Alcohol Consumption and Hypertension

STEPHEN MACMAHON

SUMMARY
An increased prevalence of hypertension in groups with high alcohol consumption has been recognized for a number of years. More recently, several studies have suggested an independent association between alcohol consumption and blood pressure levels in samples from general populations. Of 30 cross-sectional population studies reviewed, the majority reported small but significant elevations in blood pressure in those consuming three drinks or more per day in comparison with nondrinkers. In 25% of studies, elevations in blood pressure were also reported at lower levels of consumption; in about 40%, the blood pressure of nondrinkers was greater than that of those consuming one to two drinks per day. In two studies, one from the United States and one from Australia, the maximum contribution to the prevalence of hypertension of alcohol consumption greater than two drinks per day was estimated to be 5 to 7%; the contribution in men (11%) was greater than that in women because of their greater alcohol consumption. A prospective association of alcohol consumption with change in blood pressure was observed in five studies. In a small number of experimental studies, short-term falls in blood pressure accompanied alcohol restriction in both normotensive and hypertensive subjects. Uncontrolled observations in heavy drinking populations suggest that the effect on blood pressure of alcohol withdrawal may be lasting. However, firm conclusions about the long-term effects of alcohol restriction, particularly in moderate consumers who represent a large proportion in many populations, must await long-term controlled trials.

(Hypertension 9: 111-121, 1987)

KEY WORDS • alcohol • ethanol • blood pressure • hypertension

IT is over 70 years since Lian 1 reported an increased prevalence of hypertension among French servicemen consuming 3 L of wine or more per day. Since this early report numerous studies have reported an increased prevalence of hypertension in heavy drinkers or alcohol-dependent populations.2 In the past 20 years attention has focused on the question of whether an association exists between alcohol consumption and blood pressure levels in wider populations not selected on the basis of alcohol intake. This question has been addressed in a large number of cross-sectional studies and in a smaller number of prospective studies conducted in populations from a variety of geographic regions, including North America, Europe, Australia, New Zealand, and Japan.

The present report reviews the epidemiological evidence for the existence of an association between blood pressure and levels of alcohol consumption. Evidence is also considered concerning the nature of the association, that is, whether the association is linear or nonlinear and whether a consumption threshold exists for blood pressure elevation. These issues bear on the important public health question of the extent to which alcohol consumption contributes to blood pressure elevation in the population.

Two other questions are also considered. The first concerns the effects on blood pressure of modification of alcohol intake. This issue has been investigated in a small number of recent trials in hypertensive and normotensive subjects. The second question concerns the mechanism(s) by which alcohol affects blood pressure; a small number of studies in animals and in humans have attempted to address this question. For neither question are the available data sufficient to allow substantive conclusions to be drawn. Directions for further investigation are considered.

In this review, for the purposes of standardization, levels of alcohol consumption in humans have been expressed, whenever possible, as the number of standard drinks per day (1 standard drink is defined here as the equivalent of 8–10 g of ethanol).
## Table 1. Studies of the Cross-sectional Association of Blood Pressure with Alcohol Consumption

