Smoking, Alcohol Consumption, and Susceptibility to the Common Cold

Sheldon Cohen, PhD, David A. J. Tyrrell, MD, Michael A. H. Russell, MD, Martin J. Jarvis, MPhil, and Andrew P. Smith, PhD

ABSTRACT

Objectives. This study was conducted to test the supposition that both smoking and consuming alcohol suppress host resistance to viral infections.

Methods. The relations between smoking, alcohol consumption, and the incidence of documented clinical colds were prospectively studied among 391 subjects intentionally exposed to one of five respiratory viruses and 26 subjects given saline. Clinical colds were defined as clinical symptoms verified by the isolation of virus or by an increase in virus-specific antibody titer. Analyses included control variables for demographics; body weight; virus; and environmental, immunological and psychological factors.

Results. Smokers were at greater risk for developing colds than nonsmokers because smokers were more likely both to develop infections and to develop illness following infection. Greater numbers of alcoholic drinks (up to three or four per day) were associated with decreased risk for developing colds because drinking was associated with decreased illness following infection. However, the benefits of drinking occurred only among nonsmokers.

Conclusions. Susceptibility to colds was increased by smoking. Although alcohol consumption did not influence risk of clinical illness for smokers, moderate alcohol consumption was associated with decreased risk for nonsmokers. (*Am J Public Health.* 1993;83:1277–1283)

Introduction

Both smoking and alcohol consumption are believed to suppress host resistance and thereby increase the risk of upper respiratory infections. In the case of smoking, epidemiological studies indicate an increased risk of serologically confirmed influenza among otherwise healthy smokers[1–3] although a study of rhinovirus colds failed to find a relation between smoking and risk of illness.[4] Because exposure to infectious agents was not controlled for in the epidemiological work, it is possible that the increased number of influenza cases among smokers was attributable to smokers having more close contacts with infected persons rather than to decreased host resistance. Moreover, the recording of illnesses in all these studies depended on persons seeking medical care. Smokers may be more likely to seek medical care when they are bothered by mild symptoms because they are aware of being at risk for serious respiratory disease. Alternatively, they may be less likely to seek care because they regard mild respiratory symptoms as normal.

Although the use of alcohol, especially in excess, is generally viewed as being immunosuppressive, it is not clear that documented alcohol-elicited changes in immune function are of clinical significance.[5,6] There are data supporting an increased incidence of bacterial infections among alcoholics.[7,8] However, these relations are often attributed to complications of alcoholism, including nutritional deficiencies, alcoholic cirrhosis, hygienic factors, and life-style.[5,9] Up until now, the relation between alcohol consumption and susceptibility to common upper respiratory infections in healthy, nonalcoholic humans has not been studied.

We present data from a prospective study of the independent effects of smoking and alcohol consumption on susceptibility to the common cold. Healthy persons were questioned about their smoking and alcohol consumption, and had blood drawn for immune and cotinine assessments. Subsequently, they were exposed to one of five respiratory viruses and monitored for the development of clinical illness. Demographic, environmental, immunological, and psychological variables that might provide alternative explanations for associations between drinking and smoking and the incidence of biologically verified colds were also assessed and controlled for in data analyses. By experimentally exposing subjects to viral agents, we eliminated the possibility that smoking or drinking resulted in exposure to the infectious agent. Moreover, by closely monitoring for the development of infection and illness, we eliminated biases that can occur when persons must seek medical care to receive a diagnosis.

Methods

Sample

The study was conducted between June 1986 and July 1989. The subjects

Sheldon Cohen is with Carnegie Mellon University, Pittsburgh, Pa. David A. J. Tyrrell is with the Common Cold Unit of the Medical Research Council, Salisbury, England. Michael A. H. Russell and Martin J. Jarvis are with the Addiction Research Unit of the Medical Research Council, London, England. Andrew P. Smith is with the University of Wales College of Cardiff.

Requests for reprints should be sent to Sheldon Cohen, PhD, Department of Psychology, Carnegie Mellon University, Pittsburgh, PA 15213.

This paper was accepted April 29, 1993.

were 154 men and 263 women who volunteered to participate in trials at the Medical Research Council's Common Cold Unit in Salisbury, England. All subjects were between 18 and 54 years of age, reported no chronic or acute illness or regular medication regimen, and were judged in good health following clinical and laboratory examination on arrival at the unit. Pregnant women were excluded. Informed consent was obtained from each subject.

