THE CONTRIBUTION OF EPIDEMIOLOGY TO THE DEVELOPMENT OF DISEASE PREVENTION POLICY

Scientists and doctors can assist the political process by providing a systematic approach to sifting through available evidence.

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The function of epidemiology in the development of disease prevention policy is to establish and quantitate causality. Through the exploration and definition of exposure-effect relationships, epidemiologic studies seek to identify the causes of occupational and environmental diseases, to determine the populations at greatest risk, and thence to provide the scientific basis for regulatory and other forms of intervention.

As a prelude to describing how epidemiology establishes the etiology of occupational and environmental disease, it will be useful to describe the rules of evidence which have been developed for assessing causality in epidemiologic studies:

- the relationship between exposure and outcome should be consistently demonstrable from one study to another;
- the relationship should be strong;
- in the relationship, exposure must be shown to precede disease;
- there should be a positive dose-response relationship between the intensity of exposure and the frequency, severity, or rapidity of onset of the disease; exposure is most convincingly established data characterizing toxic exposures are available;
- the relationship should be biologically plausible, and should be consistent with the results of experimental evidence.

It will be useful also to describe the guidelines that have been developed for the evaluation of "negative" epidemiologic studies, that is, for studies which appear to find no association between an occupational exposure and subsequent risk of malignancy. Such studies must be scrutinized for such flaws in design as:

- dilution - the inclusion of unexposed persons in an allegedly exposed group;
- misclassification of subjects in regard to either exposure or outcome;
- premature examination of subjects for diseases, particularly for cancers, which require the passage of many years from first exposure to clinical appearance of disease;
- low statistical power, a phenomen which results when the number of subjects examined is small and the study consequently has limited ability to detect an effect, even if present;
- improper comparison - a common conseqeuence of improper comparison is the "healthy worker effect", in which the mortality experience of a group of workers is compared to that of the general population and is found to be superior; such comparisons tend to overlook the point that persons able to enter active work are a selected subset of the population.

Studies which have examined the association between occupational exposure to benzene and subsequent death from leukemia illustrate the application of epidemiology to the development of preventive policy. The association between benzene exposure and leukemia was first recognized in a series of case reports published from the 1890's to the 1960's. To evaluate this association more systematically, the National Institute for Occupational Safety and Health undertook a combined epidemiologic and industrial hygiene study. The epidemiologic study employed a retrospective cohort design. It examined a population of 748 workers who had been exposed to airborne benzene vapors at two rubber plants in Ohio. The study succeeded in tracing 98 per cent of the cohort. Examination of death certificate diagnoses indicated that 7 of the

workers exposed to benzene had died of leukemia - all of acute myelogenous leukemia - whereas only 1.25 leukemia deaths would have been expected. This association was strong - 5.6 times the expected - and consistent with previous data. Further, a positive dose-response relationship was demonstrated between duration of benzene exposure and the strength of the assocation: for workers employed less than 5 years, the relative risk was 2; for those employed for five or more years, the relative risk was 21. ← "clear evidence of cause & effect relationship" Says Ott study is consistent

The industrial hygiene evaluation showed that benzene exposure had been higher in the early years of the plants' operation and lower more recently. It appears, however, despite the occasional occurence of excursions that workers' exposure to benzene had generally been below whatever limit constituted the maximum allowable exposure at the time that the measurements were undertaken; those permissible exposure limits delcined from 100 ppm in the early years of the plants' operation to 10 ppm in 1969.

From the combined epidemiologic and industrial hgyiene data obtained in this study it was possible to undertake a quantitative assessment of the risk of exposure in workers exposed for a working lifetime (40 years) to benzene vapors. In this risk assessment, it was calculatee that in a population of 1000 workers exposed for a working lifetime at 100 ppm benzene vapor, 140 excess deaths from leukemia would be projected to occur. Also, at a lifetime exposure of 10 ppm, 14 excess leukemia deaths would be projected to occur.

Because 10 ppm is the current legal standard for occupational exposure to benzene, and because the foregoing quantitative risk assessment indicates that an unacceptably large number of leukemia deaths will result in a population of

workers exposed to benzene for a working lifetime at that level, there exists a scientific justification for lowering the current legal standard for occupational exposure to benzene. Accordingly, the National Institute for Occupational Safety and Health has recommended that the permissible exposure limit for occupational exposure to benzene should be reduced to a time-weighted average value of 1 ppm.

This provides "powerful tool for policy makers".

In conclusion, the role of epidemiology in the development of prevention policy is to establish causality and then to delineate in quantitative terms the strength of causal associations between toxic exposures and disease outcomes. Epidemiology is not an ideal tool for the shaping of preventive policy, because disease and death must occur in sufficient numbers to be detected before epidemiologic studies can be undertaken. Epidemiologic data possess, however, the great advantage over the results of animal studies that they pertain directly to man. For that reason, properly conducted epidemiology studies, particularly studies which have been replicated in various populations under varying conditions of exposure, constitute a powerful resource for the development of health policy.