<table>
<thead>
<tr>
<th>Reference</th>
<th>Year</th>
<th>Study</th>
<th>No. of subjects</th>
<th>Male subjects (%)</th>
<th>Age (yr)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>North American</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Clark et al.</td>
<td>1967</td>
<td>Los Angeles Heart Study</td>
<td>865</td>
<td>100</td>
<td>21+</td>
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<tr>
<td>Dyer et al.</td>
<td>1977</td>
<td>Chicago W. Electric Study</td>
<td>1,899</td>
<td>100</td>
<td>40-55</td>
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<tr>
<td>Klatsky et al.</td>
<td>1977</td>
<td>Kaiser-Permanente I Study</td>
<td>83,947</td>
<td>45</td>
<td>15-79</td>
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<tr>
<td>Harburg et al.</td>
<td>1980</td>
<td>Tecumseh Study</td>
<td>3,390</td>
<td>47</td>
<td>18+</td>
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<tr>
<td>Criqui et al.</td>
<td>1981</td>
<td>Lipid Research Clinics Study</td>
<td>4,783</td>
<td>52</td>
<td>20+</td>
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<tr>
<td>Kagan et al.</td>
<td>1981</td>
<td>Honolulu Heart Study</td>
<td>8,006</td>
<td>100</td>
<td>46-68</td>
</tr>
<tr>
<td>Fortmann et al.</td>
<td>1983</td>
<td>Stanford Five City Study</td>
<td>1,842</td>
<td>48</td>
<td>20-74</td>
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<tr>
<td>Coates et al.</td>
<td>1985</td>
<td>Canada Health Study</td>
<td>1,418</td>
<td>51</td>
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<tr>
<td>Gruchow et al.</td>
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<td>NHANES Study</td>
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<tr>
<td>Klatsky et al.</td>
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<td>Kaiser-Permanente II Study</td>
<td>66,510</td>
<td>44</td>
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<tr>
<td>Gordon and Doyle</td>
<td>1986</td>
<td>Albany Study</td>
<td>1,910</td>
<td>100</td>
<td>38-55</td>
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<tr>
<td><strong>European</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gyntelberg and Meyer</td>
<td>1974</td>
<td>Copenhagen Study</td>
<td>5,249</td>
<td>100</td>
<td>40-59</td>
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<tr>
<td>Kozararevic et al.</td>
<td>1980</td>
<td>Yugoslavia Study</td>
<td>11,121</td>
<td>100</td>
<td>35-62</td>
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<tr>
<td>Milon et al.</td>
<td>1981</td>
<td>Lyon Study</td>
<td>1,134</td>
<td>100</td>
<td>20-59</td>
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<td>Salonen et al.</td>
<td>1983</td>
<td>North Karelia/Kuopio Study</td>
<td>8,479</td>
<td>50</td>
<td>30-64</td>
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<td>Cairns et al.</td>
<td>1984</td>
<td>Munich Blood Pressure Study</td>
<td>3,198</td>
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<td>Kornhuber et al.</td>
<td>1985</td>
<td>Wurttemberg Study</td>
<td>3,351</td>
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<td>Zutphen Study</td>
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<td><strong>Australian and New Zealand</strong></td>
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<td>Mitchell et al.</td>
<td>1980</td>
<td>Tasmania Study</td>
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<td>100</td>
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<tr>
<td>Baghurst and Dwyer</td>
<td>1981</td>
<td>CSIRO Study</td>
<td>350</td>
<td>100</td>
<td>23*</td>
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<tr>
<td>Cooke et al.</td>
<td>1982</td>
<td>Sydney Hospital Study</td>
<td>20,920</td>
<td>65</td>
<td>18-70</td>
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<tr>
<td>Arkwright et al.</td>
<td>1982</td>
<td>Perth Study</td>
<td>491</td>
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<td>20-45</td>
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<tr>
<td>Savdie et al.</td>
<td>1984</td>
<td>Medicheck Study</td>
<td>11,000</td>
<td>75</td>
<td>43*</td>
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<tr>
<td>MacMahon et al.</td>
<td>1984</td>
<td>Australian RFPS Study</td>
<td>5,550</td>
<td>50</td>
<td>25-64</td>
</tr>
<tr>
<td>Paulin et al.</td>
<td>1985</td>
<td>Milton Study</td>
<td>901</td>
<td>56</td>
<td>19+</td>
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<tr>
<td>Jackson et al.</td>
<td>1985</td>
<td>Auckland Study</td>
<td>1,429</td>
<td>66</td>
<td>35-64</td>
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<tr>
<td><strong>Japanese</strong></td>
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<tr>
<td>Ueshima et al.</td>
<td>1984</td>
<td>Osaka/Akita Study</td>
<td>887</td>
<td>100</td>
<td>40-69</td>
</tr>
<tr>
<td>Kondo and Ebihara</td>
<td>1985</td>
<td>Minamikawachi Study</td>
<td>3,083</td>
<td>37</td>
<td>53*</td>
</tr>
</tbody>
</table>

NHANES = National Health and Nutrition Examination Survey; CSIRO = Commonwealth Scientific and Industrial Research Organization; RFPS = Risk Factor Prevalence Study.

*Mean age.

### Cross-sectional Association of Blood Pressure and Alcohol Consumption in Samples from General Populations

#### North American Studies

The association of blood pressure with alcohol consumption has been investigated in at least 12 cross-sectional studies in North American populations (Table 1). 3-14 The study populations ranged in size from 865 in the Los Angeles Heart Study to 83,947 in the first Kaiser-Permanente Study. 3 With one exception, 11 all of these studies have reported a significant positive association of blood pressure and alcohol consumption. In multivariate analyses the association was shown to be independent of a variety of potential confounding factors, including age, relative body weight, exercise, and smoking status, that are known to be or are likely to be related to both blood pressure and alcohol consumption.

A number of these studies suggested that the association of blood pressure and alcohol consumption may be nonlinear. In the first Kaiser-Permanente Study 5...
little difference was observed in systolic or diastolic blood pressures between nondrinking men and men consuming one to two drinks per day; in women, systolic and diastolic blood pressures were greater in nondrinkers than in those consuming one to two drinks per day, thereby producing a J-shaped association. The authors suggested that the results of their study indicated a threshold effect of three drinks per day for blood pressure elevation in both sexes and in all racial groups.

Similar associations in men were observed in the Lipid Research Clinics (LRC) Prevalence Study and in the Albany Study. In the LRC Study, the association in women was more closely U-shaped, with the blood pressure of nondrinkers being approximately equivalent to that in the highest consumption group (≥2-3 drinks per day). A U-shaped association in women was also reported in the Tecumseh Study and the Framingham Study. Both of these studies also reported a J-shaped association in men, in whom the blood pressure of those consuming two to three drinks or more per day appeared to be greater than that of drinkers consuming fewer than two drinks per day. This result was similar to that reported by the Honolulu Heart Program for systolic blood pressure; diastolic blood pressure in this population appeared to increase linearly with increasing levels of alcohol consumption.

Both linear and nonlinear associations also were observed in the Stanford Five City Project and the second Kaiser-Permanente Study. The Stanford Study reported a J-shaped association in men aged 35 to 49 years, a linear association in men aged 50 to 74 years, and a curvilinear association in women aged 50 to 74 years. In the second Kaiser-Permanente Study of 66,510 men and women, the association appeared to be linear in men of most age groups and J-shaped in women. A linear association in men was also reported in the Chicago Western Electric Company Study.

