Laminar Airflow Protection In Bone Marrow Transplantation

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A laminar airflow room was used to provide a low-pathogen environment for a child with lymphopenic immune deficiency transplanted with paternal bone marrow. Comparison of flora from the patient, personnel, and the environment indicated that no colonization with exogenous organisms occurred in the patient during the 45-day period of study. The number of organisms recovered from the laminar airflow room was exceedingly small. Conventional hospital isolation rooms contained more bacteria and fungi than the laminar airflow room, even when strict aseptic procedures were followed in the former. Patients with lymphopenic immune deficiency and agranulocytosis admitted to conventional isolation rooms were colonized with exogenous organisms within 1 week. Each developed infection with these strains, and one patient died. Laminar airflow isolation seems at present the best means to prevent exogenous infection during hospitalization of patients with lymphopenic and other severe immune-deficiency diseases and may be essential when bone marrow transplantation is performed to treat their immunological defect.

Patients who have undergone bone marrow transplantation (BMTP) for lymphopenic immune deficiencies (LID) are exceptionally prone to severe infection (7). Lacking humoral and cellular immunities, they are often susceptible to infection by organisms normally nonpathogenic to healthy individuals. After BMTP, they may also suffer from graft-versus-host (GVH) disease which further depresses already impaired immunity (2, 8).

Laminar airflow (LAF) rooms have recently been adapted for care of patients with a high risk of infection. When combined with strict aseptic technique, they provide maximum protection against microbial contamination from the environment (3, 15). However, it has remained unproven that these rooms can prevent colonization of patients with environmental organisms.

In the present study, we describe a 1-year-old boy with LID who received a paternal bone marrow transplant and subsequently developed GVH disease. He was cared for in an LAF room under strict aseptic procedures. Extensive microbiological monitoring of the patient, medical personnel, and the LAF room was carried out to ascertain whether the patient could be protected from acquisition of exogenous flora over a protracted time period while undergoing critical-care nursing. Comparative results from the patients and environment of six conventional isolation and hospital rooms are also presented.

These observations establish that a patient with LID can be cared for successfully in an LAF room without detectable acquisition of environmental pathogens. In contrast, patients cared for in conventional isolation and hospital rooms were continually exposed to a large number of environmental pathogens.

In view of the extreme susceptibility of LID patients to infection, an effective protective environment should be used as an adjunct to the clinical management of these patients and other patients with immune deficiencies, particularly when BMTP is performed to treat their immunological defect.

MATERIALS AND METHODS

Case history. The patient was a 12-month-old boy hospitalized to receive a BMTP for LID, i.e., sex-linked lymphopenic hypogammaglobulinemia, a consistently fatal disease. In the patient's family, over the last three generations, 12 male infants less than 1 year old had died from repeated infections. In the absence of siblings, the father was selected as the bone marrow donor. Three days before transplantation, the patient...
was admitted to the LAF room. Initial bacterial cultures were obtained and a single bath with 70% alcohol and a hexachlorophene detergent was given. At this time, pulmonary infection with *Pneumocystis carinii* was suspected, and the patient was treated with pentamidine isethionate. Prophylactic antimicrobial therapy was not instituted. To modify the course of the expected GVH disease, the bone marrow was purified by albumin gradient centrifugation (5), antilymphocyte serum was administered before transplantation, and methotrexate was given at regular intervals after transplantation.

Three weeks after transplantation, GVH disease developed; 3 weeks later, the patient suddenly developed gram-negative sepsis with severe shock and died within 3 hr. Autopsy revealed extensive intestinal ulceration and scattered bilateral pneumonia.

**Laminar airflow room and conventional isolation and hospital rooms.** The principles of LAF rooms, their operation, and efficiency have been described (3, 15, 16). The present unit was a prototype of a commercially available model (kindly provided on loan by the Applied Science Division of the Litton Co., Minneapolis, Minn.) designed for ready installation in existing hospital rooms. Figure 1 illustrates the unit. One entire wall was made up of HEPA filters capable of removing 99.97% of all particles at 0.3 μm. Virtually all bacteria, fungi, and protozoa are filtered out at this efficiency, and virus particles which may exist as individual particles below 0.3 μm are also removed by virtue of Brownian movement.