Procedures

During their first 2 days at the unit, subjects underwent a thorough medical examination; completed a series of questionnaires designed to produce measures of smoking and alcohol consumption, psychological stress, and personality; and had blood drawn for immune and cotinine assessments. Subsequently, subjects were given nasal drops containing a low infectious dose of one of five respiratory viruses: rhinovirus types 2 (n = 86), 9 (n = 122), or 14 (n = 89); respiratory syncytial virus (n = 39); or coronavirus type 229E (n = 55). An additional 26 subjects were randomly assigned to receive saline. For 2 days before and 7 days after the viral challenge, the subjects were quarantined in large apartments (alone or with one or two others). Starting 2 days before viral challenge and continuing through 6 days after challenge, each subject was examined daily by a clinician using a standard checklist of respiratory signs and symptoms.[10] Approximately 28 days after challenge, the subjects' own physicians collected a second serum sample for serological testing.

Both the subjects and the investigators conducting the study were blind to immune and cotinine assessments, to whether subjects received virus or saline, and to the purpose of the study. Investigators were also blind to questionnaire responses.

Smoking Status

Cotinine, a metabolite of nicotine, provided biochemical measures of smoking status. Cotinine levels were measured in serum by gas chromatography.[11] The average of the two cotinine measures (before and 28 days after challenge) was used as an indicator of smoking. Persons with average cotinine levels of 15 ng/mL or more were defined as smokers while those with levels of less than 15 ng/mL were defined as nonsmokers.[12] This cutoff is closely related to that found in self-reports of smoking status when smokers are defined as persons smoking at least one cigarette per day. There was 96.4% agreement between self-reported status and status as determined by cotinine.

Of the subjects exposed to a virus, 104 (26.6%) were defined as smokers. Sixty-two reported smoking 1 to 15 cigarettes per day, and 42 reported smoking more than 15. Because preliminary analyses indicated that smoking status reliably predicted clinical colds but that smoking rate did not, subjects were categorized only by smoking status (smokers or nonsmokers) for the purpose of this article.

Alcohol Consumption

Alcohol consumption was measured by questions that separated weekday and weekend drinking. A half pint, a bottle or can of beer, a glass of wine, and a shot of whiskey contain approximately equal amounts of ethanol and were each treated as a single drink. The average number of drinks subjects consumed on weekdays when they drank was multiplied by the number of weekdays on which they drank. Similarly, the average number of drinks subjects consumed on weekend days when they drank was multiplied by the number of weekend days on which they drank. The sum of these two measures was then divided by seven, resulting in the average number of drinks per day. Persons indicating that they were occasional drinkers—that is, those who did not drink every week—were assigned 0 drinks per day. Never drinkers (n = 46) and occasional drinkers (n = 100) were collapsed to allow for a measure of a continuous drinking rate. This decision was justified by similar rates of clinical colds for the two groups (41.3% and 46.0%, respectively; $\chi^2 = .28$, $P = .60$). The number of drinks per day was used as the measure of continuous drinking rate. For the purpose of calculating odds ratios (ORs), daily alcohol consumption was broken into four categories: nondrinkers (n = 146), 0.1 to 1.0 drinks (n = 101), 1.1 to 2.0 drinks (n = 74), and more than 2.0 drinks per day (n = 70). Median daily consumption for these groups was 0.0, 0.6, 1.4, and 3.4 drinks, respectively.

Viral Isolates and Virus-Specific Antibody Levels

Nasal wash samples for viral isolation were collected before viral inoculation and on days 2 to 6 after inoculation. Samples were mixed with broth and stored in aliquots at −70°C. Rhinoviruses were detected in O-Hela cells, respiratory syncytial virus in Hep2 cells, and coronavirus in C-16 strain of continuous human fibroblast cells. When a characteristic cytopathic effect was observed, the tissue culture fluids were passaged into further cultures and identity tests on the virus were performed. Rhinoviruses and coronaviruses were confirmed by neutralization tests with specific rabbit immune serum, and respiratory syncytial virus was confirmed by immunofluorescent staining of culture cells.

Levels of neutralizing antibodies and of specific antiviral IgA and IgG were determined before and 28 days after challenge. Neutralizing antibodies (for rhinoviruses only) were determined by neutralization tests with homologous virus.[13] Results were recorded as the highest dilution showing neutralization, and a fourfold rise was regarded as significant. Suitable neutralizing tests were not available for respiratory syncytial virus and coronavirus.

Specific IgA and IgG levels for rhinoviruses,[14] coronavirus,[15] and respiratory syncytial virus[15] were determined by enzyme-linked immunosorbent assay. This test detects the antibody that correlates with neutralization titers, that is associated with resistance to infection, and that increases in response to infection.[13]

Infections and Clinical Colds

A subject was deemed infected if virus was isolated after challenge or if there was a significant increase in virus-specific serum antibody over baseline levels. A significant increase was defined as either a fourfold increase in neutralizing antibody (rhinoviruses) or an increase in IgG or IgA levels of more than two standard deviations above the mean of nonchallenged subjects (all viruses). Eighty-two percent (322) of subjects inoculated with a virus were infected.