**European Studies**

The association of blood pressure with alcohol consumption has been investigated in at least seven European studies (see Table 1). The study populations ranged in size from 794 in the Zutphen Study to 11,121 in the Yugoslavia Cardiovascular Disease Study. All of these studies found evidence of an association of blood pressure with alcohol consumption independent of a variety of potential confounding factors. In the Munich Blood Pressure Study and in the studies of Gyntelberg and Meyer and Milon et al., the blood pressures of nondrinkers generally were either greater than or no different from those of persons consuming one to two drinks per day. In the latter two studies, blood pressure was greater in drinkers than in nondrinkers at consumption levels between three and five drinks per day. In the Munich Blood Pressure Study, blood pressure was greater in drinkers than in nondrinkers at consumption levels between six and eight drinks per day. The nature of the blood pressure-alcohol consumption association was not clearly specified in the other studies.

**Australian and New Zealand Studies**

There are six Australian studies and two New Zealand studies of the association of blood pressure and alcohol consumption (see Table 1). The study populations of these studies ranged in size from 85 in the study of Mitchell et al. to 20,920 in the study of Cooke et al. Only one of these studies failed to observe a significant independent association of alcohol consumption with blood pressure. The nature of the association, however, varied between studies. J-shaped or U-shaped associations were observed in the National Heart Foundation of Australia Risk Factor Prevalence Study and in the study of Jackson et al. Both of these studies found evidence of an attenuation of the difference in blood pressure between nondrinkers and those consuming one to two drinks per day after adjustment for possible confounding factors such as age, body mass index, and smoking status. In both studies, there was evidence of greater blood pressure in drinkers than in nondrinkers at levels of consumption greater than three drinks per day. In contrast to these results, Mitchell et al., Cooke et al., Arkwright et al., Savdie et al., and Paulin et al. all reported a linear association of blood pressure with consumption of alcohol.

**Japanese Studies**

The association of blood pressure with alcohol consumption has been investigated in at least two Japanese studies (see Table 1). Ueshima et al. investigated the association in 887 men from urban and rural populations; Kondo and Ebihara investigated the association in 3083 men and women from a rural population. Ueshima et al. reported independent linear associations in both the urban and the rural populations. Kondo and Ebihara observed an independent positive association of blood pressure with alcohol consumption in men but not in women, 56% of whom were nondrinkers. In the total study population the blood pressure of drinkers was greater than that of nondrinkers at levels of alcohol consumption equivalent to two to four drinks per day.

**Comment**

The results of these studies conducted in a variety of populations are largely consistent in demonstrating a positive cross-sectional association of blood pressure with alcohol consumption that is independent of a variety of confounding factors, such as age and body mass index. However, the evidence is conflicting as to whether the blood pressure of persons consuming small amounts of alcohol (1-2 drinks per day) is greater, less, or no different than that of nondrinkers. The blood pressure of nondrinkers was greater than that of minimal alcohol consumers in most of the U.S. studies but in only a minority of the studies from other countries. In some studies it was not clear whether confounding factors such as obesity might have contributed to the finding of a higher blood pressure in nondrinkers, as was observed in the Australian Risk Factor Prevalence Study and the study of Jackson et
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al. In other studies, however, the difference was shown to be independent of several factors, including age, body mass index, smoking, and exercise, raising the possibility of a hypotensive effect of modest regular alcohol consumption in some populations.

The reason for the inconsistency of the results with regard to relative blood pressures of nondrinkers and light drinkers is uncertain. It may reflect differences in the characteristics of the study populations (e.g., the exclusion of persons being treated for hypertension in some studies) or differences in the methodology of alcohol consumption data collection (e.g., 7-day recall vs estimate of usual consumption). However, a systematic association of these particular design characteristics with the study findings was not discernible. Similarly, there was no discernible association of study outcome with study population size, suggesting that the differences could not be explained by differential statistical power. The inconsistency of the results may simply indicate random variation in outcomes, with little or no true difference in blood pressure between nondrinkers and light consumers.

A more consistent finding was an elevation in both systolic and diastolic blood pressures at levels of consumption of three or more drinks per day. In general, the elevation in systolic pressure was greater than that in diastolic pressure. Most studies observed that in subjects consuming three drinks per day, systolic blood pressure was 3 to 4 mm Hg greater and diastolic blood pressure 1 to 2 mm Hg greater than that in nondrinkers. In subjects consuming five to six drinks per day, systolic blood pressure was 5 to 6 mm Hg greater and diastolic blood pressure 2 to 4 mm Hg greater than that in nondrinkers. There were no systematic differences in the degree of blood pressure elevation at these levels of consumption between those study populations in which a blood pressure elevation was observed at low levels of consumption (i.e., 1-2 drinks per day) and those in which blood pressure elevation was only observed at higher levels. A number of studies reported the prevalence of hypertension at various levels of alcohol consumption. Although there were differences in the definition of hypertension, the change in prevalence with increasing alcohol consumption was similar in most reports; at three to four drinks per day the prevalence of hypertension was approximately 50% greater than that in nondrinkers, and at six to seven drinks the prevalence was 100% greater.

