

amount of research to be completed. Examples of products for which commitments have been made by sponsors are presented in the table.

FDA also administers certain portions of the Orphan Drug Act previously described, namely, advice on studies needed for marketing approval and the designation, when appropriate, of drugs as "orphans" so that tax credits can be claimed by sponsors and an exclusive marketing license obtained for nonpatentable drugs. In September 1983, FDA issued guidelines for sponsors, describing the information to be submitted in order to obtain orphan drug designation and protocol assistance. Regulations are expected to be issued in 1984.

FDA has received an appropriation from the Congress to support orphan products research. This appropriation

is separate from that provided by the Orphan Drug Act. In fall 1983, FDA made 12 awards for clinical study of unmarketed orphan drugs and of new uses for marketed products.

## Summary

Through the combined efforts of agencies and organizations in the public and private sector, drugs have been made available that would not have been at hand without a specific focus on the orphan drug issue. It is anticipated that these cooperative efforts will continue beyond the first enthusiastic burst engendered by the inception of new and interesting activities.

---

## The Population Attributable Risk of Hypertension from Heavy Alcohol Consumption

E. B. LARBI, MD  
J. STAMLER, MD  
A. DYER, PhD  
R. COOPER, MD  
O. PAUL, MD  
R. B. SHEKELLE, PhD  
M. LEPPER, MD

Dr. Larbi, Dr. Stamler, and Dr. Dyer are with the Department of Community Health and Preventive Medicine, Northwestern University Medical School, Chicago. Dr. Cooper is with the Department of Cardiology, Cook County Hospital, Chicago. Dr. Paul is with the Department of Medicine, Harvard Medical School, Boston, Mass. Dr. Shekelle and Dr. Lepper are with the Department of Preventive Medicine, Rush-Presbyterian-St. Luke's Medical Center, Chicago.

Tearsheet requests to Jeremiah Stamler, MD, Northwestern University Medical School, 303 E. Chicago Ave., Chicago, Ill. 60611.

### Synopsis .....

*The association between alcohol consumption and hypertension was studied in 11,899 men aged 40–55 years.*

*The prevalence of hypertension among heavy drinkers was significantly higher than among those who did not drink heavily. Heavy drinking was defined as consumption of five or more drinks daily or four or more drinks daily. A total of 136 persons fulfilled the five drinks or more per day definition and 230, the four drinks daily definition.*

*The population-attributable risk of hypertension contributed by heavy drinking, depending on the diagnostic criteria used to define each endpoint, varied from 3 to 12 percent. There is reason to suspect that the contribution of alcohol to hypertension in the general population may be somewhat higher at the present time than in the late 1950s when the study was conducted.*

*Moderation of alcohol consumption, in addition to weight reduction and salt restriction, is another important nonpharmacological means to control hypertension.*

THE ASSOCIATION BETWEEN EXCESSIVE alcohol consumption and hypertension, first suggested at the turn of the century (1), has been found in several clinical and epidemiologic studies (2–13). While some studies have shown a linear relationship, others indicate a U-shaped or threshold response. The association is independent of age, sex, race, smoking, coffee use, educational attain-

ment, adiposity, social class, and physical fitness. Former heavy drinking is not associated with high blood pressure; current consumption of alcohol seems to be the essential factor.

It has been suggested that 10–20 percent of essential hypertension in the United States and Australia (5–14) may be due to alcohol use. Recent data from the Kaiser-

Permanente program provided an estimate of 5 percent for the population attributable risk of hypertension associated with heavy alcohol use (15). We report further here on the contribution of alcohol use to hypertension in an employed population.

## Methods

The association between alcohol consumption and hypertension was studied in 1,899 white men, aged 40–55 years, employed by the Hawthorne Works of the Western Electric Company of Chicago. Details of the Chicago Western Electric Company study have been reported elsewhere (16). In brief, all men in the sample had a complete physical examination including blood pressure measurement at entry into the study in 1957–58. Assessment of alcohol consumption was based on the maximum intake reported on three questionnaires administered yearly (10, 17). It was expressed as the number of drinks per day for all kinds of alcohol combined, that is, including beer, wine, and hard liquor. The number of drinks was coded based on the alcohol content; a drink for each type of beverage contained the same amount by weight of alcohol—approximately 13 gm—in a 12 oz. can of beer (4 percent by weight of alcohol), 1.25 oz. of whiskey (40 percent alcohol), the average cocktail (38 percent alcohol), and 4 oz. of table wine (10 percent alcohol). Two levels of heavy drinking were defined—one as five or more drinks per day and the other as four or more drinks per day. The population attributable risk, that is, the proportion of all hypertension in the population attributable to heavy drinking, was calculated using the formula (18):

$$\text{Attributable risk (AR)} = b(r - 1) \div b(r - 1) + 1 \times 100$$

Prevalence of hypertension in two groups of heavy drinkers and in nonheavy drinkers, by stipulated criteria, and the overall population risk of hypertension attributable to heavy drinking (percentages)

