cutaneous mycoses such as mycetoma due to *Madurella mycetomatis*[10] and conidiobolomycosis.[11] It is also particularly useful for certain systemic fungal infections, including all cases of paracoccidioidomycosis,[12] and localised disseminated forms of histoplasmosis,[13] blastomycosis,[14] and coccidioidomycosis.[13] Assessing the clinical response to treatment in systemic opportunistic fungal infections is often difficult, so that the evidence that ketoconazole is effective in these disorders is not complete. Some specific uses have been reported, however, such as for localised deep candidal infections in patients with acquired immune deficiency syndrome[15] and systemic candidiasis in heroin addicts.[11] In patients who are seriously immunocompromised oral antifungal prophylaxis remains a logical approach even though there are few studies confirming its value in preventing systemic infection. Ketoconazole is effective as a prophylactic, and in some studies it appears to have been superior to alternatives such as nystatin,[16] although the emergence of carriage of other potentially pathogenic yeasts such as *Candida (Torulopsis) glabrata* in treated patients may be another factor that has to be taken into account.

So long as ketoconazole is reserved for specific indications use may be made of its distinctive features without exposing patients to an unnecessary hazard, however rare. Ketoconazole also remains an alternative method of antifungal treatment where other drugs cannot be used, each case being carefully considered on its individual merits. Patients receiving the drug should be told to report the specific side effects and both their clinical state and their liver function values should be monitored. A recent analysis of 33 cases of symptomatic hepatic injury due to ketoconazole reported in the United States estimated the incidence at roughly one in 15 000 exposed patients, and showed that liver damage might occur at any time between 11 and 168 days of treatment, was commoner in women over 40, and was not necessarily associated with high doses. Clinicians should continue to report as many data as possible on the adverse effects of ketoconazole as this information is essential for all using the drug.

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Risk of leukaemia associated with cancer chemotherapy

The objectives of the treatment of cancer must be to restore a good quality of life and when possible cure. The experienced clinician should be able to weigh the risks of temporary morbidity associated with a particular treatment against the prospect of achieving these objectives. As the results of treatment improve and survival is prolonged new clinical events may become manifest in association either with the disease or with its treatment. When this happens the late effects of treatment must be distinguished from those of the disease itself.

Potentially one of the most serious late events is the induction of a second cancer. An association between the administration of arsenic and the development of squamous cell carcinoma was recognised a century ago, and in the late 1940s an antineoplastic drug was shown to have carcinogenic properties.[1] Of the various classes of anticancer drugs the alkylating agents, which so effectively damage DNA, might be expected to induce malignant change in a predictable fashion. Proving this suspicion conclusively and in a way that might usefully modify clinical practice has been a difficult and lengthy exercise. Plainly the problem is not substantial, for despite the widespread use of chemotherapy second cancers are rare (though this may partly reflect the limited survival of many of those treated). When second malignancies do occur the epidemiologist might reasonably argue that these may be spontaneous in patients with an increased tendency to malignant change. Both features might be expected to be more apparent in patients whose survival is increased. At present measurement of the risk of malignancy induced by treatment depends on the relation between the observed number of cases and those which might be expected for the population studied. Identifying this denominator is a weak link in the calculation but one that may be strengthened by comparing different types of populations theoretically at risk.

Exposure to radiation might be regarded as the benchmark for comparison. The Japanese populations exposed to whole body irradiation from the atomic bombs showed an increase in acute non-lymphoblastic leukaemia after some years and in solid tumours after a much longer latent period. For this type of exposure a dose relation may be identified, whereas that resulting from high dose fractionated irradiation is much more haphazard. The relation between exposure to radiation and the induction of cancer is highly complex, so that comparisons with exposure to radiation may not be appropriate or helpful in understanding the risks of leukaemia induced by chemotherapy.[2]

The mechanism of induction of malignant change is almost certainly unrelated to immunosuppression even though the incidence of some types of malignant tumours does increase in patients who are immunosuppressed (by whatever means).[3] Acute non-lymphoblastic leukaemia features only rarely among the resulting tumours.

Retrospective analyses of patients with cancer who have received different permutations of treatments indicate that in some groups the incidence of acute non-lymphoblastic leukaemia seems to be increased above that expected. The problems of relating this to treatment should not be underestimated, but a certain consistency in outcome is apparent among the surveys from different centres. An increased incidence (observed over expected) has been seen in patients

treated for Hodgkin's disease, ovarian carcinoma, breast carcinoma, and multiple myeloma, and also in non-malignant diseases treated with cytotoxic drugs.[4] The risk of malignancy appears to be increased after treatment, the alkylating agents and the nitrosoureas being particularly incriminated.[5] The most comprehensive investigations have been in patients with Hodgkin's disease, but the absolute risk remains difficult to measure.

