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From: Lloyd Etheredge lloyd.etheredge@policyscience.net>

Subject: An NIH Cross-Institute Rapid Discovery Project: Marmot, Neuroscience, and the Primate Subordination Syndrome Hypothesis

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Dear Dr. Lauer (and Colleagues):

I write in your leadership and planning capacity for NIH-wide initiatives and also in response to your editorial in <u>JAMA</u>. In the editorial you discussed the research challenge that "Despite 50 years of epidemiologic knowledge and despite numerous therapeutic advances, risk factors among minority populations are unacceptably high and consequential" (and the <u>Los Angeles Times</u> headlined its news story: "Blacks Twice as Likely to Die of Coronary Disease as Whites"). I write to suggest a cross-Institute rapid learning project, partly arising from my areas of public policy work in the social sciences, that may be relevant to these challenges and other difficult societal and behavioral problems within the purview of NIH.

Connecting the Dots: A Primate Subordination Syndrome?

Several years ago it occurred to me that a new connect-the-dots theory of a <u>Primate Subordination Syndrome</u>, emerging from new neuroscience investigations, could explain an unrecognized causal pathway for a range of effects observed in unsolved public policy problems in lower status human populations. In other primates an inherited brain mechanism, activated by social dominance hierarchies, appears to cause a package of motivational, stress, endocrine, postural, and health effects and (perhaps) other effects. In human brains, the activating and sustaining pathways would likely be hierarchical dramas of identity and to involve the visual cortex. I enclose a copy of a review article in <u>Science</u> by Sapolsky touching on some of this emerging evidence.

Associated Predictions

- A network of observed public health links also could be explained by this model. A strong, hierarchical experience of a relationship to a loving God might, for example, be one of the pathways by which strong traditional religious faith (e.g., in Judaism and/or Christian religious fundamentalism) provides a prevention and empowerment function. If it becomes a central drama of identity, it may thereby provide protection from the lower status effects in secular reality. Similar preventive effects may operate, via disabling this social subordination pathway, in Buddhism.
 - -I also enclose a brief summary diagram from the classic psychoanalytic study by Kardiner and

Ovesey, <u>The Mark of Oppression (1951)</u>. They suggested a brain/behavioral syndrome that, today, might be established by direct neuroscience measurement as the <u>Primate Subordination Syndrome</u>.

The Possibility of Societal Learning and Evidence-Based Dialogue

In America, Republicans tend to explain motivational and other effects associated with problems of social, economic, and political participation and education attainment in lower status populations, as effects of a dependency syndrome induced by an overly benevolent government and welfare state. [Part of the moral commitment of leaders like Governor Romney or President Reagan is their belief that they, too, are fighting for strong, healthy, self-starting individuals.] The theory of a <u>Primate Subordination Syndrome</u> suggests that these causal views are a misinterpretation. However, as there also are shared commitments to strong, healthy, self-starting individuals, a productive, evidence-based dialogue could emerge for the country. Also, once brain and other pathways are clarified, new and straightforward (biological and other) solutions may be invented that assist minority and other affected populations..

Collaboratory Database Requirements

An NIH cross-Institute project would be hard work, and require the development and validation of new measures. Breakthroughs also may require including relevant neuroscience measures and data in NIH Collaboratory records. However, this would be exciting and possibly transformational research. with rapid benefits in the US minority populations [cited by Dr. Lauer] with unexplained and unprevented additional health problems. Worldwide, discrimination is ubiquitous and NIH research could expand a sense of shared humanity, and be a catalyst to remove some of these barriers to human potential on a wider scale.

Big Data Puzzles

I understand that Kaiser is finding that its "dual eligible" populations - i.e., that are the most likely to reflect a lower status/Primate Subordination Syndrome sense of their place in society - do not respond to their standard medical treatments in the same way as other populations with the same diagnoses. If NIH Collaboratory databases quickly confirm this, the discovery also suggests that an unrecognized, shared causal mechanism (consistent with Marmot's investigations) may be at work in lower status/minority populations and that the predicted existence of a Primate Subordination Syndrome would be worth evaluating as an explanation of these observations and additional causal pathways affecting public health.

With my best regards,

Lloyd Etheredge

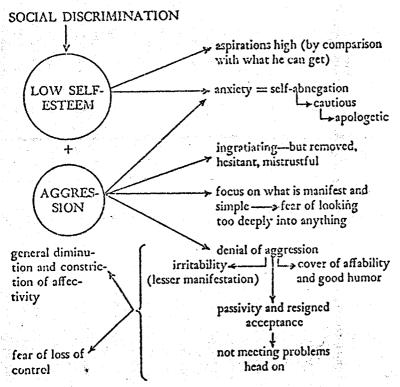
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from Abraham Kardener & Janel Overey, The Mark ! Oppression; 9.303

PSYCHODYNAMIC INVENTORY OF NEGRO PERSONALITY

because the individual, in order to maintain internal balance and to protect himself from being overwhelmed by it, must initiate restitutive maneuvers in order to keep functioning—all quite automatic and unconscious. In addition to maintaining an internal balance, the individual must continue to maintain a social façade and some kind of adaptation to the offending stimuli so that he can preserve some social effectiveness. All of this requires a constant preoccupation, notwithstanding the fact that these adaptational processes all take place on a low order of awareness. The following is a diagram of a typical parallelogram of forces:



In the center of this adaptational scheme stand the low self-esteem (the self-referential part) and the aggression (the reactive part). The rest are maneuvers with these main constellations, to prevent their manifestation, to deny them and the sources from which they

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The Influence of Social Hierarchy on Primate Health

Robert M. Sapolsky

Dominance hierarchies occur in numerous social species, and rank within them can greatly influence the quality of life of an animal. In this review, I consider how rank can also influence physiology and health. I first consider whether it is high- or low-ranking animals that are most stressed in a dominance hierarchy; this turns out to vary as a function of the social organization in different species and populations. I then review how the stressful characteristics of social rank have adverse adrenocortical, cardiovascular, reproductive, immunological, and neurobiological consequences. Finally, I consider how these findings apply to the human realm of health, disease, and socioeconomic status.

ne of the greatest challenges in public health is to understand the "socioeconomic gradient." This refers to the fact that in numerous Westernized societies, stepwise descent in socioeconomic status (SES) predicts increased risks of cardio-vascular, respiratory, rheumatoid, and psychiatric diseases; low birth weight; infant mortality; and mortality from all causes (1–4). This relation is predominately due to the influence of SES on health, rather than the converse, and the disease incidences can be several times greater at the lower extreme of the SES spectrum.

One set of questions raised by the gradient concern its external causes. Despite human aversion to inequity in some settings (5), many Westernized societies tolerate marked SES gradients in health care access. Is this the predominant cause of the health gradient, or is it more a function of differences in lifestyle risk factors or of the psychosocial milieu in which poverty occurs?

Another set of questions concern the physiological mediators of the SES-health relationship—how, in a frequently used phrase in the field, does poverty get under the skin? These physiological questions are difficult to study in humans, and an extensive literature has focused instead on nonhuman animals. Despite the demonstration that some nonhuman species can also be averse to inequity (6), groups of social animals often form dominance hierarchies, producing marked inequalities in access to resources. In such cases, an animal's dominance rank can dramatically influence the quality of its life. Does rank also influence the health of an animal?

The study of rank-health relations in animals has often been framed in the context of stress

Departments of Biological Sciences, Neurology and Neurological Sciences, Stanford University, MC 5020, Stanford, CA 94305–5020, USA, and Institute of Primate Research, National Museums of Kenya. E-mail: sapolsky@stanford.edu and the idea that animals of different ranks experience different patterns of stress (Fig. 1). A physical stressor is an external challenge to homeostasis. A psychosocial stressor is the anticipation, justified or not, that a challenge to homeostasis looms. Psychosocial stressors typically engender feelings of lack of control and predictability and a sense of lacking outlets for the frustration caused by the stressor. Both types of stressor activate an array of endocrine and neural adaptations (Fig. 2). When mobilized in response to an acute physical challenge to homeostasis (such as fleeing a predator), the stress response is adaptive, mobilizing energy to exercising muscle, increasing cardiovascular tone to facilitate the delivery of such energy, and inhibiting unessential anabolism, such as growth, repair, digestion, and reproduction. Chronic activation of the stress response by chronic psychosocial stressors (such as constant close proximity to an anxiety-provoking member of one's own species) can increase the risk of numerous diseases or exacerbate such preexisting diseases as hypertension, atherosclerosis, insulin-resistant diabetes, immune suppression, reproductive impairments, and affective disorders (7).

In most social species, dominance rank influences the extent to which an individual sustains physical and psychosocial stressors. Thus, dominance rank can potentially influence an individual animal's vulnerability to stress-related disease. In this review, I first consider which social ranks are most stressful, with an emphasis on nonhuman primates; stress can be experienced by both high- and low-ranking animals, and it varies as a function of the social organization in different species and populations. I then review the pathology that occurs in animals suffering from the most rank-related social stress. Finally, I consider the relevance of these hierarchy/health relationships to humans.

Which Ranks Are More Stressful?

No consensus exists as to whether dominant or subordinate animals are more physiologically "stressed." Research in the 1950s, since discredited, argued that high rank was more physiologically stressful (that is, the "executive stress syndrome," which was purportedly valid for both humans and other primates) (8). By the 1960s, the prevailing view had become that lower dominance rank carries the greatest risk of stress-related disease (9). It has now become clear that this too is an incorrect generalization. The contemporary view reflects the heterogeneity that is the core of ethology: Rank means different things in different species and populations. Patterns that occur amid this heterogeneity help to resolve many inconsistencies in the data, showing that the rank that experiences the most physical and psychological stressors tends to display the most severe stress-related pathologies (Fig. 2).

Resource inequity. The extent to which resources are divided unequally among individuals varies as a function of the dominance style of different species. At one extreme are top-down "despotic" hierarchies in which resource access is skewed markedly and dominant positions are attained through aggression and intimidation. In contrast, bottom-up "egalitarian" hierarchies have more equal resource distribution, and dominance is attained with the support of subordinate individuals (10). As will be seen, social subordination in despotic species can be associated with the greatest physiological indices of stress. In contrast, this is not a feature of subordination in egalitarian species.