At the end of the trial, the clinician judged the severity of each subject's cold on a scale ranging from nil (0) to severe (4). Ratings of mild cold (2) or greater were considered positive clinical diagnoses. Subjects also judged the severity of their colds on the same scale. Clinician diagnosis was in agreement with self-diagnosis for 94% of the subjects. Subjects were defined as having developed clinical colds both if they were infected and if they were diagnosed by the clinician as having a clinical cold. Of the 391 subjects inoculated with a virus, 38% (148) developed clinical colds.

Mucus Weights

Because clinical diagnoses can be influenced by how subjects present their symptoms, associations were indepen-

dently evaluated between smoking status, drinking rate, and a clinical sign that is not subject to self-presentation bias: mucus weights. Mucus weights were determined by collecting tissues used by subjects and sealing them in plastic bags. The bags were weighed, and the weight of the tissues and bags was subtracted. The prechallenge measure was based on the sum of mucus weights from the 2 days before challenge; the postchallenge measure was based on the sum of mucus weights from days 2 to 6 after challenge. The base-10 logarithm of total mucus weights was used in the analyses.

Standard Control Variables

A series of control variables was assessed to see if alternative explanations might exist for relations between smoking and illness and between alcohol consumption and illness. These variables include serologic status for the experimental virus before the challenge, age, sex, education, allergic status, body weight, season, number of subjects housed together, whether a subject housed in the same apartment became infected, and identity of the challenge virus.

Serologic status was defined as positive when a subject had a baseline neutralizing antibody titer above 2 for rhinoviruses and a baseline antibody level greater than the sample median for coronavirus or respiratory syncytial virus. Forty-three percent of subjects were seropositive before the challenge.

Because age was not normally distributed, it was scored categorically as above or below the median: 18 through 33 or 34 through 54 years. Education levels were classified on a 9-point scale ranging from no schooling (0) to doctoral degree (8). Subjects who reported any allergy (food, drug, or other) were defined as allergic. A ponderal index (body weight in kilograms divided by the cube of height in meters) was used to control for body weight. The number of hours of daylight on the first day of the trial was used as a continuous measure of season. Number of daylight hours is correlated ($r = .80$, $P < .001$) with average temperature on the same day. Control for the possibility that person-to-person transmission rather than viral challenge might be responsible for infections or clinical colds was also included. Because person-to-person transmission would have been possible only if a subject sharing the same housing had been infected by the viral challenge, a control variable indicated whether any subject sharing the same housing was infected. Finally, the challenge virus was a categorical variable that indicated the experimental virus to which a subject was exposed.

Psychological and Immunological Control Variables

Several additional psychological and immunological variables were assessed prior to viral challenge to clarify their potential roles in relations between smoking and illness and drinking and illness. Psychological stress was assessed because we reported in an earlier paper that stress is a risk factor for colds for these subjects.[16] Smoking and drinking have both been associated with higher levels of stress,[17] and it is important to demonstrate that the associations reported in this article are independent of the relation between stress and colds.[18] The psychological stress index combines recent negative life events, perceptions of being overwhelmed by demands, and negative emotions.[16]

Both smoking and drinking have been associated with the personality characteristic introversion-extraversion.[19,20] To ensure that associations between smoking and illness and drinking and illness could not be attributed to this personality characteristic, introversion-extraversion was measured using the Eysenck Personality Inventory.[20]

Finally, smokers have been found to have elevated white cell counts,[21,22] and both smokers and drinkers show alterations in immunoglobulins.[23,24] To determine whether either factor might be responsible for links between smoking and illness or drinking and illness, these immune parameters were assessed from blood and nasal secretions collected before the viral challenge. White cells were counted with an automatic cell counter, and differential counts (lymphocytes, monocytes, and neutrophils) were calculated from 200 cells in a stained film. Total serum and nasal wash IgA and IgE levels, and total nasal wash protein levels were assessed by enzyme-linked immunosorbent assay.[15] Base-10 logarithms of each differential count and immunoglobulin measurement were used.

Statistical Analysis

As expected, none of the subjects receiving saline developed colds, and analyses are based on the 391 subjects receiving a virus. A logistic regression procedure was used that provides coefficients and odds ratios for each variable adjusted for all other variables in the equation.[25] The odds ratio approximates how much more likely it was that the outcome (infection or clinical colds) would be present among smokers as compared with nonsmokers, or among persons with various drinking rates as compared with nondrinkers. Interactions were tested by determining whether the interaction term entered the model after all the main effect terms were entered. Multiple linear regression was used in analyses of postchallenge mucus weights.[26]

A sequential series of analyses is reported. In the first analysis, only smoking status and drinking rate are entered into the equation. Then a model is fitted in which the set of standard control variables is entered into the regression along with smoking status and drinking rate. A final set of analyses examines the possible role of the psychological and immunological variables by entering them into the equation with the standard controls, smoking status, and drinking rate.

