
Invited Commentary

Invited Commentary: Cassel's "The Contribution of the Social Environment to Host Resistance"—A Modern Classic

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John Cassel's 1976 paper "The Contribution of the Social Environment to Host Resistance" (*Am J Epidemiol.* 1976;104(2):107–123) is widely regarded as a classic in epidemiology. He makes the compelling argument that the quality of a person's social relationships, that is, the degree to which her relationships are more stressful than supportive (or vice versa) influences her susceptibility to disease independent of genetic endowment, diet, physical activity, etc. Cassel's provocative thesis was anchored in a cogent synthesis of findings from animal experiments and observational studies on diverse human populations. Beginning in the late 1970s, the paper stimulated an explosion of epidemiologic research on social support and human health. Beyond advancing epidemiologic theory, Cassel showed how findings from various epidemiologic study designs could be marshalled to build a persuasive causal argument that impaired social bonds increase the risk of premature disease and death. The paper also foreshadowed core ideas of later theoretical constructs, such as weathering and allostatic load, regarding the power of chronic environmental stressors to accelerate biological aging across multiple organ systems. Cassel's assessment of the research and practice implications of his conclusions has remarkable contemporary resonance for the field of epidemiology.

generalized susceptibility; host resistance; interventions; rapid sociocultural change; social support; stress

John Cassel's paper "The Contribution of the Social Environment to Host Resistance" (1) was originally the fourth Wade Hampton Frost Lecture, which he delivered at the 1975 meeting of the American Public Health Association. The lecture was published the following year, which was the year of Cassel's death at age 55 years. Thus, although the paper is a tribute to Wade Hampton Frost, the pioneering infectious disease epidemiologist, it might also be understood as Cassel's grand summary of what his experiences as a primary care physician in his native South Africa during the 1950s (2) and his experiences as an epidemiologist and chair of the Department of Epidemiology at the University of North Carolina at Chapel Hill during the 1960s and early 1970s taught him about the importance of social relationships with regard to human health and disease.

If a classic is a "work of enduring excellence" (3, p. 211), then this paper deserves the designation for the following reasons. First, by explicating how the social environment, specifically whether social relationships are more stressful than supportive, undermines resistance to disease, Cassel broadened our view of the sources of "host resistance." He also showed how the host-agent-environment triad of disease causation,

which had served Frost's generation of infectious disease epidemiologists so well, could be updated to incorporate the destabilizing effects of rapid sociocultural change on human relationships in both developed and developing societies, thereby increasing population-wide susceptibility to noninfectious diseases (4).

Second, he illustrated the centrality of an interdisciplinary perspective to major advances in epidemiology. He did this by drawing on research from both the social and biological sciences that showed that stressful social relationships alter the neuroendocrinal milieu for humans and nonhumans alike in ways that lower resistance to microorganisms that might otherwise remain harmless. Third, by showing how consistently epidemiologic research had implicated impaired social bonds as a risk factor for poor health, Cassel underscored the contribution that different study designs (from ecological to randomized controlled trials) can make to building a convincing causal argument. The causal argument is further strengthened when, as in the example of impaired social bonds and reduced health, animal experiments (5) support observational research on humans (6).

Fourth, Cassel was clearly impressed by the fact that the relationship between impaired social bonds, measured in

multiple ways (5, 6), and heightened disease risk was observed for multiple health outcomes, both sexes, young and old, and diverse racial groups (6–8). This made him inclined to believe that nurturing social relationships is a precondition for healthy human development. Cassel's personal experiences as a primary care physician for black South Africans in the 1950s who were struggling to hold onto their traditional social support systems in the face of mounting pressures from Apartheid and rapid urbanization likely further informed his view that powerful social stressors reduce population-level host resistance by eroding vital social support systems (2). The Jim Crow South provided him with another example of how government-sanctioned subordination of blacks could undermine social bonds among the latter so severely that negative health effects attributable to weak community support systems would be much greater for blacks than whites (7, 9, 10).

Fifth, Cassel dealt forthrightly with the research and practice implications of his conclusions. With epidemiologists in mind, he argued for intensifying research to identify features of the environment, both social and physical, that undermine host resistance, especially in highly vulnerable populations. With health-care professionals in mind, he advocated increasing their capacity to address the needs of highly vulnerable populations by training and deploying, with appropriate supervision, resourceful lay people to work in communities in which stressful environments routinely overwhelmed available social support resources. Given their focus on improving the environment, these suggestions echo time-tested principles of epidemiology (11, 12).

