

Cancer Epidemiology

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These reviews provide an overview of the mature science of cancer epidemiology and the rapidly evolving field of cancer genetics. Parkin describes the large and still mainly unexplained international variations in cancer incidence, which have puzzled epidemiologists for at least 40 years. Boffeta summarizes environmental and occupational carcinogenesis. McCullough and Giovannucci navigate the minefield of diet and cancer, while Calle and Thun focus specifically on obesity. Kinlen reviews viral carcinogenesis and the effects of immunosuppression, including his own remarkable discoveries in relation to childhood leukaemia and population mixing. Viral carcinogenesis is also discussed by Haverkos, who focuses on the co-carcinogenic effects of viruses and chemicals in relation to cervical cancer, hepatocellular carcinoma and Kaposi's sarcoma. Pike *et al.* update the long-established thesis that incidence patterns for cancers of the breast and other hormone-dependent tissues reflect the mitotic effects of hormonal stimulation. They suggest that chemoprevention may soon have a major impact on several of these cancers. Wakeford's comprehensive review of radiation carcinogenesis covers microwaves, low-frequency electric and magnetic waves and ultrasound as well as ionizing radiation. Stiller discusses the genetics as well as the epidemiology of childhood cancers. Highly penetrant genes are reviewed by Nagy *et al.*, and Bocchetta and Carbone discuss the mechanisms by which these and other genes affect carcinogenesis. Franco *et al.* review the epidemiological association between SV40 and human cancer, and Fisher and Fisher review the risk factors associated with the marked increase of lymphomas in recent decades.

Wu *et al.* provide a detailed account of recent work (much of it from the MD Anderson) on polymorphic variants and their effects on susceptibility to tobacco

carcinogenesis. They discuss candidate genes for carcinogen metabolism, methylation, DNA repair, cell cycle control and apoptosis, and their associations with phenotypic markers as well as with cancer. Vineis also discusses individual susceptibility to carcinogens due to polymorphisms in genes involved in carcinogen metabolism and DNA repair, focusing on colon cancer. Houlston and Peto review the potential importance of low-penetrance genes and the ways in which they may be discovered.

The carcinogenic effect of tobacco remains the most important discovery in the history of cancer epidemiology. The global impact of tobacco smoking underlies many of the associations described in these reviews, including international differences in tobacco-related cancers (Parkin), differences in susceptibility to tobacco carcinogenesis (Wu *et al.*), and interactions with other carcinogens. Obesity may be the largest avoidable cause of fatal cancer in nonsmokers, but tobacco is far more important than the combined effects of all other avoidable causes among those who still smoke (Peto, 2001).

Insights into the mechanisms of carcinogenesis were drawn from cancer epidemiology, and particularly from lung cancer rates in relation to dose rate, age and duration of smoking, before the discovery of HPV16, *Helicobacter pylori* or the first specific genetic alteration in a human cancer. Doll's (1978) seminal article, 'An epidemiological perspective of the biology of cancer', shows how much could be inferred from rigorous analysis of the limited data then available, and provides a perspective on the impact of technology on scientific progress in health research. Time will tell whether the spectacular advances in cell and molecular biology of the last quarter century will lead to commensurate public health benefits, particularly in the developing world where smoking-related mortality is still rising, obesity is increasing in many countries, and cervical screening is ineffective or nonexistent.

References

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