Recent advances

Oncology

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Cancer is an increasing cause of morbidity and mortality in most countries. It has recently overtaken heart disease as the commonest cause of death in the United Kingdom. "Breakthroughs" in cancer research are reported regularly in the media. Some reports are based on new results that show potential for improved treatments, but others are premature or publicity seeking, and the motivation behind them is questionable. The public has high expectations that basic science cancer research will translate into improved cancer cures and care. Yet awareness and understanding of the clinical trials that are essential in establishing the effectiveness of new treatments is limited. Recruitment to randomised clinical trials evaluating new cancer treatments is often slow, partly because people are convinced that all new treatments are likely to be an improvement and partly because of unease about the process of randomisation. Better public education about categories of evidence in relation to health interventions might contribute to speedier and more appropriate evaluation of promising treatments.

Public confidence that cancer care in the United Kingdom is optimal has been shaken by reports that outcomes for some common cancers differ in countries in western Europe, and that survival rates in Britain for 18 of 25 cancer types studied are poorer than in most other European countries.^{1,2} Better than average outcomes were seen in Switzerland, Finland, and Holland. These reports, together with evidence that cancer survival rates differ within a country according to the pattern of care, prompted review of the provision of care for cancer patients in the United Kingdom and in parts of Australia.³⁻⁶ Optimal organisation of cancer care might achieve appreciable gains. In the case of breast cancer, this could amount to a 5% improvement in the survival rate at five years. Such a gain would be viewed as a major breakthrough if it were the result of a new treatment.

In this article we discuss five important recent advances in oncology. Four advances are related to the organisation of care, and are as important, in terms of a deliverable improved outcome, as any recent research findings or new treatments. These four advances are: the multidisciplinary cancer treatment team; supportive care for cancer patients; definition of treatment goals; and the status of clinical trials. In addition, we discuss the exciting treatment advances in

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Multidisciplinary treatment teams specialising in specific organ sites have been recognised as being important for optimal cancer care and for improving outcome

The organisation and delivery of supportive care to patients with cancer has improved

Treatment goals are more clearly defined

Public awareness and understanding of the clinical trials that are driving clinical research has increased

Research has started on potential treatments such as matrix metalloproteinase inhibitors, gene therapy, and cancer vaccines

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areas other than radiation therapy and cytotoxic chemotherapy.

Methods

The references in this review were taken from the authors' knowledge base and recent presentations. They include Medline reviews of the topics discussed. The authors feel that the importance and relevance of the advances described here reflect a perspective focused on the patient.

Multidisciplinary cancer treatment team

Only 30 years ago, competition for patients between surgeons, radiation oncologists, and medical oncologists was an important factor influencing cancer care. Indeed, the initial testing of cancer chemotherapy in patients with leukaemia and lymphoma was partly related to the fact that surgeons and radiation oncologists were not competing to treat these patients. The later emergence of multidisciplinary treatment teams in childhood cancer care paved the way for multidisciplinary treatment teams specialising in specific organ sites—these are now common in major institutions treating large numbers of patients with cancer. In most

cases the general practitioner is still the gatekeeper in referral of patients with cancer, but screening services may influence increasingly referral to specialised care.

Several studies of outcomes in patients with cancer treated surgically indicate that not only the skills of the surgeon but also the number of cases treated are important factors.^{3 4 6 7} Within large hospitals, surgical subspecialisation and agreement between surgeons may lead to patients being referred to surgeons with a particular training or interest. This site specialisation provides the concentration of expertise essential for clinical trials and further facilitates recruitment of patients to these. However, developments in interventional radiology and fine needle aspiration cytology now influence how cancer is diagnosed and the entry point of patients to specialised care.

General practitioner's role

Although the route by which cancer patients reach specialised care is changing, general practitioners retain an important position. This is because better informed patients may seek their general practitioner's advice when presented with treatment options—which will happen increasingly with a multidisciplinary team—and because cancer treatment is largely an outpatient activity. General practitioners need better education in cancer care if they are to continue their gatekeeper and care roles. They must also promote primary prevention and effective cancer screening. Good communication between the cancer treatment team based at the hospital and the general practitioner is very important, though the best way of achieving this has not yet been determined. The letter to the general practitioner from the cancer treatment team is an important educational tool as well as a means of documenting what has been proposed and what the patient has been told.⁸ General practitioners are rarely comfortable if their patients know more than they do about their disease and its management.