Maintenance of dominance. In some species, rank is lifelong and inherited (for example, in female rhesus monkeys); in others, it may fluctuate, reflecting what has been aptly termed shifts in group "politics" (11). In species where ranks shift, how does an individual, once attaining a high rank, maintain it? At one extreme among species with despotic hierarchies, high-ranking individuals frequently and aggressively reassert their domination over the subordinate cohort (even in the absence of an overt challenge). In such species, which include dwarf mongooses, African wild dogs, and ring-tailed lemurs, dominant individuals have the greatest physiological indices of stress, most plausibly reflecting the physical demands of frequent fighting (12, 13). In contrast, in other

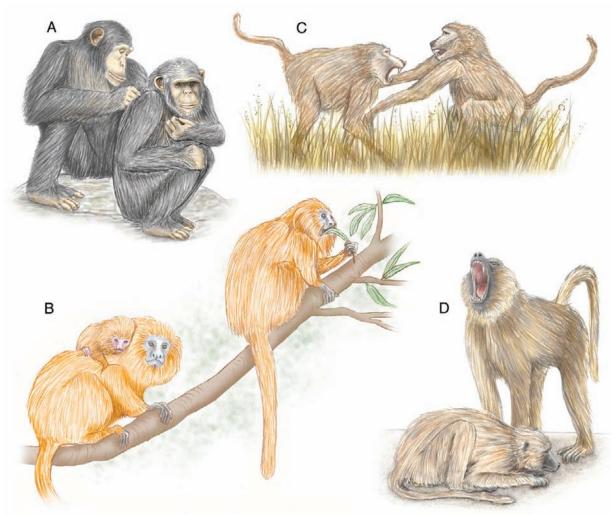


Fig. 1. (A and B) Affiliative behavior among subordinates can reduce the effects of stress. (A) Chimpanzees engage in social grooming. (B) A female tamarin monkey cares for another's young while the mother feeds. (C and D) Stressful dominance behavior may take physical or psychosocial forms. (C) Male savanna baboons may fight over a kill. (D) A dominant male baboon intimidates a subordinate. [Image credit: Carin Cain/Science]

despotic species, high-ranking individuals maintain dominance through psychological intimidation rather than aggression (where, for example, mere eye contact with the alpha individual might elicit subordination gestures). In such cases (e.g., savanna baboons, rhesus and squirrel monkeys, mice, rats, and white-throated sparrows), subordination is associated with the greatest physiological indices, plausibly reflecting the frequent psychological stressors for subordinates and the paucity of physical stressors for dominant individuals (12–18).

Breeding style. In many species, including some Old World primates, dominant alpha individuals of both genders monopolize breeding through aggression and intimidation. This can be sufficiently stressful to impair fertility in subordinates, producing "social contraception." A different picture occurs in cooperative breeders, where one breeding female dominates other females, who are anovulatory. However, this subordination is minimally stressful, not involving aggression or harassment by the dominant female. Instead,

the anovulatory individuals are mostly younger sisters, waiting their turn to breed and helping to raise nieces and nephews (19). Among cooperative breeders such as marmosets, ring-tailed lemurs, marmots, wolves, and Florida scrub jays, subordinates show no more stress-related pathophysiology than do dominant individuals and may even have fewer indices (13, 19–21).

Stability of social ranks. When the hierarchy is stable in species where dominant individuals actively subjugate subordinates, it is the latter who are most socially stressed: this can particularly be the case in the most extreme example of a stable hierarchy, namely, one in which rank is hereditary. This reflects the high rates of physical and psychological harassment of subordinates, their relative lack of social control and predictability, their need to work harder to obtain food, and their lack of social outlets such as grooming or displacing aggression onto someone more subordinate. During major hierarchical reorganization, however, dominant individuals at the center of the social tensions typically experience the greatest amounts of physical and

psychological stress. As a result, during such reorganization among wild baboons or soon after group formation among species of captive primates, dominant individuals have the greatest physiological indices of stress; this has been shown in talapoin monkeys, squirrel monkeys, various macaque species, wild baboons, and chimpanzees. Once hierarchies stabilize, subordination becomes associated with the greatest physiological indices of stress (22).

Subordinate coping strategies. Stress-related physiological endpoints not only reflect the frequency and severity of stressors but also the availability and efficacy of coping outlets. Such outlets most commonly involve social support (such as grooming, physical contact, or coalition formation). Moreover, the occurrence in some species of reconciliative behaviors between two individuals shortly after a competitive interaction can be interpreted as a coping outlet for the loser of that interaction (23). The issue of coping outlets has been examined in a meta-analysis of rank-physiology relationships in both genders of an array of primate species.

Numerous variables related to social structure were considered, and three were collectively highly predictive of the occurrence of elevated stress hormone levels among subordinate animals: (i) high rates of being subjected to stressors; (ii) low availability of social support; and (iii) minimal presence of kin (24).

Subordinate avoidance of dominants. The inability to physically avoid dominant individuals is associated with stress, and the ease of avoidance varies by ecosystem. The spatial constraints of a two-dimensional terrestrial habitat differ from those of a three-dimensional arboreal or aquatic setting, and living in an open grassland differs from living in a plain dense with bushes. As an extreme example, subordinate animals in captivity have many fewer means to evade dominant individuals than they would in a natural setting (25). Thus, although dominant wolves have elevated stress hormone levels in the wild (21), subordinates demonstrate this trait in captivity (26).

