Current Status of Immunotherapy

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The rationale underlying all forms of immunotherapy for human cancer is that there exist on the cancer cell certain differences which enable the body to recognise, and to mount an immune response against, the cancer cell. The presence of such differences, called tumour antigens, has been extensively documented both in experimental animal tumours [1, 2] and in many forms of human cancer [3]. It can readily be shown that many cancer patients are attempting to reject their own cancer. Indeed, it is possible that such immunological defence against human cancer may sometimes be successful, resulting in the eradication of the cancer before it has developed sufficiently to allow diagnosis [4], and the same mechanism may also be responsible for the infrequent cases of spontaneous regression of an established cancer. It is apparent, however, that in the vast majority of patients who present clinically with cancer, the immune response has failed and the balance between tumour growth and body defences becomes tipped progressively in favour of the tumour.

Immunotherapy attempts to reverse this balance in favour of the patient, by promoting an increased intensity of immune response to the cancer. This may be done by stimulating the patient’s own immune system (active immunotherapy) or by providing an immune response ready made (passive or adoptive immunotherapy). It is quite clear, both from studies in experimental animals [5, 6] and from clinical experience, that none of the available forms of immunotherapy is able to cope successfully with large masses of tumour tissue. The corollary of this observation is that, in most cases, successful immunotherapy requires that the tumour mass be reduced by surgery, radiotherapy or chemotherapy, either before immunotherapy or concurrently. All of these ancillary forms of treat-

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ment tend to depress the immune response, and it is therefore necessary to time the administration of active immunotherapy to take advantage of periods when such depression is minimal or absent.

Although attempts at active immunotherapy date from the early years of this century [7], the modern phase of such treatment is undoubtedly due to the work of Mathé and his colleagues at Villejuif [8] which he describes in a special article in this issue (see page 411). They used active immunotherapy to treat patients with acute lymphatic leukaemia, in whom the tumour mass had been reduced by prior chemotherapy. The method used was a combination of non-specific immunological stimulation with a living mycobacterial vaccine (Bacillus Calmette-Guerin, BCG) and, later, the administration of leukaemia antigen in the form of irradiated leukaemic cells to provide specific antigenic stimulus. The results clearly showed that the patients so treated survived longer than those treated by conventional chemotherapy.

Similar results have been obtained in patients in the remission phase of acute myeloid leukaemia treated with BCG and leukaemic cells by a group at St. Bartholomew's and Royal Marsden hospitals in England [9] and by the South-eastern Cancer Study Group in the United States, who used only BCG [10]. Other reports of successful active immunotherapy in malignant melanoma [11] and lymphomas [12] have recently appeared, while at the Second International Congress of Immunology earlier this year Israels reported prolongation of survival in patients with metastatic breast carcinoma by the addition of the non-specific immunostimulant Corynebacterium parvum to multiple drug chemotherapy. These results are highly encouraging, and suggest that the proven value of active immunotherapy in the maintenance phase of the acute leukaemias may extend to a wider range of cancers.

So far so good. Immunotherapy has emerged, after an inordinately long gestation, as a technique of proven value in the treatment of some forms of cancer. Certain questions, however, remain. Is immunotherapy, or a regimen including immunotherapy, the best form of treatment for any particular type or stage of cancer? This must be judged against the dramatic advances being made in chemotherapy, particularly in the leukaemias. It seems likely that immunotherapy will add to survival gained by any chemotherapy regimen which is not of itself severely immunosuppressive. Such immunosuppression is an undesirable side-effect per se, since it predisposes to intercurrent infections, and chemotherapy regimens are therefore likely to evolve so as to avoid immunosuppression as much as possible.

Granted that immunotherapy should continue to be investigated in the search for the optimal combination for each form of cancer, what form of immunotherapy should be used? Which strain of BCG? Is BCG really better than C. parvum? Should tumour cells be administered, and, if so, should they be autologous or allogenic? Should they be irradiated, or is the risk of tumour