The possibility of a differential association of alcohol consumption with blood pressure levels according to patterns of consumption and type of alcoholic beverage cannot be addressed by the available data. However, the consistency of results across such a wide range of study populations from cultures with widely divergent drinking patterns and beverage types suggests that these factors are not likely to be central to the observed overall positive association of alcohol consumption and blood pressure.

Some studies presented evidence of a trend toward a greater effect of alcohol on blood pressure in older than in younger men. In most studies the elevations in blood pressure and hypertension prevalence were similar in the two sexes; however, the number of women who consumed three or more drinks per day was small and often not sufficient to detect moderate blood pressure elevations. In a number of studies the blood pressure of female nondrinkers, particularly in older age groups, was considerably greater than that in minimal alcohol consumers, producing a U-shaped association. This association may be related to the finding in some studies of a greater body mass index in nondrinking women than in women of any other alcohol consumption category. However, a possible role of hormonal changes associated with menopause in determining the effect of alcohol consumption on blood pressure cannot be excluded.

Prospective Studies of the Association of Blood Pressure with Alcohol Consumption

There are at least six prospective, observational studies of the association of blood pressure with alcohol consumption (Table 2). For the most part, the results of these studies were consistent with those of the cross-sectional studies and indicated a positive association of blood pressure with alcohol consumption that appeared to be independent of such confounding factors as body mass index and smoking status at baseline and at follow-up. The first of the prospective studies was probably the Chicago People's Gas Company Study, which observed that the rise in systolic and diastolic blood pressure over a 4-year period among employees classified as problem drinkers was greater than that in so-called non-problem drinkers; more precise alcohol consumption data were not collected. The Chicago Western Electric Study reported that among employees who had a diastolic blood pressure less than 90 mm Hg at baseline, the rise in blood pressure over 4 years of follow-up was significantly greater in those consuming six or more drinks per day than in those consuming less. In those consuming fewer than six drinks per day, there appeared to be no prospective association between change in blood pressure and the level of alcohol consumption.

The prospective association of blood pressure and alcohol consumption over 4 years has also been investigated in the Framingham Study. It was observed in both men and women that change in alcohol consumption was positively associated with change in systolic and diastolic blood pressures. An increase in consumption over 4 years was associated with a significant increase in blood pressure, whereas a decrease in consumption was associated with a significant decrease in blood pressure. A similar association of change in systolic pressure with change in alcohol consumption independent of change in body mass index was reported over 5 years of follow-up in the Zutphen Study; a similar but weaker association was observed over 10 years. In this study change in alcohol consumption was not significantly related to change in diastolic blood pressure. During 18 years of follow-up the Albany Study observed that among men who stopped drink-
ing or reduced their consumption, there was a significantly smaller than average increase in blood pressure over the follow-up interval; this difference was independent of age, changes in weight, and changes in smoking status. The results of these studies are consistent with observations from a trial of a multifactorial intervention for the treatment of hypertension in patients withdrawn from long-term drug treatment, which reported that the consumption of five or more drinks per day was often associated with a rise in blood pressure, necessitating return to drug treatment. The Honolulu Heart Study may be the only prospective study that has reported no association of systolic or diastolic blood pressure at follow-up with alcohol consumption either at baseline or at follow-up.

**Contribution of Alcohol Consumption to the Prevalence of Hypertension**

On the basis of mortality data Mathews has estimated that as much as 30% of hypertension in developed countries such as England and the United States may be attributable to alcohol use. However, blood pressure data from the Australian Risk Factor Prevalence Study and the first Kaiser-Permanente Study suggested that the proportion in these study populations was considerably smaller. In both of these studies, the prevalence of hypertension was high and significant associations were observed between blood pressure and alcohol consumption. The Australian Risk Factor Prevalence Study estimated that 7% of the prevalence of hypertension (systolic blood pressure ≥ 150 mm Hg or diastolic blood pressure ≥ 95 mm Hg, or both) could be attributed to alcohol consumption (population attributable risk). The Kaiser-Permanente Study estimated that 5% of the prevalence of hypertension (systolic blood pressure ≥ 160 mm Hg or diastolic blood pressure ≥ 95 mm Hg or both) could be attributed to alcohol consumption. These estimates of population attributable risk do not take into account possible confounding factors such as age and body mass index.

In these two studies, despite their differing definitions of hypertension, it was estimated that a maximum of 11% of hypertension in men, but considerably less in women, could be attributed to alcohol consumption. In the Risk Factor Prevalence Study, alcohol consumption could account for no more than 1% of hypertension in women. The sex difference in the proportion of hypertension prevalence associated with alcohol consumption is most likely to be the consequence of greater consumption of alcohol by men than women.

Thus, although blood pressure levels and the relative risk of hypertension have been shown to be greater at higher levels of alcohol consumption in most populations, the actual contribution of alcohol consumption to the prevalence of hypertension may be smaller than previously has been suggested. In estimating the contribution of alcohol consumption to the prevalence of hypertension in communities, however, it is important to consider the representativeness of alcohol consumption in the study population in comparison with the community from which it is drawn. If heavy drinkers are proportionately underrepresented in sample surveys, then the contribution of alcohol consumption to the prevalence of hypertension may be underestimated. In the Australian Risk Factor Prevalence Study the prevalence of very heavy alcohol consumption (i.e., ≥ 9 drinks per day) in men in this study population was somewhat less than that claimed in previous Australian studies; the prevalence in women was similar. This difference might indicate that the 11% of hypertension in men potentially attributable to alcohol consumption is a conservative estimate.