It would be difficult to overstate the impact of Cassel's paper on the field of epidemiology, especially social epidemiology, the growth of which over the past 40 years owes so much to the ideas presented in that article. Indeed, it could be argued that the paper itself marked a paradigm shift in epidemiologic research in that it made the study of the availability and quality of social relationships as important as the study of socioeconomic status, dietary habits, smoking, physical activity level, medical care, etc. to our efforts to understand the distribution of premature disease and death in human populations. Cassel's paper, along with a briefer but important 1976 paper by Cobb (13), is widely regarded (14) as the launching pad for the explosion of research on social support (and related concepts like social networks, social capital, etc.) and health that began in the late 1970s.

Given the general acceptance today of epidemiologic research dealing with the effects of stress on human health, it is easy to forget the disarray that characterized stress research during the 1950s and 1960s. As Cassel pointed out in his paper, Selye and Wolfe, the pioneering stress researchers of the 1930s and 1940s, carefully distinguished between "stressor" (a noxious external stimulus) and "stress" (neuroendocrinal disturbance caused by the stimulus). This distinction was often ignored in the 1950s and 1960s by nonlaboratory stress researchers. As Cassel saw it, the resulting semantic confusion, combined with stress researchers' inability to explain why a given putatively noxious social stimulus was disturbing to some people but not others, eventually cast stress research into disarray.

The above semantic problem was fairly easy to solve: Researchers should simply abide by the distinction of Selye

and Wolfe between stressor and stress. However, Cassel's most important contribution to research on the stress–social support–health nexus would seem to be his clear distinction between psychosocial factors that act as stressors (i.e., they disturb neuroendocrinal balance) and those that act as buffers (i.e., they prevent or reduce such disturbance). He further suggested that the thorny problem of stress researchers' inability to know what makes a given stimulus a stressor for some individuals but not others could be solved if we raised our level of abstraction. What, he asked, might all social stressors have in common? Similarly, what might all buffers have in common? A common property of all stressors, he suggested, is their power to signal that the individual's actions are not leading to the expected result. Here, Cassel is less explicit than we might wish, but he strongly implied that certain results are expected because the norms of reciprocity that usually govern human relationships predispose people to believe that if they do X and do it well, then Y should result. A disconfirmation of this expectation is likely to be stressful and lead to feelings of rejection and exclusion. Conversely, its confirmation is validating and reassuring and is likely to result in feelings of acceptance and inclusion. The power of Cassel's reasoning here is its potential to shed light on a number of first-order contemporary problems in social epidemiology. These include but are not limited to the excess risk among persons from lower socioeconomic backgrounds of premature disease and death from a variety of causes (15); the puzzling deterioration of the health of immigrants (especially immigrants of color) from a developing country as their length of stay in a more developed country increases (16); and the persistent finding that blacks have poorer health than do their white peers at all levels of socioeconomic status, even after researchers control for numerous standard risk factors (17, 18).

Cassel's thesis that a social environment characterized by a severe imbalance between social stressors and support resources compromises host resistance anticipated by more than a decade the concepts of weathering (19) and allostatic load (20), each of which echoes and extends Cassel's thesis by positing that chronic exposure to stressors accelerates biological aging of multiple organ systems. Although Cassel was sympathetic to this idea of a stress-induced generalized susceptibility to disease, he remained open to the possibility that certain social stressors, particularly those involving social dominance and submission (and subsequent social rank) might dysregulate the hypothalamic-pituitary-adrenal axis in ways that could determine differential risk for specific diseases. Although it has been suggested in some recent experimental work (21, 22) on the physiological correlates of sudden conflict-laden changes in social rank among non-human primates that there is an element of target-organ specificity, whether chronic exposure to difficult social stressors leads to an increase in organ-specific (vs. generalized) susceptibility to disease among humans remains an open question.

Finally, by urging epidemiologists to intensify research aimed at identifying and then intervening on features of the environment that compromise host resistance, Cassel foreshadowed Rose's cogent argument (23) that primary prevention efforts should focus more on identifying high-risk populations rather than high-risk individuals. Looking back over the past 40 years,

Cassel's skepticism of the ability of multiphasic screening and programs to reduce multiple risk factors in order to improve population health while also reducing social inequalities in health seems well founded. It is also clear, however, that he overemphasized social support interventions to the neglect of broad-based, social policy interventions that we now know can improve the health of whole populations (24). This shortcoming aside, Cassel's paper is not only a tour de force of epidemiologic reasoning, it is an enduring gift to the field of epidemiology from one of the most influential epidemiologists of the 20th century.

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