

## CANCER

For the first time rational planning of cancer research at the national level in Great Britain was made possible by the formation of a British Cancer Council and by the agreement of the Medical Research Council, the Imperial Cancer Research Fund, and the Cancer Research Campaign (formerly the British Empire Cancer Campaign for Research) to form a Co-ordinating Committee for Cancer Research. The International Agency for Research on Cancer (IARC), though still waiting to move into new laboratories in Lyons, France, was actively promoting studies of the role of environmental factors in the etiology of human cancers. Recent advances in knowledge most relevant to problems of human cancer, however, stemmed from epidemiological studies. Among the most spectacular of these was a report that when Japanese migrated to the United States from Japan, where cancer of the stomach is prevalent and cancer of the colon rare, their risk of stomach cancer fell and of colon cancer rose. Such studies indicated that environmental factors may be more important than genetic factors in the cause of some forms of human cancer. The IARC hoped, by sponsoring field studies and supporting Regional Cancer Registries, to obtain data concerning cancer risks among various populations, and then, by correlating this information with that of risks in various communities, to identify environmental factors that cause cancer in man.

The discovery in 1969 that prolonged feeding to rats of a 10:1 mixture of sodium cyclamate and sodium saccharin (and in other tests using cyclamate alone) predisposed them to cancer of the bladder led to the banning of the use of cyclamates as artificial sweeteners in food in many countries. It may be relevant that certain gut bacteria can convert cyclamate to cyclohexylamine which is related to dicyclohexylamine previously shown to be carcinogenic in rats. No carcinogenic effect has been observed in mice fed cyclamates in high dosage for periods up to 18 months. The banning of cyclamates marked a turning point in the attitude of legislative authorities and of members of the public toward the use of animal tests for the prediction of cancer hazard for man. The question was raised as to why the carcinogenicity of cyclamates was not discovered in the course of tests reported in 1951. Other questions concerned the justification of withdrawing a valuable product from the market in the light of equivocal laboratory evidence, and pointed out that I. I. Kessler found no excess of bladder cancer in his survey of cancer in diabetics who had been heavily exposed to cyclamates. All he found was the expected excess of cancers of the pancreas known to exist in 1934, ten years before cyclamates were used as sweeteners.

Doubts of the predictive value of carcinogenicity tests on laboratory animals also stemmed from a report from J. R. M. Innes and colleagues that 11 widely used chemical pesticides predispose to the development of tumours of the liver, and in some cases also of the lung and lymphoid systems, in mice; and from the observation that liver tumours and lung tumours tend to occur much later in germ-free mice than in mice carrying a normal gut flora. In one area at least, however, there appeared to be a correlation between what happens in man and what happens in the rat: R. Montesano and Magee showed that human liver can metabolise dimethylnitrosamine at a rate comparable with that of rat liver and that similar levels of methylation of nucleic acids occur in the two species. If the carcinogenicity of this compound depends on such methylation then the results suggest that man is susceptible to its carcinogenic action.

E. D. Acheson and his colleagues reported a greatly increased risk of nasal and nasal sinus cancers in woodworkers and shoemakers in Britain and a report in the *Journal of the National Cancer Institute* suggested that cancer of the pancreas occurs unexpectedly frequently among members of the chemical profession. I. A. Evans and colleagues in Bangor, Wales, reported the induction of cancers in rats fed on the same species of bracken as that eaten by humans in Japan.

The risk of scrotal cancer among tool setters working automatic lathes cooled and lubricated by circulating mineral oils was highlighted by litigation proceedings in Birmingham, Eng. The observation by J. G. Holmes and others that second primary cancers, mostly of the lung and digestive tract, occur significantly more often than expected in men with previous scrotal cancer may point to a hazard from the mineral oil mist frequently generated by automatic cutting machines. The presumption that the carcinogenicity of mineral oil is attributable almost solely to its content of polycyclic aromatic hydrocarbons was seriously questioned by new evidence of the importance of co-carcinogenic straight-chain aliphatic constituents of the oil.

Isoenzyme studies suggested that Burkitt's lymphoma usually arises from a single cell. R. J. Huebner and G. G. Todaro's hypotheses that most vertebrate species have normally "switched-off" C-type RNA virus genomes that are vertically transmitted from parent to offspring and that the derepression of these represents the long-sought final common pathway in carcinogenesis awaited critical evaluation. (See *Occupational Medicine*, below.) (F. J. C. R.)