

The overall survival for patients with malignant carcinoid tumors and the carcinoid syndrome has increased for the last two decades from medium two years to more than nine years today. Improved diagnosis and treatment are the best explanation for this improvement.

In the future new therapies will emerge mostly based on current tumor biology including tyrosin kinase and angiogenesis inhibitors. New somatostatin analogues (som 230) are also in the pipeline for testing in neuroendocrine tumors and further development of tumor targeted radioactive treatment is ongoing. Vaccination programs are about to start and also gene therapy protocols.

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Genetic counselling for cancer predisposition

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The availability of diagnostic molecular testing for inherited cancer calls for health care professionals to identify families at risk and to advise them of surveillance and prevention strategies. The demand for specialized Cancer Genetics Services is increasing rapidly because of heightened public awareness of genetic aspects of cancer susceptibility and because of requests from primary care physicians for risk assessment and recommendations for appropriate management options for families with an inherited cancer susceptibility. However, the complex medical, ethical, legal and psychosocial issues brought by our ability to test healthy individuals for cancer predispositions and the rapid pace of new research findings pose great challenges to the medical community. The setup and provision of Cancer Genetics Clinics and presymptomatic Molecular Testing Services for inherited cancer as well as the education and training of health professionals involved in the provision of Cancer Genetics Services across Europe will be reviewed and issues such as how these services may best be organized and evaluated as well as the question at which level of care families at slightly, intermediately and highly elevated risk for cancer should be managed will be discussed.

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Recording of morbidity

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All modalities employed for the treatment of the patient with cancer are associated with a risk of side effects but with most these become evident during or soon after treatment. Radiotherapy, however, differs in that the dose-limiting side effects commonly occur many months and sometimes many years after the treatment. The recording of the morbidity of treatment presents a special challenge for the

Radiation Oncologist.

The description of individual cases prevailed in the first half of this 20th-century but as we moved into the world of the randomised controlled clinical trial there was a need for a systematic approach which could be applied on an international basis. The WHO (1979) was essentially developed for the recording of the morbidity associated with cytotoxic chemotherapy but the RTOG/EORTC system for the acute and late morbidity of radiotherapy soon followed. The Franco-Italian Glossary proved valuable for the recording of morbidity due to both radiotherapy and surgery in gynaecological cancer.

All stagings were a combination of symptoms, signs, investigations and treatment and the European Dictionary was introduced in 1989 to capture the elements making up morbidity. In 1995 the LENT/SOMA was introduced as an advance on the original RTOG/EORTC in that it gave a more detailed description of the morbidity of radiotherapy with some separation of the elements making up that morbidity. In the United States the CTC version 1 (1984) built upon the original WHO was updated to version 2 in 1998 covering the sites of morbidity in much greater detail and an attempt was made to include the morbidity of all cancer treatment. In 2003 the CTC version 3 included over 500 criteria to cover all the morbidity of cancer treatment. The exact value of this system and the preceding ones needs careful consideration.

As we enter the 21st century we are aware that patients and their families have become more critical of cancer care demanding not only cure but freedom from side effects. In order to deal with this we must have accurate data as to the incidence. The complex systems required for careful assessment of morbidity in randomised controlled trials are quite unsuitable for the assessment of morbidity in the general care of all patients with cancer. Until recently this has been given very little attention now however systems are under study which may well satisfy this need.

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Nuclear medicine in the diagnosis and treatment of paediatric tumours

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In recent years the contribution of nuclear medicine has been of increasing interest to paediatric oncology, in particular in imaging for diagnosis, staging and follow-up, in quantitative function analysis of organs at risk during oncological therapy, as well as in radionuclide therapy.

For tumour imaging a great number of tumour-seeking radiopharmaceuticals are available, exploiting various metabolic and biological properties of individual tumours; several of these agents can also be applied for radionuclide therapy. More recent tracers allow the characterization of tumours, highlighting features like hormone receptors, hypoxia, MDR and apoptosis. New techniques in paediatric oncology include PET and probe-guided surgery. A summary of applications and major indications will be presented.