Criteria for hypertension	5 or more drinks per day				4 or more drinks per day			
	Prevalence of hypertension in—		Ratio: col. 3 ÷ col. 2 × 100 4	Population attributable risk 5	Prevalence of hypertension in—		Ratio: col. 7 ÷ col. 6 × 100 8	Population attributable risk 9
	Nonheavy drinkers (N = 1,763) 2	Heavy drinkers (N = 136) 3			Nonheavy drinkers (N = 1,669) 6	Heavy drinkers (N = 230) 7		
SBP ≥ 140 mm Hg ..	36.9	55.9	51.5	3.6	36.1	53.9	49.3	5.6
SBP ≥ 160 mm Hg ..	11.5	28.7	149.6	9.7	11.3	23.5	108.0	11.6
DBP ≥ 90 mm Hg ..	41.9	64.0	52.7	3.6	41.1	60.4	47.0	5.4
DBP ≥ 95 mm Hg ..	20.3	39.0	92.1	6.2	19.7	36.1	83.2	9.2
SBP ≥ 140 mm Hg or DBP ≥ 90 mm Hg .	50.1	68.4	36.5	2.7	49.3	67.4	36.7	4.3
SBP ≥ 160 mm Hg or DBP ≥ 95 mm Hg .	22.7	42.6	87.7	5.9	22.2	38.7	74.3	8.3

NOTE: SBP - systolic blood pressure, DBP - diastolic blood pressure.

Where  $r$  = relative risk and  $b$  = proportion of the population consuming five or more drinks per day or four or more drinks per day.

## Results

With the five or more drinks per day definition, there were 136 heavy drinkers and 1,763 nonheavy drinkers in the Western Electric Company sample in the late 1950s. The table shows the prevalence of hypertension in the two groups based on six criteria for hypertension. Prevalence of hypertension among heavy drinkers was significantly higher than that for nonheavy drinkers with each criterion. The extent of hypertension in the population overall attributable to heavy drinking varied from 3 to 10 percent depending on the criterion used for hypertension. It was highest (9.7 percent) when hypertension was defined as systolic blood pressure (SBP) ≥ 160 mm Hg. With the four or more drinks per day definition, there were 230 heavy drinkers and 1,669 nonheavy drinkers (see table). Prevalence of hypertension among heavy drinkers was again significantly higher than for nonheavy drinkers with each criterion. The extent of hypertension in the population overall attributable to heavy drinking varied from 4.3 to 11.6 percent, depending on the criterion used for hypertension. It was also highest (11.6 percent) when hypertension was defined as SBP ≥ 160 mm Hg.

## Discussion

The association between excessive alcohol consumption and hypertension is by now well established. In this study heavy drinkers had a much higher prevalence of hypertension by any criterion than the nonheavy drink-

ers—from 36.5 percent to 149.6 percent higher. However, heavy drinkers made up only 7.2 to 12.1 percent of the population, depending on the criterion. Hence in this population of middle-aged employed men surveyed in the late 1950s, the proportion of prevalent hypertension attributable to heavy drinking was in the order of 3.6–11.6 percent.

In the years since the late 1950s, the per capita consumption of alcohol by Americans has increased steadily, by more than 30 percent for beer, about 100 percent for wine, and about 50 percent for distilled spirits (19,20). Epidemiologic studies have shown a close correlation between mean per capita consumption of alcohol and the prevalence in the population of heavy drinking and problem drinking (21). Therefore, it is reasonable to infer that the population risk of hypertension attributable to heavy drinking is now higher among U.S. adults than the estimate produced here from the Western Electric study findings on white middle-aged men in the late 1950s. The conclusion is reinforced by the numbers of those outside the labor force because of their problem drinking and the prevalence of both heavy drinking and hypertension in the black population nowadays (22–25).