Results

Preliminary analysis indicated no statistically significant interactions between standard control variables and either smoking status or alcohol consumption in predicting clinical colds.[26] Hence, the relations we report are similar for the five viruses and for groups defined by serologic status, age, sex, allergic status, education, body weight, season, number of subjects sharing an apartment, and whether another subject housed in the same apartment was infected.

Table 1 presents data on select control variables separately for those who developed clinical colds and those who did not. There are associations between clinical illness and four control variables: serologic status ($P < .001$), virus ($P < .001$), whether another subject sharing the same apartment was infected ($P < .014$), and psychological stress ($P < .026$).[16]

Smoking Status, Alcohol Consumption, and Clinical Colds

Thirty-six percent of nonsmokers, 40% of light smokers (1 to 15 cigarettes per day), and 48% of heavy smokers (>15 cigarettes per day) developed clinical colds. However, neither the continuous nor the categorical smoking *rate* variables were statistically significant predictors of clinical illness. As a result, we used smoking *status* in all remaining analyses. The odds ratio for smoking status adjusted for drinking rate was 1.67 (95% confidence interval [CI] = 1.03, 2.70). Adding the standard control variables to the equation produced

TABLE 1—Descriptive Statistics (Select Control Variables) Separately for Subjects Who Developed Clinical Colds and Those Who Did Not

	Subjects Not Developing Clinical Colds (n = 243)	Subjects Developing Clinical Colds (n = 148)
Mean age, y	34.4 (0.67)	32.4 (0.90)
Mean education level[a]	3.7 (0.10)	3.6 (0.12)
Mean number of roommates	1.3 (0.04)	1.3 (0.05)
Mean ponderal index[b]	14.0 (0.15)	14.0 (0.21)
Mean number of hours of daylight on first day of trial	13.0 (0.18)	12.7 (0.26)
Mean psychological stress[c]	7.2 (0.16)	7.9 (0.21)
Female, %	59.7 (3.2)	65.5 (3.9)
Seropositive, %	54.3 (3.2)	25.7 (3.6)
Allergic, %	22.6 (2.7)	21.6 (3.4)
With an infected roommate, %	72.8 (2.9)	83.8 (3.0)

Note. Standard errors in parentheses.
[a]Computed on a 9-point scale ranging from no schooling (0) to doctoral degree (8). (Mean education levels between 3 and 4 represent completion of secondary education.)
[b]Body weight in kilograms divided by the cube of height in meters.
[c]Measured by an index ranging from 3 to 12 that was derived by summing subjects' quartile rankings (1 to 4) on a life events scale, perceived stress scale and negative affect scale.

TABLE 2—Comparison of Drinkers in Each Alcohol Consumption Category with Nondrinkers in the Prediction of Clinical Colds

	Variables Controlled for in Analysis[a]					
	Smoking Status		Smoking Status and Standard Controls		Smoking Status, Standard and Additional Controls	
Alcoholic Drinks per Day	OR	95% CI	OR	95% CI	OR	95% CI
Entire sample (n = 391)						
0.1–1.0	0.81	0.48, 1.36	0.75	0.42, 1.34	0.67	0.37, 1.23
1.1–2.0	0.53	0.29, 0.97	0.45	0.23, 0.87	0.41	0.21, 0.82
2.1 or more	0.43	0.23, 0.81	0.39	0.19, 0.80	0.36	0.17, 0.76
Nonsmokers only (n = 287)						
0.1–1.0	0.80	0.45, 1.43	0.69	0.36, 1.33	0.60	0.30, 1.19
1.1–2.0	0.50	0.25, 1.01	0.38	0.17, 0.84	0.34	0.15, 0.79
2.1 or more	0.20	0.07, 0.56	0.16	0.05, 0.49	0.13	0.04, 0.43

Note. Analyses include all subjects exposed to a virus. Standard control variables include serologic status for the experimental virus before the challenge, age, sex, education, allergic status, body weight, season, number of subjects housed together, whether a subject housed in the same apartment became infected, and identity of the challenge virus. Additional control variables include psychological stress; introversion-extraversion; numbers of lymphocytes, monocytes, and neutrophils; total serum and nasal wash IgA and IgE; and total nasal wash protein.
[a]For the subsample of nonsmokers, smoking status was not a variable controlled for in analysis; thus, column 1 for nonsmokers is based on no control variables.

a similar odds ratio, 2.08 (95% CI = 1.18, 3.70). Increased alcohol consumption was related to *decreased* susceptibility to clinical colds ($P < .004$). Odds ratios based on an analysis of reference-coded drinking rates are presented in Table 2, column 1, under "Entire sample"; and the addition of the standard control variables to the equation (column 2) did not alter this association. A test of the linearity (polynomial contrasts) of the relation between drinks per day and colds indicates that there is a linear (dose-response) relation ($P < .005$).

