The use of plastic isolators to prevent infection in neutropenic patients

J. M. Goldman*  
B.M., M.R.C.P.

A. S. D. Spiers*  
M.D., F.R.A.C.P.

P. C. Trexler†  
M.S.

H. Gaya†  
M.B., ChB., M.R.C.Path.

A. M. Gordon†  
M.Phil., M.R.C.P., M.R.C.Psych.

*M.R.C. Leukaemia Unit, Hammersmith Hospital, London W12 0HS,  
†The Royal Veterinary College, Royal College Street, London NW1 0TU, and  
‡St Mary's Hospital Medical School, London W2 1PG

Summary
Over the last 5 years plastic isolators have been used for the prevention of infection in patients with severe neutropenia. Fifteen patients in differing stages of acute myeloid and chronic granulocytic leukaemia were managed in isolators for a total of 110 patient-weeks. The mean duration of isolation for each patient was 7-4 weeks with a range of 2-14 weeks. There was no evidence that any of the isolated patients acquired infection with any exogenous micro-organism. The psychological problems of isolation proved less onerous for the patients than had been anticipated by the medical and nursing staff and no patient had to be removed from isolation for psychiatric reasons. Unfortunately the reduced incidence of clinical infection in the isolated patients was not obviously associated with an increase in effectiveness of their anti-leukaemic treatment.

Introduction
Patients with acute leukaemia have an increased susceptibility to infections of all kinds and infection is the principal cause of death in patients who fail to achieve complete remission (CR) (Hersh et al., 1963; Schimpff et al., 1972). This increased susceptibility results in part from the reduction in numbers of functioning granulocytes in the peripheral blood that characterizes leukaemic relapse (Bodey et al., 1966) and may be accentuated by the use of cytotoxic drugs. Moreover there is evidence that even the residual granulocytes may have impaired microbical function (Goldman and Th'ng, 1973). It is well established that many infections in patients with acute leukaemia are due to organisms that originate from the hospital environment and colonize the patient's intestinal tract (Hersh et al., 1963; Levine et al., 1974; Jameson et al., 1971). Other infections are caused by organisms that were originally present in the patient or have been introduced from without during certain invasive procedures. Various approaches to the prevention of infection in susceptible patients should thus be considered: (1) Measures to prevent environmental organisms from reaching the patients (e.g. laminar air flow rooms, isolators); (2) measures to reduce the patients' endogenous bacterial and fungal flora (e.g. oral non-absorbable antibiotics); (3) reduction of invasive procedures which may lead to introduction of infection (e.g. intravenous or urinary catheters); (4) efforts to bolster host defence mechanisms (e.g. vaccines, prophylactic granulocyte transfusions).

The use of plastic isolators in the prevention of infection in patients with leukaemia and aplastic anaemia is now discussed and some associated psychological implications are reviewed.

Choice of protected environment
Conventional 'reverse-barrier' nursing has been used in the management of granulocytopenic patients for some years. The patient is confined to a bacteriologically clean room and attending medical and nursing staff don masks, caps and gowns as for a surgical procedure before entering. The method can be used in any general hospital but is costly in disposable gloves and linen. The time necessary to prepare the visitor for entry is considerable and patients may feel deprived because they cannot see the full faces of relations and professional personnel. Laminar air flow rooms depend on the provision of air flowing in a horizontal plane that has been filtered to remove particles greater than 0·3 μm (Penland and Perry, 1970; Schimpff et al., 1975). If
Plastic isolators for neutropenic patients

the attendant remains always ‘downwind’ of the patient, the number of microbes that reach the patient from the attendant should be substantially reduced. The system is convenient for the patient and does not expose him to any feeling of confinement or isolation.

The design and use of the ‘Trexler’-type plastic isolator have been described in detail (Spiers and Trexler, 1973; Trexler, Spiers and Gaya, 1975) and will be given here in outline only. The isolator consists of a rectangular envelope made of transparent polyvinyl chloride film, 0-2–0-3 mm thick. The envelope is 1·9 m long, 1·8 m wide and 2·0 m high and is supported by a light metal frame attached to the hospital bed. There are four half-suits attached to the vertical side walls, two on either side of the bed. Each suit consists of a clear plastic face-piece supported by an adjustable head harness and attached to a conical invagination of the plastic wall which bears the sleeves and gloves. An attendant can enter one of these half-suits and move freely within it. The patient enters the isolator through an oval entry port which is situated at the foot of the bed. When the patient is inside the isolator the entry port is closed by appropriate positioning of a supply isolator 1·3 m long, 0·75 m wide and 1·0 m high. The latter provides storage space for sterile supplies and also a means for introducing them. Supplies are introduced vertically upwards through a horizontal oval port in the floor of the supply isolator against a stream of sterile air which emerges in a downward direction from the port. At the foot of the bed on the patient’s right there is a small oval port in the main isolator which is used for the removal of soiled materials such as linen and bedpan liners.

