Today's Treatment

Blood and Neoplastic Diseases

Solid Tumours

T. J. McELWAIN, M. J. PECKHAM

British Medical Journal, 1974, 4, 584-585

The term "solid tumour" is loosely employed to draw a broad distinction between malignant disease arising from epithelial, glandular, and connective tissues (including bone and muscle) and neoplasms of the leukaemia-lymphoma complex. In this context solid tumours collectively represent the major part of the cancer problem. Perhaps the main advantage of an empirical division of this kind is to concentrate on the outstanding problems of managing many common forms of malignant disease and away from the leukaemias and lymphomas, which have received a great deal of attention during recent years.

Most common solid tumours in man—which include carcinomas of the breast, large bowel, bladder, prostate, cervix and corpus uteri—still pose considerable problems of management and in many sites only limited progress has been made. Recent developments in radiotherapy and chemotherapy, the increasing integrated use of different treatment modalities used in planned combination, together with improved techniques of tumour localization, offer the prospect of future advances in several areas.

Causes of Treatment Failure

It is important to define the obstacles to the successful use of currently available forms of treatment, and considerable attention has been paid to the study of the causes of treatment failure. In the case of surgery, the causes are often self-evident: locally advanced bulky tumours (which if considered operable are associated with a high risk of local recurrence) and metastatic disease. Failure of treatment after radiotherapy may occur as a result of the difficulty of eradicating locally advanced primary tumour, the presence of distant metastases, or a combination of both factors. For chemotherapy the problems are poorly defined but are likely to include the inherent limited responsiveness of tumour cells to available agents: the limitations imposed by normal tissue tolerance; access of the cytotoxic agent to the tumour substance; and the development of drug resistance. In the case of bulky primary tumours the combination of surgery and radiotherapy offers attractive advantages and this aspect is being actively explored at several sites—notably in the head and neck, bladder, and rectum.

The problem of local control in radiotherapy has received a great deal of attention and measures based on the hypothesis that hypoxic tumour cells may be the determinant of treatment

failure are discussed in our second article. The combination of irradiation and chemotherapy has proved of value in the management of several paediatric tumours, particularly neuroblastoma, rhabdomyosarcoma, and Ewing's sarcoma. The use of chemotherapy in these conditions, particularly the latter two tumours, depends on its effectiveness in dealing with small, clinically inapparent metastases—while radiation is reserved for the treatment of the bulky primary disease. An extension of this approach may be envisaged at other sites—for example, for soft tissue carcinomas, osteogenic sarcomas, and carcinoma of the breast.

Tumour Curability

In England in 1972 cancer accounted for one-fifth of all deaths.¹ Of over 110,000 deaths from cancer occurring in that year, just over 30,000 were due to lung cancer (40% of male cancer deaths); 38,000 to malignancy of the digestive system (most commonly stomach); 13,000 deaths to cancer of the urinary tract; and almost 12,000 to genital cancer. Of female cancer deaths, 20% were due to breast cancer. Neoplasms of the lymphatic and haemopoietic system accounted for 6% of cancers. Thus carcinoma of the bronchus, breast, stomach, and gastrointestinal tract collectively account for over half the deaths from malignant disease in England.

The time between primary treatment of the patient and relapse or death will vary very considerably, depending on the tumour type. Late relapses in carcinoma of the breast are well recognized; relapses in head and neck cancer generally appear within two years, and of large bowel cancer within five years; while tumours such as glioblastoma multiforme run a rapidly fatal course, usually within one year.

Discussion of methods for evaluating treatment results are beyond the scope of this review. The relative survival rate proposed by Easson and Russell² adjusts for normal mortality: when the expectation of life for the cancer patient is identical to that of anyone else of the same age and sex living in the same area, the patient is considered cured.

Tumours which are associated with a high probability of cure include skin cancer, and early-stage carcinomas at many sites, including the head and neck, bladder, breast, cervix, and rectum, testicular seminoma and rarer tumours such as neuroblastoma and female chorioncarcinoma. To the list may now be added localized prostatic cancer and stage I and II Hodgkin's disease. Localized carcinomas at several sites may be managed equally effectively by radiotherapy and surgery and the functional result will determine the choice of treatment. For example, in glottic carcinoma radical irradiation eradicates the tumour and leaves a normally functioning larynx. The curability of these localized tumours (including prostate) depends on a tumour of small volume and the ability to deliver the high radiation doses necessary to eradicate the tumour. In seminoma and Hodgkin's

The Royal Marsden Hospital, Sutton, Surrey

T. J. McELWAIN, M.B., M.R.C.P., Consultant Physician
M. J. PECKHAM, M.D., F.F.R., Professor of Radiotherapy

disease the inherent radioresponsiveness of the tumour enables cure to be obtained even when large volumes of the body need to be irradiated. In nephroblastoma and chorioncarcinoma the tumours are chemosensitive, and here chemotherapy plays a curative part—alone in the case of chorioncarcinoma and combined with irradiation in nephroblastoma.

