be social as well as medical. How was progress to be monitored? Virchow's answer was clear[6(p684)]: "Medical statistics will be our standard of measurement: we will weigh life for life and see where the dead lie thicker, among the workers or among the privileged."

Documenting injustice is not enough. Virchow knew that; he was at the Barricades in 1848; his cause did not win, but he never gave up the fight. Martin Cherkasky knew that; a "premature" antifascist, he was on the American Medical Association's list of enemies for his advocacy of group health plans and national health insurance; he, too, never gave up that fight.

The evidence is clear: inequalities in health and differential access to care by social class persist and plague the disadvantaged, a plague made worse when market forces were substituted for coherent federal policy. The only way to ensure access, equity, effectiveness, and efficacy in health care is through coverage, universal for all citizens, and an organized health care delivery system.

Which side are we on?

REFERENCES

1. Eisenberg L. What makes persons patients and patients well? *Am J Med.* 1980;69: 277–286.
2. Haldane JBS. Natural selection in man. *Acta Genet Stat Med.* 1956/1957;6:321–332.
3. Black FL. Infectious diseases in primitive societies. *Science.* 1975;187:515–518.
4. Black FL. Why did they die? *Science.* 1992;258:1739–1740.
5. Eisenberg, L. Rudolf Ludwig Karl Virchow: where are you now that we need you? *Am J Med.* 1984;77:524–532.
6. Virchow R, cited in G Rosen, What is social medicine? A genetic analysis of the concept. *Bull Hist Med.* 1947;21:674–733.
7. Raoult D, Ndihokubwayo JP, Tissot-Dupont H, et al. Outbreak of epidemic typhus associated with trench fever in Burundi. *Lancet.* 1998;352:353–358.
8. Kass EH. Infectious diseases and social change. *J Infect Dis.* 1971;123:110–114.
9. McKeown T. *The Role of Medicine: Dream, Mirage or Nemesis?* London: Nuffield Hospital Trust; 1976.
10. Himsworth HP. Diabetes mellitus: its differentiation into insulin-sensitive and insulin-insensitive types. *Lancet.* 1936;1:117.
11. Hattersley AT. Genes versus environment in insulin-dependent diabetes: the phoney war. *Lancet.* 1997;349:147–148.
12. Mutoni SA, Fonte MT, Stoduto S, et al. Incidence of insulin-dependent diabetes mellitus among Sardinian-heritage children born in Lazio region, Italy. *Lancet.* 1997;349:160–162.
13. Cavalli Sforza LL, Piazza A. Human genomic diversity in Europe: a summary of recent research and prospects for the future. *Eur J Hum Genet.* 1993;1:3–18.
14. Krolewski AS, Warram JH. Epidemiology of late complications of diabetes. In: Kahn CR, Weir GC, eds. *Joslin's Diabetes Mellitus.* 13th ed. Philadelphia: Lea and Febiger; 1994:605–619.
15. Salmeron J, Manson JE, Stampfer M, et al. Dietary fibre, glycemic load and risk of NIDDM. *JAMA.* 1997;277:472–477.
16. Zimmet PZ. Kelley West lecture. Challenges in diabetes epidemiology—from West to the rest. *Diabetes Care.* 1991;15:232–252.
17. Neel JV. Diabetes mellitus: a thrifty genotype rendered detrimental by "progress"? *Am J Hum Genet.* 1962;14:353–362.
18. Dowse GK, Zimmet PZ, Finch CF, Collins V. Decline in incidence of epidemic glucose intolerance in Nauruans: implications for the "thrifty genotype." *Am J Epidemiol.* 1991; 133:1093–1104.
19. Feudtner C. The want of control: ideas, innovations, and ideals in the modern management of diabetes mellitus. *Bull Hist Med.* 1995;69(1):66–90.