Further studies of the population attributable risk of alcohol consumption for hypertension prevalence would be valuable. Such studies should more carefully consider the possible effects of confounding factors such as age and body mass index. It would be of interest to determine whether estimates of the attributable risk are greater in study populations in which the association of blood pressure with alcohol consumption is linear rather than nonlinear (as in the Australian Risk Factor Prevalence Study and the Kaiser-Permanente Study). It would also be of interest to determine, from prospective observational studies, the population attributable risk of alcohol consumption for hypertension incidence.

**Validity of Alcohol Consumption Data**

The question of the validity of self-reported alcohol consumption data requires examination in any consideration of the association of alcohol consumption and blood pressure in population studies. The possible underreporting of alcohol consumption could affect the

### Table 2. Prospective Observational Studies of the Association of Blood Pressure with Alcohol Consumption

<table>
<thead>
<tr>
<th>Reference</th>
<th>Year</th>
<th>Study</th>
<th>No. of subjects</th>
<th>Male subjects (%)</th>
<th>Age range (yr)</th>
<th>Follow-up (yr)</th>
</tr>
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<td>Dyer et al.</td>
<td>1977</td>
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<td>1340</td>
<td>100</td>
<td>40-59</td>
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<td>1981</td>
<td>Chicago W. Electric</td>
<td>871</td>
<td>100</td>
<td>40-55</td>
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<td>Reed et al.</td>
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<td>6858</td>
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<td>Gordon and Doyle</td>
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<td>Albany</td>
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<td>100</td>
<td>38-55</td>
<td>18</td>
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observed association between alcohol and blood pressure in a number of ways. The entire association between blood pressure and alcohol could be an artifact of underestimation of consumption only if those with lower blood pressure were to underestimate consumption to a greater extent than those with higher blood pressure. However, there is no reason to believe that the validity of alcohol consumption data should be related to blood pressure in this way.

If all people were to underestimate alcohol consumption to a similar degree, then the observed cross-sectional association would remain an accurate estimate of the true association, but the level of consumption associated with increased blood pressure would be underestimated. Friedman et al.38 argued that if heavy drinkers were to underestimate alcohol consumption to a greater degree than others, an underestimation of the overall association between alcohol and blood pressure might result, by decreasing the blood pressure difference between lighter and heavier drinking groups. However, such selective underestimation by heavy alcohol consumers would also contribute to the increased blood pressure observed at lower levels of consumption. If blood pressure were only truly increased in heavy consumers, then an increasing proportion of "underestimating" heavy consumers across the range of lighter alcohol consumption categories could contribute to the dose-response type of relationship seen in cross-sectional studies. Similarly, denial of alcohol consumption by heavy consumers could contribute to the J-shaped association of blood pressure with alcohol intake observed in a number of studies.

Although the ultimate effects of underestimation of alcohol consumption are unknown, it clearly is unlikely to account for the entire association between alcohol and blood pressure. However, underestimation by everyone, or selectively by heavy consumers, could result in underestimation of the level of consumption at which blood pressure levels are increased.

**Trials of Alcohol Restriction**

In their review of studies of the prevalence of hypertension in high alcohol consumption groups, Ashley and Rankin2 observed that in two hospital inpatient studies a marked decrease in blood pressure and the frequency of hypertension was noted a few days after admission. They also observed that similar reductions in blood pressure following admission had been reported in a number of other studies of inpatient groups undergoing treatment for alcoholism, and at least one study had reported a reduced prevalence of hypertension in recovered alcoholics compared with current heavy drinkers. Ashley and Rankin suggested that the hypertension associated with heavy alcohol consumption may be reversible on cessation of drinking.

Subsequent work by Saunders et al.39 gave further support to this proposition of reversibility. In a study of 132 alcoholic patients consuming in excess of eight drinks per day, 52% were reported to have had blood pressures exceeding 140/90 mm Hg at the time of presentation. They reported that blood pressures fell after detoxification and remained reduced after discharge in those known to be abstinent. However, this study was uncontrolled, as were those reviewed by Ashley and Rankin.2 To my knowledge, the first controlled (though not randomized) trial of the effects on blood pressure of reduction in alcohol consumption was that of Potter and Beeveres, involving 16 men with moderate hypertension whose usual alcohol consumption averaged six to eight drinks per day. With the use of a crossover design, they observed that blood pressures remained high when alcohol consumption was maintained at baseline levels but fell significantly (systolic, 13 mm Hg; diastolic, 5 mm Hg) when alcohol was withdrawn for 3 to 4 days. The reintroduction of similar amounts of alcohol produced significant increases in both systolic and diastolic blood pressures. Thus, the results of this study suggest both a pressor effect of moderate to heavy alcohol consumption in hypertensive men and short-term blood pressure reductions following complete withdrawal of alcohol.