Data from Stanford University indicate no increased risk in patients receiving radiotherapy or chemotherapy alone but a mean actuarial risk of developing acute leukaemia within seven years of diagnosis of 3·9% in those receiving treatment with both.[6] The crude risk for the entire group of 680 patients was 1·2%. Virtually all reports incriminate dual treatment with radiotherapy and chemotherapy, and several associate increasing age with an increase in risk. A recent report from the National Cancer Institute identified eight cases of acute non-lymphoblastic leukaemia in 473 untreated patients with Hodgkin's disease. The 10 year estimated risk of leukaemia by treatment was assessed for radiotherapy only as zero; for chemotherapy only as 0·02; for initial combined modality therapy as 0·06; and for salvage combined therapy as 0·09.[7] The risk of leukaemia was not raised in patients who began treatment for Hodgkin's disease over the age of 40. Time is required to document observations of this kind; the median latent period between starting treatment for Hodgkin's disease and the emergence of leukaemia is around six years.

One of the larger surveys has collected information from nine groups taking part in the National Cancer Institute's surveillance, epidemiology, and end results programme.[8] The study population was 440 000 patients with various cancers diagnosed between 1973 and 1980. Thirty four cases of acute non-lymphoblastic leukaemia were subsequently diagnosed among 70 674 known to have received initial chemotherapy; this compared with an expected number of 7·6. As in other reports an excess incidence of acute non-lymphocytic leukaemia was seen after chemotherapy for breast carcinoma, ovarian carcinoma, and multiple myeloma. Patients initially treated with radiotherapy also had a higher risk, particularly those with carcinoma of the body of the uterus. The lack of detailed knowledge of the treatments (character and duration) and of patient characteristics in this very large patient group limits the conclusions, but clearly some increase in the risk of acute non-lymphocytic leukaemia is likely, particularly in certain histological and treatment groups. Sporadic reports have also appeared of cases of acute non-lymphocytic leukaemia in other types of cancer. In a recently published series of 158 patients with small cell lung cancer treated with chemotherapy and prophylactic cranial irradiation (with or without irradiation to the chest) 21 survived for two years or more.[9] Of these, three developed acute non-lymphocytic leukaemia—2·3, 2·7, and 3·0 years from diagnosis. Some cases have also been noted in germ cell tumours,[9a] but most were seen in patients treated before the introduction of current combination therapy which does not contain alkylating agents.

The better prognosis of patients selected for adjuvant chemotherapy means that they may be exposed to anticancer drugs for prolonged periods. If the risk of inducing a malignancy is real then there are grounds for serious concern. Lerner *et al* looked at 2020 patients who had received chemotherapy over a 15 year period and found that most of the new cancers had developed in patients receiving adjuvant chemotherapy.[10] These were primarily patients with breast cancer who had received alkylating agents. The difficulty of interpreting this and other reports is, however, compounded by the fact that acute non-lymphocytic leukaemia will occur de novo in patients with breast cancer who have not received either radiotherapy or chemotherapy, and in relatively small series the excess may be difficult to determine.[11] In another recent study methyl lomustine was implicated as a possible cause of seven cases of acute non-lymphocytic leukaemia seen in patients receiving adjuvant chemotherapy for carcinoma of the colon.[12] These were among 621 patients randomised after curative surgical resection to four treatment arms, two of which received adjuvant chemotherapy. The evidence strongly suggests that prolonged treatment with alkylating agents is a potential cause of acute leukaemia. The risk is almost certainly related to total dose administered and the duration of treatment and may be enhanced by exposure to radiation.[13]

Further reports may be expected incriminating chemotherapy as a cause of acute non-lymphocytic leukaemia, but until those cases induced by treatment can be identified with certainty, the precise risk will be difficult to measure. Possibly cytogenetic studies might help to do this.[14] More recently Pedersen-Bjergaard *et al* found clonal cytogenetic abnormalities of the bone marrow in 44 patients with acute non-lymphocytic leukaemia, preleukaemia, or acute myeloproliferative syndrome presumed to be induced by treatment. Defects of chromosome 7 were observed in 24 patients (predominantly −7) and of chromosome 5 in 14 (predominantly 5q−), whereas some abnormalities seen in de novo cases of acute non-lymphocytic leukaemia such as +(B;21) and +(K;17) were not seen.[15] This is one of several reports indicating a difference in chromosome banding patterns between bone marrow cells from leukaemias induced by treatment and those arising de novo. If karyotypic abnormalities prove sufficiently characteristic to permit the recognition of leukaemias induced by treatment, we may be able to modify treatment to reduce this risk. Moreover, leukaemias induced by treatment appear more refractory than primary malignancies. In the series studied by Pedersen-Bjergaard *et al* the median survival of the whole group was seven months but was longer for the subgroup of 11 patients with a normal karyotype.[15]

Morbidity induced by treatment is not limited to cancer, but the other side effects should largely be temporary. Many current treatments are highly effective; it is only their misuse or uncritical application which brings them into disrepute. Cancer chemotherapy has suffered in this way, largely because it is so easily prescribed, but rising standards of clinical care should reduce the incidence of adverse effects to a minimum. In any circumstance acute leukaemia is unwelcome. It appears more likely to arise after therapeutic success when survival is prolonged, and so is doubly unwelcome. As a complication it is extremely rare, however, and probably avoidable once the risk factors become known. These data need to be gathered prospectively as comprehensive information is essential for monitoring the true effects of treatment on the clinical course of disease.