Moreover, if it is assumed, as has been found in several studies, that the relationship of alcohol use and blood pressure is linear, then in countries such as the United States, where the per capita consumption is high (26,27), the population at risk of alcohol-related hypertension is enormous. For this reason as well, therefore, the contribution of alcohol to the prevalence of hypertension is almost certainly greater than that estimated in this study, in which only heavy drinkers were considered. Conservatively, at least 30 million people in the United States—and as many as 60 million—are estimated to have hypertension (28). If the contribution of heavy drinking is 6 percent, then as many as 3,600,000 persons may have alcohol-related hypertension. Reduction of alcohol consumption could thus result in a substantial saving in lives. Potential hypertensives will also be saved the unpleasant side effects of anti-hypertensive therapy. It would seem appropriate that, in addition to weight reduction and salt restriction, moderation of alcohol intake is another important measure in the nonpharmacological control of hypertension.

## References

1. Lian, C.: L'alcoolisme, cause d'hypertension arterielle. *Bull Acad Med* 74: 525–528 (1915).
2. D'Alonzo, C. A., and Pell, S.: Cardiovascular disease among problem drinkers. *J Occup Med* 10: 571–581 (1968).
3. Kannel, W. B., and Sorlie, P.: Hypertension in Framingham. *In Epidemiology and control of hypertension*, ed-

ited by O. Paul. Stratton Intercontinental Medical Book Corp., New York, 1974, pp. 553–592.

4. Gyntelberg, F., and Mayer, J.: Relation between blood pressure and physical fitness, smoking and alcohol consumption in Copenhagen males aged 40–59. *Acta Med Scand* 195: 375–380 (1974).
5. Mathews, J. D.: Alcohol use, hypertension and coronary heart disease. *Clin Sci* 51 (supp.): 661–663 (1976).
6. Klatsky, A. L., Friedman, G. D., Siegelaud, A. B., and Gerrard, M. J.: Alcohol consumption and blood pressure. *New Engl J Med* 296: 1194–1200 May 26, 1977.
7. Dyer, A. R., et al.: Alcohol consumption. Cardiovascular risk factors and mortality in two Chicago epidemiologic studies. *Circulation* 56: 1067–1074 (1977).
8. Kozarevic, D. J., et al.: Frequency of alcohol consumption and mortality and morbidity. *Lancet* I: 613–616, No. 8169 (1980).
9. Mitchell, P. I., et al.: Role of alcohol in the aetiology of hypertension. *Med J Aust* II: 198–200 (1980).
10. Dyer, A., et al.: Alcohol, cardiovascular risk factors and mortality. The Chicago experience. *Circulation* 64 (suppl III): 20–27 (1981).
11. Saunders, J. B., Beevers, D. G., and Paton, A.: Alcohol induced hypertension. *Lancet* II: 653–656, No. 8248 (1981).
12. Beilin, L. J., et al.: Alcohol and hypertension. *Lancet* II: 1286, No. 8258 (1981).
13. Arkwright, P. D., et al.: Effects of alcohol use and other aspects of lifestyle on blood pressure levels and prevalence of hypertension in a working population. *Circulation* 66: 60–66 (1982).
14. Mathews, J. D.: Alcohol and hypertension. Editorial. *Aust NZ J Med* 9: 124–128 (1979).
15. Friedman, G. D., Klatsky, A. L., and Seigelaub, A. B.: Alcohol, tobacco, and hypertension. *Hypertension* 4 (suppl. III) 143–150, September-October 1982.
16. Paul, O., et al.: A longitudinal study of coronary heart disease. *Circulation* 28: 20 (1963).
17. Dyer, A., et al.: Alcohol consumption and 17-year mortality in the Chicago Western Electric Study. *Prev Med* 9: 78–90 (1980).
18. Levin, M. L.: The occurrence of lung cancer in man. *Acta Unio Internat Contra Cancrum* 9: 531–541 (1953).
19. Bureau of the Census: Statistical abstracts of the United States. Ed. 96, U.S. Department of Commerce, Washington, D.C., 1975, p. 750.
20. Bureau of the Census: Statistical abstracts of the United States. Ed. 100, U.S. Department of Commerce, Washington, D.C., 1979, p. 815.
21. Faris, D.: The prevention of alcoholism and economic alcoholism. *Prev Med* 3: 36–48, March 1974.
22. Stamler, J., et al.: Hypertension screening of 1 million Americans. Community Hypertension Evaluation Clinic (CHEC) Program, 1973 through 1975. *JAMA* 235: 2299–2306, (1975).
23. Hypertension Detection and Follow-up Program Cooperative Group. Race, education and prevalence of hypertension. *Am J Epidemiol* 106: 351–361 (1977).
24. National Center for Health Statistics: Blood pressure of persons 18–74 years, United States, 1971–1972. Series 11, No. 150. U.S. Department of Health, Education, and Welfare, Washington, D.C., 1975.
25. Terris, M.: Epidemiology of cirrhosis of the liver: national mortality data. *Am J Public Health* 57: 2076–2088 (1967).