The unit was designed to operate at airflow rates of 30, 60, or 90 ft/min. The highest velocity resulted in approximately 400 air changes per hour and was used for maximum activity situations. The crib was oriented perpendicular to the airflow at the filter wall of the room so that all activities took place downstream from the patient.

All materials entering the facility, including food, were presterilized by steam autoclaving or ethylene oxide gaslaving. Certain items, such as thermometers which could not be heated above 100 F (ca. 38 C), were sterilized by a 24-hr exposure to ethylene oxide at room temperature. All items were double wrapped before sterilization.

All personnel entering the facility performed a 3-min hand scrub with 3% hexachlorophene emulsion and dressed in special uniforms in a 3 by 3 ft entryway ("buffer zone area") which was marked off by floor tapes at the room opening. The uniforms consisted of special presterilized hoods, laboratory coats, and calf-length boots, all made from Bar-Bac cloth (Angelica Uniform Co., St. Louis, Mo.); conventional presterilized disposable masks and surgical gloves were worn. Room furnishings and floor surfaces were cleaned thoroughly once daily by the nurses using 3 to 4 sterile, single-use cleaning cloths and a phenolic detergent-disinfectant solution (15). The whole procedure lasted about 30 min.

For purposes of comparison, non-LAF hospital rooms, with mechanical ventilation of less than five air changes per hour, were included in the study. In three hospital isolation rooms, the isolation and housekeeping procedures were the same as in the LAF room except that the food and equipment were not sterilized. The patients occupying these rooms were 0.5, 3, and 10 years old and suffered from LID, meningomyelocele, and agranulocytosis, respectively. All were completely confined to bed during their stay in the hospital. None had open wounds.

Less rigid isolation procedures were followed in three other single-bed hospital rooms. Persons entering these rooms used sterile gowns and masks. Bed clothes were changed every morning and the rooms were cleaned with a phenolic detergent-disinfectant. The patients occupying these rooms were 3, 22, and 43 years old and suffered from purulent meningitis, paraplegia, and cancer of the colon, respectively. They were all confined to bed during their stay in the hospital.

**Microbiological methods.** Specimens from patients and personnel were obtained, usually at 4- and 7-day intervals, respectively, with cotton swabs moistened with sterile saline. The technique has previously been described (17). Nose and throat swabs were streaked on 5% sheep blood-agar (SBA) plates, 5% rabbit blood-agar plates [both having Trypticase Soy Agar base (BBL)], and on Levine’s eosin-methylene blue (EMB) agar plates (BBL). Skin swabs were inoculated on 5% SBA and EMB plates and on plates containing 5% sheep blood in Columbia selective agar (CSA, BBL).

A quantitative platinum loop (0.001 ml) was used for streaking urine specimens onto 5% SBA and onto EMB plates. Stools were inoculated on 5% SBA, EMB, and CSA plates; a 5% SBA plate and a plate containing phenylethyl alcohol in 5% sheep blood-agar were incubated anaerobically.

A Saboraud agar (Difco) plate with 2% added
dextrose and 0.05% chloramphenicol was used periodically to detect the presence of yeast.

Organisms from sources other than urine were evaluated by using a semiquantitative rating of less than 10 colonies (+), 10 to 30 colonies (++) greater than 30 colonies but no growth in the third segment of streaking (+++), and greater than 30 colonies and growth in all streaking segments (++++)

Rodac plates containing 15.5 ml of medium were used for surface sampling (4) and Casella slit-samplers, for air sampling. The sampling medium was Trypticase Soy Agar. For the Rodac plates, a neutralizer system (0.5% Tween 80 and 0.07% soya lecithin) was incorporated in the medium.

