
This book contains papers read at the Conference on Paraneoplastic Syndromes held in New York in March 1973. The importance of this conference and the publication of its proceedings for collating and disseminating information about paraneoplastic syndromes is obvious from the introductory remarks made by Hall who said that at ‘any given time 20% of a group of cancer patients in all stages of their diseases will be suffering from a paraneoplastic syndrome and that 75% of all patients will develop one during the course of their disease.’

The book is subdivided into ten parts: (1) Generalised perturbations in host physiology caused by localised tumours; (2) Endocrine-metabolic syndromes; (3) The spectrum of tumour-induced alterations in haematopoietic function; (4) Altered coagulability in tumour patients; (5) Gastrointestinal cancer syndromes; (6) Neurogenic paraneoplastic syndromes; (7) A spectrum of tumours that produce paraneoplastic syndromes; (8) A spectrum of organ systems that respond to the presence of cancer; (9) Other causes, diagnosis, and treatment of syndromes, and (10) Newer concepts in pathogenesis. It is a daunting task for any reviewer to review a book so extensive in scope as this one, and I shall therefore confine myself to the discussion of the features which in my view are the most salient.

In Part I, Bodel describes investigations into the production of pyrogen by tissues from cancer patients and demonstrates its production in vitro by some of the cells in these tissues. Bodel indicates the possibility that some activator might interact with the pyrogen-producing cells and also suggests possible pathways in the processes of activation and pyrogen production. Following this there is a review of the cachexia-anorexia syndrome in cancer patients which Theologides ends with a hypothesis of his own which has neither much experimental basis nor is amenable to experimental tests. More concrete data on the anorexia syndrome is presented by de Wys (in Part 8) which appear to indicate that this syndrome may have its basis in abnormalities in taste sensation. Weinhouse and Gold emphasise the role of loss of enzyme adaptation for energy conservation in the causation of the anorexia, asthenia and loss of body tissues. This section also highlights the possibility of alterations in immune function and induction of autoimmunity in association with neoplasms. Friou, for example, considers dermatomyositis as an autoimmune paraneoplastic disease. Tumour cells may bear surface antigens which might be identical in part of their structure with antigenic determinants in muscle cells. This is an interesting possibility because of the possible viral aetiology of some forms of cancer and the ability of viruses to induce autoimmunity. However, much of these data come from animal models and very few cancer patients with dermatomyositis have been studied. Towards the end of the book, Hall also considers autoimmune diseases as representing paraneoplastic syndromes and postulates ‘oncocognitive autoimmunity’, in which macromolecules associated with normal epithelial cells, which are prevented by the basement membrane from alerting the immune system in the normal course of events, are suggested as possible immunogens.
A perusal of Part 2 leaves one with the impression that ‘ectopic’ production of certain hormones indicated in some endocrine-metabolic syndromes is still an open question. Marks seems to have reservations about the belief that paraneoplastic hypoglycaemia is due to production by the neoplasm of a substance with insulin-like activity. But Amatruda and Upton have reported extraction of ACTH and corticotropin-releasing factor from tumours from 3 patients with ‘ectopic ACTH’ syndrome. They also state that much of the activity of their preparation resided with peptides of the same size as ACTH of pituitary origin. The ectopic hormone differed from that of pituitary origin in amino acid composition, and contained threonine and isoleucine. Gordon, on the other hand, presents some definitive evidence that hypercalcaemia occurring in association with breast cancer is not due to ‘ectopic’ production of parathyroid hormone. While tumours other than breast cancer may have demonstrable parathyroid hormone, the latter is nevertheless distinguishable from the normal hormone. From a study of more than 340 cases of erythrocytosis Hammond and Winnick arrive at the conclusion that whilst in a number of nonmalignant tumours hypoxia of the kidney results in the production of the erythropoietic factor, the major mechanism might yet be elaboration of an erythropoietin-like factor by the tumours themselves.

The causes of altered coagulability presented by cancer patients are discussed in Part 4 of the book which contains formal presentations on certain aspects of this syndrome. Increased fibrinogen turnover frequently accompanies neoplasms, and since this seems to occur in and around the tumour itself the relationships between tumour cells and their products and the coagulation mechanisms have received much attention. Pineo describes the release of mucus from adenocarcinomas and points out that extracts of the mucus can initiate coagulation. The active component is said to be a glycoprotein different from thromboplastin. When the malignancy involves marrow or spleen, thrombocytopenia is a major complicating factor. For these cases the use of inhibitors of platelet function is no answer because decreased production is the cause of thrombocytopenia. Nor does anticoagulation affect the bleeding due to thrombocytopenia. The best means to manage patients with altered coagulability, argues Merskey, is therapy directed at the tumour itself, or aimed at reversion of the alterations in coagulability using hormones or antimetabolites.

In the section devoted to neurogenic paraneoplastic syndromes, Joynt examines the aetiology of carcinomatous neuromyopathies. This seems to be little understood except for multifocal leukoencephalopathy. Of this Richardson has given an excellent account. The virus in this case appears to be a papova type virus, very similar to, if not identical with, Simian virus-40. Other syndromes involving nerve and neuromuscular junction also remain as yet unexplained.

Part 9 contains a number of papers dealing with complications of cancer chemotherapy, the effectiveness of corticoids, and a panel discussion on therapy.

New concepts based on animal models to explain the pathogenesis of paraneoplastic syndromes are described in the final section. Inglesias describes some interesting experiments of implantation of testicular tumours in rats which result in the development of pituitary and mammary tumours. Inglesias traces the chain of events beginning with estrogenic activity of the implanted tumour causing hyperplasia or tumour of the pituitary and subsequently, through mediation of prolactin, resulting in mammary neoplasia. Inglesias thus not only traces the possible mediators but also the specific responses of target organs. While this is an ‘at-a-distance’ effect, one of the mechanisms implied in Sherbet’s hypothesis for the pathogenesis of
these syndromes is close cell-to-cell interactions. Nathanson and Hall have suggested mechanisms like derepression of the genome in the tumour cells. In the same strain a more detailed explanation of the derepression mechanisms has been attempted by Sherbet, who proposes the ‘precessive competence’ hypothesis which also appears to have a predictive value with respect to the incidence of a particular syndrome in association with a given neoplasm. The book contains more than 2,000 references in the literature and incorporates a vast body of information, interpretation and analysis. The emphasis is quite clearly on understanding the mechanisms involved. The conference has resulted in a better understanding of paraneoplastic phenomena and a number of new concepts have emerged.

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