The Emergence of New Tumour Lines during Therapy

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During the relapse from an initial response to treatment with cyclophosphamide or melphalan, evidence that their tumour had 'changed its spots' was found in 45% of 155 patients in the first MRC myeloma trial. These changes all seemed to evolve a tumour with a faster growth rate and this occurred either alone, growth rate escape (2%), or with other changes: Bence Jones escape (32 + 3%) was seen as a disproportionate increase in Bence Jones proteinuria relevant to the initial proportions of Bence Jones to whole paraprotein and in a few patients Bence Jones appeared where it had not formerly been detected in urine concentrated 300 times (de novo 3%). Mutation escape (5%) was the emergence of a new paraprotein closely related (eg, one amino acid difference) to the parent one: non-paraprotein escape (3%) was seen as terminal reticulo-sarcoma with very little paraprotein, but enough to relate the primitive tumour to the initial myeloma. In this series monocytic leukaemia has not yet been seen.

All these new lines emerged mostly two to five years after treatment and have rarely been witnessed in the natural history of the disease. Successful prolongation of life could have allowed a natural tumour progression to show, but I fear the treatment, which acts by altering DNA, may have induced mutants, the most prolific of which are seen in the relapse. This explanation could also apply in patients given immunosuppressive therapy for renal transplants. Cytotoxic drugs are best reserved for otherwise fatal diseases.

Fibrin in the Kidney in Myelomatosis

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Renal involvement in myelomatosis is a frequent occurrence both as a mode of presentation and as a cause of death. The nature of the renal involvement is varied but the precise mechanism by which renal failure occurs is obscure. Attention has recently been focused on the role of fibrin in the development of renal lesions, both in the experimental and clinical situations. The deposition of fibrin has been shown in the renal glomeruli proliferative glomerulonephritis but not in membranous glomerulonephritis or in the nonproliferative phases of the nephrotic syndrome. This correlation of fibrin with proliferation has been confirmed in the experimental model. We have conducted a retrospective study of the renal histology in a necropsy series of 32 cases of myelomatosis. Intravascular fibrin was demonstrated within the glomeruli of more than one third of the cases and this was usually associated with proliferation of the mesangium. The presence of intravascular fibrin and mesangial proliferation was not associated with any particular immunoglobulin abnormality or with the presence or concentration of Bence Jones proteinuria. In addition to fibrin within the glomerular capillaries, fibrin was also demonstrated in intertubular capillaries in three cases of myelomatosis with acute tubular necrosis.

Although the precise significance of the presence of fibrin within the renal glomeruli in myelomatosis is obscure, we believe that it may be of importance in the pathogenesis of the renal dysfunction which occurs in myelomatosis, and that this merits further study.

Production of Lymphomata following Intraperitoneal Inoculation of Silica

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Crystalline silica was injected into the right pleural cavity of Wistar rats at 6-10 weeks of age. Alkaline-washed quartz, less than 5μ in size, was used. Approximately 37% developed tumours belonging to the reticuloses group, whilst another third had an altered or hyperplastic reaction. Very few tumours have been reported previously following exposure of various animals to silica by other routes. The distribution of the tumours was from 300 to 1 000 days in a spread out fashion. They were mainly found in the medastinum and on the diaphragm, as were the benign silicotic nodules. The majority of tumours were believed to be malignant histiocytoses, although some malignant lymphomas with a predominant lymphoblast or mature lymphocyte were found. A few spindle cell sarcomas were also found.

In order to study the development of these tumours, rats were killed at five-week intervals after intraperitoneal injection of silica. The distribution of the dust was noted and it was found to reach the tracheo-bronchial lymph nodes and the region of the thymus. Eventually it entered the thymus. The thymus appeared to be involved in the tumours: likewise silica and tumour tissue was also, but not always, found in the spleen, liver, and in occasional abdominal lymph nodes.