Methods of organism identification follow guidelines described elsewhere (11). Sensitivity determinations were done by using either the twofold serial tube dilution method [employing Mueller-Hinton broth (BBL) and an inoculum of approximately 10^4 to 10^6 organisms per ml] or the single high-potency disc technique (1). Serological typing of *Escherichia coli* was done through the courtesy of Albert Balows at the Center for Disease Control, Atlanta. Pycnotyping of *Pseudomonas aeruginosa* was done by Shirley Parker of the University of Manitoba, Winnipeg. *Klebsiella* strains were serotyped in the laboratory of one of the authors (JMM; 13). Phage typing of *Staphylococcus aureus* was performed as previously described (17). Identity of bacterial strains was documented by antibacterial spectra and biochemical testing in addition to routine cultural methods. Serological, pycnion, and phage typing were performed as indicated above.

**RESULTS**

Patients and medical personnel. On admission to the hospital, the bone marrow transplant patient was directly transferred to the LAF room where he stayed for 45 days. Samples from his nose, throat, axillae, groin, perineum, stool, and urine were obtained immediately before he entered the LAF room and later usually at 4-day intervals. Table 1 shows the organisms isolated from the patient's nose, throat, perineum, and stool during his stay in this room. Before admission to the LAF room, he was heavily contaminated with gram-negative rods which showed a tendency to build up during hospitalization, not only in the nose and throat, but also in the perineum and stool. The more benign organisms, such as diphteroids and *Neisseria* sp., disappeared early during hospitalization. *P. aeruginosa* was isolated from the nose and throat before the patient entered the isolation room; later, identical strains were isolated not only from these sites, but also from the perineum and stool. *E. coli* and *Klebsiella* sp., identical to the organisms in the stool and perineum, invaded the nose and throat. *S. epidermidis* was cultured from the axillae before the patient was placed in the isolation facility. Identical strains were later recovered from the nose, throat, and perineum. All staphylococcal strains were characteristic in being coagulase-negative and exhibited the identical antibiogram, being resistant to both penicillin and methicillin. The urine was sterile. Organisms isolated from the groin were identical to those in the perineum. *E. coli* and *P. aeruginosa* identical to the organisms isolated from the patient before and during his entire stay in the LAF room were cultured from the blood, before and immediately after his death, and from lung specimens obtained at autopsy. *P. carinii* organisms were also identified in lung specimens.

Cultures from the nose and throat of the personnel entering the LAF room were obtained with 1-week intervals. During the first 5 weeks, identical strains were not isolated from these individuals and the patient. But later, *P. aeruginosa* identical to the patient's strain was isolated from the nasal samples of one of the nurses. No organisms from the environment or from the personnel entering the room were cultured from the patient during his stay in the LAF room.

Samples from the nose, throat, perineum, stool, and urine of the patients occupying the conventional isolation and hospital rooms were obtained at 3- to 6-day, usually 4-day, intervals. The patients with LID and agranulocytosis were colonized with environmental organisms during the first week in the hospital and the other patients within less than 3 weeks, the organisms most frequently isolated being gram-negative rods and *Candida albicans*. The patients with LID and agranulocytosis developed infection with these organisms, and the patient with agranulocytosis died of the infection.

Laminar airflow room and conventional isolation and hospital rooms. Table 2 shows the microbial contamination of surfaces and furnishings in the LAF room and the other hospital rooms 4 to 6 hr after the beds were made and the rooms cleaned. The blankets and pillows in the conventional isolation and hospital rooms had 5 to 10 times more bacterial and fungal contaminants, and the floors, walls, and furniture usually 100 to 300 times more bacterial and fungal contaminants than did the LAF room.