Nationally agreed protocols

Drug treatment prolongs survival in patients with metastatic cancer of several types. Outcomes in childhood cancer have improved dramatically; in about 60% of children diagnosed with cancer, the disease is eliminated by complex and intensive treatments. This is largely because treatment for children has been

organised on a national and international basis.⁹ Children with a relatively rare tumour, such as a Wilms's tumour, are treated according to nationally agreed protocols. This enables prognostic categories to be defined and treatment to be tailored to risk. Patients categorised as having a good prognosis can be given less toxic treatment that is better tolerated and has fewer sequelae, whereas those with a low chance of cure may benefit from intensive, more prolonged treatment. Because of the numbers involved the results are sufficiently robust to justify changes in treatment over the years, resulting in better outcomes and fewer late adverse effects. The work of the Wilms Tumour Study Group in the United States is a model of how cancer treatments should evolve and is based entirely on specialisation and cooperation in clinical trials.

Palliation

Some metastatic cancers in adults are also very sensitive to drug treatment, and long term survival is not unusual in adults with lymphoma, germ cell tumours, and some variants of acute leukaemia. However, where solid tumours common in adults have metastasised, drug treatment prolongs average survival by only a few months at best, even though tumour regression is documented in around half of the patients. These disappointing results mean that the treatment goal is palliation for most adults with metastatic cancer, and the effects of treatment on tumour size must be balanced against the side effects. Patients' understanding of the aim of treatment in these settings is commonly different from that of their doctors.¹⁰

Adjuvant therapy

The beneficial effect on overall survival of adjuvant drug treatment after surgical resection of apparently localised disease has been documented in large randomised trials in patients with breast and large bowel cancers.^{11 12} This has led to an increasing use of chemotherapy after surgery in these common cancers, particularly when patient care is coordinated by a multidisciplinary cancer treatment team.⁴⁻⁶ Treatment outcomes in breast cancer and some other cancers have been related to management by a multidisciplinary group.^{4-6 13 14} Interventions such as pain control have also been shown to be more effective when coordinated through a multidisciplinary team.¹⁵

Team structure

The structure and membership of multidisciplinary cancer treatment teams vary considerably, in part according to the type of cancer being treated.¹⁶ The team generally includes a surgeon with a special interest, a medical oncologist, and a radiation oncologist. In an ideal world, other clinicians such as a specialist pathologist, a palliative physician, and sometimes a radiologist would be included. Paramedical members of the team will usually include specially trained nurses, a radiographer, a psychologist, and sometimes a physiotherapist, occupational therapist, and speech therapist. Good communication between team members is crucial for the best results, and successful teams are built on mutual respect.

Paramedical members of the multidisciplinary cancer treatment team usually include specially trained nurses

Supportive care

The supportive care needs of cancer patients are now widely acknowledged. Providing information to patients with cancer and to their families has become a major task of cancer treatment services. Pamphlets, telephone information lines, and patient support groups have contributed to better informed patients, who increasingly want to be involved in decisions about their treatment.¹⁷ Some cancer consultations are now spent reviewing information of variable quality derived from the internet.

Pain and symptom control

Control of pain remains an important goal but is not always achieved. New opiate preparations with sustained action and new routes of administration can improve control. Bisphosphonate drugs are important new palliative treatments for hypercalcaemia and metastatic bone disease.¹⁸ They have analgesic effects in bone pain, and also reduce bone fracture rates in patients with breast cancer and myeloma. New radiopharmaceutical products and radiation fractionation schedules are also improving treatment of bone pain in cancer patients. External beam radiotherapy in one or five fractions has largely replaced the prolonged treatment courses of past years.¹⁹ Strontium-89 is a bone seeking radioisotope that reduces the bone pain caused by sclerotic bone metastases. Samarium-153 is another radiopharmaceutical product that reduces bone pain and therefore analgesic use in patients with breast cancer and prostate cancer.^{20 21}

Technical developments are also enhancing palliation in patients with obstructive syndromes. New materials and developments in interventional radiology mean that stents can be placed to bypass obstructions caused by tumour, thereby reducing the need for palliative surgery. New antiemetic drugs, the serotonin antagonists, mean that vomiting is no longer the most feared side effect of cancer chemotherapy, but nausea and hair loss remain major concerns of patients.²² Out-patient treatment for cancer—both chemotherapy and radiotherapy—has an increasing impact on patients' families, a fact that may not always be acknowledged by doctors.^{22 23}

Defining treatment goals

Defining the goals of treatment is important for both the patient and oncologist. Is the realistic treatment goal prevention, cure, or palliation? Has this objective been agreed in a full and frank discussion between patient and doctor? By consciously and explicitly defining realistic goals, doctors can agree appropriate end points with their patients, and this clarity generally brings with it improved relationships between the patient and doctor. Explicit disclosure of the expectation of treatment is slowly becoming more widespread—often because patients (and the public) are better informed.