The interaction between smoking status and drinking rate was also significant ($P < .009$ without control variables, $P < .008$ with controls). The interaction indicates that the relation between drinking rate and clinical illness differs depending on whether a person smokes. The nature of the interaction is depicted in Figure 1. As apparent from the figure, smokers remain at highest risk irrespective of their drinking rate, but the risk for nonsmokers is modified by drinking alcohol, with greater drinking associated with less risk. To provide accurate estimates of the relation between drinking and illness for smokers and nonsmokers, we fit separate regression models for each of these groups. Alcohol consumption was not related to illness for smokers but was related to it for nonsmokers ($P < .001$). The odds ratios are presented in Table 2, column 1, under "Nonsmokers only"; and the addition of standard control variables to the equation (column 2) did not alter this association. A test of the linearity (polynomial contrasts) indicates a linear (dose-response) relation ($P < .001$).

To determine whether the relation between drinking and colds was primarily attributable to weekend or weekday drinking, we conducted two additional analyses. Both included smoking status and standard control variables. In one, we entered weekend drinking rate as the measure of alcohol consumption; in the other, we entered weekday drinking rate. In both cases, increased rates of alcohol consumption were similarly associated with decreased risk of colds ($P < .02$ and $P < .03$, respectively). Analyses including only nonsmokers indicated similar results ($P < .002$ and $P < .001$).

Our sample did not include enough subjects who drank more than three drinks per day for us to accurately assess whether higher rates of drinking are associated with increased or decreased incidence of illness. (Only 10.0% of the entire sample and only 5.6% of nonsmokers drank more than three drinks per day). In an attempt to estimate whether illness incidence increased or decreased as drinking rates exceeded three drinks, we compared the proportion of colds for persons above and below the median drinking rate (3.4 drinks) in the "2.1 or more" drink category. The proportions were not reliably different either in the entire sample (29% colds for those below the median and 28% for those above) or in the subsample of nonsmokers only (15.0% and 12.5%, respectively).

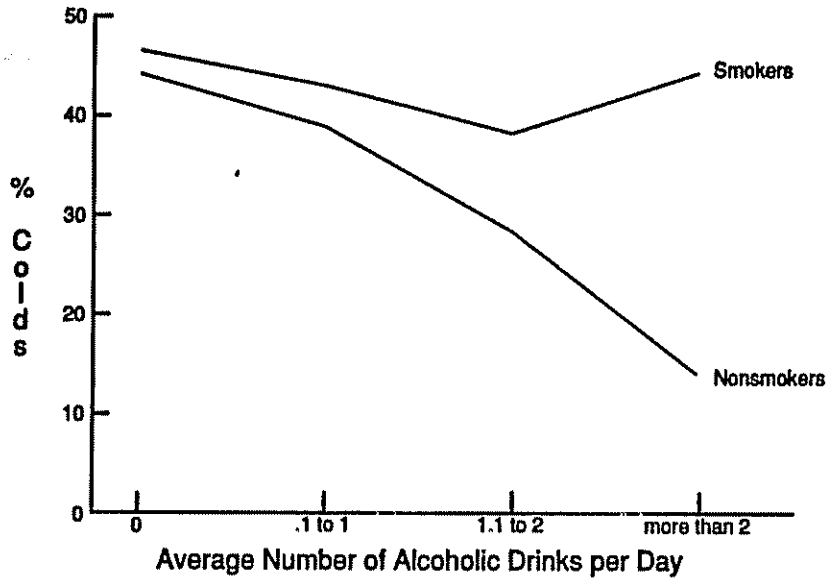
We were also interested in testing the possible roles of psychological stress, immunity, and personality in the relations between smoking status and illness and alcohol consumption and illness. Thus, an analysis predicting cold incidence was conducted in which measures of psychological stress; introversion–extraversion; number of circulating monocytes, neutrophils, and lymphocytes; total serum and nasal wash IgA and IgE; and total nasal

wash protein levels were all added to the regression equation, along with the 10 standard control variables, smoking status, and drinking rate. The results for both smoking status (adjusted OR = 1.93; 95% CI = 1.03, 3.62) and drinking rate (see Table 2 [entire sample], column 3) were relatively unaltered by the addition of the stress, immunity, and personality control variables. The results of adding these control variables to the analysis that included only the nonsmokers were equivalent. The results for drinking rate (see Table 2 [nonsmokers only], column 3) were relatively unaltered. Hence, these relations cannot be accounted for by differences between smokers and nonsmokers or between persons of various drinking rates as measured by any of these variables.

Infection or Symptoms for Infected Persons?

Subsequent analyses including the 10 standard control variables indicate that smoking status predicts both incidence of infection (adjusted OR = 2.23; 95% CI = 1.03, 4.82) and clinical diagnosis for infected persons (adjusted OR = 1.83; 95% CI = 1.00, 3.36). Although continuous drinking rate does not predict incidence of infection, it does predict clinical diagnosis among infected persons ($P < .013$). The odds ratios and their confidence intervals are presented in Table 3. Analysis of only nonsmokers similarly indicates that drinking rate does not predict infection but does predict clinical diagnosis for infected persons ($P < .001$ for continuous drinking).

