Surgery-Related Immune Suppression in Cancer Patients

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This study developed from investigations of factors predictive of outcome for melanoma.1 Prognosis could be estimated with acceptable accuracy, using a multifactorial clinicopathological score sheet. However, it was clear that factors other than those determined by inspection and microscopy were important. One factor that was considered relevant was the role of the immune system in neoplasia. The late 1960s was a period of great activity in tumor immunology and the Karolinska's Department of Tumor Biology, with George Klein and Eva Klein, was a mecca to aspiring tumor immunologists. Two years spent there implanted a firm conviction that immune factors are important in human cancer and should most properly be studied in man.

Back in Glasgow a decision was made to study cellular immunity in melanoma because of broad hints from the clinic that this was an immunogenic tumor and breast cancer (because of its frequency and frequently fatal outcome). A highly enthusiastic team formed: Roaa M., Mackie, lecturer in dermatology with an interest in melanocytic tumors; Walter G.S. Spieg, lecturer in pathology, interested in experimen
tal pathology; and Cathie E. Thomas, a biology doctoral student interested in working with human material. This was a democratic group in which all were involved in study design, acquisition of mate
tials, and benchwork (though Katie did most experiments).

The experiments were to demonstrate cellular immunity to tumor-derived materials in vitro and to determine whether similar results were obtained in longitudinal studies of individual patients. They were not, and this triggered spirited discussions of experimen
tal technique until for a time. Ignored that the apparent inconsistencies were related in time to the intervening surgical operation. Further experiments confirmed transient immune suppression following surgery, possibly caused by the metabolic consequences of surgery and the effects of anesthetic and other drugs. This raised concern that treatment of immune suppression might facilitate the establishment of tumor cells disseminated during surgical manipulations. Such a possibility is hard to study in humans and, despite its importance, has yet to be conclusively proved or disproved. That this was one of the earliest convincing demonstrations of postoperative immune suppression and continuing concern that this event may facilitate metastases are the most plausible explanations of the article's popularity.

Impressed by the possibility that tumor progression might relate to immune suppression, we went on to examine many facets of the immune response in patients with cancer at various stages of progression. We found that general immune competence was maintained in most patients until their disease advanced and they were subject to multisystem failure.2

The team dissolved amicably in the late 1970s, Mackie becoming professor of dermatology at the University of Glasgow, Spieg becoming clinical director of the Karolinska's Department of Medical Immunology, and Thomas, having obtained her PhD, marrying and giving up science, at least for a time. I moved to Los Angeles to join other devotees of melanoma immuno
nology at the University of California, Los Angeles. Mackie, in Glasgow, continues to work on a wide range of aspects of melanoma, contributing to World Health Organization clinical studies of the value of nonspecific therapeutic stimulation and EORTC studies of the specificity and sensitivity of a wide range of antimalignoma monoclonal antibodies.

Since coming to Los Angeles I have again become interested in the problems of immune suppression and cancer. In a series of papers,25 we have shown that the lymph nodes nearest to melanoma are immune-suppressed, contain abundant suppressor cells, and permit the survival of small numbers of tumor cells. We have also shown that melano
noma-derived products, such as gangliosides, pros
taglandins, and membrane lipoproteins, can down
tegrate normal lymph node cells.6 We consider that local immune suppression induced by tumor products facilitates the survival of tumor cells and their expansion into metastases. This occurs in patients who are generally immune-competent.


Cell-mediated immunity to tumor-associated antigens was measured before and after surgery (leukocyte migration inhibition test) in 12 patients with breast carcinoma and 12 with malignant melanoma. Postoperatively leukocyte migration inhibition was reduced in all patients for a period from 6 to 22 days. (The 

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