ORIGINAL ARTICLES

Controlling the exotic diseases: 1. Isolation facilities

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The exotic diseases are highly virulent transmissible conditions that include Lassa fever, some viral hemorrhagic fevers, smallpox and plague. Any of these diseases could be brought into or diagnosed in Canada as the result of natural or laboratory acquired infection. The patients must be isolated until the presumptive diagnosis is proved. High-security isolation is necessary and needs to be backed up by high-security laboratory services. In Canada facilities for high-security isolation are generally not available; therefore, hospitals must preplan and be ready to effect the best possible isolation under the existing conditions. The plan should address construction, ventilation, filtration, temperature and humidity, together with protective measures for staff and careful handling of laboratory specimens. Materials the patient has contacted and areas or vehicles he or she has been in will have to be decontaminated, and appropriate, safe disposal of corpses must be considered.

Les maladies exotiques sont des affections transmissibles fortement virulentes qui comprennent la fièvre de Lassa, certaines fièvres hémorragiques virales, la variole et la peste. Chacune de ces maladies pourrait être importée ou diagnostiquée au Canada à la suite d'une infection acquise naturellement ou accidentellement en laboratoire. Les malades doivent être isolés jusqu'à ce que le diagnostic de présomption soit démontré. Une zone d'isolation à sécurité maximum est nécessaire et elle doit être renforcée par des services de laboratoire à sécurité maximum. Au Canada des installations permettant une isolation à sécurité maximum ne sont généralement pas disponibles; en conséquence, les hôpitaux doivent planifier et être prêts à assurer la meilleure isolation possible dans les conditions actuelles. Ce plan doit tenir compte de la construction, de la ventilation, de la filtration, de la température et de l'humidité, ainsi que des mesures de protection pour le personnel et une manipulation soigneuse des échantillons de laboratoire. Les objets avec lesquels le malade est venu en contact de même que les endroits ou les véhicules qu'il a occupés devront être décontaminés, et on devra considérer une façon sûre et appropriée de disposer des corps.

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The exotic diseases can be defined as highly virulent transmissible conditions caused by dangerous pathogens, for which patients require specialized handling and care. These diseases include Lassa fever, Marburg virus disease, Ebola virus disease, Argentinian hemorrhagic fever (Junin), Bolivian hemorrhagic fever (Machupo), smallpox and pneumonic plague.[1]

The aim of this paper is to emphasize the lack of facilities and knowledge for handling patients suffering from these conditions, and to outline methods of providing safe care and preventing spread of the infecting organisms from the patient to others and into the ecosystem.

Epidemiologic considerations

Lassa fever, after its identification in 1969, originally appeared to be highly transmissible and was responsible for several extensive nosocomial outbreaks in West Africa. Since 1969 there have been six cases imported from Africa, but apart from laboratory acquired infection there have been no secondary cases.[2] Marburg and Ebola virus diseases seem to be more transmissible; laboratory acquired, other secondary and even tertiary cases have been recognized.[3-6] The two South American hemorrhagic fevers have not been recognized outside of their indigenous areas except as laboratory acquired disease.[2] Smallpox is probably the most highly transmissible of the exotic diseases.[7] Its natural form appears to have been eradicated from the world, but the one laboratory acquired case and one subsequent secondary case in Birmingham, England in August and September 1978 indicate that the threat of this disease is still present.[2] Pneumonic plague, the only bacterial disease on the list, is also highly transmissible, but its natural pneumonic form is now rare; in recent years the only recognized case was laboratory acquired, in California in August 1977.[8]

Thus, there are two concerns about containment of organisms causing the exotic diseases: first, the infrequent importation of a case into a country in the Western world; and, second, the recognition and handling of laboratory acquired cases.

Although these diseases vary in transmissibility and virulence, they have one feature in common — unpredictability. It is this unpredictability that necessitates high-security isolation to protect attending medical staff and to prevent virulent organisms from escaping into the ecosystem and possibly infecting humans and animals.