Audit

Audit has emerged as an important tool in developing cancer services and in the competition for resources. The reorganisation of cancer care in the United Kingdom under Calman and Hine will focus not only on evaluating the hub and spoke organisational model

Macmillan Cancer Relief funds specialist nurses and doctors who provide expert care and support to patients and their families

represented by cancer centres and units but also on addressing the “unexplained” geographical disparities in outcomes of treatment. Audit results are informing the restructuring of hospital departments.²⁴ In some large general hospitals, the traditional disciplinary divisions of medicine, surgery, obstetrics, and gynaecology are being replaced by disease and organ based multidisciplinary groupings. The development of cancer centres in large general hospitals is justified and will probably result in more efficient interdisciplinary care and better education of cancer specialists. These changes will facilitate audit of cancer treatments and may lead to more and better coordinated community based initiatives in cancer prevention and screening.

Clinical trials

The need to evaluate efficiently and appropriately promising cancer treatments and variations in approaches to treatment provides further impetus to a reorganisation of cancer care services. Better organised cancer treatment services allow more rapid evaluation of experimental treatments and provide an important opportunity for doctors and patients to evaluate new treatments and treatment strategies. Pharmaceutical and other companies are now major sources of funding for medical research, but the research priorities of the industry are driven by the market and are not always the same as those of the doctors, the patients, or the community that ultimately pays. The pharmaceutical industry has come to dominate the clinical trials programmes in all developed countries where charges for new drugs restrict research initiated by clinicians. Nevertheless, the interests of patients and the community are best served by identifying quickly the effective treatments, discarding treatments which are not effective, and determining the most efficient use of resources.

Problems of recruitment

Slow recruitment to clinical trials is an important problem in cancer care, and the time and effort involved in submitting proposals to ethics committees, enrolling patients, and collating the necessary data is costly in terms of resources, particularly staffing. The reasons for slow recruitment are also cultural and have

been investigated in a number of studies.^{25 26} Surprisingly, these studies have shown that it is resistance of doctors and not reluctance among patients that is the major obstacle.²⁷ Better dissemination of information, the development of consumer advocate groups, and greater use of the worldwide web allow patients to seek out new treatments and the opportunity to participate in clinical trials. Multidisciplinary cancer centres are ideally suited to conduct clinical trials research provided that they are adequately resourced. There is evidence for several types of cancer that patients in clinical trials have a better outcome.²⁸ These data should be used to inform patients and the community that well designed and conducted clinical trials are an essential and desirable aspect of high quality cancer care.

New treatments

Improved understanding of the molecular biology of cancer will ultimately mean that the current, empirically derived cytotoxic drugs and radiation therapy will be superseded by cancer treatments based on specific genetic and phenotypic abnormalities in cancer cells. Though this goal is still a dream, advances in cancer biology are identifying targets for new treatments, and some of these will prove to be the Achilles' heel of cancer cells. In the meantime, new cancer treatments currently being tested in clinical trials are discussed below.

Matrix metalloproteinase inhibitors—Matrix metalloproteinases are a family of proteases involved in the invasion of the basement membrane, and hence the process of invasion and metastasis. Several inhibitors of these enzymes are now being evaluated in patients with advanced cancers including gastric, pancreatic, and ovarian cancer. If these drugs are found to be effective, they may, like established hormonal treatments such as tamoxifen, have a role as adjuvant therapy in patients at high risk of disseminated disease.

Gene therapy—Inherited or acquired genetic changes are implicated in the behaviour of malignant cells that arise in both familial and sporadic cancer. Gene therapy aims to exploit differences between malignant and normal cells. There are now over 100 trials of gene therapy in humans—most involving treatment of cancer.²⁹ Selective targeting at deposits of tumour cells is a problem yet to be solved.

Immunotherapy—Immune recognition of cancer cells has long been the hope of tumour immunology. The potential of vaccines to protect people from cancers caused by viruses is still a dream, though expectations are high for hepatitis and cervical cancer. The long held notion that treated cancer cells might be used as a vaccine has recently resurfaced.³⁰ New techniques modify tumour cells so that molecules enhancing immune recognition and responsiveness are expressed.³¹ These approaches will have to be evaluated critically before the expectations of tumour immunology enhance cancer control and treatment.

Conclusions

Our ageing population and progress in the prevention and treatment of heart and cerebrovascular disease increase the importance of cancer as a cause of morbidity and mortality.³² Changes in the way cancer

care is organised have the potential not only to improve the outcome of treatment but also to streamline the appropriate evaluation of breakthroughs in cancer treatment that are anticipated from the rapidly advancing knowledge of cancer biology.³³

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