Filters for sterilizing the entering and exhaust air are placed at the top of the isolator envelope. The blower unit which pressurizes the filters is in a sound-absorbing box below the bed and has an alarm system in case of failure (which is extremely rare). The flow of air entering the supply filter is controlled by a ball valve at the foot of the bed and the flow is indicated by a gauge. The extract filter is connected to the blower through a ball check valve which is adjusted by a mechanical linkage to the roof of the isolator and controls the interior pressure.

Once inside the isolator the patient is remarkably unrestricted in his daily life. He is free to move normally on the bed and has an area approximately 0·6 m wide along the length of the bed where he can

FIG. 1. A diagram of the Trexler bed isolator showing a patient in bed and two nurses using half-suits. A third nurse is working with the supply isolator (left). The bed isolator communicates with the supply isolator at the patient entry port (A). Note also the control mechanism for regulating pressure in the isolator (B), the air filter for the supply isolator (C), the downflow supply port (D), the air-supply line to half-suit (E) and an unoccupied half-suit (F).

(This diagram is reproduced by permission of the Editor of the British Medical Journal.)
stand upright and walk. A chair can be placed underneath the isolator at the foot of the walkway so that the patient may sit out of bed. At the head of the bed a bedside table may be inserted into a pocket sealed into the wall of the isolator. By making use of one of the half-suits, members of the medical or nursing staff can attend the patient in a near-normal manner. For example, a doctor may carry out physical examination with very little encumbrance or a nurse may help a patient to feed himself. An X-ray machine can be introduced into a half-suit and the plates placed beneath the plastic film, the entire unit still remaining outside the protected area. When the patient wants to make telephone calls the telephone receiver is introduced into a special sleeve of thin plastic which transmits sound.

Preparation of the patient for isolation

Before entering the isolator the patient must be made as free as possible of micro-organisms. This preliminary decontamination is carried out over a 3-day period during which the patient is nursed in a reverse-barrier room. He eats only sterile food. Chlorhexidine preparations are used on the skin, hair, ears, nose and throat. Chloramphenicol and saline enemas are given 24 and 4 hr before entering the isolator. Immediately before entry two gloved and gowned nurses place the patient on a sterile sheet on a trolley and spray his entire body excluding the face with chlorhexidine aerosol. The patient is then assisted through the entry port into the isolator. Once the patient is inside the main isolator the supply isolator is moved into place and thereby seals the entry port.

Clinical use of the isolator

In the past 4 years we have treated fifteen patients with acute myeloid leukaemia (AML) or chronic granulocytic leukaemia (CGL) in plastic isolators for a total of 110 patient-weeks. The mean duration of treatment for each patient in the isolator was 7-4 weeks with a range of 2–14 weeks. The diagnoses of these patients and the outcome of isolation are given in Table 1. During isolation repeated bacteriological examinations were made of the urine, stool and saliva, and of swabs from the ears, nose and throat, axilla, umbilicus, groin and vagina. During 110 weeks of isolation in fifteen patients there was no evidence of acquisition of any exogenous micro-organism and the patients' endogenous flora remained satisfactorily suppressed and free from potential pathogens such as Pseudomonas aeruginosa, the Enterobacteriaceae and Staphylococcus aureus. From time to time patients in the isolator developed fevers but blood cultures were regularly negative and the fever usually resolved without explanation. One case of septicaemia with P. aeruginosa was documented. The probable source of this organism was a site of apparently quiescent chronic osteomyelitis.

At the beginning of the study the use of isolation was reserved for patients whose prognosis was regarded as especially grave, such as those with AML resistant to primary therapy, those in relapse after maintained remission of AML or those in transformation of CGL. Later the isolator was used to treat patients with newly diagnosed AML and in two cases for intensive chemotherapy of patients in the chronic phase of CGL.

In addition to the patients with leukaemia, two patients with aplastic anaemia were managed in isolators while they were being prepared for allogeneic bone marrow transplantation (Table 1). Both patients survived the critical periods before and immediately after the graft.

