Immunology and Cancer

BY

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It has been shown that human neoplastic cells possess tumour specific antigens, which are not the normal antigens of the host. The immunological screening mechanisms, in consequence, mount an immune response to these intruders. Why the antigenic structure of cancer cells differs from that of normal cells is not understood, but it may be a produce of their dedifferentiation. Alternately, cancer cells may be of embronic origin and bear antigens which are normally not apparent to the immune mechanism. The demonstration of colonic embryonic antibody in the serum of patients with gastro-intestinal tract carcinoma supports this theory.

The response induced by neoplasia differs in its intensity in that the widely metastasing tumour provokes a poor protective response, while tumours which remain small, or in extreme cases regress, provoke a strong protective response.

This response depends on two factors; the innate antigenicity of the tumour cell and the competence of the immunological mechanism of the host. The former factor is shrouded in mystery at present, but the latter depends on the patient's age, the presence of immunological deficiency states and the exhibition of immuno-suppressive agents, e.g.

1. Radiation.
2. Corticosteroids.
3. Alkylating agents.
4. Anti-metabolites.

Some authorities feel that a poorly-differentiated cancer can suppress the immune response, and allow rapid spread of tumour cells. Thus it is not known whether a cancer metastases readily because the immune response is poor, or whether it is able to render the immune mechanism incompetent. Some cancers may be less antigenic than others, and not invoke a satisfactory protective response. The tumour enhancement phenomenon must be mentioned here. This is when humoral antibodies are accepted by tumour cellular antigens leaving the cell free to by-pass cellular antibodies and continue on its evil path, and when it lodges in tissue there is no tissue response to its masked antigens.

The main response is cellular and is mediated by the intestinal lymph aggregates alerted by macrophage surveillance of tumour antigen and the subsequence production of plasmablasts and later, lymphocytes or immunologically competent cells. The reaction occurs in the tissues and is analogous to the host-graft reaction (rejection). It is considered likely that graft-host reactions also occur with circulating tumour cells, but are definitely of low incidence.

The importance of immunology in a neoplastic context concerns the place of immunotherapy in the treatment of cancer. The immune cells, unlike chemotherapeutic agents, do not act according to first order kinetics, (i.e., killing a certain number of cells according to dosage) but may, in fact, completely exterminate the cancer deposits.

Hitherto, tumours were thought to be small because they were of lowgrade malignancy or had been discovered at an early stage. Now it is seriously proposed that small masses without metastases may also be the result of a strong host immune reaction which causes their rate of expansion and destruction to be in some degree of equilibrium.

Were it posible to tip the balance of this equation in the host's favour, we would have a tremendously important ally in our battle against cancer, and, therefore, much research effort is to-day being centred around immunotherapy which exists in several forms:

1. Active specific immunotherapy in which antibodies are fabricated to a patient's tumour cells. The difficulties inherent in this process are those of serum sickness and the other malevolent responses which result from the use of foreign or zenogenic sera as a vehicle for these antibodies. In addition, a method of culturing tumour cells and thus producing antibodies in volume has yet to be devised. Prolonged therapy is needed as tumours continue to grow and means the battle must be continued until all cells (100 per cent.) are killed. The possibility of producing a "polyvalent vaccine" for human cancer has largely been discounted due to the multiplicity of antigens possessed by these tumours (each individual tumour seems to possess different antigens). However, certain virus-produced cancers in animals have common antigens, and in leukaemias similarities appear to exist, thus encouraging hope for the future.

2. Passive immunotherapy is, for the same reason, not a viable proposition although is has been successful, in one case of a malignant melanoma when a regression of long duration was demonstrated.

3. It is in the field of immunological stimulation that the greatest hope lies. B.C.G., Freunds adjuvant, C. Parvum, Bordetella pertussis and the synthetic polynuclectides (poly-IC and poly-AU) have been used in a variety of inconclusive experiments in cancer therapy. Albeit that these experiments were inconclusive, evidence exists that immunological stimulation of this nature increases the body's resistance and may succeed in tipping the balance in favour of the host.

Surgery for cancer has been based on anatomical lines since the epic work of Virchow, but, it is now felt that the regional lymph nodes must play a part in the immune response, and that their removal might actually decrease the patient's chances. Also, radiotherapy and chemotherapy are both immune-suppressive and must play a part in further reducing the response. There is a firm balance in all these mechanisms as on discontinuing immune-suppressive type therapy, the body's immune responses usually return to normal and in some cases are even enhanced.

Evidence of the state of the delayed hypersensitivity reaction before therapy, and the histological response in the regional lymph nodes should be an indication of the immune status, and the likely outcome of the battle between the host's defences and the cancer. This information could govern our future thinking on therapy in any given case. Immunological stimulation in cases with a poor response, early surgery in cases with a good response and so on. It is, therefore, likely that the future use of immunotherapy will be an adjunct to surgery in the treatment of cancer.