

*Middle Articles***Immunological Aspects of Cancer—Part I**

On 16 and 17 October the Royal Medical Society of Edinburgh held a conference on the "Immunological Aspects of Cancer." Shortened versions of all the papers have been prepared—the first part, comprising six contributions, is printed below.

Immunological Factors Affecting Tumour Growth

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The existence of antigenic differences between tumours and genetically compatible hosts has been most clearly shown in rodent tumours induced by chemical carcinogens and by oncogenic RNA or DNA viruses. Whether "spontaneous" tumours also show such differences is more debatable, though at least some are clearly, if weakly, antigenic.

The antigenic behaviour of the different aetiological groups of tumours differs considerably in features such as immunogenicity, immunosensitivity, and the relative "strength" of the immune response that can be mobilized against them.

At present many laboratories are studying the antigenic properties of human tumours. Immune responses by the host against tumour-associated antigens have been shown by various methods, particularly in Burkitt's lymphoma, nasopharyngeal carcinoma, osteogenic sarcoma, malignant melanoma, neuroblastoma, and carcinoma of the colon and bladder. Moreover, some findings suggest that immune responses may also be provoked by several other tumours.

Nature of Response

The immune response against tumours resembles a homograft reaction when the histocompatibility antigens are relatively weak. With the possible exception of some lymphomas and one virus-induced mouse sarcoma, cell-mediated immunity plays the major part in this immune response. Humoral antibodies, on the other hand, are either ineffective or actually block the rejection reaction, thereby enhancing the growth of the tumour.

The antigens responsible for inducing the immune response against tumours are probably all localized on the outside of the cell membrane, like ordinary transplantation antigens. It is not known whether they are analogous to ordinary transplantation antigens or are completely different. But we do know that the cell membrane of some virally induced tumours contains structures derived from the viral envelope; moreover, the immune response directed against these can lead to rejection of the tumours.

Escape Mechanisms

Tumour cells could theoretically escape rejection in several different ways. Firstly, their antigenic make-up might be changed or lost altogether; though these possibilities have not been proved we do know that tumours induced by RNA and

DNA viruses as well as chemical carcinogens may develop immunoresistance associated with a decreased concentration of surface antigen.

Secondly, at the host level, immunosuppression by means such as neonatal thymectomy, treatment with antilymphocytic serum, or whole body irradiation can eliminate or decrease the resistance to tumour spread, allowing the growth of antigenic tumour cells that would otherwise have been rejected. At present it is not clear whether true immunological tolerance can exist against antigens associated with tumours. Nevertheless, the lack of any rejection reaction in newborn animals exposed to the agents causing murine leukaemia or mammary tumours resembles immunological tolerance. Possibly this lack of reaction merely reflects a persistent excess of antigen—as occurs, for example, in viraemia.

Thirdly, insufficient release of antigen before the tumour has reached an irreversible size could be an important mechanism in why the cells fail to be rejected. This is particularly well shown with the oncogenic DNA viruses. The formation of blocking antibodies is another important mechanism, which is known to operate in both animal and human tumours. If the tumour is inaccessible to the host defences, it may also escape rejection, as for example in the case of neoplastic cells lodged in the central nervous system.

Conversely, experimentally, "immunological reinforcement" by specific or non-specific means during the latent period before cancer appears can reduce the incidence of tumours in such situations.

Application of Study

The results of the studies on tumour immunology might be applied in four main ways. Firstly, the identification of group-specific antigens in tumours of unknown aetiology may help to uncover new clues to their aetiology. Secondly, knowledge of the changes in the surface of the cancer cell may help to increase our understanding of how neoplastic cells differ from the corresponding normal cells. Thirdly, specific or non-specific measures designed to prevent the development of tumours may be considered, provided that the antigenic behaviour of a particular tumour is understood and the risk of enhancing its growth can be avoided. Fourthly, immunological reinforcement may serve as an adjuvant to other forms of treatment, particularly in eliminating relatively small numbers of disseminated tumour cells, and thereby decreasing the risk of recurrence and metastasis. In particular the last will apply when the tumour is relatively antigenic and there are relatively few residual tumour cells present.

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