persist for weeks in an individual patient, typically the disease is self-limiting.

A fatal form of CMV infection has now been described\(^3\) as a result of a prospective study of virus infections in renal transplant recipients. This variant was identified in eight of 377 patients who had received 441 transplants over six years. The illness started with a spiking fever and in the first week there was hypotension; hypoxaemia (with no other clinical or radiological signs of a lung disorder); thrombocytopenia; lymphopenia; and deterioration in renal function. In the second week the patient became lethargic, weak, and bedridden, with peripheral oedema, muscle wasting, and hypoxaemia. All these features became more severe during the next two weeks, liver and kidney function deteriorating further and diffuse interstitial pneumonia developing. The eight patients described all died during the fourth week with acidosis, irreversible hypotension, and pulmonary oedema. At necropsy all had pneumonitis and multiple scattered ulcerations of the gastrointestinal tract, but the grafted kidneys showed no evidence of acute rejection, and chronic rejection was present in only three of the eight patients.

No evidence of infection could be obtained during the first week, and the only evidence in the second week was the occurrence of CMV inclusion bodies in cells obtained in bronchial washings. Nevertheless, in the third and fourth weeks cytomegalovirus was cultured from urine, sputum, bone marrow, or renal biopsy specimens in six of the eight cases. At necropsy CMV inclusions were seen and virus was isolated from lung, brain, liver, kidney, and the gastrointestinal tract. Intestinal bacteria and fungi (especially aspergillus and candida) were also isolated from the lungs, gastrointestinal tract, heart, and blood. CMV antibody could not be detected in any of the patients throughout the illness—except that in one patient a titre of 1/64 was found on the day before death.

Pneumonitis associated with CMV has been described repeatedly in immunocompromised patients. In a period of four years at Stanford CMV was isolated from the lungs of nine recipients of organ transplants and seven patients with tumours.\(^7\) All had fever, non-productive cough, and dyspnoea. Twelve (of whom 11 died) had hypoxaemia, whereas all those without hypoxaemia survived. Only seven showed a CMV antibody response. In another series, of 150 patients given bone marrow transplants, over half developed interstitial pneumonitis within the first four months and in half the patients the pneumonia was a fulminant lethal illness.\(^8-10\) CMV was recovered from lung tissue in over half those with pneumonitis, but a definite rise in the CMV antibody titre was found in only about a third of them. The prognosis was much worse if there was no antibody response: indeed, in one series\(^16\) all 13 such patients with CMV pneumonitis died.

CMV pneumonitis in recipients of organ transplants may, then, be a transient condition with recovery associated with a specific antibody response. Alternatively, severe pneumonitis may occur with death from respiratory failure in the absence of an antibody response. The fatal form seems to develop in about 2% of recipients of renal transplants but it may be ten times more frequent in recipients of marrow transplants. Other organisms (Pneumocystis carinii, fungi, intestinal bacteria) may be isolated from the lungs of some of these patients, but in some at least CMV is the only pathogen isolated. Definite antemortem diagnosis depends on finding CMV in lung aspirate or biopsy material. Culture of the virus may take weeks, but rapid diagnosis may be possible by staining for CMV antigen by immunofluorescence.

No specific prevention or treatment is available at present.

Nevertheless, since the fatal form appears to be related to a lack of an immune response by the host, the doctor must consider decreasing the immunosuppression in any patient with a typical clinical illness in whom a renal biopsy specimen shows no evidence of rejection.

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**Utility of needle aspiration of tumours**

The surgical world is divided into two classes: those who believe it is wrong to assault a tumour by anything less than its formal excision and those who are prepared to pass needles of varying size into it to reach either a cytopathological\(^1\) or a histopathological\(^2\) diagnosis ahead of definitive treatment.

There is no satisfactory evidence in man on whether needle aspiration is dangerous or safe, so that the choice between the conservative and interventionist schools is an article of faith. Nevertheless, it is incumbent on the interventionist to prove utility before the practice is widely adopted.

Utility is built on three foundations: practical success, sensitivity, and discrimination. Success with needle aspiration means the production of a satisfactory specimen by the clinician and the preparation of a reportable smear by the cytopathologist. Though results in different centres and for different organs vary, the going rate for unrepresentable specimens should be certainly less than 10%, and probably less than 5%.\(^3-5\) Most of the failures will result from the needle’s missing the lesion, but sometimes the target may be so acellular that a good sample is impossible. Success rates may be artificially inflated if specimens such as cyst fluid are included.\(^4\) Sensitivity means the ability to detect malignancy when it is present. Again, rates vary. In the breast 90% sensitivity has been reached and in other tissues (for example, the lung) it may be higher.\(^6\) Discrimination depends on the results of the procedure of sorting clinically dubious lesions into benign and malignant. Here achievement is less impressive—50-60% only are correctly assigned.\(^4\)

But utility must be judged on more than correct assignment to diagnostic classes: the final arbiter is how a technique influences clinical practice for good or ill. With cytological tests the question cannot be answered directly, since those interested have not expressed their results in such terms, accepting instead the premise that if something works it is thereby useful. When challenged, most of those who seek cytological specimens would agree that a histopathological diagnosis is necessary before ablative surgery or other radical treatment, such as chemotherapy or radiotherapy. If that is the case, what is the use of needle aspiration cytology? Where does it fit in the diagnostic sequence? The answer remains uncertain but should probably not be sought in the black-and-white terms of the dichotomy between benign and malignant. Different frames of reference should be used: firstly, how may
the procedure alter decision-making about the next step in the management sequence for the individual patient, and, secondly, how does it help in the discussions between doctor and patient over the likely cause of the problem? For needle aspiration cytology we do not have the requisite information, though again some clinicians would claim that as their experience grows subtle changes are manifest in clinical practice. In this, as in so many other diagnostic topics, a prospective survey which addresses the final problem of utility is needed rather than repeated publications which attest to the technical success, sensitivity, and discrimination of the method.

