Social Status and Susceptibility to Respiratory Infections

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ABSTRACT: Adults and children of lower socioeconomic status (SES) are at higher risk for a wide range of communicable infectious diseases, especially respiratory infections. Greater risk for infectious illness among people with lower SES is thought to be attributable to increased exposure to infectious agents and decreased host resistance to infection. We summarize three studies that examine the prospective association of several markers of social status (unemployment, perceived and observed social status) with host resistance to upper respiratory infections. Unemployment was associated with increased susceptibility to infection in adult humans. Lower social status in male monkeys was also associated with increased susceptibility, as was lower perceived social status in humans. The association of social status and susceptibility was accounted for primarily by increased risk in the lowest social status groups. However, further increases in social status were associated with further decreases in susceptibility in both monkeys and humans.

INTRODUCTION

Adults and children of lower socioeconomic status (SES) are at higher risk for a wide range of communicable infectious diseases, especially respiratory infections. For example, in China low income and poor living conditions were associated with greater incidence of acute upper respiratory tract infections.[1] In Guatemala, children of parents with lower levels of education had higher rates of respiratory illnesses than those with less educated parents.[2] Similarly, in India acute respiratory episodes among children were greater for those from families with lower per capita income and lower literacy rates.[3] British children from lower social classes were found to be absent from school more often as a result of upper respiratory and ear infections.[4] U.S. studies have found similar relations. Lower levels of formal education and unemployment have been associated with greater incidence of acute lower respiratory tract infections[5] and otitis media.[6–8] Similarly, U.S. children from poor families missed more days of school and spent more days in bed as a result of acute respiratory illnesses.[6] Children (up to 17 years old) from families who received federal assistance were also more likely to die of pneumonia or influenza compared to those from families not receiving federal assistance.[9]

The evidence discussed so far is primarily from studies comparing those below the poverty level to others in the population. However, there is substantial evidence

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for a graded relation between SES and health with each increase in SES associated with increased health and lessened mortality.[10] A study of tuberculosis in an adult U.S. sample provides some evidence for a graded relation between SES and incidence of an infectious respiratory illness. Although the link between tuberculosis and poverty has been established for many years,[11] in this study, risk of contracting tuberculosis was found to increase uniformly with decreases in income and education and increases in poverty and public assistance.[12]

Why are people with lower SES at greater risk for infectious illness? There are two categories of explanation (see TABLE 1). One attributes greater incidence to increased *exposure* to infectious agents with decreased SES. Lower SES families often have more children and live in more crowded quarters, both environmental conditions conducive to transmission of infectious agents.[5,13] Poor environmental sanitation and poor hygienic practices might also increase exposure among poorer and less educated groups. Alternatively, SES may increase risk of infection and infectious illness because it alters the *body's ability to fight off infection.* For example, those with lower SES may lack information about vaccination, lack access to medical care, or be unable to afford vaccinations.[14] Vaccinations boost the immune system's ability to respond to specific infectious agents and hence reduce incidence and severity of illness. Inadequate nutrition among lower SES groups may also contribute to poorer host resistance. Malnutrition is known to suppress the immune system's ability to fight off infections and has been identified as a pathway linking poor children to disease risk.[3] Health practices that worsen with decreasing education are also thought to act as pathways linking SES to infectious susceptibility. For example, greater rates of smoking contribute to greater susceptibility to respiratory infectious illness among teenagers and adults,[1,15,16] whereas passive smoke exposure increases susceptibility among children.[16] Other health practices associated with increased risk of respiratory infection such as inadequate physical exercise and poor sleep quality are also more prevalent among those lower on the SES gradient.[15,17] Occupational exposure to immune-altering substances can also alter host resistance. For example, workers in occupations associated with low socioeconomic status have higher risk for tuberculosis, presumably because of higher occupational exposure to agents that increase the risk of progressing from latent infection to active TB.[18] Finally, lower levels of SES are associated with reporting more stressful life events,

TABLE 1. Pathways linking lower socioeconomic status to increased risk for infectious illness

Increased Exposure to Infectious Agents
greater crowding and family size
poorer sanitation
poorer hygienic practices
Decreased Host Resistance to Infection
less access to immunizing vaccinations
poorer nutrition
more smoking (passive and active)
more psychological stress

perceptions of stress, and negative affective states including depression and anger.[17] Greater stress and negative affect are risk factors for upper respiratory infections in community studies,[19,20] as well as in viral-challenge studies where exposure to the pathogenic agent is controlled.[21–23]