Occurrence of cases

Cases of the exotic diseases can be encountered in one of four circumstances:

- As a result of a purposeful importation — that is, a dedicated aeromedical evacuation, in which one aircraft and its crew are dedicated to transporting and caring for one patient. There are no other passengers, with the possible exception of the patient's immediate family.
- When a passenger on an aircraft or at a port of entry is noted to be ill.
- When a person falls ill soon after arriving in the country.
- As a result of exposure or an accident in a laboratory.

Handling of cases

Isolation should begin as soon as a presumptive diagnosis of an exotic disease is made. There will almost always be a delay in the definitive diagnosis. The delay may be a matter of hours for a serologic diagnosis; for example, fluorescent antibody testing for Lassa fever can demonstrate the presence of antibodies within a few hours, although the antibody titre does not rise until several days after the disease begins. Culture and identification of the virus, however, take up to 5 days.

Isolation can consist of residential quarantine or isolation in a private home, the degree of isolation varying with the degree of suspicion of the diagnosis, or full containment isolation in a hospital.[1] If necessary the patient can be transported in a containment stretcher isolator or containment aircraft transit isolator to an isolation ward or facility or into a containment bed isolator.[2]

High-security isolation

Ideally a high-security isolation facility should consist of a purpose-designed unit with containment bed isolators. There are few, if any, such units in the world. A 10-bed unit is being constructed in Australia. In Canada a recommendation was made to the federal government to build a six-bed unit, but fiscal restraints make it unlikely that this will be done in the near future.

The ideal facility should be constructed with either a differential pressure system in three separate zones or a directional air flow and filtration system for each of the areas where a patient would be cared for in a containment bed isolator.

There are seven containment bed isolators in Canada. Four are owned by the federal government; two are at the National Defence Medical Centre in Ottawa and two are in storage. The government of New Brunswick has one, and in Alberta there are two, one in Calgary and one in Edmonton. Other provinces, particularly Ontario, are considering buying these isolators, and they should be the definitive high-security isolation units in the next few years.

Since an ideal purpose-designed clinical isolation facility does not exist in Canada, the existing facilities must be used. Such facilities can consist of areas within a hospital with containment bed isolators or any available ward space; with preplanning and thought, ward space can be rapidly prepared and utilized when the need arises. Before describing the type of planning and modification that might be undertaken, we will briefly mention laboratory facilities.

High-security laboratories

Laboratories suitable for handling specimens from patients with exotic diseases are lacking. Such a laboratory needs containment level F capability[9] (level P4 and category IV in the United States and the United Kingdom respectively); this is the highest level of containment and represents an isolation unit geographically separated from other areas by means of a separate building or a separate air system in a multipurpose building. At this time only three laboratories in the world are capable of handling specimens from patients with all seven exotic diseases: the Center for Disease Control, Atlanta, Georgia; the Centre for Applied Microbiological Research (formerly the Microbiological Research Establishment), Porton Down, England; and the Prince Leopold Institute of Tropical Medicine, Antwerp, Belgium. The government of Ontario is proposing to build a laboratory in Toronto that will adequately serve Canada's needs in this respect.

Surveillance of staff

All staff designated as having close contact with an exotic disease must be placed under personal surveillance throughout the incubation period of the disease. Close contact can be defined as contact during the 3-week infective period of the following types: face to face contact; sharing the same residence; close exposure during travel; or exposure to infected biologic specimens. During the period of surveillance the individual's temperature must be noted daily and a report made of any symptoms. If fever or other signs or symptoms suggesting the disease develop, the individual must be isolated immediately and further investigation done.

Exclusion of other diagnoses

Procedures for specimen collection, including handling, packaging, labelling and transportation, have been fully described in the Canadian contingency plan for the management of exotic diseases.[1]

About 45% of patients suspected of having viral hemorrhagic fever turn out to be suffering from malaria.[10] It is therefore important that blood be collected to exclude malaria as soon as possible after the patient has been seen. Extreme care must be taken so that the individual collecting the blood and the laboratory processing the sample do not become contaminated. Such patients are usually placed in high-security isolation and kept there until the disease is shown to be other than one of the exotic diseases.

