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Pointers

Immunity and Malignancy: In his Goulstonian lecture Dr. G. Hamilton Fairley examines evidence for the existence of tumour-specific antigens and considers how to increase their activity (p. 467). Leader at this page.

Hodgkin's Disease: Changes in circulating lymphoid cells similar to those in conditions of antigenic challenge (p. 473).

Active Labour: Properly supervised stimulation of labour with intravenous oxytocin ensured delivery within 24 hours. This proved safe and beneficial to both mother and baby (p. 477).

Iatrogenic Septicaemia: Three patients receiving antibiotic by intravenous infusion developed secondary septicaemia originating from the cannula site (p. 481) ; Leader at p. 462.

Platelet Inhibitor: New pyrimido-pyrimidine compound proves in vitro to be a potent inhibitor of platelet aggregation and adhesiveness (p. 483).

Heart Rate and Hypertension: "Intrinsic" heart rate (produced by blocking both sympathetic and parasympathetic stimuli) was decreased by reserpine (p. 486).

Great-toe Reflexes: Extensor reflexes are difficult to elicit, but found specially useful in assessing lesions of fifth lumbar nerve root (p. 487).

Cardiogenic Shock: Almost complete suppression of insulin secretion observed in four patients after cardiac infarction (p. 490).

Placental Metastases: From maternal bronchial carcinoma. Mother died eight months after birth of apparently unaffected infant (p. 491).

Diabetic Children: Management (p. 493).

Today's Drugs: For thyrotoxicosis (p. 496).

Coronary Care: Results from a five-bed unit in a general medical ward compared favourably with those from more highly staffed purpose-built units (p. 502).

Interference with Demand Pacemakers: By radio monitoring equipment (p. 504).

Personal View: Dr. Clifford Hawkins (p. 508).

Letters: On pulmonary blood flow; women doctors; "normal" values; dangers of dry-cleaning machines; *Medical Directory*; and hospital salaries (pp. 509–516).

Parliament: Nurses' pay; Mr. Crossman on abortion, N.H.S. charges, and G.P.s in hospitals (p. 521). Leader at p. 466.

G.M.S. Committee: Meeting report (*Supplement*, p. 91).

Immunity to Cancer

It is no longer in dispute that cancer in man and animals may provoke immune responses by the host. In so far as cancers are part of the host, the responses are a form of autoimmunization. Some of the evidence that they occur has long been available, but a fuller appreciation of it has come from developments in the science of immunology and the elucidation of the role of the lymphoid cells and their products, the immunoglobulins.

Morphological distinctions between tissues depend on differences in protein composition, and they confer a different antigenic structure. The repetitive histological features of certain kinds of tumour that permit histopathologists to label and classify them demand some characteristic composition and hence antigenicity. The reaction of the host's system of immunity to the tumour antigens constitutes the immune response to cancer.

It is a sign of the times that for this year's Goulstonian lecture at the Royal College of Physicians Dr. G. Hamilton Fairley took as his subject "Immunity to Malignant Disease in Man." His scholarly survey, reported in this issue of the *B.M.J.* at page 467, presents a historical account of the accumulated evidence that tumours in man provoke immune reactions and lays suitable stress on their value to the host. It ends appropriately enough on a guardedly optimistic note about the prospect for immunotherapy. The conclusion from observations made by research workers in several countries is compelling that immune responsiveness to tumours has a favourable effect on limiting their growth and on their susceptibility to other forms of treatment. Contrariwise, it seems sure that deficient immunity favours the occurrence, growth, and spread of tumours. It may be that an immune reaction will develop only when tumours possess antigens entirely new to the body, though we might be allowed the optimistic speculation from analogy with autoimmune disease that sometimes immunological rejection processes may occur even in the absence of such absolute novelty.

New antigens in human tumours have been only rarely found. The Burkitt lymphoma does possess foreign antigenic material, which is viral in nature or at least virus-dependent, and the victims of this tumour have a high titre of circulating antibodies to the tumour cells. It is unlikely to be a coincidence that this tumour is remarkably sensitive to chemotherapy, with a high rate of clinical cure. Much the same considerations may also apply to uterine chorionepithelioma, which also responds favourably to chemotherapy. Antigenic dissimilarity of this tumour from the host, owing to its possession of paternal antigenic determinants, could be the important factor here.

New methods of antigenic analysis of cells in vitro and of detecting specific serum antibodies and lymphocytic reactivity have been devised lately. The more precise of them depend largely on microscopical examination of cytological and serological reactions, and they include immuno-

fluorescence, mixed-cell agglutination techniques, and cytotoxicity studies. The detection of immune reactions at the surface of the tumour cells will be particularly important in assessing whether an effective in vivo immune response is likely. Autoantibodies against internal cytoplasmic constituents, sometimes present, may merely reflect a response to unusual breakdown products of a tumour rather than any attempt at the immunological rejection of it.