Subordinants' use of alternative strategies. Implicit in being subordinate are the notions that one has reduced access to desirable resources and that this can translate into reduced Darwinian fitness. Sometimes, however, subordinate animals can pursue alternative behavioral strategies that, in effect, move them outside the hierarchy. For example, low rank among males of various Old World monkey species, as the result of male-male competition, has been thought to mean minimal reproductive access to females. However, females actually have considerable control over who they mate with. These are often low-ranking individuals with whom they have affiliative relationships (such as

Brain

Dendritic atrophy, impaired neurogenesis

frequent, nonsexual bouts of reciprocal grooming) (27). Such males not only have greater reproductive success than originally thought but also fewer physiological indices of stress than would be expected for their rank (28).

A different alternative strategy occurs among orangutans. Dominant males have pronounced secondary sexual characteristics, whereas subordinate individuals appear "juvenile." This appearance is not merely a chronological stage. Instead, it is a state of arrested development in the presence of a dominant male and can persist for years. When the dominant male is removed, the apparently juvenile individual develops secondary sexual traits. This arrested state might seem to be a case of stress-induced social contraception. However, "juvenile" males are fertile, have some reproductive success (as they will force copulations when a dominant male is absent), and do not have elevated stress hormone levels or stressrelated reproductive impairments. Rather than a stress-induced pathology, the arrest appears to be an alternative strategy. It is actually males in the process of the conspicuous, slow transition to the dominant form with the most marked physiological indices of stress (29).

Stress of dominating mating. In species with a sharply demarcated mating season, or where a few males disproportionately dominate mating, male-male competition for mating access can be fierce, dangerous, and at the cost of feeding and of affiliative behaviors. This raises the ironic possibility that dominant males may be sufficiently stressed by such competition that their testicular axes are suppressed. However, various endocrine mechanisms have evolved

that buffer reproductive physiology under that circumstance, either through blunting the release of stress hormones or blunting their ability to suppress the testicular system (30).

Atmosphere and culture. The nature of dominance varies with species and gender. Additionally, different populations of a species vary in their social milieu, and rank-physiology relationships can vary as well. For example, patterns of foraging by subordinate female spotted hyenas differ markedly between the enclosed Ngorongoro Crater and the open Serengeti Plains in East Africa, and only in the latter is subordination associated with elevated stress hormone levels (31). As another example, the elevated stress hormone levels observed among subordinate female macaques do not occur in a troop with atypically high rates of affiliative support (32, 33). In the realm of animal "culture," multigenerational transmission of a culture of low aggression and high affiliation in a troop of wild baboons results in subordinate males that do not display the stress-related pathophysiology found in other troops (34).

Personality. Precedent exists for modulation of stress reactions by individuals' personalities. For example, independent of rank, primates who distinguish poorly between threatening and neutral stimuli, lack social outlets for support, and are hyperreactive to novelty have elevated stress hormone levels (35, 36) and increased rates of atherosclerosis (37).

Thus, under a variety of circumstances, social dominance can be associated with the most stress-related pathology, whereas in other situations, this is a trait of subordinate individuals. Are there common themes underlying this variability? Broadly and logically, adverse physiological profiles are most pronounced among animals of the rank exposed to the most physical and psychological stressors. This can arise from (i) low degrees of social control and predictability (as in dominant animals in unstable hierarchies and subordinate animals in small living spaces); (ii) a paucity of outlets after exposure to stressors (such as subordinate individuals in species lacking alternative strategies to hierarchical competition); (iii) a paucity of social support (for example, subordinate animals in settings with few kin and little access to social grooming); or (iv) high rates of physical stressors (such as dominant individuals who, as a function of their species or the instability of their hierarchy, must constantly reassert their dominance by physical means). Moreover, these links between rank and pathology can be made even more dramatic by the culture of a particular social group and by a personality prone toward interpreting ambiguous social circumstances as psychologically stressful.

and synaptic plasticity, enhanced benzodiazepine tone **Immune System** Basal immunosuppression and decreased immune responsiveness to challenge Heart Basal hypertension, sluggish response to and recovery from stress, pathogenic **Adrenal Gland** cholesterol profile Elevated basal levels of glucocorticoids sluggish response to and recovery from stress, feedback resistance Ovary Decreased levels of gonadal 0 Testis hormones, increased risk of Testicular atrophy, decreased levels anovulation and miscarriage of hormones of the gonadal axis

Fig. 2. Physiological correlates of the more stressful social rank. [Image credit: Bayard Colyear, Stanford Visual Arts Services]

Negative Physiological Effects of Stressful Social Ranking

Studies of both feral and captive animal populations show that animals with specific

dominance ranks tend to show characteristic stress-related physiological profiles (Table 1). We know that a particular rank gives rise to a particular physiological profile, rather than visa versa, because studies of individual captive animals before they are placed in social groups indicate that physiological profiles of singly-housed subjects do not predict their subsequent ranks in a social group (38).

Several stress-related physiological endpoints have been found to be sensitive to rank. The most frequently studied endpoint is the blood level of glucocorticoids (GCs), adrenal steroid hormones that are secreted during stress, such as cortisol or hydrocortisone in primates and corticosterone in many rodent species. GCs typify the double-edged nature of the stress response, as they help mediate adaptation to short-term physical stressors yet are pathogenic when secreted chronically.