Guidelines for high-security isolation

The following guidelines and recommendations cannot be undertaken by most Canadian hospitals. However, attempts should be made to provide as much as possible for safe patient management.

Isolation suite

The isolation suite should be on the top floor of the hospital, with a dedicated elevator and entrance, or in a separate building. If, however, the suite is on the ground floor, with an air-lock entrance, then extracted air can be vented to the roof or to a suitable stack. Air must be extracted in such a manner as to prevent contamination and directed to ensure that there is no possibility of its being drawn into the hospital's air intake system.

The suite should consist of the patient room or rooms and one or, preferably, two anterooms connecting the patient area, nursing station, shower facilities, storage rooms and so forth. The remaining area or wing of the hospital should be cleared of all other patients unless they have the same disease as the original patient.

The floor, walls and ceiling of the patient room should be constructed of nonporous materials that are resistant to disinfectants. Smooth, clean, impervious surfaces where dust cannot accumulate are desirable. Easy cleaning is important for the nursing staff, who will be obliged to undertake daily cleaning.

The approach to the room must be through an anteroom of sufficient size to permit staff to dress in protective clothing before entering the patient area and suitable for receiving contaminated clothing before the staff leave. Preferably there should be two anterooms, one for the entry routine and one for the departure routine. Shower, washing and disinfection facilities should be available near and preferably between the anteroom and the patient room. The patient room must be close to an autoclave and incineration facilities.

The nursing station should be near the patient room and in contact with it, either (preferably) by intercom and television surveillance or by direct vision through a glass partition. Nurses and other attendant staff should be able to reach the patient room without having to cross other patient areas.

Engineering aspects

Air flow and ventilation: The first principle of air flow in a high-security isolation suite is that air must be directed out of the patient area to the outside after undergoing appropriate filtration or sterilization. A simple air extractor can be built into the ceiling and, provided an air flow of 0.1 to 0.2 m^3/s is maintained, microorganisms will not escape into the corridor. The density of air varies with temperature changes, so an air flow of 0.3 to 0.4 m^3/s will produce a safe environment under most conditions.

An entrance lobby and pass-through hatches with directional air flow can be used relatively inexpensively. The lobby, or air lock, greatly improves the isolation, largely because the two-door principle (keeping one door shut while the other is open) prevents backward flow of air from the contaminated area. Therefore, because only one door is open at a time, a much smaller air flow, about 0.05 to 0.1 m^3/s, is adequate to maintain the desired direction of air current. In an emergency it is possible, but not really desirable, to set up a large fan in the door of the patient room and direct the air flow to an opened window. Alternatively, a window extractor fan or air-conditioning unit can be similarly used.

Filtration and sterilization of extracted air: All air extracted from the high-security isolation suite must pass through high-efficiency particulate air filters, which allow penetration of less than 0.03% of a sodium chloride aerosol with a particulate diameter ranging from 0.2 to 2 μm or less than 0.03% of dioctyl phthallate particles 0.3 μm in diameter.[11] It is clearly a more expensive operation, but effluent air can be sterilized by incineration if desired.

Temperature and humidity: The ideal temperature in a high-security isolation suite is between 20 and 23°C and the ideal relative humidity is 45%.

Maintenance: Isolation suites and modifications should be designed, when possible, in such a manner that engineering maintenance can be undertaken by personnel working outside the patient area. Consideration can be given to designing units so that they can be used for immunosuppressed patients when not being used for patients with exotic diseases. This would, however, present a moral problem if a unit were being used for an immunosuppressed patient when another patient with an exotic disease arrived at the hospital.

Chemoprophylaxis and immunoprophylaxis

Protecting medical and nursing staff caring for patients in high-security isolation units does not mean simply providing containment facilities. There are chemoprophylactic and immunoprophylactic measures that provide partial protection and can be applied as part of the preplanning; similarly, on occasion chemotherapy and immunotherapy very early in the course of the disease will furnish valuable protection (Table I).