26. Kaelber, C., and Mills, G.: Alcohol consumption and cardiovascular diseases. Introductory remarks. *Circulation* 64 (supp. III) 1-6 (1981).
27. Third special report to the U.S. Congress on alcohol and health. DHEW Publication No. (ADM) 78-569. U.S. Government Printing Office, Washington, D.C., 1978.
28. Public Health Service: Health United States 1980 with prevention profile. DHHS Publication No. (PHS) 81-1232. U.S. Government Printing Office, Washington, D.C., 1981.

## Over-the-Counter Drugs: Factors in Adult Use of Sedatives, Tranquilizers, and Stimulants

RALPH BELL, PhD

Dr. Bell is professor in the Division of Health Administration, School of Health Professions, Governors State University, Park Forest South, Ill. 60466.

This work was supported by grant C7-0079-01 from the Illinois Dangerous Drugs Commission.

Tearsheet requests to Dr. Bell.

### Synopsis .....

*Despite a growing research interest in over-the-counter (OTC) drug use, little information has been available about the determinants of use for this category of medications. The researcher examined the effects of demographic, need, and physician utilization measures on the use of 10 OTC drugs that were categorized as sedatives, tranquilizers, or stimulants. A statewide survey in 1975*

*of drug-using behavior in the previous year by Illinois adults ages 18-59 resulted in 2,738 questionnaires that could be analyzed. Thirteen variables, representing the demographic, need, and physician utilization characteristics of the respondents, were entered as predictors into logistic multiple regression models to estimate their effects on drug use.*

*Only 10.37 percent of the respondents indicated that they had used any of the OTC drugs in the previous year. Sedative use was found to be increased in persons who were tense or were having trouble sleeping. Having trouble sleeping also increased the probability of using OTC tranquilizers and stimulants. Women had a much higher probability of using OTC tranquilizers than men, and men had a higher probability of using stimulants. Non-whites had a higher probability of using tranquilizers than did whites. Stimulants were more likely to be used by younger adults and unmarried adults. Physician utilization, measured by the number of visits to physicians, did not significantly affect OTC drug use.*

**S**ELF-MEDICATION THROUGH THE USE of proprietary or over-the-counter (OTC) drugs represents one aspect of a growing movement toward medical self-care (1,2). OTC use is a cost-effective way of treating minor illnesses and alleviating related symptoms (1). Despite a growing interest among researchers in the use of OTC drugs and in the self-care movement in general, we still know little about who does or does not use different types of OTC drugs.

This research focused on the use of three broad classes of proprietary drugs by a cross section of adults: sedatives, including Nytol, Somnex, and Sleep-Eze, that are commonly used to alleviate insomnia; tranquilizers, including Compoz, Cope, and Nervine, that are commonly used to relieve minor tension or anxiety; and stimulants, including No-Doz, No Nod, Vivarin, and caffeine tablets, that are used to combat drowsiness. All three types of drugs are readily available over the counter in retail pharmacies and stores.

Although several studies on OTC use have been conducted, there remains a dearth of empirical data on the

correlates and predictors of use. Much of the empirical data available are limited because they are based on small samples or on particular segments of the population and cannot be used as a basis for generalizations. Bryar's study of self-care among British university students, for example, was based on only 28 persons (3). Similarly, Freer's research results are based on a sample of 26 women (4). The data presented by Knapp and Knapp were based on a sample of 275 households with children in Columbus, Ohio (5).

Anderson and coworkers have provided an excellent and comprehensive review of the literature on self-medication and self-care in general (2).

Several large-scale studies of OTC drug use have also been conducted. Data on whether the drugs had ever been used or used in the past year were collected for the National Commission on Marijuana and Drug Abuse (NCMDA) (6). Its results provide a base from which to examine demographic differences among users and non-users of sedative, tranquilizer, and stimulant proprietary drugs for a national sample of adults. The OTC drugs