The microbial air contamination was measured before, during, and after bedmaking (Fig. 2). Four experiments were performed in the LAF room and two experiments in each of the other hospital rooms. In the conventional hospital rooms, the mean air contamination increased from 9 colonies/ft^2 before bedmaking to 33 colonies/ft^2 during bedmaking, and then de-
### Table 1. Microorganisms isolated from the patient during stay in laminar airflow unit

| Samples from | Organisms                        | No.\(^a\) of organisms isolated on day |
|--------------|----------------------------------|----------------------------------------|
|              |                                  | 1\(^b\) | 3 | 8 | 11 | 15 | 22 | 26 | 29 | 32 | 36 | 40 | 43 | 45 |
| Nose         | Diphtheroids                     | +       |    |    |    |    |    |    |    |    |    |    |    |    |
|              | *Escherichia coli*              | +       |    |    |    |    |    |    |    |    |    |    |    |    |
|              | *Klebsiella sp.*                | +       |    |    |    |    |    |    |    |    |    |    |    |    |
|              | *Pseudomonas aeruginosa*        | +       | +  | +  | ++ | ++ | ++ | ++ | ++ | ++ | ++ | ++ | ++ | ++ |
|              | *Staphylococcus epidermidis*    | ++      | ++ |    |    |    |    |    |    |    |    |    |    |    |
|              | *Viridans group streptococcus*  | +       |    |    |    |    |    |    |    |    |    |    |    |    |
| Throat       | Diphtheroids                     | +       |    |    |    |    |    |    |    |    |    |    |    |    |
|              | *E. coli*                       | +       |    |    |    |    |    |    |    |    |    |    |    |    |
|              | *Klebsiella sp.*                | +       |    |    |    |    |    |    |    |    |    |    |    |    |
|              | *Neisseria sp.*                 | +++     | +++| +++| +++| +++| +++| +++| +++| +++| +++| +++| +++| +++|
|              | *P. aeruginosa*                 | ++      | ++ | ++ | ++ | ++ | ++ | ++ | ++ | ++ | ++ | ++ | ++ | ++ |
|              | *S. epidermidis*                | +       |    |    |    |    |    |    |    |    |    |    |    |    |    |
|              | *Viridans group streptococcus*  | +++     | +++| +++| +++| +++| +++| +++| +++| +++| +++| +++| +++| +++|
| Perineum     | *E. coli*                       | +++     | +++| +++| +++| +++| +++| +++| +++| +++| +++| +++| +++| +++|
|              | *Klebsiella sp.*                | +++     | +++| +++| +++| +++| +++| +++| +++| +++| +++| +++| +++| +++|
|              | *Proteus mirabilis*             | +++     | +++| +++| +++| +++| +++| +++| +++| +++| +++| +++| +++| +++|
|              | *P. aeruginosa*                 | +       |    |    |    |    |    |    |    |    |    |    |    |    |    |
|              | *S. epidermidis*                | +       |    |    |    |    |    |    |    |    |    |    |    |    |    |
|              | *Enterococcus*                  | +       |    |    |    |    |    |    |    |    |    |    |    |    |    |
| Stool\(^c\) | *E. coli*                       | +++     | +++| +++| +++| +++| +++| +++| +++| +++| +++| +++| +++| +++| +++|
|              | *Clostridium perfringens*       | +       |    |    |    |    |    |    |    |    |    |    |    |    |    |
|              | *Klebsiella sp.*                | +       |    |    |    |    |    |    |    |    |    |    |    |    |    |
|              | *P. mirabilis*                  | +++     | +++| +++| +++| +++| +++| +++| +++| +++| +++| +++| +++| +++| +++|
|              | *P. aeruginosa*                 | +       |    |    |    |    |    |    |    |    |    |    |    |    |    |
|              | *Enterococcus*                  | +       |    |    |    |    |    |    |    |    |    |    |    |    |    |

\(^a\) Symbols: +, fewer than 10 colonies; ++, 10 to 30 colonies; ++++, more than 30 colonies but no growth in the third segment of streaking; ++++, more than 30 colonies and growth in all streaking segments.

\(^b\) Immediately before entering the laminar airflow unit.

