

Prevention of Infection in the Immunocompromised

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Abstract

Infection is an important cause of morbidity and mortality in immunocompromised patients. The high risk of infection is not only the consequence of the underlying disease but also the result of the diagnostic, monitoring and therapeutic procedures performed on these patients. Infections may be exogenous or endogenous in origin. The prevention of exogenous infections requires a high standard of hygiene. As many infections are acquired in hospitals, an effective control of nosocomial infection programme is crucial in preventing infections in the immunocompromised. Prevention of endogenous infections involves suppression of the aerobic bacterial flora (selective decontamination) and measures to maintain gastrointestinal epithelial integrity to reduce risk of translocation of intestinal flora. Boosting the host immunity through passive and active immunisation should also be considered. Prevention of infection in the immunocompromised is no easy task and requires a multidisciplinary approach.

Ann Acad Med Singapore 1997; 26:331-5

Key words: Antibiotic prophylaxis, Host-pathogen relationship, Immunisation, Nosocomial infection, Selective decontamination

Introduction

As a result of improvements in medical technology, doctors are now able to prolong the lives of patients suffering from many of the previously so-called "incurable" diseases. This is often achieved at the expense of the immune status of the patient. The patient's immunodeficiency is not only the result of the underlying condition but is also often due to the adverse effects of the treatment themselves. Consequently there is an increasing number of patients with compromised immune status who are predisposed to severe and often life-threatening infections. These infections can be caused by even pathogens of low virulence (opportunistic infections). Such infections occur frequently in the immunocompromised patients. A survey of infections among immunocompromised patients has estimated that nearly 12% of patients with solid tumours acquired an infection while in patients with acute myelogenous leukaemia the rate of infection was as high as 30.5%.¹ A study of mortality patterns in a medical intensive care unit (ICU) in Singapore showed a high mortality rate (26% in ICU and 42% in hospital). Among the factors strongly associated with mortality were infection and the immunocompromised state.²

The host-pathogen relationship represents a balance between the virulence of the pathogen and the immune status of the host. When the virulence of the pathogen outweighs the immune status of the host, infection will

result. The position of the fulcrum in this system may either favour the pathogen or the host and is influenced by environmental factors that either promote or hinder the transmission of infection (Fig. 1). Attempts in prevention of infection in the immunocompromised should therefore focus on restoring the balance by measures to hinder the transmission of infection and to boost the host's immune status. The purpose of this article is to review briefly some of the more important strategies involved in general infection control for immunocompromised patients in a hospital setting. It will not cover strategies for the prevention of specific infections in defined categories of patients like HIV-infected persons.

Sources and Transmission of Infection

There are two primary sources of infection in the immunocompromised patient. Infections can arise from the resident flora of the patient (endogenous) or from sources outside the patient (exogenous). It has been estimated that among immunocompromised patients the number of endogenous infections is about equal to that of exogenous infections.³

Exogenous sources would include people (other patients and hospital staff) or environmental sources. Environmental sources are many and varied and include food and drink, dust and aerosols, baths and sinks, instruments and even disinfectants that come into

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direct contact with the patients. Exogenous infections are transmitted to the patient via direct contact, the air-borne route and the oral route. Many infections are transmitted from patient to patient via the hands, gloves and gowns of health care personnel. By far the most important vehicle for the spread of infection are the hands of these health care personnel.

Many endogenous infections especially among hospitalised patients are caused by microorganisms from exogenous sources which have colonised the skin and other epithelial surfaces of these patients. Among such bacterial colonisers *Pseudomonas aeruginosa* has been found to be the most likely to result in subsequent infection.⁴ The ability to resist such colonisation in the gastrointestinal tract is termed colonisation resistance and is an important factor in the host defences. Colonisation resistance is conferred by the presence of the normal gastrointestinal flora; in particular the anaerobic organisms. Antibiotics, radiation and anticancer chemotherapy are known to lower colonisation resistance.⁵ Bacteria resident in the gastrointestinal tract gain access into the blood stream via the wall of the viscus, a process referred to as *translocation*.⁶

Strategies for Prevention of Infection

Exogenous Infections

In preventing exogenous infections the primary objectives should be to:

- (i) eliminate the source of infection and
- (ii) to prevent the transmission of the organism from source to patient.