Decontamination

Concurrent disinfection and terminal disinfection are the same procedure performed at different times. Concurrent disinfection is undertaken using techniques by which infected articles, materials and fomites that may or may not have further use or may require rehandling by unexposed personnel are rendered incapable of further transmitting the causal organism. Terminal disinfection must be done in buildings and locations the patient has been in; this includes ambulances, aircraft, hospital rooms and isolation facilities. All persons engaged in disinfection must wear protective clothing appropriate to the degree of disinfection being carried out.

As all but one of the exotic diseases are caused by viruses, we will consider only virucidal disinfection.[12] The following four products are highly effective against these viruses and against *Yersinia pestis*, the bacterium that causes pneumonic plague:

- Sodium hypochlorite, 5.25%. This agent is remarkably virucidal and bacteriocidal, and is recommended for use in general cleaning. It is readily available as household Javex or Chlorox. Unfortunately it corrodes metal, including stainless steel.
- Glutaraldehyde, 2% aqueous, alkalinized with sodium bicarbonate. This agent is ideal for disinfecting instruments, and is preferred for items that might be damaged by alcohol, hypochlorites or heat sterilization.
- Formaldehyde. This is the best gaseous disinfectant available. It is inexpensive and does not harm fabrics (including wool and leather), rubber, paint, metal and most plastics.
- Ethylene oxide. This is also an effective fumigant and is particularly useful for disinfecting instruments and medical equipment. It can, however, discolour some plastics and can be retained in the pores of the plastic for some time.

Nondisposable items and instruments can be concurrently disinfected by being immersed in 2% aqueous glutaraldehyde for at least 10 minutes or by being heat sterilized in an autoclave in double bags. Incineration is preferred for disposable and waste materials.

After the patient's discharge, when all disposable and removable objects have been taken out of the room for appropriate handling, the walls, floor and ceiling of the room should be mopped with a 1:10 solution of sodium hypochlorite, 5.25%, then the unit must be fumigated with formaldehyde. The personnel preparing the unit should be wearing protective clothing that includes rubber boots. The temperature should be kept at not less than 18°C and the relative humidity over 60%, preferably 80% to 90%. If the area is overhumidified, however, formaldehyde fumigation is less effective. The room should be exposed to the gas for not less than 6 hours. Following fumigation the area must be well ventilated. Full details of the techniques of fumigation are found in the Canadian contingency plan.[1]

Handling and disposal of corpses

Although corpses must be handled and disposed of in accordance with provincial regulations, certain procedures are necessary. Before removal from the bed the body should be sealed in a strong polythene bag that is then sprayed with 10% formalin. The body should be removed by persons wearing protective clothing and placed in a coffin that contains sawdust or tow impregnated with 10% formalin. An air valve must be provided in the plastic bag. The body should be covered with more sawdust or tow and then further impregnated with formalin. Once sealed, the whole coffin should be sprayed with formalin solution.

Conclusion

There is a risk, albeit not high, that an exotic disease may be imported into Canada or may be acquired in a laboratory. Hospitals generally do not have adequate facilities to care for patients with such a disease. However, with foresight, planning and some expenditure, existing facilities can easily be modified to provide reasonably safe medical care.

