Memoranda
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Memoranda are statements concerning the conclusions or recommendations of certain WHO scientific meetings; they are signed by the participants in the meeting.

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Essential drugs for cancer chemotherapy: Memorandum from a WHO Meeting*

Essential drugs for cancer chemotherapy were reviewed in a consultation convened by WHO in Geneva. General principles regarding the proper role of cancer chemotherapeutic agents in relation to other established treatment modalities and the classification of tumours with respect to curative potential are discussed. Curable cancers and those cancers where the cost-benefit ratio clearly favours drug treatment can be managed appropriately using only 14 drugs.

The health needs of many countries far exceed available medical resources. To best serve these populations it may be necessary to have priorities for allocation of scarce resources. The choices that have to be made between therapeutic options are affected by numerous factors — for instance by the prevalence of tumour types, by the socioeconomic, geographical and political conditions, by the availability of appropriate medical personnel or equipment to deliver therapy, and by local definitions of a good quality of life. Since 1975, WHO has encouraged local health administrators to develop lists of basic or essential drugs as part of this process of resource allocation and has convened expert committees at regular intervals to initiate or update lists of essential drugs that might be used as models to be adapted to local conditions. As part of this process WHO invited medical oncologists from Africa, North and South America, Asia, Australia, and Europe to formulate an essential drug list for the treatment of cancer. The group met in October 1983, and this memorandum is a summary of their report and contribution to the further development of the essential drugs concept.

The members of this consultation first agreed upon general principles for the proper role of these agents in relation to other established modalities for the treatment of cancer and defined the situations in which chemotherapy is apt to be most useful. The most common tumours were then reviewed and classified into one of five categories. For each of the common tumours in the first four of these categories (i.e., those for which the benefit of treatment with drugs is beyond doubt), a list of drugs was developed such that regimens containing them might be curative or clearly benefit patients with that disease. From this list of tumours and drugs, one essential drugs list was devised.

GENERAL PRINCIPLES OF CANCER THERAPY

Although cancer is an important cause of mortality in most countries, nearly 40% of malignant tumours may now be cured if diagnosed sufficiently early and given appropriate treatment, while the remainder can be palliated for varying periods. To achieve these results it is necessary to make judicious use of surgery, radiotherapy, and cytotoxic and endocrine therapies, as well as supportive care measures such as treatment with analgesics, antibiotics, and blood products. A few tumour types can be managed optimally in almost any area of the world, but for many other tumours the patient's primary physician may need to consult frequently with one or several cancer specialists in surgery, radiotherapy, or medicine. Some tumours, such as the acute leukaemias, are treated ideally in

* This Memorandum was drafted by the signatories listed on page 1002 on the occasion of a WHO Consultation in Geneva in October 1983. Requests for reprints should be addressed to Cancer Unit, World Health Organization, 1211 Geneva 27, Switzerland. A French translation of this Memorandum will appear in a later issue of the *Bulletin*.

large medical centres under the direct supervision of specialists.

Cancer chemotherapy, using either cytotoxic agents or hormones, is a relatively new form of cancer treatment. Under some circumstances these drugs may be used on their own to cure patients; more often they are used in conjunction with surgery or radiation therapy. Many of the drugs cause unpleasant side-effects such as nausea, vomiting, diarrhoea, mucositis, and alopecia. Myelosuppression may occasionally result in fatal infections or haemorrhages. Some of these drugs are also quite expensive. For these reasons it is important to define the objectives of therapy before embarking on treatment that may be costly and accompanied by severe side-effects.

Some principles of chemotherapy are well established. First, for most drug-sensitive tumours a combination of drugs, each used at an optimum dose, is more likely to induce a response and result in either cure or significant prolongation of survival than sequential single drug therapy. Second, the first therapy employed is often the most important in determining patient survival. Therapy should not be delayed nor should a suboptimum course of treatment be prescribed as a trial if the tumour is potentially curable. Finally, toxic multidrug combinations may not be needed to palliate the symptoms of an incurable cancer; the inappropriate use of intense chemotherapy regimens may cause morbidity and increase the patient's suffering without palliating symptoms or prolonging survival.

Prior to the initiation of any cancer treatment, the goal of therapy must be realistically defined. Although a particular tumour type may be curable in some instances, not all patients with that tumour type may be cured. Individual prognostic factors should be considered, including the stage (extent) of disease, the sites of metastases, the particular histology of the tumour, the functional status of vital organs, the nutritional status of the patient, the patient's willingness to accept the toxicity of the therapy, and the availability of necessary facilities and medical personnel to treat any complications arising from the therapy. In most cases cancer chemotherapy requires some access to laboratory facilities to monitor white blood cell and platelet counts. In addition, assessment of tumour response must be made at appropriate intervals to determine if it is in the patient's best interest to continue therapy.

There are a number of cancers that shrink as a result of treatment with one or a combination of drugs, but for many of these tumours it has not been established that this response necessarily palliates symptoms or prolongs survival. It is possible that the quality of life of some patients will be compromised to provide a remission of short duration for only a few patients. Examples of tumours presently in this category are epidermoid and large cell carcinomas of the lung, malignant melanoma, colorectal carcinomas, and cervical carcinomas.