In the analyses presented so far, diagnosis of illness is based on clinical judgment. Additional analyses investigated the associations of smoking and drinking with a purely objective measure of disease manifestation: total mucus weights. Only persons defined as infected were included (n = 322). There were no differences in before-challenge mucus weights of smokers and nonsmokers. However, smokers had higher mean after-challenge mucus weights (18.4 g) than nonsmokers (13.5 g; $F[1,305] = 12.86, P < .001$). Surprisingly, greater rates of drinking were associated with lower mucus weights *before* viral challenge ($F[3,304] = 4.27, P < .007$) (Table 4). Hence, the analysis of after-challenge mucus weights controlled for before-challenge mucus weights. Again, increased alcohol consumption was related to less mucus production ($F[3,303] = 3.77, P < .012$). Although alcohol consumption was not reliably associated with before-challenge mucus weights when only the nonsmokers were included in the analysis ($P = .10$), drinking rates were similarly associated with decreases in after-challenge mucus weights ($F[3,212] = 3.87, P < .011$).



Note. For 0, 0.1 to 1.0, 1.1 to 2.0, and more than 2 drinks per day, cell sample sizes for nonsmokers are 118, 80, 53, and 36, respectively, and for smokers are 28, 21, 21, and 34, respectively.

FIGURE 1—Observed association between number of alcoholic drinks per day, smoking status, and incidence of clinical colds.

TABLE 3—Comparison of Drinkers in Each Alcohol Consumption Category with Nondrinkers in the Prediction of Infection and Clinical Colds among Infected Subjects

	Entire Sample				Nonsmokers Only			
	Infection (n = 391)		Colds for Infected Subjects (n = 322)		Infection (n = 287)		Colds for Infected Subjects (n = 230)	
Alcoholic Drinks per Day	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI
0.1–1.0	0.60	0.29, 1.23	0.82	0.44, 1.55	0.75	0.34, 1.65	0.70	0.34, 1.43
1.1–2.0	0.53	0.24, 1.18	0.45	0.22, 0.92	0.52	0.21, 1.28	0.35	0.14, 0.83
2.1 or more	0.48	0.20, 1.15	0.41	0.19, 0.89	0.45	0.16, 1.24	0.16	0.05, 0.51

Note. Standard control variables were included in the equations from which these odds ratios were derived. (In analyses of the entire sample, smoking status was also included in the equation.) Standard control variables include serologic status for the experimental virus before the challenge, age, sex, education, allergic status, body weight, season, number of subjects housed together, whether a subject housed in the same apartment became infected, and identity of the challenge virus.

Discussion

Smoking was associated with an *increased* risk of acute infectious respiratory illness. In contrast, alcohol consumption was associated with a *decreased* risk of respiratory illness. This was a dose-response relation, with each increase in drinking up to approximately three to four drinks per day associated with a decreased risk of illness. However, the relation between alcohol consumption and illness was modified by smoking status. Smokers were at relatively high risk irrespective of how much alcohol they consumed. Nonsmokers who did not drink were at equally high risk as smokers, but as their consumption of alcohol increased, their risk for illness decreased. These relations were relatively unaltered by the 10 standard control variables as well as by the additional controls for psychological stress, introversion-extraversion, and immune

TABLE 4—Mean Mucus Weights (in grams) for Infected Subjects Before and After Viral Challenge for Each Alcohol Consumption Category

Alcoholic Drinks per Day	Entire Sample (n = 322)		Nonsmokers Only (n = 230)	
	Before	After	Before	After
0.0	1.30	17.48	1.15	15.66
0.1–1.0	0.88	17.43	0.94	16.00
1.1–2.0	0.46	11.95	0.40	9.18
2.1 or more	0.59	8.70	0.62	5.92

characteristics including total immunoglobulins and white cell differentials.

Increased risk of illness among smokers was attributable to both increased incidence of infection and increased symptomatology among infected persons. However, the decreased risk of illness associated with increased drinking was attributable to decreased symptoms among infected persons but not to decreased incidence of infection.

Although there was some person-to-person transmission of virus in this study, the associations between smoking and colds and drinking and colds were independent of whether such transmission was possible (i.e., whether a subject shared housing with another infected subject). Moreover, these associations were similar for those with and without infected apartment mates. In short, smoking and drinking were associated with host resistance, not with differential exposure.