Malhotra et al.41 addressed the question of whether such reductions in blood pressure could be observed following restriction of alcohol intake in both normotensive and hypertensive subjects. The effects of an alcohol intake of approximately six drinks per day in comparison with total abstinence were investigated in a 10-day sequential study (5 days of alcohol consumption followed by 5 days of abstinence). Thirty men were studied: 10 normotensive and 10 hypertensive subjects who all reported consuming fewer than two drinks per day, and 10 hypertensive subjects who reported consuming up to six drinks per day. In both hypertensive groups, standing systolic and diastolic blood pressures were significantly lower during the abstinence phase (systolic, 10–12 mm Hg; diastolic, 6–8 mm Hg). In normotensive subjects systolic and diastolic blood pressures were 1 to 3 mm Hg lower during the abstinence phase, but this decrease was not statistically significant. While these results appear to confirm those of Potter and Beeveres and extend them to hypertensive subjects with a history of light alcohol consumption, important methodological problems were associated with this study that must be considered when interpreting the results. First, the effects of habituation to blood pressure measurement and regression to the mean were not controlled for; there was no parallel or crossover control condition. Second, there was no mention of the use of blinded observers or random zero sphygmomanometers in the measurement of blood pressure during the trial. The possibility that there was some carryover effect from the alcohol consumption phase to the abstinence phase that may have accounted for the failure to observe a significant difference in blood pressure between phases in the normotensive group could not be excluded.

To my knowledge, the first randomized, controlled trial of the effect of restriction of alcohol consumption was that of Puddley et al.32 In this study 48 normotensive men who reported consuming an average of four to five drinks per day were studied in a 12-week cross-
over trial in which subjects consumed approximately three drinks per day for 6 weeks and three drinks per week for 6 weeks. In contrast to the findings of Malhotra et al., standing and supine systolic blood pressures were significantly lower (4 mm Hg) during the low alcohol consumption phase than during the high alcohol consumption phase; changes in diastolic blood pressure were smaller (1.4–2.5 mm Hg) and not statistically significant. Changes in both systolic and diastolic blood pressures were correlated with reported changes in alcohol intake. Howes has observed similar effects of alcohol restriction in normotensive subjects with moderate drinking habits. Ten subjects (5 men and 5 women) were studied in an eight-day randomized crossover trial in which subjects consumed eight drinks per day for 4 days and were abstinent for 4 days. Both systolic and diastolic blood pressures were significantly lower (8 mm Hg and 6 mm Hg, respectively) during the period of abstinence.

In summary, the results of these studies suggest a short-term pressor effect of levels of alcohol consumption between three and eight drinks per day in both hypertensive and normotensive subjects. Similarly, the results indicate that the total withdrawal of alcohol or its restriction to less than one drink per day results in short-term falls in blood pressure. These results are suggestive of a therapeutic benefit of alcohol restriction in hypertensive subjects and a preventive benefit in normotensive subjects; however, this possibility needs to be confirmed in long-term, randomized controlled trials. The results of the trials, taken together with the findings in the cross-sectional and prospective observational studies, are supportive of the hypothesis of causality in the relationship between alcohol consumption and blood pressure.

Possible Mechanisms

The mechanism by which regular alcohol consumption leads to chronic elevations in blood pressure is uncertain and has been the subject of comparatively few investigations. A number of studies have investigated the mechanisms by which alcohol ingestion results in acute changes in blood pressure; however, there are problems in extrapolating from the results of such studies explanations for the chronic blood pressure elevation associated with long-term regular consumption.

One hypothesis has developed from observations of the acute effects on blood pressure of alcohol withdrawal. The degree of blood pressure elevation was found to be related to the severity of alcohol withdrawal in heavy drinkers during detoxification. Subsequently, it was suggested that long-term alcohol consumption leads to a state of intermittent withdrawal even at low levels of consumption that may be responsible for the elevation in blood pressure. This hypothesis is consistent with observation in the LRC Prevalence Study that blood pressure (measured after 12 hours of fasting) was more closely associated with alcohol consumed in the previous 24 hours than with alcohol consumed in the previous week. However, the hypothesis is not consistent with the observation in studies such as that of Potter and Beevers that a fall in blood pressure occurred immediately after abstinence from alcohol (within 24 hours), with no obvious peak in blood pressure before the fall. The withdrawal hypothesis is undoubtedly worthy of further investigation. Collection of data on "hours since the last drink" would be of value in any future epidemiological studies. Withdrawal in certain individuals may account for some, though not necessarily all, of the association between blood pressure and alcohol consumption.

The observation that psychological stress results in acute increases in blood pressure has led to the hypothesis that stress may independently predispose to both hypertension and alcohol use. While there are many difficulties in measuring stress, there are instruments for measuring a variety of psychological characteristics often considered to be influenced by stress. In the Australian Risk Factor Prevalence Study and in a study by Arkwright et al., the association of blood pressure with alcohol consumption was shown to be independent of a number of such psychological characteristics, including type A behavior, trait anxiety, recent life stress, neuroticism, and extroversion or introversion. Furthermore, the observation in intervention studies of a reduction in blood pressure following the withdrawal of or reduction in intake of alcohol suggests that the association of blood pressure with alcohol consumption is not an artifact of the association of the latter with any factor that may predispose to alcohol use.

