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World No-Tobacco Day: 31 May 1992

TO HELP protect the health of the world's population from the tobacco epidemic, the WHO Tobacco or Health programme [1] plays a leading role in promoting the concept of tobacco-free societies and lifestyles as a positive social norm. The aim of the programme is to attain an immediate decrease in, and ultimate prevention of, tobacco-related diseases, which are currently killing 3 000 000 each year. To attain this goal WHO has been mandated to employ various media to develop informed public opinion on health matters. This information is crucial if governments, the population at large and relevant target groups—such as the health and teaching professions, community leaders and decision-makers—are to be convinced of the extent and gravity of the tobacco problem and the feasibility of control measures.

As a tool for public information and education, WHO has been requested to coordinate the worldwide celebration of the World No-Tobacco days held on 31 May each year. Originally, this day was set aside to appeal to all those who smoke or chew tobacco to stop for at least 24 h, as a first step towards ceasing their harmful and wasteful behaviour. Currently, World No-Tobacco days are also seen as opportunities for WHO to call for action in the tobacco or health area and to initiate research on specific themes and subsequently disseminate information.

This year, World No-Tobacco Day is dedicated to workers and has the theme: tobacco-free workplaces, safer and healthier. The workplace is one of the places where people spend most of their lives, so the least they can expect is to be able to breathe clean healthy air at work, unpolluted by tobacco smoke.

The combined effect of smoking and occupational hazards has shown that there are significant differences between the morbidity of smokers and non-smokers in many occupations, and that the interaction of the two types of hazard can, in certain circumstances, increase the risk of many diseases, particularly the chronic obstructive lung diseases, lung cancer and cardiovascular diseases, as well as specific disabilities. Tobacco smoking is not only dangerous to smokers but also to non-smokers and acute effects and increased risks are caused by exposure to environmental tobacco smoke (ETS) (passive smoking) [2, 3]. For these reasons, over the past few years the trend towards tobacco-free workplaces has accelerated and legislation, regulations and efforts to liberate workplaces from tobacco smoking have been devised, but more needs to be done.

To support the celebration of the Day, the WHO is publishing an advisory kit and a press kit containing information on tobacco-free workplaces, the health effects of occupational hazards and smoking, the economic burden it entails, the laws and regulations necessary to promote a tobacco-free workplace and the means of creating a tobacco-free workplace. This information is distributed worldwide and is available from the Tobacco or Health programme at WHO in Geneva. The Director-General of WHO is calling on all those concerned by these issues to work together in their preparations to ensure that World No-Tobacco Day, 31 May 1992, is a global endeavour.

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Epigenetic Effects on Radiosensitivity: the Extracellular Matrix and Growth Factors

THE ACCOMPANYING paper by Fuks *et al.* [1] is a provocative and intriguing report which builds upon previous work from his laboratory which demonstrated that basic fibroblast growth factor (bFGF) induced potentially lethal damage repair in bovine aortic endothelial cells (BAEC) [2]. In this article the authors report that when radiation survival of BAECs is assayed in dishes precoated with autologous natural basement membrane-like extracellular matrix, a survival advantage is observed when compared with cells plated on plastic or cells treated with biologically unrelated (mouse) HR9-bFGF/ECM. The authors point out that although the media of either tissue culture was not supplemented with bFGF, these culture systems are still exposed to stimulation by bFGF produced following irradiation.

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Thus the authors conclude that the matrix upon which the irradiated endothelial cells are plated is capable of modulating the repair capacity of radiation induced lesions. They further suggest that there is sensitivity to specific matrix components in terms of expression of metabolic functions involved in DNA repair.

There are several points of interest for radiation oncologists and biologists. The first is in the context of normal tissue tolerance to radiation. Although the exact balance between stem cell "drop out" and vascular damage in the pathogenesis of late radiation effects on normal tissues is debated, there is little doubt that microvascular degeneration is important in some component of the long term effects of radiotherapy. Studies in embryogenesis have shown the importance of cell to cell contact, cell orientation and tissue gradients of secreted tumour factors in development [3]. Fuks *et al.* have taken these concepts one step further in the context of survival of bovine aortic endothelial cells following radiation. The ability of endothelial cells to survive radiation depends upon specific endothelial cell matrix interactions, as well as growth factors secreted by irradiated cells. Thus, epigenetic factors influencing the cytotoxic effects of radiation on the genome are important. This concept is likely to apply to organs other than the endothelial cell/subendothelial basement membrane complex. These investigators, as well as our group have commented on the potential importance of radiation induced growth factors and cytokines and their potential paracrine, autocrine and endocrine effects in radiotherapy [2, 4]. In the bovine aortic endotheliál cell system, bFGF enhances the repair of radiation damage. The interactions between radiation induced growth factors and cytokines will depend upon the specific cytokine induced and the cells with which it interacts. For example, tumour necrosis factor α is reported to protect haematopoietic cells from the cytotoxic effects of radiation while sensitising a wide variety of human tumour cells to the killing effects of X-rays [5, 6]. The presentation of TNF α to its receptor(s) in the context of the cellular-matrix interaction may explain the different radiobiological effects.

The second point of interest is in the context of prediction of radiocurability. The authors suggest that the most accurate prediction of tumour radiocurability will need to come not only from investigation of individual radiosensitivity of human tumour cells but the interaction of tumours with their matrix substrata. The closest approximation of the tumour microenvironment is likely to give the best estimate of cellular radiosensitivity *in vivo*. This is likely to be very difficult to accomplish experimentally because matrix substrata are likely to vary more in tumours than in normal tissue. Nonetheless, laboratories interested in predictive assays should attempt to approximate the tumour microenvironment as closely as possible.

In summary, a variety of epigenetic factors that effect survival of cells to radiation is just beginning to be investigated. The concepts proposed by Fuks *et al.* for bovine aortic endothelial cells are likely to have importance in other normal tissue and tumours. The ability to modify the matrix components may make it possible to favourably alter the therapeutic ratio in some circumstances.

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