high-risk groups (including both the "worried well" and those with the prodromal symptoms). Included in this area are risk-assessment studies to refine procedures for differentiating which individuals with AIDS or in high-risk populations are likely to experience emotional disturbance or psychological dysfunction as well as studies examining the relationship among social, behavioral, and psychological factors and the course and prognosis of the illness.

Interventions aimed at reducing behaviors that may be linked to transmission or development of AIDS and treating or preventing the mental health sequelae of the disease need to be assessed in a rigorous manner, both to ensure effective care for those affected by AIDS and to assist in developing effective strategies for other, similar situations. Specific educational strategies for modifying risk-related behaviors of persons at risk should be evaluated. The relative roles of generic treatment approaches, such as stress reduction and counseling, and specific techniques for treating mental health syndromes manifested in AIDS patients (for example, particular somatic treatments, specific forms of psychotherapy, and support group systems such as the Shanti project) should be assessed in terms of both reducing psychiatric symptoms and altering the course and progression of the illness itself. There is also a need for research assessing the effect of *preventive* interventions in reducing stress and the incidence of emotional disturbance and psychological dysfunction in AIDS patients, members of high-risk populations, bereaved partners and family members of AIDS patients, and health care workers treating AIDS patients.

Finally, cutting across all of these research areas are important methodological issues that need to be addressed. That is, given the unique subcultural contexts of this syndrome, researchers will need to examine these issues within the perspective of the gay culture, the drug abuse culture, and so on, in order to maximize validity. Methodological studies and the development of instruments sensitive to such issues as response bias and response validity, with regard to subcultural and related issues, are critical.

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LETTERS TO THE EDITOR

Cigarette Smoking: Example of Behavioral Regulation of Physiological Homeostasis?

In a recent study on life expectancy of nonsmoking men and women over age 30, Miller and Gerstein (*1*) reported that " . . . differential rates of cigarette smoking are apparently the overwhelming cause of the male-female longevity difference." They also concluded that " . . . virtually all the increase in the difference . . . since 1930 is attributable to the effects of cigarette smoking." Since the data presented were statistical rather than biological, such causality claims are questionable. Differences among smokers would not be differences due to smoking if smokers differ constitutionally from nonsmokers. It is well known that an hypothesis can be rejected but not validated by statistical methods (*2,3*). Moreover, as Berkson advised: "Cancer is a biologic, not a statistical problem" (*4*).

Holden (*5*) cited investigations that have shown that human females live longer, on average, than males. For example, among Seventh Day Adventists (nonsmoking vegetarians), women survive about 3 years longer than men (*5*). In an insurance study, life-expectancy for 32-year-old male nonsmokers was about 76 years, compared with about 80 years for nonsmoking females (*5*). Comfort stated: "Women—and all female mammals—tend to live longer than males" (*6*). A physiological component of this difference seems clear (*7*).

Behavioral regulation of physiological homeostasis, or ethological homeostasis (*8–10*), has been investigated by, among others, Richter (*11,12*), Mitchell (*13*), Wurtman et al. (*14*), and Lytle (*15*). Richter (*11*) observed that " . . . the results of our experiments indicate that in [humans] and animals the effort to maintain a constant internal environment or homeostasis constitutes one of the most universal and powerful of all behavioral urges or drives." In fact, survival depends on such maintenance.

The assertion—"Nicotine has no therapeutic application" (*16*)—is incompatible with contrary evidence (*17–25*). For some, ulcerative colitis is a "nicotine-deficiency" affliction, which smoking or nicotine alleviates. Since nicotine releases cellularly-stored biogenic monoamine neurotransmitter hormones such as epinephrine and norepinephrine (*26*), the therapeutic effect of smoking on ulcerative colitis may result from normalizing their levels (*25*). The finding of Gyde et al. (*27*) that ulcerative colitis patients showed lower systolic and diastolic blood pressures than controls ($P < 0.01$) is consistent with anomalies in control of one or more neurotransmitter hormones such as epinephrine in these individuals (*25*). Moreover, blood pressure response to challenge is atypical in persons with phenylketonuria; sufferers react unusually strongly to epinephrine (*28*).