SES EFFECTS IN THE VIRAL-CHALLENGE MODEL

As discussed earlier, greater incidence of infectious illness among those with lower SES may be attributable to either greater exposure to infectious agents or to lower host resistance. In this article, we discuss three viral-challenge studies that investigated the role of SES in host resistance. In all three studies we use an upper respiratory disease model that allows us to experimentally control exposure to a virus and to monitor the development of both infection and clinical illness. In short, *after* characterizing subjects on markers of social status (as well as behavioral, endocrine, and immune factors), we inoculate them with an upper respiratory virus. After exposure they are closely monitored (in quarantine) for the development of infection and illness. There is considerable variability in response to these viruses in terms of both whether subjects become infected, and whether they express symptoms. This paradigm eliminates the possibilities that associations we find between social status and susceptibility are attributable to any of the following: *previous exposure* to the virus (we measure prechallenge antibody to the experimental virus); *differential exposure* to the virus (we expose subjects to controlled doses of the virus); or *illness-causing changes* in social status (we accept only healthy subjects into the trials and assess social status before viral exposure).

We will briefly discuss two studies with human subjects and one with nonhuman primates. The distributions of income, education, and occupational status in our human studies tend to be constrained and somewhat unrepresentative. Many of our volunteers have relatively low incomes, and about 30% are college students. Because the traditional markers of SES are not well represented in our samples, we have pursued other markers of SES as predictors of infectious illness. In the first (human) study, we examine under- and unemployment, and in the second (monkey) and third (human) studies we examine observed (monkeys) and perceived (humans) social status.

UNEMPLOYMENT AND SUSCEPTIBILITY TO CLINICAL COLDS

The data on unemployment derive from a study of 276 volunteers.[22] The major focus of the study was identifying the types of stressful life events that increased risk for infectious illness. We assessed life events before exposing volunteers to one of two rhinoviruses and then followed them for five days after exposure to monitor infection (viral shedding) and signs/symptoms (e.g., mucus weights, congestion) of the common cold. The major outcome in the study was clinical illness, which was defined as both infection by the challenge virus and expression of symptoms (see Ref. 22).

We used an interview, the Life Events and Difficulties Schedule[24] (LEDS), to assess the existence of enduring (one month or longer) and consensually threatening (agreement by judges) stressful events. Twenty-eight (9%) of the volunteers were identified as being unemployed or underemployed according to these criteria. (To simplify presentation, we will refer to this group as unemployed.) This is a different approach than just asking about employment status. For example, instead of treating all unemployed persons the same, the LEDS differentiates leaving an unsatisfying job because of lack of financial need (not coded as an unemployment stressor) from being fired following 20 years of dedicated and fulfilling service (coded as unemployment stressor).

The data were analyzed to determine whether unemployment predicted who developed clinical colds. The analyses included eight control variables that might provide alternative explanations for the relation between unemployment and colds. These included antibody to the experimental virus before inoculation, age, body mass index (weight in kilograms divided by height in meters^2), season (fall or spring), race (Caucasian or not), gender, education (high school graduate or less, some college, and bachelor's degree or greater), and virus type (RV39 or Hanks). The result indicated that even after accounting for all of these variables, those who were unemployed were 3.4 times ($p < 0.03$) more likely to develop colds than the remainder of the volunteers.

We also attempted to identify possible behavioral and biological pathways that might link unemployment to susceptibility. The analyses indicated that at least part of the association could be attributed to unemployed people smoking, having poorer sleep quality, and elevated levels of norepinephrine (a stress hormone).

SOCIAL STATUS AND SUSCEPTIBILITY TO INFECTION: THE MONKEY STUDY

Several years ago, we conducted a study in which the objective was to assess the roles of social stress and social status in susceptibility to upper respiratory infection.[23] Sixty male cynomolgus monkeys were randomly assigned to stable or unstable social conditions for fifteen months. Two markers of social status, social rank (based on who wins encounters with other animals) and percent of behaviors that were submissive, were assessed at independent observation periods. Social rank was assessed monthly, and submissive behaviors were measured during intensive monitoring of the animals' behavior during the 11th and 14th months of the study. Endocrine and immune responses were each assessed at three-month intervals. At the beginning of the 15th month, all animals were exposed to a virus (adenovirus) that causes a common cold-like illness. The primary outcome was whether or not an animal developed a biologically verifiable infection (shed adenovirus) following viral exposure.