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Table I—Immunologic and therapeutic measures available for protecting against the exotic diseases

Disease	Immuno-prophylaxis	Chemo-prophylaxis	Immuno-therapy	Chemo-therapy
Lassa fever			×*	
Marburg virus disease			×*	
Ebola virus disease			×*	× (interferon)†
Argentinian hemorrhagic fever				
Bolivian hemorrhagic fever			×*	
Smallpox	×		×	× (Marboran)
Pneumonic plague	×	×		×

*Specific immune plasma has been prepared, but the supplies are small and the efficacy is largely unproven.
†Has been given with immune plasma on one occasion.[5]

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Controlling the exotic diseases: 2. Nursing management

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Advance planning can facilitate the care of a patient with an exotic disease who is admitted to a hospital that lacks facilities for high-security isolation. The Department of National Health and Welfare contingency plan for dealing with such patients lacks specific information in a number of areas of medical care, as described in this paper. Consideration must be given to the number of personnel trained and readied for employment, the criteria for selection and special preparation. The protective clothing generally used for hospital isolation procedures is inadequate. Several types of special clothing, including a respirator, are available for total protection of personnel; the clothing may be uncomfortable when worn for long periods, and does restrict movement, vision and communication. All persons entering the isolation suite must change into fully protective clothing, and double layers of clothing are required for direct patient care. All personnel must shower and change before leaving the isolation suite. Suitable facilities for dressing and showering, together with entry and exit routines, must be considered. Hand washing, daily cleaning procedures and disposal of liquid and solid wastes all require special procedures. The social and psychologic problems of patients and their families must also be considered. Preplanning is required to decrease the risks involved in monitoring vital signs and implementing emergency procedures requiring contact with the patient's blood.

Une planification par anticipation peut faciliter les soins au malade atteint d'une maladie exotique accueilli dans un hôpital dépourvu d'installations pouvant assurer une isolation à sécurité maximum. Tel que décrit dans cette publication, le plan d'urgence du service de la Santé et du Bien-être national pour faire face à de tels malades ne contient pas d'informations spécifiques relatives à un bon nombre de domaines des soins médicaux. On doit considérer le nombre de personnes formées à cet effet et prêtes à l'emploi, les critères de leur sélection et leur préparation spéciale. Les vêtements protecteurs habituellement utilisés à l'hôpital pour les procédures d'isolation sont insuffisants. Plusieurs types de vêtements spéciaux, incluant un respirateur, sont disponibles pour assurer une protection totale du personnel; ils peuvent être incomfortables lorsqu'ils sont portés pour des périodes prolongées, et ils limitent les mouvements, la vue et les communications. Toute personne entrant dans la zone d'isolation doit passer un vêtement à protection complète, et une double épaisseur de vêtements est nécessaire pour les soins directs au patient. Tous les employés doivent passer sous la douche et se changer avant de quitter la zone d'isolation. On doit prévoir des installations adéquates pour la douche et l'habillage ainsi que des procédures d'entrée et de sortie. Le lavage des mains, le nettoyage quotidien, l'élimination des déchets liquides et solides exigent tous des procédures spéciales. Les problèmes sociaux et psychologiques des malades et de leurs familles doivent aussi être envisagés. Une planification par anticipation est nécessaire pour diminuer les risques encourus pour la surveillance des signes vitaux et la mise en oeuvre des mesures d'urgence nécessitant un contact avec le sang du malade.

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The nursing of patients suffering from the exotic diseases has been described elsewhere,[1-4] particularly with respect to the use of a containment bed isolator. In West Africa, patients with Lassa fever have been cared for with the use of barrier nursing techniques and isolation techniques appropriate to that setting.

In the United States the one patient with Lassa fever in 1976 was cared for with the use of modified high-security isolation techniques.[5] The patient was quarantined in a private room with suitable ventilation, and all persons entering the room wore complete protective clothing and respirators. In South Africa in 1975 the patients with secondary cases of Marburg virus disease were cared for in an isolation ward, and the medical staff wore disposable clothing, plastic goggles and thick disposable face masks.[3] In the United Kingdom two of the three cases of Lassa fever were diagnosed when the patient's condition had improved; special precautions had not been taken during the acute phase of the illness. In the third case the patient died within 24 hours of admission to hospital, at which time the true diagnosis was not suspected; strict isolation techniques, however, were carried out in an isolation ward. Finally, the patient with laboratory acquired Ebola virus disease was cared for in a containment bed isolator for 42 days.[6]

Thus, the experience in the world during the last few years clearly supports the need for high-security