The quality of air in relation to microbial content is an important consideration in the prevention of infection among the immunocompromised. One strategy which has been used to prevent air-borne infections is to nurse the patient in a total protected environment (TPE). This is a strategy which requires the construction of special HEPA (high efficiency particulate air) filtered rooms equipped with a laminar air-flow system. When used together with other measures that include strict disinfection measures, decontamination of the patient's gastrointestinal tract with antibiotics, skin asepsis and semi-sterile diets, it has been shown to reduce the occurrence of infections including aspergillosis in severely immunocompromised patients.⁷⁻⁹ This is however, a very expensive option and would not be readily available in many developing countries where resources are limited. In the University Hospital Kuala Lumpur, bone marrow transplants have been performed using reverse barrier nursing techniques. This centre has reported an overall survival rate of 73% with the majority of survivors leading normal lives. The early and late infection rates were 46% and 13% respectively and these figures are comparable to those in other centres.¹⁰ How-

ever, the use of positive air pressure rooms, proper maintenance of air-conditioning filters and avoidance of activities that redisperse microorganisms into the air would help to minimise the risk of air-borne infections.

Legionellosis is an air-borne infection which may affect immunocompromised patients in hospitals. Prevention of legionellosis entails the removal of the source of infection, often the potable water system or the air-conditioning cooling towers. This may be achieved by heating or treatment of the contaminated water with biocides.¹¹ Outbreaks of aspergillosis has been attributed to reconstruction works in hospitals. Whenever such work is being carried out, efforts must be made to seal off the dust from areas under renovation.¹²

Many infections in the immunocompromised patients are transmitted to them from other patients via the hands, gloves and gowns of doctors, nurses and other health care personnel. The hands are probably the most important vehicle of transmission of infection and handwashing is probably the single most important measure in the prevention of infection. When nursing immunocompromised patients, stringent precautions have to be taken to minimise transmission of infection through barrier nursing techniques and meticulous observation of aseptic techniques. A recent survey on the practice of aseptic technique in Malaysian hospitals has shown that there is still much room for improvement in routine nursing procedures like handwashing, gloving, gowning, wound dressing and urinary catheterisation. In general nurses perform better than doctors.¹³ These and other measures of nosocomial infection control like setting up a good infection surveillance system, appropriate use of sterilisation and disinfection, isolation practices and good catheter care, all play important roles in the prevention of infection in immunocompromised patients in hospitals.

Microorganisms may also be acquired through food and drink. It is therefore important that immunocompromised patients be served only thoroughly cooked food and filtered or boiled water for drink. Uncooked food like salads and fresh fruits should be avoided. In many Southeast Asian countries, it is not an uncommon practice for relatives to bring food and drink when visiting the patient. Such practices should be discouraged in the immunocompromised, and patients and visitors should be educated on the importance of avoiding such foods and drinks.

Endogenous Infections

The primary objective in measures to prevent endogenous infection is to suppress the number of potential pathogens in the gastrointestinal flora of immunocompromised patients. This is through the use of antibiotics which is primarily directed against the aerobic bacteria and yeasts. The anaerobic flora should be preserved in

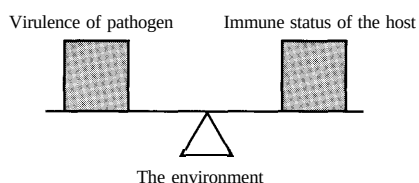


Fig. 1a. The host-pathogen relationship in balance

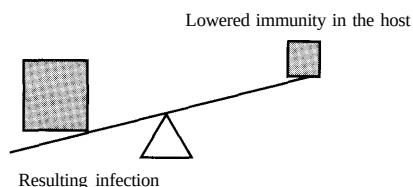


Fig. 1b. The immunocompromised host.

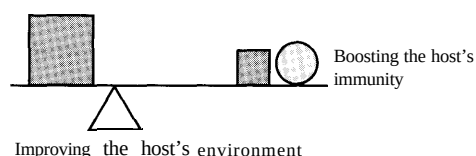


Fig. 1c. Restoring the balance.

Fig. 1. The host-pathogen relationship.

order to maintain colonisation resistance. Such an approach has been termed selective *decontamination*.¹⁴ The prophylactic antibiotics are usually administered during periods of neutropenia or in critically ill patients in intensive care units. The orally administered antibiotics which have been used include both non-absorbable and absorbable agents like aminoglycosides and polymyxins, cotrimoxazole and, more recently, aztreonam and the quinolones. The antibacterial agents may be administered together with an antifungal agent like nystatin, amphotericin B or one of the azoles. Selective decontamination has been practised in intensive-care patients to prevent nosocomial pneumonia. In addition to the oral antibiotics, a parenteral antibiotic like cefotaxime is also administered as pre-emptive treatment of lower respiratory pathogens. Many papers have been published on these prophylactic trials both for the prevention of bacteraemia in the neutropenic as well as pneumonia in the critically ill. However, the results of these trials are difficult to interpret due often to inadequate sample sizes, the heterogeneity of the underlying disease, the severity of the illness and in the case of pneumonia, disagreement with diagnostic criteria. Results may also be confounded by other concomitant preventive measures undertaken. Generally all trials report a beneficial effect from the use of these regimens in terms of reduction of infection rates. Nevertheless it is more difficult to establish reductions in mortality.^{15,16}

The decision to institute such prophylactic antibiotics should be made on a case-to-case basis taking into

account the severity of neutropenia, the presence of other risk factors, environmental and personal factors.¹⁷ It should always be remembered that prophylactic antibiotics are not without disadvantages and potential adverse effects of prophylaxis should be weighed against the benefits in each patient. The adverse effects of such regimens include the risk of emergence of resistance in the resident flora, the increased risk of being colonised and infected by resistant organisms and the side effects of the antibiotics themselves. Such regimens are also very expensive and this should merit serious consideration in countries where resources are scarce.

