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Smoking and leukaemia

Leukaemia commoner among smokers but why?

Cigarette smoking has been so extensively researched and linked to so many different diseases that there is an initial sense of disbelief at the suggestion that it may cause yet another disease—namely, leukaemia. That the possible link has not received much attention is not surprising because only a few prospective studies of smoking are large enough to detect even a 100% increase in the risk of leukaemia in smokers, and many case-control studies of leukaemia have not obtained information on smoking.

In 1985 Austin and Cole reviewed the epidemiological evidence and suggested that there was an association between smoking and leukaemia, especially acute myelocytic leukaemia.¹ They said that confirmation was needed, and since then confirmation has been found. A case-control study showed that cigarette smoking was associated with a significantly increased risk of acute myelocytic leukaemia (relative risk 1.78, 95% confidence interval 1.01 to 3.15). Now Kinlen and Rogot report the largest prospective study smoking and leukaemia (p 657). It provides the results of 16 years of follow up from the United States veterans study (eight years longer than was available to Austin and Cole in their review) and includes details of the type of leukaemia. The study shows a significant increase in the risk of leukaemia associated with smoking (relative risk 1.53, $p < 0.005$) together with a dose-response relation between cigarettes smoked and risk; the relative risks were 1.34, 1.56, and 1.59 for people smoking less than 10, 10 to 20, and more than 20 cigarettes daily. Again the strongest effect was found for leukaemia of the myeloid and monocytic types.

The association between smoking and leukaemia is undoubtedly real, but is it one of cause and effect? Could it be an artefact of diagnosis? Metastatic lung cancer, for example, producing leucoerythroblastic cells in the peripheral blood, might be misdiagnosed as leukaemia. This type of error is

unlikely to have occurred often enough however, to account for the observed relative risk. Associations with a relative risk of about 1.5 may be due to an indirect association: smoking may thus be associated with some other (confounding) factor that is itself associated with leukaemia. But identifying such a factor is difficult. Consumption of alcohol, for example, is greater in smokers than in non-smokers but is not known to cause leukaemia. Social class would if anything tend to mask the association between smoking and leukaemia as leukaemia is more common in social class I (professional occupations) but smoking is more common among people in partly skilled and unskilled occupations. If the association is one of cause and effect no mechanism has been identified. Benzene and Benzene and ionising radiation cause leukaemia in man, and tobacco smoking is a source of both—but in quantities so small that they are unlikely to make any material contribution to the excess risk of leukaemia in smokers.

Whatever the mechanism, the balance of evidence suggests that smoking may cause leukaemia. This cancer can now be added to the list of tobacco related causes of death summarised by the World Health Organisation,³ including it along with diseases such as bladder cancer in the category "diseases for which the excess mortality in smokers may be partly or wholly attributable to smoking".

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