Consistently, animals who are more socially stressed by the dominance hierarchy show indices of hyperactivity of the GC system. This includes elevated basal levels of GCs, the enlarged adrenal glands that accompany such increased secretion, a sluggish GC stress response in the face of a major homeostatic challenge, and impaired sensitivity of the system to negative feedback regulation.

In some cases, it is dominant individuals who show this profile. This includes species where dominant individuals have to repeatedly and physically reassert their rank (e.g., feral populations of dwarf mongooses, African wild dogs, female ring-tailed lemurs, and male chimpanzees) (12, 13, 39); those that are cooperative breeders (feral wolves and captive marmosets and tamarins) (16, 21); and those with transient periods of major rank instability (feral baboons and captive populations of talapoin, squirrel, and rhesus monkeys) (22).

In contrast, this profile is seen among subordinate individuals in species where high rank is maintained through nonphysical intimidation and the hierarchy is stable (feral male baboons and captive populations of squirrel and rhesus monkeys, tree shrews, rats, and mice) (22, 40, 41); where subordinates are exposed to frequent social stressors amid low availability of social support and minimal presence of kin (feral ring-tailed lemurs and captive populations of male rhesus or female talapoin monkeys) (13, 24); and when animals are in an enclosure too small to allow subordinate individuals to eyade dominant ones (26).

A second prominent feature of the stress response is secretion of the catecholamine hormones (epinephrine and norepinephrine). These hormones of the sympathetic nervous system are secreted within seconds of the onset of a stressor (versus minutes for GCs) and have many of the same effects as GCs upon metabolism and cardiovascular tone. Thus, as with GCs, although the acute secretion of catecholamines is adaptive, prolonged secretion can be pathogenic. The

speed with which catecholamines are secreted typically precludes measuring basal circulating levels (because of the stress caused by the restraint of subjects for taking blood samples), and the hormones are poorly and variably preserved in urine and feces. Thus, little is known about rank-catecholamine relationships.

Prolonged stress adversely affects cardiovascular function, producing (i) hypertension and elevated heart rate; (ii) platelet aggregation and increased circulating levels of lipids and cholesterol, collectively promoting atherosclerotic plaque formation in injured blood vessels; (iii) decreased levels of protective high-density lipoprotein (HDL) cholesterol and/or elevated levels of endangering low-density lipoprotein (LDL) cholesterol; and (iv) vasoconstriction of damaged coronary arteries. A small literature demonstrates that animals who are more socially stressed by the dominance hierarchy demonstrate (i) basal hypertension; (ii) a sluggish activation of the cardiovascular stress response after a challenge and delayed recovery when it abates; (iii) a pathogenic cholesterol profile; and (iv) increased vulnerability to the atherogenic effects of a highfat diet. These are traits of subordinate individuals when the dominance hierarchy is stable (among captive fascicularis macaques of both genders and among feral male savanna baboons) but of dominant individuals of the same populations when the hierarchy is unstable (37, 42, 43).

Chronic stress inhibits reproduction in both genders, a classic example of stress suppressing a costly anabolic process until more auspicious times. In females, this suppression can take the

form of delayed puberty, decreased levels of estrogen and progesterone, increased incidence of anovulatory cycles, impaired implantation, greater risk of miscarriage, prolonged interbirth intervals, and accelerated reproductive senescence. Primate studies show that the stress of subordination in a stable hierarchy (of cynomolgus monkeys) is associated with decreased gonadal hormone levels (42); there are conflicting data as to whether dominance or subordination in stable hierarchies of feral baboons is associated with higher rates of miscarriage (44, 45).

Among males, prolonged and major stress can suppress fertility; at an extreme in teleost fish, this includes atrophy of testes and of hypothalamic regions responsible for gonadotropin release (46). More commonly, stress can suppress circulating testosterone levels (9). However, there are many exceptions, as numerous species are resistant to this effect when the stressor is male-male competition during mating seasons; moreover, it is not clear how often these lower testosterone levels actually affect behavior or fertility. There is no consensus as to whether more socially stressed individuals have lower basal testosterone levels. However, such individuals (in this case, subordinate male baboons in a stable hierarchy) are more vulnerable to the suppressive effects of stress on basal testosterone levels (9).

Stress has complex time- and severity-dependent effects upon immunity. In general, mild to moderate transient stressors enhance immunity, particularly the first phase of the immune response, namely innate immunity. Later

Table 1. Influence of societal characteristics on stress experienced by high- and low-ranking individuals. An asterisk indicates no rank-related trend.

individuals. An asterisk indicates no rank-related trend.		
		ndividuals experiencing the most stress
Domir	nance style and means of maintaining despotic don	ninance
Despotic hierarchy maintained through frequent physical reassertion of dominance		High-ranking
Despotic hierarchy maintained through intimidation Egalitarian hierarchy		Low-ranking *
8	Style of breeding system	
Cooperative Competitive	-9,	High-ranking *
	Stability of ranks	
Unstable Highly stable	· · · · · · · · · · · · · · · · · · ·	High-ranking Low-ranking
0)	Availability of coping outlets for subordinates	· ·
High availability Low availability		* Low-ranking
	se with which subordinates avoid dominant individ	
Easy avoidance		*
Difficult avoidance		Low-ranking
Av	railability of alternative strategies to overt competi	
Present		*
Lacking	Personality	Low-ranking
Dominants perceive neutral interactions as challenging; subordinates take advantage of coping strategies		High-ranking
Dominants are adept at exerting social control and highly affiliative; subordinates are poor at exploiting opportunities for coping and support		Low-ranking