4 Coleman, D, et al, Clinical Oncology, 1975, 1, 27.

Non-endemic Burkitt's lymphoma

In 1958 Burkitt described a clinical entity seen in East African children: the association between sarcomas of the jaw and abdominal tumour masses of similar histological appearance.1 Though this combination is highly characteristic of Burkitt's lymphoma, these clinical features may be closely mimicked by other neoplasms and cannot by themselves be used to define the tumour.2 Furthermore (a fact not generally appreciated) the jaw tumours in Burkitt's lymphoma are related to age; they occur less often after the age of 3 years and are present in only half of Ugandan cases.3 Many older patients present with abdominal tumours or other lesions that are not clinically unique. Burkitt's lymphoma presents a characteristic cytological and histological picture, however, and it is by these features that the tumour is usually defined.4 The use of histopathological criteria to identify the tumour soon led to a spate of reports of sporadic cases from all over the world, recently expanded by a series of eight cases from Italy.5 The clinical and anatomical similarity of these to African cases of Burkitt's lymphoma gives credibility to the histopathological definition of the tumour,6 though in general the non-African cases have a higher incidence of bone marrow and peripheral lymph node deposits and of abdominal tumours.7

The first intimation that a patient has Burkitt's lymphoma is usually provided by the diagnostic histopathologist. Ideally good quality paraffin sections should be supplemented by cytological preparations, plastic-embedded sections, and electron microscopy in arriving at the diagnosis. Presented with this diagnosis the physician may well ask: What is Burkitt's lymphoma? What is the aetiological relation of the sporadic cases to the endemic African disease? What is the ideal treatment and what is the prognosis? To answer the first question, Burkitt's lymphoma is a tumour of B-lymphocytes usually expressing membrane immunoglobulins and complement receptors.8 It has been argued that it is a follicular centre cell lymphoma on the basis of its B-cell characteristics and the observation that it sometimes appears to arise within germinal follicles.8 Against this hypothesis is the observation that the tumour usually avoids peripheral lymph nodes (unlike all other follicular centre cell lymphomas) and that it never has a follicular pattern.

Much of the interest in African Burkitt's lymphoma was generated by its remarkable epidemiological features. In Africa the distribution of the tumour appears to depend on climate, and in some areas it shows both time-space clustering and epidemic drift, suggesting an infectious aetiology.9 The Epstein Barr virus (EBV) has emerged as the strongest contender, possibly in combination with falciparum malaria.10 Some authors have accepted the aetiological role of EBV in Burkitt's lymphoma as proved11; others dispute it.12 One of the difficulties is that the known distribution of this virus cannot be related to the geographical pattern of Burkitt's lymphoma, though recent studies by de Thé have shown that the virus may have unique seroepidemiological features in African children.13 These studies need to be extended. In the meantime the non-African cases may shed light on the tumour-virus relationship.

About a quarter of American patients with Burkitt's lymphoma have serological patterns of antibodies against EBV similar to those of African children, and in some of these the virus genome is present within the tumour cells.14 Few non-African cases of Burkitt's lymphoma have been studied by these techniques, and clinicians caring for such patients should do their utmost to obtain serum and fresh tumour cells for this purpose.

Dramatic and sustained responses to chemotherapy, with 55% survival rate reported from Uganda, attracted further attention to Burkitt's lymphoma.15 These encouraging results have not been duplicated in non-African cases.16,17 though Ziegler—who has had considerable experience in treating Burkitt's lymphoma in both Uganda and America—has reported18 a 54% two-year survival in his younger American patients. Good prognostic features include age of less than 12 years and minimal tumour burden either at presentation or after surgical removal of the tumour. Central nervous system relapse is a major problem, occurring in up to 45% of African patients. Intrathecal methotrexate rarely produces long-term remission, and the results of preventive treatment using cyschloroethyl-nitrosourea (CCNU) and early craniopsint irradiation have not been encouraging.19 Prolonged intrathecal chemotherapy during remission may prove to be more successful.

The diagnosis, management, and investigation of patients with Burkitt's lymphoma demand pathological and clinical skills at the highest order. These may be rewarded by good remissions and prolonged survivals, and the detailed investigation of these cases may provide clues to aetiology. In America setting up a Burkitt lymphoma registry has done much to further the treatment and study of this tumour.19 Britain and possibly Europe should follow suit.

1 Burkitt, D, British Journal of Surgery, 1959, 46, 218.
10 Burkitt, D, Journal of the National Cancer Institute, 1969, 42, 19.
15 Ziegler, J L, Cancer, 1972, 30, 1534.