Although the social stability manipulation was associated with increased agonistic behavior (as indicated by minor injuries) and elevated norepinephrine responses to social reorganizations, the manipulation did not influence the probability of being infected by the virus. However, low social status (as assessed by either rank or percent of behaviors that were submissive) was associated with a substantially greater

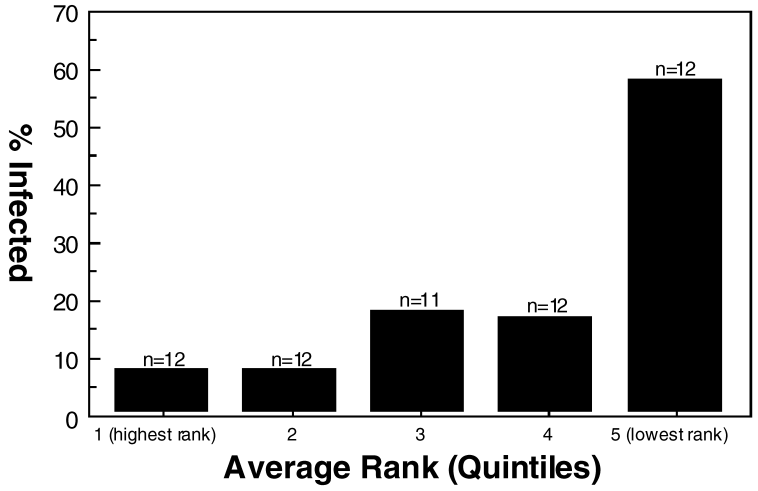

FIGURE 1. Percentage of animals infected by the virus presented by average social rank (quintiles); *1* refers to the highest rank and *5* to the lowest. Adapted from the original figure (see Ref. 23), with permission from the American Psychological Association.

probability of being infected. As apparent from FIGURE 1, although the association of social status and susceptibility was accounted for primarily by increased risk in the lowest social status groups, there was evidence for a graded relation with further increases in social status associated with further decreases in susceptibility. Lower social status was also associated with less body weight, greater elevated cortisol responses to social reorganizations, and less aggressive behavior. However, none of these characteristics could account for the relation between social status and infection.

SOCIAL STATUS AND SUSCEPTIBILITY TO INFECTION: THE HUMAN STUDY

The relationship between social status in the animals and susceptibility led us to consider the possibility that a similar relationship might occur in humans. However, it was not entirely clear how social status in monkeys (based on winning confrontations with other animals in their social group) might apply to humans. One possibility was that the traditional measures of SES—income, education, and occupational status—are the appropriate analogues in humans. However, these are all measures of status in relation to the larger society as opposed to the individuals' own social groups.[25] Instead, we used a measure of perceived social status in one's own community developed by the MacArthur Foundation's Network on Socioeconomic Status and Health. This measure is very simple to complete. The subject is presented

with the picture of a ladder with nine rungs and is asked to indicate (with an X) where they stand in their own community.

This study design was similar to the human study described earlier. One hundred and six subjects were administered the ladder as well as other psychological, behavioral, and biological measures. They were then exposed to a rhinovirus (RV23) and followed in quarantine for five days and monitored for the development of infection (viral shedding or fourfold increase in RV23 antibody titer). We have just begun to analyze these data. Our initial analyses focused on the association between perceived social status and infection. Control variables were the same as described in the previous study. The preliminary results were surprisingly similar to those of the monkey study. Lower perceived social status was associated with greater susceptibility to infection. This association was accounted for primarily by increased risk in the lowest social status groups. However, there was also evidence for a graded relation with further increases in social status associated with further decreases in susceptibility. Interestingly, perceived social status was not associated with smoking status, sleep efficiency, alcohol consumption, or exercise. Nor was it associated with circulating levels of catecholamines. Consequently, we currently do not have any evidence for a behavioral or biological pathway linking perceived status to susceptibility to infection.

CONCLUSIONS

We have provided evidence from three prospective studies for the relation between markers of SES and susceptibility to upper respiratory infectious illness. This includes a substantial association between unemployment and greater susceptibility. Unemployment has been associated with a broad range of disease risk in past studies,[26] and documenting its relation to host resistance to infection further justifies the centrality of work in our lives and the magnitude of stress generated when we lose our livelihood. We have also found provocative evidence in regard to the relation of social status and host resistance to infectious disease. This includes greater susceptibility among monkeys who tend to lose encounters with other animals and people who rate themselves as having relatively lower status in their own communities. Although it is those of the lowest social status who are at greatest risk, for both monkeys and man there is some evidence for a graded relation with increased status associated with less risk. This work raises many interesting questions that have not yet been addressed. For example, to what degree is perceived social status a function of traditional measures of SES such as income, education, and occupational status? To what degree does it reflect components of status among one's own social network that are not highly correlated with traditional measures? To what degree is it a biased report reflecting dispositional characteristics such as neuroticism or depression? What are the pathways that link social status (real or perceived) to susceptibility to infectious agents? Does it operate through stress and stress hormones or through other biological or behavioral concomitants of social status?

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