There are now more than 60 cytotoxic agents that have been shown to have some biological activity in humans, and many more are currently being investigated. However, only a few of these have been shown to cure some cancer patients or prolong survival either as single agents or in multidrug combinations. Some of these drugs are redundant, since others may be equally effective at less cost and have lower toxicity. Some drugs may shrink a small number of tumour types but have side-effects that outweigh their benefits. Finally, few drugs are effective only against extremely rare tumours.

The state-of-the-art in cancer chemotherapy is changing continuously, and it is likely that many new drugs will be introduced over the next five years. However, therapeutic claims supported only by anecdotes, testimonials, and unpublished or irreproducible trials should be ignored when selecting therapy for an individual patient. Drugs should be accepted as effective only on the basis of scientifically organized, controlled clinical trials in carefully defined populations, and the results obtained should be available for scrutiny in peer-reviewed, scientific journals; moreover, one such trial is usually not sufficient. These criteria have been used in selecting the essential drugs listed in this report.

ESSENTIAL DRUGS LIST

It is difficult to define a single list of essential drugs for cancer chemotherapy for every part of the world, and the one shown below may need to be modified slightly for each country or area depending on the prevalence of various cancers there, the financial resources available to treat cancer, and the expertise of the personnel who will be using the drugs. In some countries drugs are used preferentially because of limited radiotherapy facilities. In other areas particular agents are impractical because of inadequate refrigeration facilities or the inability to administer the drug intravenously. Finally, appropriate treatment of very rare tumours and some cancer symptoms may require additional agents.

The list does not include all that might be effective in every situation. However, all curable tumours and those cancers where the cost-benefit ratio clearly favours chemotherapy can be managed appropriately using only the following 14 drugs.

Cytotoxic Agents

Bleomycin
Cisplatin
Cyclophosphamide
Cytarabine
Dactinomycin
Doxorubicin
Etoposide
Mercaptopurine
Methotrexate
Procarbazine
Vincristine

Hormones

Corticosteroids
Estrogens
Tamoxifen

This list is not meant to be a guide for the treatment of individual patients or a substitute for formal training and experience in cancer management. The instances when a single drug or a single modality can be used to treat, especially to cure, cancer are so rare and the definitions of optimum treatment change continuously that it is not likely that algorithms for therapy will be available in the near future. However, it is anticipitated that this list will be of value to health planners, in consultation with physicians, in drawing up an essential drug list for cancer chemotherapy in their country, region, or hospital.

TUMOUR CATEGORIES

The definition of each of the five tumour categories used in constructing the list together with the tumours included in each of these categories are as follows.

Category 1

Tumours for which there is evidence that the use of one drug or a combination of drugs, alone or in conjunction with other therapeutic modalities, will cure or significantly prolong the survival of *some* patients with this tumour type.

Acute lymphoblastic leukaemia
Acute non-lymphoblastic or myelogenous leukaemia
Hodgkin's disease
Non-Hodgkin's lymphoma
Burkitt's lymphoma
Gestational/trophoblastic cancers
Germ-cell cancers of the testis
Wilms' tumour
Ewing's sarcoma
Paediatric soft tissue sarcomas
Lung cancer—small-cell type
Kaposi's sarcoma

Category 1-2

Tumours not fulfilling all the criteria for category 1 but for which there is controversial evidence that treatment may prolong survival.

Breast cancer
Osteosarcoma

This applies only to the use of chemotherapy as an adjuvant to surgery for patients in this category. For breast cancer it is limited to premenopausal women with early stage cancer and histologic node involvement.

Category 2

Tumours for which there is evidence that the use of one drug or a combination of drugs will cause tumour shrinkage and almost certain improvement in the quality of life. Marginal prolongation of survival *may* occur as well, but this is not well established.

Chronic lymphocytic leukaemia
Chronic myelogenous leukaemia
Multiple myeloma
Ovarian carcinoma
Endometrial carcinoma
Prostate cancer
Neuroblastoma

Category 2-3

Tumours not fulfilling the criteria for category 2 but for which there is evidence that tumour shrinkage may occur; however, for these tumours it is not clear that the clinical benefit outweighs the toxicities of the drugs, and any improvement in survival remains marginal and controversial.

Gastric cancer[a]
Head and neck cancers
Primary cancers of the central nervous system
Bladder cancer (intravesical)
Adrenal cell cancer
Hepatoma

Category 3

Tumours for which there are no effective drugs. Although some drugs may have been shown to shrink these tumours, the effect is so marginal that it is unlikely the quality of life of the patient will be improved, except in extremely rare instances, and it is possible that the quality of life of the majority of patients will be compromised and their survival time shortened as a result of chemotherapy.

[a] The data suggesting a benefit of adjuvant chemotherapy for early gastric cancer are inconsistent between countries. It is possible that this cancer has different chemosensitivities in different areas of the world.

Lung—epidermoid, adenocarcinoma, and large-cell type
Oesophageal carcinoma
Colorectal carcinoma
Pancreatic carcinoma (non-endocrine)
Cervical carcinoma
Penile carcinoma
Renal nephroblastoma
Melanoma

The drugs included in this list are those felt necessary for the appropriate treatment of the tumours included in the first four of the above categories, i.e., tumours in categories 1, 1–2, 2, and 2–3.

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