Rats have also been given intraperitoneal coal and carbon, but no tumours have developed. Three different types of silica have been used, and tumours have developed with all three types when given by this route. However, when the silica was given intravenously and intra-peritoneally, tumours were not found.

Two Cases of Haemangioepycytomatosis Arising in the Uterus

HILDA R. HARRIS (Maerlor General Hospital, Wrexham)

The first case occurred in a woman aged 39 years, who for three months had pro-

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longed scanty menstrual loss. Her uterus was the size of an eight-week pregnancy, but pregnancy tests were negative. Within the uterine wall there was a cystic, trabeculated, reddish-grey tumour with an ill-defined capsule.

The second case was in a woman aged 68 years who complained of abdominal pain and had an irregular pelvic tumour which was undergoing torsion. The uterus contained cervical and endometrial polypi, multiple fibroids, one of which had undergone torsion, and a yellowish white lobulated tumour with an ill defined capsule which was situated in the myometrium of the uterine fundus.

Both tumours had similar histological features. They were vascular, and many of the small blood vessels were surrounded by a cuff of collagen. Between the blood vessels the neoplastic cells with their vesicular nuclei were packed together and had a whorled appearance. They lay outside the reticulin sheath of the blood vessels, whose endothelium was normal and were surrounded by reticulin fibres.

These tumours were differentiated from stromal endometriosis, unusually vascular fibroids and leiomyosarcoma, by the inability to demonstrate muscle fibres in the growth or a connexion with the overlying endometrial stroma. The reticulin pattern of the growths conformed with the criteria laid down by Stout and Murray for the diagnosis of haemangiopericytoma.

The patients were well three and a half years after the growths had been removed, which supports the concept that uterine haemangiopericytoma are more benign than when they arise elsewhere in the body. This may be due to the complete removal of the neoplasm when the uterus is taken out.

Significance of Asbestos in Lung Tissue

J. C. WAGNER (Pneumoconiosis Research Unit, Penarth)

In 1964 a working group studied the available information concerning the cancers that were associated with exposure to asbestos dust. Recommendations were made for an international study of the problem by a number of scientific disciplines under the headings of epidemiology, pathology, and dust physics and chemistry. Information was required to ascertain whether a certain type of asbestos was responsible for the development of mesothelomas of the pleura and peritoneum and carcinoma of the lung; if a particular type of fibre could be implicated, it might be possible to define the risk of exposure to other types of fibre. After eight years the results of most of these investigations are being correlated. At present it appears that a certain type of fibre is more dangerous than the others. The use of this material has been restricted in Britain.

In this paper I shall present the evidence for incriminating a certain type of fibre.

'Retention Lung' in Infants

JOHN L. EMERY (Sheffield)

Young children frequently present with consolidating conditions of the lung which are diagnosed as pneumonia and treated with antibiotics.

Histological features are described of the changes found in a particular group of such children in which the consolidation is not inflammatory but due to the inability of the bronchi to eliminate fluid and cell debris.

Factors leading to 'retention lung' include congenital squamous dysplasia of bronchi, the secondary effects of virus infections, and oxygen therapy.

The importance of the condition lies in its recognition both clinically and at necropsy and that treatment lies in physical rather than in antibiotic therapy.

Some Observations on Peripheral Sponge Biopsy of the Lung

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Whilst the diagnosis of bronchogenic carcinoma was relatively easy in conditions within the reach of the bronchoscope, distal lesions were more difficult and in spite of bronchography and sputum cytology there remained a number of peripheral lesions which, although showing an apparently characteristic radiographic appearance, were found on thoracotomy not to be malignant.

The use of sputum cytology was well recognized and was a useful diagnostic weapon but it was time consuming.

Brush or abrasive methods of obtaining material from peripheral lesions had been described by several workers. Methods included the use of radio-opaque catheters, abrasive instruments, and sponges. The latter included acetone-soluble material and also acrylic sponge-capable of being processed in the same way as tissue for paraffin sections.

In this investigation a new design of
Two cases of haemangiopericytomata arising in the uterus.

H R Harris

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