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Why keep hospital clinical records?

National Health Service hospital records are public records[1] and the DHSS has issued guidance on their retention and destruction.[2] The most recent DHSS guidelines recommended new minimum periods of retention for personal health records with a view only to their possible use in litigation.[3] They did not, however, give guidance on the destruction of records.

The recommended minimum retention periods are 25 years for obstetric records; until the patient's 25th birthday or eight years after the last entry if longer for records relating to children and young people (including paediatric, vaccination, and community child health service records); and 20 years for records relating to mentally disordered persons within the meaning of the Mental Health Act 1959, and taken from the date at which, in the opinion of the doctor concerned, the disorder has ceased or diminished to the point where no further care or treatment is considered necessary. For all other personal health records the minimum period is eight years after the conclusion of treatment, and the same minimum of eight years applies after the death of a patient (or, in the case of obstetric records, death of a child—but not of the mother).

For various reasons many hospital clinical records have survived beyond these minimum retention periods. Their storage, however, is causing immense problems—and these are becoming more acute as hospitals close down or find that the space taken by clinical records is not cost effective. For example, the Norfolk and Norwich Hospital, which has 762 beds, creates some 30 000 new files every year.[4] Merely handling this information and retrieving it for current use are the main occupations of most medical records officers, without their worrying about long term preservation. This problem of longer term preservation has already been recognised, and concern has been expressed intermittently over the years. This concern led in 1977 to a one day conference at the King's Fund Centre, which found that the threat to medical records was if anything more serious than had been assumed and concluded "that the danger to medical records was so great that it was not possible to rely on long term action by central authorities to amend and enforce official guidelines. In the short term it was essential that the various interest groups acting in partnership at the local level should pool their efforts to ensure vigilance in respect of the preservation of medical records, and to introduce practical schemes for their retrieval, safe deposit, and accessibility to scholars and medical workers" (C Webster, paper presented at conference 25 May 1977).

The conference did much to alert interested parties to the dangers of the destruction of medical records including clinical records: as a result various local initiatives were taken. A survey of hospital records undertaken by the Contemporary Medical Archives Centre at the Wellcome Institute for the History of Medicine found that many administrative records had found their way into local authority record offices; in some areas offices had been actively locating and acquiring archives from hospitals. Clinical records, however, were seen as a distinct and less attractive group, and many record offices specifically excluded them when taking in other materials.

The problem caused by clinical records was next faced by a committee under the chairmanship of Sir Duncan Wilson which was appointed by the Lord Chancellor to investigate the workings of certain provisions of the Public Records Acts. Its report was published in March 1981.[5] Its chapter on NHS records suggested that they were of value in both medical and associated scientific research and historical and social studies. The committee thought that "the long term value of clinical records is less clear cut than that of the administrative and non-medical NHS records." It recommended, however, that clinical records reserved for research should remain the responsibility of the health authorities, who should arrange for their housing and maintenance; that the DHSS should invite the Medical Research Council to convene an advisory group to identify NHS clinical records of research potential and that, after consultation with the Public Record Office, it should issue guidance to health authorities on the periods for which records should be retained for research purposes; and that the NHS should designate a specified record officer for each region to take responsibility for the general supervision and handling of its records.[5]

The government responded to this report with a White Paper.[6] Accepting that guidance given to NHS authorities should be revised, this went on to state that "The revised guidance would also effectively remove clinical records of individual patients from the scope of the Public Records Act." The government has made no recommendations on the retention or destruction of clinical records except in so far as it recommends minimum retention periods for possible use in litigation.

So the problem remains: what should be done with these records?—and it becomes increasingly critical as more and more clinical records are created. Some hospitals (particularly teaching hospitals) have overcome the problem by microfilming. Some have resorted to computerisation of information, which brings additional problems for archivists and historians. But often a large amount of older material has survived, frequently in bound volumes, for which the cost of retrospective microfilming is thought to be unjustified.

Before any work can be done on seeking to improve the present haphazard arrangements affecting the survival of hospital clinical records, a vital question needs to be posed—do these records need to survive? Medical historians, epidemiologists, and others may well claim that they should and indeed must survive. They will recount stories such as the fortuitous survival of Richard Napier's 17th century case