The role of catecholamines in mediating the acute effects on blood pressure of alcohol administration has been investigated in a number of studies. Ireland et al. have observed acute increases in blood pressure and plasma epinephrine immediately following alcohol ingestion in normotensive men. These authors have suggested that repeated activation of this adrenergic system may produce a slow pressor effect involving small increments in plasma epinephrine and resulting in chronic increases in blood pressure. However, Potter et al. and Howes and Reid have shown that the short-term rise in blood pressure in normotensive subjects is followed by a fall in pressure to control levels or lower a few hours after ingestion. In both these studies, the short-term increase in blood pressure was associated with a longer increase in heart rate. In the study of Howes and Reid, alcohol administration was associated with a transient increase in plasma norepinephrine. Such increased norepinephrine levels may reflect an increase in sympathetic nervous activity; however, other studies of the acute effects of alcohol ingestion suggest that the increase in norepinephrine may be the consequence, at least in part, of a reduced clearance and metabolism rather than an increased secretion. Potter et al. also measured plasma renin and cortisol levels and reported that neither appeared to be affected by the administration of alcohol.

The role of circulating levels of these pressor hor-
mones in maintaining chronic elevations in blood pressure associated with moderate levels of regular alcohol consumption has been investigated in one study in rats and in three studies in humans. In a recent study of rats made hypertensive by chronic alcohol consumption, Chan et al.\(^51\) observed a 20 to 30% increase in plasma norepinephrine in alcohol-fed animals in comparison with controls given an alcohol-free diet. Arkwright et al.\(^52\) measured levels of various pressor hormones in 30 male nondrinkers and in a group matched for age and body mass index with an average consumption of five drinks per day. They observed that, although blood pressures were greater among the drinkers, there were no significant differences between the groups in plasma epinephrine, norepinephrine, cortisol, or renin at rest or during physiological stress. In a similar study by Ibsen et al.,\(^53\) plasma norepinephrine and renin levels were compared in a group of 16 men consuming an average of five or more drinks per day and in 17 men consuming fewer than three drinks per day. As in the study of Arkwright et al.,\(^52\) blood pressure levels were significantly greater in the heavier consumption group; however, plasma renin levels were also greater in this group. Potter and Beevers\(^40\) found that plasma cortisol but not plasma renin increased during the alcohol consumption phase and fell during the abstinence phase. The reason for the inconsistency of these results is uncertain. Further studies of the long-term effects of alcohol manipulation both on levels of these pressor substances and on levels of blood pressure would be of value.

A number of recent reviews have drawn attention to the possibility that chronic levels of alcohol consumption might be directly related to peripheral vascular tone and vascular smooth muscle cell membrane transport.\(^54\)\textsuperscript{-57} Acutely, the effect of alcohol consumption is predominantly vasodilative\(^58\); there is also evidence that it reduces vascular reactivity to pressor substances such as methoxamine.\(^59\) In contrast, however, Altura and Altura\(^58\) have observed that local or systemic administration of alcohol in rats results in potentiation of the constrictor responses of certain arterioles to locally administered catecholamines in animals maintained for two to six weeks on liquid diets containing ethanol but not in animals maintained on an alcohol-free diet. These authors suggest that an increased sensitivity of blood vessels to pressor substances in subjects with a higher regular alcohol intake is a possible mechanism by which chronic levels of alcohol consumption could affect blood pressure levels. This is an important hypothesis that requires further investigation in animals and humans.

It has been proposed that an alcohol-induced, chronic increase in vascular sensitivity might be mediated by changes in calcium transport into vascular smooth muscle cells.\(^58\) In the short-term alcohol-loading study of Potter et al.,\(^49\) plasma calcium levels fell significantly after alcohol ingestion. Urinary calcium was not measured, but the authors noted that it has been reported that urinary calcium excretion is not increased after the administration of alcohol in rats and dogs. Although this finding requires verification in humans, it raises the possibility that the hypocalcemia may reflect the transfer of calcium from the plasma into tissues with a rise in intracellular calcium in smooth muscle cells, thereby facilitating vasoconstriction. A study in rats made hypertensive by chronic alcohol consumption was unable to demonstrate any gross cell membrane transport changes in erythrocytes.\(^60\) However, further animal and human studies of cell membrane transport, intracellular calcium concentrations, and peripheral vascular reactivity in relation to acute and chronic levels of alcohol consumption would be of value.

In summary, the results of these studies raise a number of possibilities concerning the involvement of neural, humoral, and renal mechanisms in the mediation of the observed association between levels of regular alcohol consumption and blood pressure. However, the actual role of each of these factors, if any, is far from clear. There is a pressing need for careful investigation of these factors in long-term experimental studies of the effects on blood pressure of alcohol manipulation.

**Conclusions and Implications for Prevention and Treatment**

The available evidence clearly indicates that blood pressure, the prevalence of hypertension, and the rate of increase in blood pressure over time are significantly increased in heavy alcohol consumers (i.e., those consuming \(\geq 6\) drinks per day). Short-term, nonrandomized, controlled studies suggest that the withdrawal of alcohol in such patients with hypertension may result in a fall in blood pressure. Uncontrolled observations indicate that in a proportion, blood pressures may fall to normotensive levels after a period of abstinence. Long-term, randomized, controlled trials of the effects of alcohol withdrawal or restriction on blood pressure in heavy consumers would be of value. An additional benefit of reduction in alcohol consumption in such patients may be an improved response to antihypertensive therapy and increased compliance with treatment\(^61,62\); this is also worthy of further investigation.

