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Does passive smoking cause heart disease?

The evidence is strong enough to warrant measures to reduce exposure

Active smoking is the most readily preventable cause of coronary heart disease. In 1986 the United States Surgeon General identified passive smoking as a cause of lung cancer and called for further research on the relation between passive smoking and cardiovascular disease.[1] Since then six cohort studies[2-9] and one case-control study[10] published in English have examined this association and an answer is beginning to emerge. The cohort studies were of variable size and included participants from the United States,[2-5 7] Scotland,[6] and Japan.[8 9] Measurement of exposure to passive smoking was based on questionnaire responses; in only one study was there objective evidence of exposure to passive smoke and the same study had information on workplace exposure.[4] All but one study[5] followed up individuals; and one study measured the stability of smoking rates part way through the follow up.[7] Several coronary heart disease end points were examined, and all the studies tried to control for other risk factors.

Collectively the cohort studies suggest a positive association between passive smoking and death from heart disease with relative risks ranging from 1·2 to 2·7. There are several possible explanations for the observed association; these include chance, bias (including publication bias), and confounding—or the association could be causal. Chance is an unlikely explanation given the precision of the results in some studies; the combined relative risks were significant in both men and women.[11]

Systematic error (bias) in measuring passive smoking is a possible explanation.[12] If the passive smoking group included active smokers who had been incorrectly classified as non-smokers the relative risk in this group would have been inflated. Only a small part of the increase in the risk of lung cancer associated with passive smoking among non-smokers, however, could have been due to this type of misclassification.[13] Active smoking increases the risk of lung cancer by about 10-fold, but its effect on heart disease is much less (roughly a doubling of risk), so misclassification is highly unlikely to be the sole cause of the observed increase in the risk of heart disease associated with passive smoking. Furthermore, since many non-smokers who do not live with smokers are known to be exposed to smoke from other sources, particularly at work, the effect of passive smoking is likely to be underestimated.[13] Publication bias, the greater likelihood of studies with positive results to be published compared with those with negative results, does not explain the association of passive smoking with lung cancer[14 15]; there is no reason to believe that it explains the association with coronary heart disease.

Confounding—that is, mixing of effects—is the most likely non-causal explanation for the observed association. Confounding might account for some or all of the association if passive smoking were associated in the population studied with other risk factors for heart disease and if these associations had been inadequately controlled in either the study design or the analysis. All six studies controlled for age, and four comprehensively controlled for the major cardiovascular disease risk factors[2 4 6 7]; the impact on the relative risk of controlling for these risk factors was in general minimal. Since non-smokers tend to come from healthy families, however, the effects of unknown confounders might still be important.[16 17]

A judgment is required to determine whether the association is causal. The temporal association is correct; the association is plausible given our knowledge of the effects of active smoking and the effect of passive smoking on other health outcomes[1]; physiological and biochemical studies suggest possible mechanisms[18]; there is some evidence of a dose response relation[6 7]; and there is consistency of results among the cohort studies. Differences between sidestream and mainstream smoke, the absence of a truly non-exposed control group in studies of active smoking, and a greater susceptibility of passive smokers to the health damaging effects of tobacco smoke may explain the apparently high relative risks of coronary heart disease associated with passive smoking compared with the relative risks caused by active smoking.

The available evidence does therefore suggest that passive smoking is a cause of coronary heart disease. Nevertheless, further epidemiological studies are required in various settings. In particular there is a need for large, well designed case-control studies that accurately measure recent and past passive smoking at home and at work and adjust for all known potential confounders, particularly socioeconomic factors. Follow up studies of people at high risk, such as survivors of a myocardial infarction, may also be worth while.

From the public health perspective this association is important because coronary heart disease is much more common than respiratory disease; most of the deaths attributed to passive smoking in the United States and New Zealand have been caused by coronary heart disease.[11 19]

Passive smoking is easier to control (by legislation and regulation) than active addictive smoking. The public health implications of the available evidence warrant continued efforts to reduce the public's exposure to other people's tobacco smoke.