20. Joslin EP. The Shattuck lecture: the treatment of diabetes mellitus. *Boston Med Surg J.* 1922;186:833–852.
21. Joslin EP. A half-century's experience in diabetes mellitus. *Br Med J.* 1950;1:1095–1098.
22. Diabetes Control and Complications Trial Research Group. The effect of intensive treatment of diabetes on the development and progression of long-term complications in insulin-dependent diabetes mellitus. *N Engl J Med.* 1993;329:977–986.
23. Diabetes Control and Complications Trial Research Group. Resource utilization and costs of care in the Diabetes Control and Complications Trial. *Diabetes Care.* 1995;18: 1468–1478.
24. Diabetes Control and Complications Trial Economic Evaluation Writing Team. Lifetime benefits and costs of intensive therapy as practiced in the Diabetes Control and Complications Trial. *JAMA.* 1995;276:1409–1415.
25. UK Prospective Diabetes Study Group. Intensive blood-glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in patients with type II diabetes (UKPDS 33). *Lancet.* 1998;352:837–853.
26. UK Prospective Diabetes Study Group. Effect of intensive blood-glucose control with metformin on complications in overweight patients with type II diabetes (UKPDS 34). *Lancet.* 1998;352:854–865.
27. UK Prospective Diabetes Study Group. Tight blood pressure control and risk of macrovascular and microvascular complications in type II diabetes (UKPDS 38). *Br Med J.* 1998;317:703–713.
28. Ohkubo Y, Kishikawah, Araki E, et al. Intensive insulin therapy prevents the progression of diabetic microvascular complications in Japanese patients with non-insulin-dependent diabetes mellitus: a randomized prospective six year study. *Diabetes Res Clin Pract.* 1995;28:103–117.
29. Nathan DM. Some answers, more controversy, from UKPDS. *Lancet.* 1998;352:832–833.
30. Walberg P, McKee M, Shkolnikov V, Chenet L, Leon DA. Economic change, crime, and mortality crisis in Russia: regional analysis. *Br Med J.* 1998;317:312–318.
31. Lynch JW, Kaplan GA, Pamuk EP, et al. Income inequality and mortality in metropolitan areas of the United States. *Am J Public Health.* 1998;88:1074–1080.
32. Joseph KS, Kramer MS. Review of the evidence on fetal and early childhood antecedents of adult chronic disease. *Epidemiol Rev.* 1996;18:158–187.
33. Rich-Edwards JW, Stamfer MJ, Manson JE, et al. Birthweight and risk of cardiovascular disease in a cohort of women followed-up since 1976. *Br Med J.* 1997;315:396–400.
34. Martyn CN, Barker DJP, Osmond C. Mothers' pelvic size, fetal growth and coronary heart disease in men in the UK. *Lancet.* 1996;348:1264–1268.
35. Lynch JW, Kaplan GA, Salonen JT. Why do poor people behave so poorly? Variation in adult health behaviors and psycho-social characteristics by stages of the socioeconomic life course. *Soc Sci Med.* 1997;44:809–820.
36. Lynch JW, Kaplan GA, Cohen RD, et al. Childhood and adult socioeconomic status as predictors of mortality in Finland. *Lancet.* 1994;343:524–527.
37. Lantz PM, House JS, Lepkowski JM, Wiliams DR, Mero RP, Chen J. Socioeconomic factors, health behaviors, and mortality. *JAMA.* 1998;279:1703–1708.
38. Kaplan GA, Lynch JW. Whither studies on the socioeconomic foundations of population health? *Am J Public Health.* 1997;87:1409–1411.
39. Rice D. The cost of instant access to health care. *JAMA.* 1998;279:1030.
40. Budetti PP. Health insurance for children—a model for incremental reform? *N Engl J Med.* 1998;338:541–542.
41. Newacheck PW, Stoddard JJ, Hughes DC, Pearl M. Health insurance and access to primary care for children. *N Engl J Med.* 1998;338:513–518.
42. Seldin TM, Banthin JS, Cohen JW. Medicaid's problem children; eligible but not enrolled. *Health Aff.* 1998;17:192–200.
43. Reinhardt U. Wanted: a clearly articulated social ethic for American health care. *JAMA.* 1997;278:1446–1447.

44. Moore RD, Stanton D, Goplan R, Chaisson RE. Racial differences in the use of drug therapy for HIV disease in an urban community. *N Engl J Med.* 1994;330:763–768.
45. Johnson PA, Lee TH, Cook EF, Rounan GW, Goldman L. Effect of race on the presentation and management of patients with acute chest pain. *Ann Int Med.* 1993;118:593–601.
46. Powe NR, Griffiths RL, deLissovoy G, et al. Access to recombinant erythropoietin by Medicare-eligible renal dialysis patients. *JAMA.* 1992;277:535–542.
47. Diehr P, Yergan J, Chu J, et al. Treatment modality and quality differences for black and white breast cancer patients treated in community hospitals. *Med Care.* 1998;27: 942–958.
48. Peterson ED, Shaw LK, DeLong ER, Pryor DB, Califf RM, Mark DB. Racial variation in the use of coronary-revascularization procedures—are the differences real? Do they matter? *N Engl J Med.* 1997;336:480–506.
49. Todd KH, Samaroo N, Hoffman JR. Ethnicity as a risk factor for inadequate emergency department analgesia. *JAMA.* 1993;269:1537–1539.
50. Eisenberg L. Managed care and the patient-doctor relationship. Paper presented at: American Psychiatric Association Annual Meeting, Toronto, June 1, 1998.
51. Cunningham PJ, Kemper P. Ability to obtain medical care for the uninsured: how much does it vary across communities? *JAMA.* 1998;280:921–927.
52. Kassirer J. Managed care and the morality of the marketplace. *N Engl J Med.* 1995;333: 50–52.
53. Virchow R. *Collected Essays on Public Health and Epidemiology.* Vol. 1. Rather LJ, ed. Canton, Mass: Science History Publications; 1849/1985:4.