Collectively, these observations suggest that a detailed history of alcohol consumption should be obtained from patients with hypertension, particularly men, in whom heavy alcohol consumption is more frequent. The measurement of biochemical markers of alcohol consumption and the assessment of other clinical signs of heavy drinking\(^63\) might also aid in the identification of heavy consumers. Such patients should be encouraged to reduce their consumption and be referred for treatment of alcohol dependence when appropriate. The importance of reducing consumption in young patients who are heavy consumers is accentuated by the finding in at least two studies that heavy alcohol consumption preceded the onset of symptoms in a large proportion of patients under the age of 55 years who suffered a stroke.\(^64,65\) Whether this association involves an acute alcohol-induced increase in
blood pressure is uncertain. However, data from the Honolulu Heart Program have indicated a positive association between levels of alcohol consumption and the risk of hemorrhagic stroke, independent of chronic blood pressure levels.

In most of the population studies reviewed, blood pressure levels were greater at moderate levels of alcohol consumption (3–4 drinks per day) than at minimal levels (1–2 drinks per day). Approximately 25% of studies reported blood pressure elevations, in comparison with pressures of nondrinkers, at consumption levels below three drinks per day. However, any estimate of the level of consumption necessary for blood pressure elevation will be an underestimate if there is a tendency for alcohol consumption to be underreported in population studies. In about 40% of studies, the blood pressure of nondrinkers, particularly female nondrinkers, was observed to be greater than that of those consuming one to two drinks per day. Whether these observations truly reflect a hypotensive effect of minimal consumption remains uncertain. This question might be addressed more effectively in an experimental study.

A number of reports found that the prevalence of hypertension, variously defined, increased with increasing levels of alcohol consumption. In population studies from the United States and Australia, it was suggested that alcohol consumption could account for as much as 11% of hypertension (150–160/95 mm Hg) in men but considerably less in women because of their lesser consumption of alcohol. Therefore, the possibility exists that reduction of alcohol consumption in men consuming three or more drinks per day could have an important role in interventions for both the treatment of hypertension and its primary prevention.

However, the short-term and long-term effects of reducing alcohol consumption in hypertensive patients who consume fewer than six drinks per day are uncertain. Puddey et al. have observed that systolic blood pressure fell in normotensive men when alcohol consumption was reduced from the equivalent of three drinks per day to fewer than two drinks per week over a 6-week period. Whether this change in blood pressure can be maintained over a longer period and whether a similar reduction in alcohol consumption will reduce blood pressure in hypertensive patients remains to be determined. The uncontrolled observations of Malhotra et al. are suggestive of a similar benefit in hypertensive subjects.

Stamler and colleagues have incorporated restriction of alcohol consumption in two controlled, multifactorial intervention studies, one concerning the prevention of hypertension in high-risk subjects and the other concerning the nondrug treatment of hypertension in subjects withdrawn from long-term drug therapy. The results of the treatment study suggested that there may be problems in long-term compliance with alcohol restriction. In this study, subjects who normally consumed three or more drinks per day were counseled to reduce their consumption to fewer than three drinks per day; after 3 years only 30% reported having achieved this goal. This finding suggests that work is needed to develop strategies to maximize adherence to regimens involving restricted alcohol consumption.

In many populations, a large proportion of men consume three or more drinks per day. If a reduction of alcohol consumption in moderate alcohol consumers could be achieved and could be shown to result in long-term reduction of blood pressure — even if only by 2 to 3 mm Hg — this could result in important reductions in both the prevalence of hypertension and the incidence of cardiovascular disease. The data from population studies and short-term trials suggest that this may be possible. However, definite conclusions about the value of reducing alcohol consumption in moderate consumers, for the treatment and prevention of blood pressure elevation, will require long-term, randomized, controlled trials in hypertensive and normotensive populations.

Acknowledgments

The author gratefully acknowledges the advice of Dr. Robyn Norton of the National Institute on Alcohol Abuse and Alcoholism, Rockville, Maryland. The assistance of Ms. Leah Thompson and Ms. Colleen Brown in the production of the manuscript is also acknowledged.

References

13. Klatsky AL, Friedman GD, Armstrong MA. The relationships between alcoholic beverage use and other traits to blood pres-
50. Chan TCK, Wall RA, Sutter MC. Chronic ethanol consumption, stress, and hypertension. Hypertension 1985;7:519-524
53. Stokes GS. Hypertension and alcohol: is there a link? J Chronic Dis 1982;35:759-762
63. Chang NC, Chao HM, eds. Early identification of alcohol abuse. Rockville, MD: National Institute on Alcohol Abuse and Alcoholism, 1985; DHHS publication no (ADM) 85-1258 (Research monograph no 17)
Alcohol consumption and hypertension.
S MacMahon

*Hypertension*. 1987;9:111-121
doi: 10.1161/01.HYP.9.2.111

*Hypertension* is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0194-911X. Online ISSN: 1524-4563

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World Wide Web at:
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