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Does treatment for cervical intraepithelial neoplasia affect fertility and pregnancy?

Little to worry about

One of the main advantages of an increasingly conservative approach to managing cervical intraepithelial neoplasia, and even microinvasive carcinoma of the cervix, is that the potential for child bearing is maintained. But does such treatment compromise either fertility or the outcome of a subsequent pregnancy?

There are three potential causes of infertility after cone biopsy or destructive methods of treatment. The first is cervical stenosis, which would have to be complete to prevent sperm from entering the endometrial cavity and is uncommon.[1,2] Luesley *et al*, however, reported symptomatic cervical stenosis in 8% of 915 patients, with 1·3% experiencing amenorrhoea due to haematometra.[3] This complication seems to be a particular risk if the cone biopsy is performed during postpartum amenorrhoea.[4] A second, somewhat more common, problem is secondary infection at the site of treatment, which may occur in up to 10% of cases. Potentially these patients are at risk of developing ascending infection with resulting tubal damage, but no studies have documented this. Lastly, we have seen several patients who have had infertility problems, particularly after laser ablative treatment, allegedly due to absence of cervical mucus. All treatment methods destroy many of the mucus secreting glands of the cervix, and such destruction may alter both the volume and the physical properties of cervical mucus. Nevertheless, there are no reports on mucus problems, or indeed on subsequent fertility, after laser treatment for cervical intraepithelial neoplasia. Weed *et al* postulated that altered mucus might be a problem after cryosurgery, but failed to prove it in a series of 412 patients.[5] They noted good spinnbarkeit and ferning in patients who were ovulating. In 30 patients treated by cryosurgery for cervical ectropion, who had normal cytological and colposcopic findings, Baram *et al* thought that this treatment improved the characteristics of cervical mucus.[6]

Most workers who have studied fertility after treatment of cervical intraepithelial neoplasia have assessed it by comparing the numbers of patients at risk of pregnancy with the number of pregnancies achieved[7-9]; others have compared the numbers of patients becoming pregnant with those complaining of infertility.[10] None have found any effect of treatment on subsequent fertility.

Complications of pregnancy after treatment of cervical intraepithelial neoplasia are more familiar, though these too are uncommon and seem to be confined largely to patients who have undergone cervical conisation. Such problems may include cervical dystocia, leading to caesarean section.[1] The incidence of second trimester abortion also seems to be increased after cervical conisation: the incidence was 15% in 88 pregnancies in 77 women.[11] Among 66 patients proceeding beyond 28 weeks preterm delivery occurred in 12, with birth weights of under 2500 g in 14.[12] The mean duration of labour was 8·5 hours for 55 multigravid patients who had undergone cone biopsy compared with 6·3 hours in 205 controls. Nevertheless, in their review of published studies, which they criticised for lack of detail about patients and limited use of controls, Weber and Obel concluded that conisation did not lead to an increased frequency of spontaneous abortion or to increased perinatal mortality.[13] Likewise, Buller and Jones concluded that spontaneous abortion rates, premature delivery, and caesarean section rates were not significantly altered by cervical conisation in 166 patients who were followed up out of an original series of 314.[10]

The findings for cryosurgery and laser vaporisation for cervical intraepithelial neoplasia seem even more reassuring. In two series of patients who underwent cryosurgery the authors found no adverse effect on the subsequent outcome of pregnancy,[14,15] and similar conclusions came from two series of patients treated by laser vaporisation.[16,17] Fertility has not been evaluated after loop diathermy excision of the cervical transformation zone, but Prendiville *et al* reported on two women treated at six weeks of pregnancy who had no subsequent complications.[18]

Patients undergoing conservative treatment for cervical intraepithelial neoplasia can therefore be largely reassured about their subsequent fertility and outcome of pregnancy, particularly if the colposcopic findings satisfy the requirements for destructive treatment techniques. Patients undergoing cone biopsy of the cervix may, however, have a slightly increased risk of complications in a subsequent pregnancy.

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