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In Doll and Peto's 1981 report to the U.S. Congress on the causes of avoidable cancer [1], the proportion of cancer deaths attributable to dietary problems was estimated at 35% with a range of acceptable estimates from 10 to 70%. The width of this range reflected, quite properly, the uncertainty of the state of knowledge at that time.

The reader of the review of diet in the aetiology of cancer by Miller and co-authors in this issue might be forgiven for feeling pessimistic about the likely success of future work after comparing our current state of knowledge according to Miller and his colleagues with Doll and Peto's report. The epidemiological literature is still contradictory and confusing. While this must reflect to some degree the varying quality of the research conducted over the intervening 12 years, the main message to emerge must surely be that the problem is too complicated to be completely solved by the relatively simplistic approach of gathering dietary data, consulting food tables, and comparing the nutrient intakes of cancer cases with appropriately chosen subjects free of the disease of interest. The tools for such studies: dietary questionnaires, food tables, computers and statistical methodology have only be generally available for one or two decades, and it was right and proper that they be applied to the problem of human cancer. But in the final analysis, it would seem that no single nutrient (macro or micro), not even fat, has yet been *unequivocally* implicated in the aetiology of any cancer. As the reviewers point out, the weight of evidence against high fat and energy intakes continues to increase, but there are still many contradictory findings.

Research in all disciplines is bounded by the information and tools currently available. Epidemiological studies of diet and cancer have concentrated heavily on the nutrients for which food composition tables are available. In some cases, associations between a nutrient and a cancer have been over enthusiastically interpreted as causal, when in fact the association can indicate no more than that the foods from which the study populations derive their greatest contributions of that particular nutrient (not necessarily the foods with the highest content!) are associated with the risk of disease within that population. The real dangers/benefits associated with certain foodstuffs may, therefore, involve mechanisms which are completely unrelated to the nutrient through which the food items were initially identified. (The reviewers appear to flirt dangerously with this approach with an initial discussion of fat, and separate discussions of vitamin C and beta-carotene, but retreat from the brink in a slightly illogical ordering with a generalised discussion of this very problem under a separate paragraph heading of 'other dietary factors'.)

So, 12 years down the track from Doll and Peto, is the most we have to offer, a broad recommendation to eat less fat and more fruit and vegetables? What happened to wholegrain breads and cereals? Evidently, one author of this review, who also co-authored a recent meta-analysis [2] of studies looking at fibre and colon cancer, was insufficiently convinced by the outcome to make any recommendation about increasing intakes of the richest sources of fibre. Perhaps he was concerned by the ambiguities of the health benefits of a nutrient which increases cell proliferation in the colonic mucosa [3]. Experimental studies (both animal and human) looking at the effects of fibre on the circulating levels of steroid hormones implicated in breast and prostate cancer [4] are still in their infancy, but it is a pity that they were not given a passing reference.

Once a nutrient has been implicated in the aetiology of a disease, we can reasonably prudently recommend to the target population that it should modify its consumption of foods contributing most of that particular nutrient, pending further evidence of a more direct and convincing nature. This evidence is most likely to be provided by an intervention study. However, the difficulties, both ethical and practical, of intervening in human populations require that the majority of intervention studies are either performed with laboratory animals, or in humans, but with some measure (a biomarker) other than clinical disease as the endpoint. With our current state of

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knowledge of most cancers, that biomarker may be only tenuously linked to the disease, so that the overall relevance of the intervention becomes difficult to assess. Nevertheless, interventions like that of fat reduction and breast cancer risk being conducted as part of the Women's Health Initiative in the U.S.A., will probably be vital in weeding out the non-causal associations thrown up by observational studies and in establishing the relevance of particular pathways to the determination of an individual's overall risk of disease [5].

It would be unfortunate if the reader of this review were to come away with no impression of the other avenues of research which may eventually prove vital. A host of exciting possibilities are being provided by different approaches. At a conference on Food and Cancer, sponsored by the Food Chemistry Group of the Royal Society of Chemistry held in Norwich, U.K. in September 1992 [6], a wealth of papers on potential mechanisms by which both nutritive and non-nutritive components of the diet may alter cancer risk was presented. A considerable number of studies were concerned with the problem of the oxidation and conjugation of non-nutritive dietary factors, and the inhibition, induction and activation of the enzymes/isozymes responsible for the biotransformation of compounds foreign to the body. It appears that relatively small amounts of these xenobiotics can have dramatic influences on the existence and availability of certain metabolic pathways. Otherwise harmless endogenous compounds (e.g. steroid hormones) and their metabolites may be raised to the status of procarcinogens in the presence of pathways induced by xenobiotics. If this is the case, are we expecting too much of the broad brush techniques of diet cancer epidemiology?

The article by Miller and his colleagues might be criticised for failing to acknowledge the exciting contributions that other research approaches are providing — even if the global picture is still very indistinct. Epidemiologists and laboratory scientists need to be guided by each others' findings if answers to problems as complex as diet and cancer are to be discovered with least delay.

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IN 1981, DOLL AND Peto provided an estimate of the proportion of cancer deaths in the United States attributable to diet of 35%, with, however, a wide range of acceptable estimates, from 10 to 70% [1].

The substantial amount of epidemiological research published over the last 12 years seems to have confirmed, at least in first approximation, the point estimate given in 1981, and somewhat restricted its range of acceptable estimates. There is, however, still scope for discussion on how wide a range can now reasonably be accepted.

Miller and colleagues (pp. 207–220), at the end of their review, provide a series of apparently precise estimates of population attributable risks and hence potential incidence reduction. These, for instance, would be of 68% for stomach cancer through reduction of nitrite, cured meats and salt-preserved foods and increase of fruit and vegetable consumption, or of 27% for breast cancer through reduction of fat and increase of vegetables.

Although we now have sufficient knowledge to restrict the original Doll and Peto's range of acceptable estimates [1], perhaps to somewhere between 20 and 50%, I am not sure that any such precise estimate for potential incidence reduction can be offered. For instance, the 27% breast cancer reduction might be consistent with the results of most [2] (though not all [3]) case–control studies, but is certainly inconsistent with the findings of most cohort studies [4–6]. Miller and colleagues indicate that "when in cohort studies less details can be collected than is possible in case–control studies, there may be much misclassification of fat intake". Further, case–control studies which relate to current or recent diet may be more appropriate to investigating some aspect of diet with a short-term (promoting) effect on the process of breast carcinogenesis [7]. One could further discuss advantages and disadvantages of case–control and cohort studies, but when the general results of the two major analytical epidemiology approaches are so inconsistent, any precise estimate of risk remains open to criticism.

This line of reasoning has at least two main implications, one in the short term on indications for prevention, and another in broader terms for perspectives of research. In principle, if our knowledge is still unsatisfactory, our focus should in fact be more on research than on prevention, and *vice versa*. In practice, other considerations should also be taken into account, including some general cost/benefit assessment of preventive indications—for cancer as well for other major diseases—and some evaluation

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