Osteosarcoma/EWING's sarcoma. In differentiated osteosarcoma bone scintigraphy and SPECT using ^{99m}Tc -diphosphonate, targeting the tumour-produced osteoid, may visualize not only the primary bone tumour and skeletal metastases, but also the extraosseous metastases. For preoperative therapy and palliation of metastases beta-emitting bone-seeking agents, such as ^{89}Sr -chloride, ^{186}Re -HEDP and ^{153}Sm -EDTMP, are available.

Lymphoma. ^{67}Ga -citrate has been used for decades in the detection, staging and follow up of lymphoma, as well as for early recognition of response to therapy. ^{201}Tl -chloride scintigraphy + SPECT and PET using ^{18}F -deoxyglucose can also be used for this purpose. ^{99m}Tc -sestamibi and ^{99m}Tc -tetrofosmin are associated with p-glycoprotein, playing a role in multidrug resistance. In adults with recurrent non Hodgkin lymphoma treatment with ^{131}I - or ^{90}Y labelled anti-CD20 antibodies is highly effective.

Thyroid carcinoma. ^{201}Tl -chloride scintigraphy together with thyroglobulin assays has become a reliable alternative to the use of ^{131}I -iodine in the follow-up of differentiated thyroid carcinoma; procedure and radiation dose to the child compare favourably with that of ^{131}I . Iodine-131 maintains its role in radionuclide therapy of thyroid carcinoma. When children become involved in the family screening of MEN 2 syndromes, a variety of tracers can be used to demonstrate medullary thyroid carcinoma:

Neuroblastoma. Because of its high sensitivity and specificity, scintigraphy using ^{123}I - or ^{131}I -metaiodobenzylguanidine (MIBG) has established its role in the diagnosis, staging and follow-up of neuroblastoma. ^{131}I -MIBG is used for the treatment of this condition. Alternatively, specific targeting may be achieved using radiolabelled peptides (e.g. ^{111}In -pentetreotide) or monoclonal antibodies (e.g. 3F8, UJ13A, BW575/9, ch14.18 and chCE7). PET using ^{18}F -deoxyglucose (FDG) and ^{11}C -hydroxyephedrin (HED) is used to image neuroblastoma and ^{124}I -MIBG and -3F8 antibodies for dosimetry prior to therapy.

Rhabdomyosarcoma. Aspecific tracers, e.g. ^{67}Ga -citrate, ^{201}Tl -chloride and ^{18}F -deoxyglucose, can be used to image rhabdomyosarcoma. An example of specific targeting of rhabdomyosarcoma is radioimmunoscinigraphy using ^{111}In antimyosin Fab fragments, but these are no longer commercially available.

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Will oral drug replace IV treatment?

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Unlike most therapeutic areas where oral treatment is standard, in oncology most drugs are given intravenously. Encouraging clinical trial results indicate that for first time many of the oral anti-cancer drugs in development are better drugs rather than pale imitations of i.v. treatments. The oral route is appropriate for schedule dependent cytotoxics e.g. fluoropyrimidines as well as novel agents including signal transduction inhibitors and anti-angiogenic agents in order to achieve prolonged exposure.

Although more than 20 cytotoxics are available orally, many such as cyclophosphamide, etoposide and topotecan are also given i.v. Currently, probably the widest use of oral chemotherapy is 6-mercaptopurine, methotrexate and busulphan in leukaemias and lymphoma. Temozolamide (for glioma, astrocytoma and melanoma) and idarubicin (principally for leukaemia) are also well established but again have had limited impact as these are not the commonest cancers. 5-fluorouracil (5-FU) is, however, widely used and oral alternatives have been developed including pro-drugs that are absorbed unchanged (capecitabine, tegafur), the addition of inhibitors of the enzyme DPD that catabolizes 5-FU (uracil, eniluracil), or a combination of the two (UFT, S1, emitfur). With capecitabine now approved in