injection of the suspect ampicillin. This batch of ampicillin was taken out of circulation immediately, and samples were sent for analysis in Europe. Chemical analysis confirmed the presence of ampicillin but also of high concentrations of *N*, *N*-dimethylanalin, a degradation product, and of another, unknown, substance.

Culture showed *Pseudomonas* spp and an unknown organism in the first two phials and *Bacillus* spp and an unknown organism in the second two phials. The laboratory suggested that, in view of the unevenness of the contamination, the route of entry could have been the perforated stoppers. The non-government organisation informed the relevant authorities.

The fact that the aluminum seals of the phials were normal while the rubber stoppers were perforated indicates that the rubber stoppers were not perforated after the manufacturing process. Thus stoppers that were already perforated were probably used in the manufacturing process. The most likely explanation is that these stoppers were second hand—in other words, disposable material had been reused. In the Indian subcontinent it is common (and dangerous) practice to collect used disposable syringes and needles from hospitals and to repackage them and sell them as new—hopefully after proper cleaning and sterilisation.

As far as I know, reuse of disposable stoppers has not been described before, but it seems possible that it is a new, illegal, probably profitable, but certainly highly dangerous enterprise.

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Alcohol consumption and risk of coronary heart disease

Studies suggest that wine has additional effect to that of ethanol

EDITOR,—In their review of the reduction in the risk of coronary heart disease due to moderate alcohol consumption Eric B Rimm and colleagues interpret the available studies as supporting a beneficial effect of alcohol without any additional effect of the specific beverage consumed (beer, wine, or spirits).[1] We do not challenge the paradigm that ethanol itself possesses some cardioprotective properties. In the Copenhagen city heart study we also found a reduction in mortality associated with occasional intake of all three types of beverage.[2] But studies that do not take into account all three types of beverage are not suitable for addressing the question of whether there is an additional effect of beer, wine, or spirits.

Rimm and colleagues included in their review 10 prospective population studies, of which three did not analyse the effect of all three types of alcoholic beverage because consumption of one or two of them was negligible. In two other studies the analysis did not take into account the intake of the other types of beverage. Of the remaining five studies, four suggested a greater beneficial effect of wine, although with different methodological and statistical strength. In Rimm *et al*'s study, which found a stronger beneficial effect of spirits, 12.2% of the male health professionals studied reported a total alcohol intake of more than 2 drinks a day.[3] A breakdown of the figures showed that the number of subjects who drank each type of beverage were small. The exact data are not given, but we are told that spirits were the beverage most frequently consumed, and the broad confidence intervals give a hint of the small number of subjects in the groups that drank beer and wine.[1 3]

Thus the ecological and prospective cohort studies, as well as pertinent clinical studies,[4 5] suggest that wine has an additional effect to that of ethanol in reducing the risk of coronary heart disease.

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Authors' reply

EDITOR,—Many of the prospective studies that we reviewed could not take into account all of the three main beverages containing alcohol (beer, wine, and spirits) because of the limited frequency of consumption of some of them. We do not agree with Mørten Gronbæk and Thorkild I A Sørensen, however, that this should necessarily prevent them from being included in a review of the benefits of moderate alcohol consumption. In the multivariate analysis of type of beverage in the Copenhagen study the authors examined the association between wine consumption and total mortality, holding the effects of spirits and beer constant statistically.[1] However, in the Honolulu heart study, in which beer accounted for almost all of the alcohol consumed,[2] and in the Italian rural cohort study,[3] in which only wine was consumed, the effects of other types of beverage were held constant implicitly.

Arguably, studies looking at only a single type of beverage may be more informative than those looking at many, since measurement of each beverage may contain error due to overreporting or underreporting or differential error due to differences in drinking patterns. The inverse association reported between moderate beer consumption and coronary heart disease in the Honolulu heart study (relative risk 0.57) was similar to the inverse association reported for wine in the Copenhagen city heart study (relative risk 0.47 (95% confidence interval 0.35 to 0.62) and for spirits in the study from eastern Finland (0.3 (0.1 to 0.7)).[4]

Gronbæk and Sørensen state that they do not challenge the paradigm that ethanol has some cardioprotective properties. In their study, however, 1-2 drinks of spirits a day increased the risk of death from coronary heart disease (1.16 (0.98 to 1.39)).[1] If the ethanol in spirits reduced the risk of coronary heart disease to a degree similar to that reported for beer consumption in their study (0.79 (0.68 to 0.91)) then some other, unknown, component of spirits must have been almost doubling the risk of death from coronary heart disease among men and women consuming 1-2 drinks a day. This seems unlikely since most other studies have reported a significant inverse association between moderate consumption of spirits and coronary heart disease.[4] Therefore, differences in relative risks between types of beverage in the Copenhagen study, and in many other studies, are more likely to have been due to differences in lifestyle characteristics, such as diet and drinking patterns, than to any additional substantial benefit from the non-ethanol components of a specific beverage.

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Association cannot be assumed to be causal

EDITOR,—The Royal College of Physicians has estimated that alcohol is responsible for 25 000 premature deaths every year.[1] Medical professionals need to be cautious about making pronouncements that might encourage people to drink more. Two recent papers in the *BMJ* that seem to provide evidence of a protective effect of alcohol in relation to ischaemic heart disease[2 3] were widely reported in the national media; it may be assumed that the net effect will be to shift upwards the distribution of alcohol consumption in the population.

Neither study provides convincing evidence that alcohol protects against heart disease. Association cannot be assumed to be causal, but the authors of both articles make this assumption. Eric B Rimm and colleagues write that "a substantial portion of the benefit is from alcohol."[2] Hans Ole Hein and colleagues discuss attributable risk among men who abstained from alcohol; this term is appropriate only to a causal relation.[3]

There are reasons to doubt a causal relation. In Hein and colleagues' study non-drinkers were older than drinkers, which suggests a lower all cause mortality. Subsequent higher mortality might be attributable to age, which would have a non-linear relation with mortality and therefore be inadequately controlled for in the regression. The authors did not analyse data from the 1971 baseline, and mortality related to alcohol before 1986 may have biased the sample. The authors dismiss the possibility of "sick quitters" causing bias but do not consider a possible "sick non-starter" effect, whereby those prone to heart disease never started drinking. Given that 87% of the non-drinkers had never drunk, this was potentially a much larger source of bias.

Rimm and colleagues base their claim for a causal relation on inconsistent observational data. Of 12 ecological studies cited, seven show a significant beneficial effect of wine, two show a harmful effect of beer, and only one shows a beneficial effect of spirits and one a beneficial effect of beer. Of three case-control studies, only one shows all forms of alcohol to be protective,