As bacteria translocate via the intestinal wall, preserving the integrity of the epithelial barrier will also help to decrease the likelihood of systemic infection. Enteral feeding is important in promoting normal gastrointestinal function.¹⁸ Other factors which may help promote intestinal epithelial integrity include the amino-acid glutamine.¹⁹ Antacids and H-2 antagonists reduce gastric acidity and may cause bacterial overgrowth and their use has been associated with a higher incidence of pneumonia. Sucralfate has been advocated to be a more suitable muco-protective agent in the critically ill since it does not increase gastric pH.²⁰ Nursing in the semi-recumbent position as opposed to the supine position has been associated with a reduction in nosocomial pneumonia among ventilated patients.²¹

Intravascular catheters are an important source of bloodstream infections in immunocompromised patients. In patients with central venous catheters the rate of bacteraemia may be as high as 30.2 per 1000 catheter days in contrast to 0 to 2 bacteraemias per 1000 catheter days in patients without central catheters.²² Since most infections are due to the patient's own resident skin flora, efforts should be directed at preventing these organisms from reaching the intravascular segment of the catheter. The use of catheter cuffs, subcutaneous tunnelling and total implantation of the whole catheter system have lowered infection rates. Improvements have also been made in catheter materials. Teflon catheters which are more inert and pliable have been associated with lower rates of infection compared to the older plastic catheters. It has also been shown that *Staphylococcus epidermidis* is less likely to adhere to Teflon. Catheters have also been impregnated with antimicrobial substances to lower the risk of bacterial adherence. The use of antiseptics to prepare the skin for catheter insertion has also been shown to be associated with lower subsequent infections. These developments in catheter technology have been recently reviewed by Goldmann and Pier.²³

Boosting Host Immunity

In neutropenic patients, attempts have been made to boost their neutrophil counts. Granulocyte transfusion

has been undertaken but this procedure has two major difficulties. Donor granulocytes are difficult to obtain. Such transfusions are also complicated by alloimmunisation and are therefore confined to situations where HLA-matched granulocytes are available. This has made granulocyte transfusion an impractical option.²⁴ Stimulating the bone marrow of the patient to increase the production of granulocytes is perhaps a more viable option. This is achieved through the use of colony stimulating factors. Both G-CSF and GM-CSF have been shown to shorten the duration or lessen the severity of neutropenia. Maintenance therapy has also resulted in reduction of frequency of infections as well as duration of antibiotic treatment.²⁵⁻²⁸

Immunocompromised patients can also be protected through the use of both passive and active immunisation. Antibody replacement therapy with intravenous immunoglobulin may reduce the frequency of infection by encapsulated bacteria in patients with haematological malignancies and in those who have received chemotherapy or undergone major surgery for other malignancies.²⁹

Immunocompromised hosts are also capable of mounting antibody responses to protein toxoids, conjugated polysaccharide and viral vaccines. Practical immunisation schedules are being developed. Such schedules should take into account the nature of the underlying condition and the timing of the immunisation.³⁰ In bone marrow transplantation, vaccination of the donor prior to the procedure should also be considered. Vaccines recommended for the immunocompromised include Hib, pneumococcal, meningococcal, diphtheria-tetanus (DT) or diphtheria-pertussis-tetanus (DPT), inactivated poliovaccine and influenza. Live vaccines are generally avoided in the immunocompromised. Higher doses for the primary vaccination and more frequent boosters may have to be given in view of the host's diminished immune response. The Centres for Disease Control and Prevention has issued guidelines for immunisation regimens in the immunocompromised.³¹

Conclusion

Prevention of infection in the immunocompromised is a difficult task and involves a variety of strategies. Measures to be taken may depend on the nature of the underlying disease and the severity of the immunosuppression. Good hospital hygiene, in particular hand washing, plays a crucial role in the prevention of infection. This is complemented but not substituted for by other strategies involving the use of antimicrobial prophylaxis, maintaining gastrointestinal epithelial integrity and immunisation of the patients. This is a multidisciplinary effort and requires close cooperation between doctors, nurses, laboratory per-

sonnel, other categories of health care workers and the patients themselves.

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