phases of the stress response are immunosuppressive, returning immune function to baseline. Should the later phase be prolonged by chronic stress, immunosuppression can be severe enough to compromise immune activation by infectious challenges (47, 48). In contrast, a failure of the later phase can increase the risk of the immune overactivity that constitutes autoimmunity. No studies have examined rank differences in the first immunostimulatory phase of the stress response or in the risk of autoimmunity if the later suppressive stage fails to occur. However, suppression of circulating lymphocyte numbers and blunted immune responsiveness to a challenge have been reported among animals socially stressed by a dominance hierarchy (subordinate rodents and pigs subject to high rates of attack and dominant chimpanzee males in an unstable captive population). Less clear is whether such rank effects are of sufficient magnitude to actually increase the risk of infectious disease (47, 49).

Animals who are socially stressed by the dominance hierarchy for prolonged periods undergo neurobiological changes as well. This can involve inhibition of neurogenesis, dendritic atrophy, and impairment of synaptic plasticity in the hippocampus (50, 51) and altered patterns of apoptotic cell death (increases in the cortex and decreases in the hippocampus) (52); these pathologies have been observed in socially subordinate rodents and tree shrews in stable hierarchies in captive populations.

Finally, a socially stressful position in a hierarchy is also associated with alterations in the neurochemistry of anxiety. Receptors exist in the nervous system for the antianxiety benzodiazepines (BDZs), which include the synthetic molecules diazepam and chlordiazepoxide hydrochloride as well as an as-yet uncharacterized endogenous BDZ. Pharmacological blockade of BDZ receptors caused the greatest disinhibition of anxietyrelated behaviors in subordinate males in a stable hierarchy among feral baboons (34). This rank difference was interpreted as reflecting the demands for anxious vigilance among such individuals, necessitating a greater counteracting effect of endogenous BDZ tone.

Human Hierarchies and Health

The literature reviewed raises the obvious question: Are these findings relevant to humans? Initially, they seem to be of minimal relevance. Humans are not hierarchical in the linear, unidimensional manner of many species. For example, humans belong to multiple hierarchies and tend to value most the one in which they rank highest (for example, a low-prestige employee who most values his role as a deacon in his church). Furthermore, the existence of internal standards makes humans less subject to the psychological consequences of rank. Finally, health-rank relations that are easy to study can be highly artificial (e.g., ex-

amining the physiological consequences of winning versus losing an athletic competition).

Despite these caveats, the SES gradient of health among Westernized humans is a robust example of social inequalities predicting patterns of disease. As mentioned earlier, stepwise descent in SES predicts a major increase in the incidence of an array of diseases and mortality (1–4).

These health effects of SES are not a result of poverty causing limited access to health care. Robust SES-health gradients exist in countries with universal health care and documented equality of access. In addition, gradients exist for diseases with incidences that are impervious to preventative health measures (e.g., juvenile diabetes) (2, 3).

Only a small portion of the SES-health relationship is due to SES-related life-style differences. In Westernized societies, lower SES is associated with higher rates of smoking and drinking to excess, less healthy diets, more sedentary life-styles, crime- and toxin-riddled communities, and fewer coping outlets (e.g., health club memberships and vacations). However, the most prominent of these factors collectively account for only a small part of the variability in the SES-health gradient (3).

Instead, increasing evidence suggests that the gradient arises from psychosocial factors. Subjective SES can be at least as predictive of health as is objective SES (1); in other words, feeling poor may be at the core of why being poor predicts poor health. In the United States, at the level of states or cities, the same low SES predicts poorer health in communities with greater income inequality (4). Whereas large inequalities decrease the availability of protective lifestyle factors for the poor in a community (what has been termed a "neomaterialist" explanation for the inequality-health relationship) (53), the disease consequences of feeling poor are often rooted in the psychosocial consequences of being made to feel poor by one's surroundings (4). Increased income inequality typically decreases a community's "social capital" (shown in decreased levels of trust and increased senses of alienation and disenfranchisement), and such decreased capital mediates the relationship between income inequality and health (2).

Conclusions

Strong associations between social status and health thus occur in numerous species, including humans, with the poor health of those in the "wrong" rank related to their surfeit of physical and psychosocial stressors. In considering these issues in nonhuman species, the variability, qualifiers, and nuances of the rank-health relationship are frequently emphasized, a testament to the social complexity of other species. In contrast, in humans, there is a robust imperviousness of SES-health associations to differences in social and economic systems. It is not plausible that this human/nonhuman contrast re-

flects human sociality being less complex than in, say, baboons. Instead, it is a testimony to the power of humans, after inventing material technology and the unequal distribution of its spoils, to corrosively subordinate its have-nots.