The relation between smoking and illness is consistent with most earlier epidemiological and immunological research.[1–3] Because smoking is related to the probability both of infection and of developing symptoms, it is probably associated with more than one process involved in susceptibility. For example, increased probability of infection among smokers could be attributable to deleterious effects of smoke on nonspecific mucosal processes that provide frontline barriers against infection. However, the relation between smoking and increased probability of symptoms is more likely due to links either between smoking and primary (nonmemory) immune processes that limit viral replication or between smoking and inflammatory processes involved in the production of symptoms.

The benefits of alcohol consumption in relation to susceptibility were unexpected. The epidemiology and experimental work with animals indicate that alcoholism and intoxication are immunosuppressive. Thus, how could moderate alcohol consumption be associated with a lower probability of symptom development? One possibility is that alcohol acts to limit the replication of the virus through a primary (nonmemory) immune process. Another is that alcohol inhibits inflammatory processes involved in symptom mediation. For example, ethanol has been found to produce up to 10-fold increases in cyclic adenosine monophosphate (AMP) concentrations in human lymphocytes.[27] Cyclic AMP is known to have a general anti-inflammatory action, including the inhibition of histamine release,[28] and hence it provides a possible pathway through which ethanol inhibits symptoms among infected persons. The relation between alcohol consumption and *before*-challenge mucus weights suggests that alcohol may have such an anti-inflammatory effect.

As discussed earlier, smoking nullifies the beneficial effects of moderate drinking. This likely occurs because of a particularly powerful influence of smoking on symptom production. For a person to receive a clinical diagnosis, symptom duration and severity must exceed a threshold. If smoking pushes people far over that threshold, alcohol consumption may not provide enough of a counter response to nullify the effects of smoking.

One problem in interpreting our data involves distinguishing between the acute and chronic effects of smoking and drinking. Subjects were allowed to smoke and drink alcohol (in moderation) during the trials. As a result, it is unclear whether the relations we report are acute effects on host resistance during viral challenge or effects of habitual drinking and smoking behaviors on chronic host resistance.

Finally, we are not suggesting moderate drinking as a prophylactic or cure for the common cold. As discussed earlier, our data are ambiguous in regard to whether it is drinking during the trial or chronic drinking rates that are associated with susceptibility. Moreover, given the serious health risks associated with exceeding two drinks per day,[29,30] increased alcohol consumption cannot be recommended. □

Acknowledgments

This work was supported by grants from the National Institute of Allergy and Infectious Diseases (AI23072) and the Office of Naval Research (N00014-88-K-0063), by a research scientist development award to Dr Cohen from the National Institute of Mental Health (MH00721), and by the Medical Research Council's Common Cold and Addiction Research units.

We are indebted to S. Bull; R. Dawes; J. Middleton; H. Parry; M. Sargent; J. Schlarb; S. Trickett; the medical, nursing, and technical staff of the Medical Research Council's Common Cold Unit; and the volunteers for their contribution to this research, and to A. Arria for her comments on an earlier draft. Statistical consultation was provided by Joel Greenhouse, Department of Statistics, Program in Biostatistics, Carnegie Mellon University.

References

1. Finklea JF, Sandifer SH, Smith DD. Cigarette smoking and epidemic influenza. *Am J Epidemiol.* 1969;90:390–399.
2. MacKenzie JS, MacKenzie IH, Holt PG. The effect of cigarette smoking on susceptibility to epidemic influenza and on serological responses to live attenuated and killed subunit influenza vaccines. *J Hyg.* 1976;77:409–417.
3. Waldman RH, Bond JO, Levitt LP, et al. An elevation of influenza immunization: influence of route of administration and vaccine strain. *Bull WHO.* 1969;41:543–548.
4. Gwaltney JM Jr, Hendley JO, Simon G, Jordan WS Jr. Rhinovirus infections in an industrial population: I. the occurrences of illness. *N Engl J Med.* 1966;275:1261–1268.
5. Adams HG, Jordan C. Infections in the alcoholic. *Med Clin North Am.* 1984;68:179–200.
6. MacGregor RR. Alcohol and immune defense. *JAMA.* 1986;256:1474–1479.
7. Austrian R, Gold J. Pneumococcal bacteremia with especial reference to bacteremic pneumococcal pneumonia. *Ann Intern Med.* 1964;60:759–776.
8. Straus B, Berenyi MR. Infection and immunity in alcoholic cirrhosis. *Sinai J Med.* 1973;40:631–640.
9. Paronetto F. Ethanol and the immune system. In: Seitz HK, Kommerell B, eds. *Alcohol Related Diseases in Gastroenterology.* Berlin, Germany: Springer-Verlag; 1985:269–281.
10. Beare AS, Reed SE. The study of antiviral compounds in volunteers. In: Oxford JS, ed. *Chemoprophylaxis and Virus Infections.* Cleveland, Ohio: CRC Press; 1977; 2:27–55.
11. Feyerabend C, Russell MAH. A rapid gas-liquid chromatographic method for the determination of cotinine and nicotine in biological fluids. *J Pharm Pharmacol.* 1990; 42:450–452.
12. Jarvis MJ, Tunstall-Pedoe H, Feyerabend C, Vessey C, Saloojee Y. Comparison of tests used to distinguish smokers from nonsmokers. *Am J Public Health.* 1987;77(11): 1435–1438.
13. Al-Nakib W, Tyrrell DAJ. *Picornviridae*: rhinoviruses—common cold viruses. In: Lennette EM, Halonen P, Murphy FA,