From the viewpoint of biobehavioral processes and psychoendocrinology, Hamburg (*29*) observed (*30*) that " . . . we may find useful guidance in the principal that *individuals seek and find gratifying those situations that have been highly advantageous in the survival of the species*. That is, tasks that must be done (for species survival) tend to be quite pleasurable; they are easy to learn and hard to extinguish. Their blockage or

deprivation leads to tension, anger, substitutive activity, and (if prolonged) depression." In contrast, however, " . . . *individuals avoid and find distressing those situations that have been highly disadvantageous in species survival*" (Hamburg's italics). Can these principles be applied to habitual cigarette smoking? Damon (*31*) reported, in studies of the practices of seven preliterate societies, that " . . . personal gratification is much stronger than social influence in maintaining the smoking habit."

The recent 10-year, $115 million MRFIT study (*32,33*) was expected to find benefits from reduced smoking, among other interventions. Results of value were few, if any. Stallones (*34*) stated that " . . . the best explanation for the failure to detect a beneficial effect in MRFIT is that no benefits accrued." If smoking is symptomatic of physiological variants that nicotine or smoking tend to normalize, then, for some, intervention should aggravate the problems rather than alleviate them. Consider, by analogy, that insulin usage is a symptom of, or a "risk factor" for, diabetes mellitus and for various afflictions to which diabetics are prone. Reduction or prevention of insulin usage, on medical advice, by diabetics who need it might constitute medical malpractice. If habitual smoking is symptomatic of a physiological need, it is not surprising that smoking intervention in MRFIT (*32,33*) failed.

The concept that smoking is symptomatic of a need that nicotine tends to alleviate is generally ignored. It should be evaluated without bias, without use of personal opinion, without selective reporting, and without misuse of statistics.

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Miller Replies

The comments by Bowers, Allen, and Hickey referring to our study (*1*) on the effects of cigarette smoking on the male-female longevity difference is a fine example of misuse of biostatistics. The writers reintroduce the "constitutional hypothesis" proposed several decades ago by the distinguished statistician Fisher (*2*). His argument with the Doll-Hill report (*3*) on the damaging effects of smoking was that inherited factors—not cigarette smoking—might be the real cause of the higher mortality rates of smokers over nonsmokers. He postulated that since cigarette smoking is a self-selection process, those with weaker constitutions might be more likely to smoke, thus creating higher mortality rates for smokers. Fisher advocated more research on this topic to determine the truth of his hypothesis. The bulk of modern epidemiological and other biomedical research on smoking has shown his hypothesis to be invalid (*4,5*).

Bowers et al. then cite a number of reports showing significant differences in male-female longevity. They overlook research showing little difference in male-female longevity in societies where there is an absence of smoking (*6,7*) and in the latest reports on third world countries—such as China, India, Indonesia, Iran, and Pakistan—where the men live as long or longer than the women (*8,9*).

These writers proceed through the whole maze of theoretical verbiage of highly questionable validity. They suggest that through the behavioral regulation of physiological homeostasis there is a therapeutic effect of smoking on ulcerative colitus which results in normalizing the levels of biogenetic monoamine neurotransmitter hormones. They also imply that, through biobehavioral processes and psychoendocrinology, personal gratification brought about by smoking may be "highly advantageous to the survival of the species."

Let us now consider the scientific evidence for two of our critics' most cogent arguments: (*a*) that smoking counteracts the symptoms of ulcerative colitus and (*b*) that the "expected benefits of reduced smoking" from the Multiple Risk Factor Intervention Trial (MRFIT) study were few, if any.

Ulcerative colitus is a fairly rare disease and it is hardly fatal. Analysis of the articles cited shows that nicotine alone without smoking will eliminate the spasms of ulcerative colitus.

With regard to the MRFIT report (*10*), Bowers et al. apparently overlooked the final results as well as the main body of the report, where the principal investigators concluded " . . . men who stopped smoking cigarettes had lower CHD [coronary heart disease] and total mortality than those who continue to smoke." The analysis of the MRFIT data showed a two-fold decrease in cardiovascular disease (CVD) for those who had stopped smoking in both groups.

The writers' suggestion that it is good for the species to ingest an addictive substance through smoking in order to counteract a rather rare ailment, while markedly increasing the risk of contracting diseases which are the leading causes of death, is totally unrealistic (*11–14*).

We therefore see no reason why the arguments of Bowers et al. based on such speculations should shake confidence in our findings or lessen anyone's confidence in the vast amount of research demonstrating that cigarette smoking is dangerous to one's health. We, of course, welcome further research on this important topic and agree with our critics that it should be free from bias and preconceived opinion. Unfortunately we must conclude that their efforts do not meet their own criteria.

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