\(^c\) Anaerobic cultures also demonstrated *Bacteroides* sp., peptostreptococci, *Lactobacillus* sp., and diphtheroids.
Table 2. Microbial contamination on surfaces and furnishings in laminar airflow room and conventional isolation and hospital rooms

| Item                | No. of Rodac plates per exp | Colonies per Rodac plate | Expt 1 | Expt 2 | Expt 3 | Expt 4 | Expt 1* | Expt 2* | Expt 1* | Expt 2* |
|---------------------|-----------------------------|--------------------------|--------|--------|--------|--------|--------|--------|--------|--------|
|                     |                             | Laminar airflow room     |        |        |        |        |        |        |        |        |
|                     |                             |                          |        |        |        |        |        |        |        |        |
|                     |                             | Conventional isolation rooms |      |        |        |        |        |        |        |        |
|                     |                             |                          |        |        |        |        |        |        |        |        |
|                     |                             | Conventional hospital rooms |      |        |        |        |        |        |        |        |
|                     |                             |                          |        |        |        |        |        |        |        |        |
| Pillows and blankets | 10                          | 10.9                     | 4.9    | 4.1    | 10.7   | 33.0   | 37.3   | 57.6   | 72.3   |
| Floors              | 15                          | 0.1                      | 0.5    | 1.0    | 0.4    | 24.5   | 25.7   | 89.0   | 99.3   |
| Walls               | 4                           | 0.0                      | 0.0    | 0.0    | 0.0    | 2.0    | 3.6    | 8.2    | 12.4   |
| Shelves and          | 15                          | 0.2                      | 0.3    | 0.2    | 0.8    | 17.7   | 25.4   | 61.4   | 72.3   |
| Chair               | 4                           | 1.0                      | 0.0    | 0.5    | 0.0    | 21.0   | 39.7   | 91.3   | 93.7   |
| Lamp                | 4                           | 0.0                      | 0.0    | 0.0    | 0.5    | 20.2   | 29.0   | 233.7  | 356.7  |

* Mean of three experiments, one in each of three different rooms.

Few organisms were isolated from the air during the entire period.

Table 3 gives the mean values of the microbial air contamination for all experiments in the three different types of rooms. The air contained 170 and 370 times more bacterial and fungal organisms per cubic foot in the conventional isolation and hospital rooms, respectively, than in the LAF room.

In the LAF room, all of the 118 colonies in the air samples, the samples from floors, walls, and furniture, and 50 randomly chosen colonies in the samples from the bed clothing were identified. For each experiment in the other six rooms, 25, 15, and 10 randomly chosen colonies in the air samples, samples from the floors, walls, and furniture, and from the bed clothing, respectively, were identified (Table 4). Far more total and pathogenic organisms (Tables 2 and 3), especially enteric and fungal strains, were isolated from the conventional isolation and hospital rooms than from the LAF room. Strains isolated were compared with organisms isolated simultaneously from the patients in each of these rooms. The majority of organisms isolated from blankets and pillows were identical to organisms isolated from the patient inhabitant of the bed (Table 5). This was true to a lesser extent when floors, walls, tables, etc., and the room air were sampled. In the LAF room, 48 or 50 colonies in the samples from the bed clothing were identical with the patient's organisms. The frequency of patient identical strains in air samples and in samples from the floors, walls, and furniture was also higher in the LAF room than in the other rooms.

**Discussion**

Patients with LID are remarkably susceptible to infection because they lack immunological...
defense of cellular and humoral types (7). Often they become chronically infected with organisms normally nonpathogenic to healthy individuals, e.g., *C. albicans* (7), and may die from systemic varicella, rubeola, BCG, and vaccinia infections (7, 9). The majority of LID patients die during their first year of life, and few, if any, reach the age of 2 years. Our experience with numerous LID patients indicates that hospitalization, even under strict conventional isolation procedures, frequently results in colonization with resistant hospital organisms, especially gram-negative bacilli (*P. aeruginosa, Klebsiella* sp., *E. coli*), fungi (*Candida* sp.) and *P. carinii* which often cause sepsis and death. In addition, if GVH disease develops after BMTP as in our patient, LID patients become even more susceptible to infection, not only with endogenous flora, but also with hospital organisms. Therefore, the capability of LAF rooms to prevent colonization