eds. *Laboratory Diagnosis of Infectious Diseases: Principles and Practice.* New York, NY: Springer-Verlag; 1988;2:723–742.
14. Barclay WS, Al-Nakib W. An ELISA for the detection of rhinovirus specific antibody in serum and nasal secretion. *J Virol Methods.* 1987;15:53–64.
15. Callow KA. Effect of specific humoral immunity and some non-specific factors on resistance of volunteers to respiratory coronavirus infection. *J Hyg London.* 1985;95:173–189.
16. Cohen S, Tyrrell DAJ, Smith AP. Psychological stress and susceptibility to the common cold. *N Engl J Med.* 1991;325:606–612.
17. Cohen S, Williamson G. Perceived stress in a probability sample of the United States. In: Spacapan S, Oskamp S, eds. *The Social Psychology of Health.* Newbury Park, Calif: Sage; 1988:31–67.
18. Smith GM. Personality and smoking: a review of the literature. In: Hunt WG, ed. *Learning Mechanisms in Smoking.* Chicago, Ill: Aldine; 1970.
19. Eysenck HJ. *Fact and Fiction in Psychology.* London, England: Penguin Press; 1960.
20. Eysenck HJ, Eysenck SBG. *Manual of the Eysenck Personality Inventory.* London, England: University of London Press; 1964.
21. Friedman GD, Siegelaub AB, Seltzer CC, Feldman R, Collen MF. Smoking habits and the leukocyte count. *Arch Environ Health.* 1973;26:137–143.
22. Tollerud DJ, Clark JW, Brown LM, et al. The effects of cigarette smoking on T cell subsets. *Am Rev Respir Dis.* 1989;139:1446–1451.
23. Chan-Yueung M, Ferreira P, Frohlich J, et al. The effects of age, smoking and alcohol on routine laboratory tests. *Am J Clin Pathol.* 1981;75:320–326.
24. Gerrard JW, Heiner DC, Ko CG, Mink J, Meyers A, Dosman JA. Immunoglobulin levels in smokers and nonsmokers. *Ann Allergy.* 1980;44:261–262.
25. Hosmer DW, Lemeshow S. *Applied Logistic Regression.* New York, NY: John Wiley; 1989.
26. Pedhazur EJ. *Multiple Regression in Behavioral Research.* Fort Worth, Tex: Holt Rinehart and Winston; 1982.
27. Atkinson JP, Sullivan TJ, Kelly JP, Parker CW. Stimulation by alcohols of cyclic AMP metabolism in human leukocytes. Possible role of cyclic AMP in the antiinflammatory effects of ethanol. *J Clin Invest.* 1977;60:284–294.
28. Bourne HR, Lichtenstein LM, Melmon KL, Henney CS, Weinstein Y, Shearer GM. Modulation of inflammation and immunity by cyclic AMP. *Science.* 1974;184:19–28.
29. LaPorte RE, Cresanta JL, Kuller LH. The relationship of alcohol consumption to atherosclerotic heart disease. *Prev Med.* 1980;9:22–40.
30. Califano JA. *Healthy People: Background Papers.* Washington, DC: US Govt Printing Office; 1979.

Call for Abstracts on Psychosocial and Behavioral Factors in Women's Health

The American Psychological Association will sponsor a national conference on "Psychosocial and Behavioral Factors in Women's Health: Creating an Agenda for the 21st Century," May 12–14, 1994, at the Hyatt Regency Hotel, Capitol Hill, Washington, DC. The goal of the conference is to highlight the importance of psychosocial and behavioral factors in women's health research and the implications for treatment, prevention, and health policy.

Major foci of the conference will include theoretical models/frameworks for conceptualizing women's health; issues in research methodology, measurement, and evaluation; new research on psychosocial and behavioral factors in women's health; implications of psychological factors in treatment, health policy, and interventions; and special issues of underserved populations (e.g., ethnic minorities, the poor, women with disabilities). Content areas of interest include sociocultural influences on health; behavioral and psychosocial risk factors; behavioral and psychosocial factors in health promotion; and coping, resilience, health, and illness.

The deadline for receipt of abstracts (800–1000 words) is *October 18, 1993.* Send abstracts to Gwendolyn Puryear Keita, PhD, American Psychological Association, 750 First St, NE, Washington, DC 20002-4242; tel (202) 336-6044; fax (202) 336-6040.