At the other end of the spectrum, tumours such as carcinoma of the pancreas, lung, stomach, grade III and IV astrocytomas, and osteogenic sarcoma still have an appalling prognosis—most patients being dead within one to two years of diagnosis.

Between these two extremes fall the large mass of common solid tumours, with survival results concealing in most cases a wide variation within each tumour type, from early to late stage tumours, with the overall treatment results depending on the relative proportions of patients within each stage category. Since curability is in many instances closely related to tumour size and localization, it is reasonable to suppose that early detection will be advantageous in improving the overall picture. This may prove to be the case in some tumours, particularly carcinoma of the prostate, breast, and cervix.

Diagnosis

Detailed histological classifications have been developed for many tumour types, which allow the clinical evolution of the disease to be predicted with some precision. Obvious examples are the Rye classification of Hodgkin's disease and the subdivisions of testicular teratomas. Histological grading, for example, in carcinoma of the breast, colorectal cancer, bladder cancer, and astrocytomas may also permit the likely behaviour of the tumour to be predicted with reasonable accuracy.

Clinical and pathological staging provides the necessary basis for choice of optimal therapy and assessment of prognosis, and facilitates comparison of treatment results between different centres. The T.N.M. system introduced by the Union Internationale Contre le Cancer, Geneva, has gradually been extended to provide a commonly accepted staging system for the majority of tumour sites.

Information about tumour extent and dimension is derived from the details of clinical assessment, radiological, isotopic, and ultrasonic examination; and in some cases by surgical exploration. Space allows only one or two examples of advances in localization techniques to be cited. Perhaps the most valuable introduction into diagnostic radiology in the cancer field in the past decade has been pedal lymphography, which demonstrates retroperitoneal nodal metastases from pelvic malignancies including carcinomas of the cervix, corpus uteri, ovary, and bladder; testicular tumours; malignant lymphomas; carcinoma

of the kidney; paediatric tumours, particularly nephroblastoma; and tumours of the limbs such as melanoma. Recent advances in nuclear medicine, including isotopic and ultrasonic scanning have also contributed to pre-treatment assessment. Isotopic scanning, with the exception of radio-iodine in well-differentiated thyroid carcinoma, is limited by the lack of radiopharmaceuticals which are specifically incorporated into tumour cells. Gallium-67 has shown promise in lymphomas, seminomas, and carcinoma of the lung, while technetium polyphosphate bone scanning is proving a valuable method of detecting clinically silent metastases, particularly in breast carcinoma.

DIAGNOSTIC ULTRASOUND

Without doubt the most exciting recent introduction into tumour localization is diagnostic ultrasound. This is a readily repeatable technique and offers considerable promise in the diagnosis of intra-abdominal, particularly hepatic, metastatic disease. The localization and details of dimension of deeply seated tumours—for example, pancreatic carcinoma—are likely to be of great value in planning radiation therapy.

Surgical staging procedures have also proved valuable—particularly in Hodgkin's disease, where laparotomy and splenectomy form part of the initial assessment of most patients with apparently localized disease. Tumour index substances have been a subject of considerable interest in recent years. These substances produced by the tumour may be of diagnostic value—for example, in neuroblastoma or useful in monitoring the progress of disease on therapy. Carcino-embryonic antigen (C.E.A.) produced by large bowel adenocarcinomas is being evaluated for monitoring the course of the disease. It may find a place in detecting recurrence, but has not proved to be reliable enough as a diagnostic screening test. Human chorionic gonadotrophin produced by male and female chorioncarcinomas is of limited value in the follow-up of therapeutic response in male teratoma, but is extremely valuable in monitoring female patients since the levels of the hormone parallel the number of tumour cells—thus providing a sensitive index of the effectiveness of drug therapy. Alpha-feto protein produced by primary hepatomas is also produced by some testicular teratomas; its potential value in the management of the latter tumour type is being investigated at present.

References

- ¹ Department of Health and Social Security, *On the State of the Public Health*. London, H.M.S.O., 1973.
- ² Easson, E. C., and Russell, M. H., *The Curability of Cancer in Various Sites*. London, Pitman Medical, 1968.

Any Questions?

We publish below a selection of questions and answers of general interest

Pseudoasthma

What is pseudoasthma and how should it be treated?

The term pseudoasthma, unlike pseudogout, is not usually used to describe a definite clinical syndrome. Most medical dictionaries state that it means "false asthma" or more commonly simply "dyspnoea." The term is occasionally used, however, to describe expiratory wheezing or grunting noises produced by voluntary spasm of the vocal cords. This may occur in some hypochondriacs or in cases of genuine asthma

with strong underlying emotional causes. In the latter case it can be very difficult to deal with. The former type may respond to reassurance or tranquillizers. Bronchodilators may also help especially if the patient is told that they are bronchodilators. The condition often improves if more serious organic illness occurs to replace it. Care should be taken to distinguish it from the intermittent asthma of young people in whom the wheeze and degree of airways obstruction are very variable and so may not be present when examined by the physician. In such cases serial measurements on a peak flow meter may reveal the true state of affairs.