These modern in vitro methods of study are now being applied to a wider range of cancers in man—as, for example, the malignant melanoma, cited by Dr. Hamilton Fairley. In sera of about 30% of patients with this tumour cytotoxic autoantibodies at least in part specific for the cancer cells have been detected by the clinical and experimental tumour immunology team at the Chester Beatty Research Institute. It would seem that in patients possessing such antibodies the tumour progresses more slowly than in others. There may also be a correlation with infiltration of the tumour by lymphocytes.

Clearly there is a need to extend these methods of investigation to other tumours. It should become general histopathological practice to assess lymphocytic and plasma-cell infiltration of any tumour to determine if possible whether it might be a host response to the living tumour or only the consequence of necrosis or infection. Then it might become feasible to correlate such specific host response with prognosis. Tumours like seminoma of the testis, squamous carcinoma of the skin, and carcinoma of the breast are obvious targets for a search for tumour-specific autoantibodies and autoimmunocytes. The lymphoid reaction in Hodgkin's disease, discussed this week by Dr. D. Crowther, Dr. Hamilton Fairley, and Mr. R. L. Sewell (page 473), is possibly an immune response by the host to reticulum-cell neoplasia. Comprehensive immunological investigation is now required to examine this hypothesis.

The lesson of the favourable response to chemotherapy of the Burkitt lymphoma and the chorionepithelioma may suggest that other tumours which excite an immune reaction could also have a better prognosis if more specific effective drugs were to become available. As to specific immunotherapy, this will become possible only when we have more information about the antigenicity of the tumours and the responses to them. We can be confident that there is nothing inherently unlikely in immunotherapy for some tumours, whether by immunocytes or by antisera. Meanwhile for immunogenic tumours, which may prove to be more numerous than is at present supposed, the best therapy will be that which disproportionately reduces the number of tumour cells while maintaining the relative efficiency of the immunological system.

Septicaemia from Infusion

Contamination by inadequately sterilized instruments, syringes, or solutions is preventable and probably rare today, but the preparation of the skin remains a weak link in the aseptic defences. The living skin cannot be sterilized, and even the best chemical disinfection will usually allow the survival and subsequent growth of some of the resident bacteria. As well as failing to sterilize, the methods used for disinfection may add contaminants. Many reports have appeared in which infection, especially with *Pseudomonas aeruginosa,* has been acquired from a solution used to disinfect the skin before incision, venepuncture, or setting up an intravenous infusion.[1-3] Quaternary ammonium compounds have been especially fallible in this respect, but aqueous solutions of other compounds including chlorhexidine and chloroxylenol and hexachlorophane detergent preparations have also been found contaminated.[3-5]

Small numbers of bacteria injected directly into the bloodstream will, in most people, be rapidly overcome by the humoral and cellular defences. But if these defences are impaired, as in patients with severe burns or in those receiving treatment with steroid and immunosuppressive drugs, there is an obvious risk of infection. Such a risk also attends patients with the lesions of rheumatic or bacterial endocarditis. In such patients, too, the risk is mainly from "opportunist" organisms, which have relatively low pathogenicity for healthy people. They include *Ps. aeruginosa,* pathogenic fungi, and other organisms difficult to exclude or to eradicate by chemotherapy. When a cannula is introduced for continuous-drip infusion there is a further hazard—the development of a thrombus in which small numbers of contaminating bacteria are likely to multiply without hindrance. The chances of contamination from the skin are obviously increased by the prolonged exposure of a drip incision, and the profuse growth of bacteria in a septic thrombus exposes the bloodstream to heavy contamination. In a patient with poor resistance this is likely to lead to septicaemia or pyaemia.[6]

A report by Dr. J. H. Darrell and Professor L. P. Garrod in the *B.M.J.* this week (page 481) gives details of three patients who developed secondary septicaemia while receiving prolonged intravenous infusion of antibiotics. Each of the patients had a disease or had received treatment which increased susceptibility to infection. Two were being treated for bacterial endocarditis when they developed a secondary infection, in one case with *Candida albicans* and *Achromobacter* sp., in the other with *Candida* sp. The third patient was being treated with prednisolone for sarcoidosis and developed cryptococcal meningitis, for which he was given an intravenous infusion of amphotericin B. During the course of this treatment he acquired a bloodstream infection with *Staphylococcus aureus,* and this organism was also found at the site of the original drip incision. Treatment with amphotericin B was successful in one of the two patients with endocarditis who developed *Candida* septicaemia. The two other patients appeared at first to respond to treatment with

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