Review article

Lung cancer from passive smoking:
hypothesis or convincing evidence?

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Summary. The epidemiological literature on passive smoking and lung cancer is reviewed and the well-known criteria for establishing a causal relationship are applied in order to determine what level of causal evidence currently exists. Three cohort studies and 12 case control studies are analysed. Of the prospective cohort studies, one contributes very little to our knowledge, one shows no risk increase and one results in a moderate risk increase of 1.74 for women married to heavy smokers. The last is the only study which has to be taken seriously, even when other considerations show that its results might be caused by chance, bias or confounding. None of the six case control studies yielding a positive relationship was conducted according to the state of art of epidemiological research, giving reasonable and sound evidence which cannot be explained by chance, bias, confounding or misclassification. Two studies contribute nothing to the evidence. None of the four case control studies yielding no risk change or a risk decrease can exclude the possibility that a causal relation exists. The epidemiological and toxicological evidence is discussed in the light of recent findings. The volume of accumulated data is conflicting and inconclusive. The observations on nonsmokers that have been made so far are compatible with either an increased risk from passive smoking or an absence of risk. Applying the criteria proposed by IARC there is a state of inadequate evidence. The available studies, while showing some evidence of association, do not exclude chance, bias or confounding. They provide, however, a serious hypothesis. Further studies are needed, if one wants to come to an adequate and scientifically sound conclusion concerning the question as to whether passive smoking causes lung cancer in man.

Key words: Passive smoking – Lung cancer – Causal connection
**Introduction**

Active smoking is the most important, avoidable health hazard in industrialized countries. If passive smoking causes lung cancer, this would be a very strong argument against active smoking. It could be the decisive argument for reducing active smoking considerably. Science should determine whether this hypothesis is true or not. If it is to do so, one must seek to state the facts and to separate these from mere speculation.

There are eight well established criteria which should be fulfilled if a causal connection in epidemiology is to be inferred:

- **Consistency** of the association in various studies. The results should be reproducible in similar circumstances.
- **Strength and intensity** of the association. Risk ratios of 5, 10 or greater are more likely to indicate a causal relationship than a risk ratio of around 2.
- **Specificity** of the association. The exposure, the effect and the way in which the exposure works should be specific. Therefore exposure and effects should be measured with sufficient validity and specificity.
- There should be a **dose-response relationship**.
- **Exclusion of bias and confounding factors**.
- There should be **statistical significance**.
- **Impact of intervention**, i.e. there should be studies showing a decrease of the effect when the exposition has been diminished.
- There should be **biological plausibility**.

Taking these criteria into consideration, the IARC has proposed four different levels of evidence [22] when evaluating the existence of a causal relationship regarding carcinogenicity in humans:

1. **Sufficient evidence of carcinogenicity**: There is a causal relationship between the exposure and human cancer.
2. **Limited evidence of carcinogenicity**: A causal interpretation is credible, however, alternative explanations (such as chance, bias, confounding) cannot adequately be excluded.
3. **Inadequate evidence**: There are few pertinent data or the available studies, while showing evidence of association, do not exclude chance, bias or confounding.
4. **No evidence**: Several adequate studies are available which do not show evidence of carcinogenicity.

In this article the available literature is examined in light of the criteria required to infer a causal connection and thus to determine what IARC level of causal evidence currently exists.

**Cohort studies**

Adequate and well conducted cohort studies can provide sound, empirical evidence on a causal relationship between exposure and event. To date, three cohort studies on passive smoking (from Hirayama, Garfinkel and Gillis et al.) have been published.