References and Notes

- 1. N. Adler et al., Health Psychol. 19, 586 (2000).
- I. Kawachi, B. Kennedy, The Health of Nations: Why Inequality Is Harmful to Your Health (New Press, New York, 2002).
- 3. J. Siegrist, M. Marmot, Soc. Sci. Med. 58, 1463 (2004).
- 4. R. Wilkinson, *Mind the Gap: Hierarchies, Health, and Human Evolution* (Weidenfeld and Nicolson, London, 2000).
- E. Fehr, B. Rockenbach, Curr. Opin. Neurobiol. 14, 784 (2004).
- 6. S. Brosnan, F. de Waal, Nature 425, 297 (2003).
- 7. R. Sapolsky et al., Endocr. Rev. 21, 55 (2000).
- 8. J. Brady et al., J. Exp. Anal. Behav. 1, 69 (1958).
- 9. R. Sapolsky, Psychoneuroendocrinology 16, 281 (1991).
- B. Thierry, M. Singh, W. Kaumanns, Eds., Macaque Societies: A Model for the Study of Social Organization (Oxford Univ. Press, New York, 2004).
- F. de Waal, Chimpanzee Politics: Power and Sex Among Apes (Johns Hopkins Univ. Press, Baltimore, MD, 1983).
- 12. S. Creel et al., Nature **379**, 212 (1996).
- 13. S. Cavigelli, Anim. Behav. 57, 935 (1999).
- 14. R. Sapolsky, Biol. Psychiatry 28, 862 (1990).
- F. Bercovitch, A. Clarke, *Physiol. Behav.* 58, 215 (1995).
 D. Abbott *et al.*, *Comp. Biochem. Physiol. C* 119, 261 (1998).
- D. Davis, J. Christian, *Proc. Soc. Exp. Biol. Med.* 94, 728 (1957).
- 18. K. Manogue et al., Primates 16, 457 (1975).
- 19. D. Abbott et al., Comp. Biochem. Physiol. C 119, 261 (1998).
- 20. S. Schoech et al., Physiol. Zool. **70**, 68 (1997).
- 21. J. Sands, S. Creel, Anim. Behav. 67, 387 (2004).
- R. Sapolsky, in *Primate Social Conflict*, W. Mason, S. Mendoza, Eds. (SUNY Press, New York, 1993), pp. 171–183.
- 23. F. de Waal, Science 289, 586 (2000).
- 24. D. Abbott et al., Horm. Behav. 43, 67 (2003)
- 25. S. Creel, Trends Ecol. Evol. 16, 491 (2001).
- 26. P. McLeod et al., Can. J. Zool. 74, 209 (1996).
- 27. B. Smuts, Sex and Friendship in Baboons (Harvard Univ. Press, Princeton, NJ, 1999).
- C. Virgin, R. Sapolsky, Am. J. Primatol. 42, 25 (1997).
 A. Maggioncalda et al., Am. J. Phys. Anthropol. 118, 25 (2002).
- 30. J. Wingfield, R. Sapolsky, J. Neuroendocrinol. 15, 711 (2003).
- 31. W. Goymann et al., Horm. Behav. 43, 474 (2003).
- 32. D. Gust et al., Brain Behav. Immun. 5, 296 (1991).
- B. Wallner, in *The Integrative Neurobiology of Affilia*tion, C. Carter, B. Kirkpatrick, I. Lederhendler, Eds. (New York Academy of Science, New York, 1996), pp. 45–51.
- 34. R. Sapolsky, L. Share, *PLoS Biol.* 2, E106 (2004).
- 35. C. Virgin, R. Sapolsky, Am. J. Primatol. 42, 25 (1997).
- 36. J. Ray, R. Sapolsky, Am. J. Primatol. 28, 231 (1992).
- 37. S. Manuck et al., Psychosom. Med. 57, 275 (1995). 38. D. Morgan et al., Am. J. Primatol. 52, 115 (2000).
- 39. N. Masataka, Ethology 85, 147 (1990).
- 40. S. Barnett, Nature 175, 126 (1955).
- 41. J. Eberhart, Physiol. Behav. 30, 361 (1983).
- 42. C. Shively, T. Clarkson, Arterioscler. Thromb. 14, 721 (1994).
- 43. R. Sapolsky, L. Share, Am. J. Primatol. 32, 261 (1994).
- 44. C. Packer et al., Nature **373**, 60 (1995). 45. I. Altmann et al., Nature **377**, 688 (1995).
- 46. M. Fox, R. Andrews, *Behaviour* **46**, 129 (1973).
- R. Ader et al., Psychoneuroimmunology (Academic Press, San Diego, CA, 2001), ed. 3.
- 48. S. Cohen et al., Psychosom. Med. 59, 213 (1997).
- F. Dhabhar, B. McEwen, Proc. Natl. Acad. Sci. U.S.A. 96, 1059 (1999).
- 50. Y. Kozorovitskiy, E. Gould, J. Neurosci. 24, 6755 (2004).
- 51. A. Magarinos *et al.*, *J. Neurosci.* **16**, 3534 (1996).
- 52. P. Lucassen et al., Eur. J. Neurosci. 14, 161 (2001).
- 53. J. Lynch et al., Milbank Q. 82, 5 (2004).
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PRESIDENT REAGAN'S COUNSELING

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For decades, economic policy has been the territory of economists, governed by their idea that we are a nation of rational choices. President Reagan has changed the assumptions. He is using ideas familiar to psychoanalysts and clinical psychologists to diagnose the problems of the American economy and design a course of treatment. He has posed a set of problems which political psychologists can solve with great benefit to the intelligence of national policy.