Psychological considerations

Patients

It was not possible to predict without previous experience whether certain patients might be unsuitable for isolation. Accordingly, the decision whether or not to isolate a patient was made on the basis of his liability to develop infection, the status of his leukaemia and the availability of an empty isolator. Psychological evaluation of a number of patients in the study was carried out in order to determine the nature of the adaptation to isolation and to define criteria for predicting, if it were possible, those patients who would be unable to tolerate isolation (Gordon, 1975a, b).

A diagnosis of leukaemia implies the risk of fatal outcome and imposes considerable stress on the capacity of the patient for psychological adaptation. The addition of a treatment regimen involving protective isolation further complicates the picture and it may be difficult to distinguish reactions due to the patient's awareness of his or her diagnosis from those resulting specifically from isolator management. In the isolated patients, differing psychological reactions were observed. Seven patients manifested a pattern of manic defence. These patients were able to acknowledge their diagnosis while attempting to master their disease and control its outcome in

<table>
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<th>Diagnosis</th>
<th>Outcome</th>
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<th>Died</th>
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<tbody>
<tr>
<td>Leukaemia</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Acute myeloid</td>
<td></td>
<td>3</td>
<td>7</td>
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<td>Chronic granulocytic</td>
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<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Aplastic anaemia</td>
<td></td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>7</td>
<td>10</td>
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TABLE 1. Details of seventeen patients treated in isolators
several ways: by eager search for knowledge of its cause, treatment and prognosis, by insisting on an explanation of all procedures, by expression of aggressively optimistic attitudes and by denial of pessimistic statements. In short they displayed an omnipotent belief in their capacity to survive leukaemia. Three other patients manifested a defence of regression: they strongly denied their diagnosis, requested little information and expressed no interest in the details of their treatment. These patients accepted medical and nursing care without protest but withdrew from close social contact and revealed little effective response. In individual patients, the use of defence mechanisms varied to some extent during treatment but major patterns emerged in every case and usually reflected the defence mechanism most commonly mobilized in the patient before the onset of his illness.

All the patients interviewed described feelings of anxiety and apprehension before entry into the isolator. The period of reverse barrier nursing that preceded isolation served apparently to heighten this anxiety but all patients subsequently found that the plastic isolator with unrestricted social contact was preferable to the reverse-barrier environment. After the initial anxiety associated with admission to the isolator, sustained disturbances of mood were not apparent. Five patients who had expressed depressive feelings before isolation continued to manifest fluctuating depression. One patient with a manic defence continued mildly euphoric throughout treatment. No patient developed a severe affective disturbance which required pharmacological management or interruption of isolation. Similarly, no patient developed florid psychiatric disturbance. One patient had a past history of phobic illness and another a history of paranoid personality traits. There was no evidence that previous psychiatric illness was a contra-indication to isolation.

**Reaction of relatives**

In general, patients' relatives reacted enthusiastically to the use of the isolator which they saw as an additional measure of protection that might improve chances of successful treatment. The principal conflict arose when it became clear that a patient in the isolator was dying. Some relatives believed that it was kinder to remove such a patient from isolation while others felt that removal from the isolator would convince the patient that hope had been abandoned. No clear guideline could be established for this situation.

**Conclusions**

Decontamination of the gastrointestinal tract by administration of antibiotics reduces the incidence of infection in neutropenic patients receiving myelo-suppressive chemotherapy (Bodey et al., 1968; Levine et al., 1973), while physical isolation of patients without gastrointestinal decontamination decreases the acquisition of pathogenic microorganisms from other patients or from hospital staff. The simultaneous application of decontamination procedures to reduce endogenous flora and of isolation to reduce the acquisition of exogenous organisms should substantially reduce the risk of infection in neutropenic patients receiving cytotoxic drugs for treatment of leukaemia. In practice, studies of the use of protected environments and 'prophylactic' antibiotics have shown a reduced incidence of infective episodes and fewer deaths from infection but an increased rate of remission of acute leukaemia has not been observed. This seeming paradox may be due to the relatively effective treatment available for the management of established infection (e.g. combination antibiotics, granulocyte transfusions) and the relative ineffectiveness of modern anti-leukaemic drugs. In other words, to increase the rate of remission in acute leukaemia we may need to resort in the future to the combined use of a protected environment and of much more aggressive (i.e. effective) chemotherapeutic schedules.

Psychological problems encountered by patients in isolation proved not to be insuperable. Indeed there was a tendency for relatively inexperienced members of the medical or nursing staff to exaggerate the problems in their own minds and this may have been involuntarily communicated to patients. As the staff became more experienced in their use of the isolator, their confidence increased and so did that of the patients. In this small series it was not possible to define a group of patients for whom isolation would be inappropriate.

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