TABLE 3. Air contamination in laminar airflow room and conventional isolation and hospital rooms

| Expt | Laminar airflow rooma (downstream) at airflow velocity of 90 ft/min | 60 ft/min | Conventional isolation roomsb | Conventional hospital roomsb |
|------|---------------------------------------------------------------|----------|-------------------------------|-------------------------------|
| 1    | 0.047                                                        | 0.050    | 8.16                          | 15.90                         |
| 2    | 0.039                                                        | 0.068    | 9.61                          | 21.56                         |
| Mean | 0.043                                                        | 0.059    | 8.89                          | 18.73                         |

a Total of 660 ft² sampled.

b Mean of three experiments, one in each of three different rooms. Total of 696 ft² sampled.

TABLE 4. Identification of environmental contaminants from laminar flow room and conventional isolation and hospital rooms

| Organisms                  | No. of colonies | Laminar airflow room | Conventional isolation rooms | Conventional hospital rooms |
|----------------------------|-----------------|-----------------------|-----------------------------|-----------------------------|
|                            | Blankets and pillows | Floors, walls, furniture, and air | Blankets and pillows | Floors, walls, furniture, and air | Blankets and pillows | Floors, walls, furniture, and air |
| *Bacillus* sp.             | 16              | 14                    | 81                           | 10                           | 63                           |
| *Candida* sp.              | 2               | 4                     | 1                             | 5                            |
| *Clostridium* sp.          | 1               |                        |                               |                              |
| *Diphtheroids*             | 2               | 3                     | 28                           | 4                            | 12                           |
| *Enterobacter*             | 3               | 2                     | 2                             | 3                            |
| *Enterococcus*             | 4               | 2                     | 2                             | 4                            | 6                            |
| *E. coli*                  | 4               | 1                     | 1                             | 1                            |
| *Herellea* sp.             | 4               | 1                     | 2                             | 2                            | 9                            |
| *Klebsiella* sp.           | 2               | 1                     | 1                             | 2                            |
| *Lactobacillus* sp.        | 1               | 2                     | 1                             | 2                            |
| *Neisseria* sp.            | 9               | 2                     | 16                            | 2                            | 21                           |
| *Proteus mirabilis*        | 3               | 1                     | 2                             | 4                            | 3                            |
| *Pseudomonas aeruginosa*   | 3               | 1                     | 2                             | 3                            | 2                            |
| *Saccharomyces*            | 2               | 1                     | 1                             | 1                            | 2                            |
| *Staphylococcus aureus*    | 3               | 1                     | 1                             | 1                            |
| *S. epidermidis*           | 3               | 1                     | 1                             | 1                            | 11                           |
| Viridans group streptococcus | 3             | 1                     | 1                             | 1                            | 2                            |
| Unidentified molds.        | 2               | 4                     | 16                            | 3                            | 20                           |
| Totals                     | 50              | 118                   | 60                           | 240                          | 60                           | 240                          |
and infection with environmental organisms was put to a severe test by our patient.

LAF systems have been described previously (3, 15, 16). Air entering the LAF room is virtually sterile: not only fungi, bacteria, and protozoa (P. carinii) but also viruses are effectively eliminated by the filtration technique used. Furthermore, if the patient is kept upstream, close to the filter wall, infectious particles originating from medical personnel will be carried downstream away from the patient by the airflow. Penland and Perry (16) described the mechanism of the LAF room in detail but reported no microbiological data. Bodey et al. (3) treated patients with leukemia in LAF rooms, but in their study no attempts were made to associate the microorganisms isolated in the LAF room with those from the patients. Therefore, colonization of patients by exogenous organisms could not be ruled out. Michaelsen et al. (15) performed the most extensive microbiological studies on LAF rooms reported to date. In their investigation, they used normal human volunteers and studied the effectiveness of the air purification system. They did not study the bacterial flora of the human subjects and did not identify the organisms isolated. Their volunteers stayed in the LAF room for 12 days only and did not need the extensive and complex care that our patient received.