The President's idea is simple. He says our economy's lack of vitality is produced because government has become a powerful, substantial presence "above" us here in America. Over the past thirty years as, in our national imagination, government became "bigger," we grew subjectively smaller to develop a national dependence. There was a "zero-sum" effect on each person's mind: as "it" (government) assumed more responsibility in national life, "we" (the people) took less. The work ethic disintegrated; productivity increases stopped; the economy stalled.

The President's economic policy follows logically. It is intellectually serious and urgent: he must provide national psychotherapy for a depressed, passive nation that expects its therapist to have a prompt and magical solution.

To effect the change he desires, our President-psychiatrist has designed a national psychodrama to inspire us, to create open space, and to reduce our idealized illusions. He is warm and supportive. He is cutting taxes and expenditures to make government above us "smaller." It may not be a cure we like, and there will be painful withdrawal symptoms, but we must again take responsibility for our own lives.

From personal experience, Dr. Reagan knows he is right. The dire predictions of his theory, made thirty years ago, appear correct to him. And in his autobiography, Where's the Rest of Me?, he sketches how he, too, was once dependent, in his case on the Hollywood studio system. He was well paid but unhappy, reading scripts written by others, never getting the leading dramatic roles he wanted to play. But then he became more

assertive, struck out on his own. Once he became his own man, life started to work for him. He made a successful

second marriage. Speaking his own ideas, he was elected Governor of California. Now, he has <u>the</u> leading role in the country.

Other aspects of the President's life and experience confirm the same intuitive truth. He enjoys exhilaration, and a sense of freedom, when he rides the open range on horseback, the experience of the open range for free entrepreneurship he has told us we will regain in our national psychology by cutting back that "big government" in the sky. When he escapes to California from Washington and clears brush on his ranch, he feels recharged. He knows we will feel that way too, as the American Congress "stays the course" to effect the psychological transformation he wants.

To be sure, this is a closed system of beliefs. Evidence is always interpreted in the light of what the President calls his "basic principles." If the economic recovery is slow, it only means problems of dependency and addiction to big government are deep in our national psyche. So he is under an even greater obligation to persevere until we regain our independence and self-confidence and restart the economy. He has no choice.

From the President's perspective there is likely a second cause of a slow recovery, a cause psychoanalysts and clinical psychologists often cite: we are resisting. To an unprecedented degree American news media refuse to discuss a national problem in the language a President uses. He has been stonewalled. <u>CBS News</u> runs nightly news stories about the sufferings imposed by Reaganomics but has not yet discussed the real national problem, our psychology of dependency. It is as though the Eastern liberal news media are so addicted to the drama of an activist government, so psychologically dependent, so accustomed to demand that the President <u>do</u> something, that they will never admit even the possibility he could be profoundly right.

If Reagan is right, these skeptics slow the cure. The President can cut taxes and expenditures; these are actions in physical reality. But the stakes are <u>psychological</u> reality. For the therapy to work we must agree - that the diagnosis of dependency is right, that big government is receding, that the therapist knows what he is doing.

It is also possible our actor-President is wrong. A powerful bond to government may be true of only 2% of the population: actors, intellectuals, reporters, the people who give money to political causes or end up in Washington. How can we tell?

The President has profoundly challenged the discipline of economics. His idea about how the economy works does not come from the hundreds of complex equations of their mathematical models. The basic problem, in his view, is simple: the economy is deeply political; we orient ourselves dependently toward government in a larger-than-life drama.

Lacking objective evidence, we now are adrift and debates about economic policy are decoupled, without intellectual integrity. Administration economists have given no evidence to support the intuitive psychological ideas about the economy the President uses to set policy. They have developed no national indicators for the substantiality of images of a "big" government in the sky, for changes in achievement motivation, for the alleged zero-sum allocations of responsibility.

Now, as we "stay the course," we navigate blind, on faith alone. Congress has applied no rules of evidence. The <u>Report</u> of the U.S. government's Council of Economic Advisers is intellectually irrelevant; it would be rejected as a test of the President's theories by any psychology department.

If the President is right, good national psychological indicators will tell us. And, refining our understanding, they might improve the President's policy. John F. Kennedy cut taxes and the economy leaped ahead - but Kennedy also talked about achievement - a New Frontier, a man on the moon by 1970. If psychodrama is needed, perhaps these are

the themes to emphasize.

The President is not speaking in metaphors. He believes he is talking about our reality: solid, strong constituents of individual's imagination so powerful in their effects as to destroy the health of a multi-trillion dollar economy and our national spirit. His theories reflect ideas many psychologists have voiced seriously in the past: psychoanalysts have told us that, via transference, many people related to government authority, in our "mass psychology," the way as children they regarded their magically powerful parents; David McClelland of Harvard explained the economic rise and fall of civilizations by changes in the imaginations of citizens.

Currently, empirical evidence bearing upon the President's fundamental assumption is indirect and inconsistent. Self-report measures seem to deny his model: Americans say they blame themselves for economic hardship. Yet macro-level studies of election results, and individual-difference measures of self-interested and "socio-tropic" voting suggest Reagan is correct and responsibility for management of the economy is assigned to the party in power.

Such measures of attitudes and voting are open to different interpretations as reflecting either rational and secular or psychodramatic processes. Alone, they cannot dispel the fog. The deeper question is the psychological nature of American government, and what is needed is that our public debates begin to be informed by evidence, from appropriate, clinically-derived measures, of the location and substance of citizens' experience of government.