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THE IMPORTANCE OF BIOLOGICAL TESTS

As of this date the tests which might in my opinion be carried out by a manufacturer taking reasonable steps to assure himself that the cigarettes he was selling were "safer" are, in decreasing order of importance:

- (1) Smoke inhalation tests which may be capable of producing undeniable lung cancers, e.g. Kotin and Wiseley's work on mice infected with influenza virus and exposed to aerosols, which Harris is trying for the Imperial Cancer Research Fund using tobacco smoke (N.B. this technique has not yet produced cancers using tobacco smoke but it seems possible that it will do so before long.)
 - (1a) Inhalation tests which produce pre-cancerous changes, e.g. epithelial proliferation as in Leuchtenburger's work on mice in smoke-filled chambers.
 - (1b) Ciliary inhibition tests. Preferably on human tissue, e.g. adenoids.
- (2) Intra-bronchial injection of smoke condensate produced lung cancer in rats (Blacklock) but this was accompanied by physical trauma. Whitehead has used intra-tracheal instillation of smoke condensate in rats, but so far, although suggestive pre-cancerous changes have been observed, no cancers have yet been obtained.
- (3) Mouse skin painting techniques which undeniably produce skin cancers, e.g. the work at Harrogate.

In writing this I am guided by the consideration that there is as yet no proof that cigarette smoking causes lung cancer, but that if one accepts this proposition as a working hypothesis, since it is also the basis on which attacks on the industry are being mounted, then the criteria for "safe" or "safer" must be tests which are capable of producing cancers in the lungs of experimental animals and of these, tests which use smoke seem preferable to those using prepared condensate which thereby introduce artificiality. Mouse skin painting tests come next because the cancers they produce are not in the lung and because at present only prepared condensate is used. Also, they may only be of limited use in testing the changes produced in smoke by selective filters since the present

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method of preparation of the condensate which involves evaporating the acetone in which the smoke has been dissolved will also remove an invariable proportion of such compounds as phenols, aldehydes, volatile acids, nitriles and ketones which we are intending to remove by our selective filters. Mouse skin painting tests of the Harrogate type may well be useless for evaluating the effect of such filters.

Smoke inhalation tests (1a) which lead to recognizably pre-cancerous conditions may be looked upon as a stepping stone between class (1) and ciliary (1b) tests, and both (1a) and (1b) have the advantage of taking less time than tests producing real cancers. For these reasons I have included them as sub-groups of class (1). All of these tests are at present comparative, and their limitations are unknown. It is probable that cases will occur from time to time where no cancers are produced or nil reaction occurs in either test or control animals, or where a reaction is found in the controls. Thus there can never be complete "safety" since the possibility always exists that with more sensitive animals or with a more sensitive test differences will be found.

In my view it is not possible to think in terms of a one hundred percent "safe" cigarette but this should not in any way deter us from making efforts to measure where we are getting, even though what we think is fifty percent "safe" turns out later to be one hundred percent "safe" or vice versa.

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