Our patient is the first human to be studied in an LAF room by extensive microbiological monitoring for a prolonged period of time (45 days) while under intensive medical care. Our microbiological studies involved not only repeated sampling of the air and surfaces of the LAF room but also extensive monitoring of the patient and medical personnel entering the room. To determine exogenous colonization of the patient, bacteria were characterized by phage typing, biochemical and serological methods, and antibiotic-sensitivity determinations.

Our observations show that no demonstrable colonization by new organisms occurred during the period of study. In addition, the microbial contamination of the air (per cubic foot), walls, floor, and furniture of the LAF room was low, and the majority of the organisms were identical to the bacteria isolated from the patient. The very few organisms which could not with certainty be traced back to the patient's flora were usually found far downstream in the LAF room and, therefore, did not constitute a major threat to the patient. By contrast, a great number of pathogenic bacteria and fungi were isolated from the environment of conventional isolation and hospital rooms, and, as documented in our study, patients occupying these rooms were readily infected by these organisms. Therefore, these rooms appeared unsuit for treatment of LID patients and other patients with markedly reduced resistance to infection.

Although the concentration of airborne microorganisms in terms of colonies per cubic foot was 170 to 370 times greater in the conventional rooms than in the LAF room in this study (Table 3), the differences in total numbers of airborne microorganisms were small because of the greater ventilation used in the LAF room. Thus, at a ventilation rate 80 times as great (400 versus 5 air changes per hour) in the LAF than in the conventional rooms, the total number, rather than the total concentration, of airborne microorganisms was only about two to four times greater in the conventional rooms.

BMTP now offers a chance of cure for patients with LID, particularly if a histocompatibility locus-A (HL-A) identical sibling is available as a donor (6, 14). However, after transplantation the majority of patients undergo GVH reactions which markedly enhance susceptibility to infection by depression of the marrow, production of lymphoid atrophy, and initiation of intestinal ulcerations. In our patient, measures were taken to modify the severity of the GVH reactions, including albumin gradient centrifugation of the marrow (5) and administration of antilymphocyte serum and methotrexate. Nevertheless, severe GVH disease with multiple intestinal ulcerations developed. Disruption of the intestinal barrier most probably facilitated seeding of gram-negative organisms into the blood and resulted in terminal septicemia. Our experience with bone marrow transplant patients (Brit. Med. J., in press) and recent studies of GVH disease in experimental animals (10, 12) indicate that LID patients considered for BMTP should undergo suppression of oropharyngeal and intestinal flora if severe GVH disease is expected. Under these circumstances, environmental protection is even more imperative since decontamination procedures in the absence of effective isolation facilities are regularly disastrous. Our patient was closely observed by skilled personal during his entire stay in the LAF room. His microbial flora was monitored continuously and found to be fairly susceptible to antibiotics, and intestinal ulcerations were not observed while the patient was alive. Therefore, prophylactic treatment with nonabsorbable oral antibiotics was not considered necessary. Our policy was immediate institution of parenteral and oral antibiotic therapy at the first signs of infection. However, the terminal episode of septicemia was so rapid in its onset and so fulminating in its course that antibiotic therapy was of no help. In retrospect, it is felt that pro-
Phylactic antibiotic therapy might have prevented this terminal septic episode. Therefore, in future BMTP, hospitalization of the patients in LAF rooms under strict isolation procedures and decontamination of the intestinal flora may be important steps in securing survival of the patients.

It should be emphasized that LAF rooms provide no protection against sepsis caused by endogenous organisms. Neither can LAF rooms be expected to function optimally unless a strict and meticulous aseptic technique is maintained. However, if good isolation procedures are followed, the LAF rooms constitute a significant advance in environmental microbial control. Nursing of patients with LID and other immunological deficiency diseases in a LAF environment seems at present the best means to prevent hospital infections in these patients and may be essential if transplantation with HL-A nonidentical bone marrow is considered.

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