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ORIGINAL ARTICLES

Surveillance report

HOSPITAL PREPAREDNESS AND MANAGEMENT OF PATIENTS AFFECTED BY VIRAL HAEMORRHAGIC FEVER OR SMALLPOX AT THE LAZZARO SPALLANZANI INSTITUTE, ITALY

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The US cases of anthrax in 2001 and the recent severe acute respiratory syndrome outbreak have heightened the need for preparedness and response to naturally emerging and re-emerging infections or deliberately released biological agents.

This report describes the response model of the Istituto Nazionale per le Malattie Infettive Lazzaro Spallanzani (INMI), Rome, Italy for managing patients suspected of or affected by smallpox or viral haemorrhagic fever (VHF) either in the context of an intentional release or natural occurrence.

The INMI is Italy's leading hospital in its preparedness and response plan to bioterrorism-related infectious agents. All single and double rooms of INMI are equipped with negative air pressure, sealed doors, high efficiency particulate air (HEPA) filters and a fully-equipped anteroom; moreover, a dedicated high isolation unit with a laboratory next door for the initial diagnostic assays is available for admission of sporadic patients requiring high isolation. For patient transportation, two fully equipped ambulances and two stretcher isolators with a negative pressure section are available. Biomolecular and traditional diagnostic assays are currently performed in the biosafety level 3/4 (BSL 3/4) laboratories.

Continuing education and training of hospital staff, consistent application of infection control practices, and availability of adequate personnel protective equipment are additional resources implemented for the care of highly infectious patients and to maintain the readiness of an appropriately trained workforce to handle large scale outbreaks.

Euro Surveill 2005;10(3):36-39 Published online Mar 2005

Key words: biological agents, bioterrorism, haemorrhagic fever, Italy, preparedness, smallpox

Introduction

The cases of anthrax in Florida and New York City in 2001, following the terrorist events in New York City and Washington, D.C. [1] and the recent severe acute respiratory syndrome (SARS) outbreak [2] have heightened the need for preparedness and response to emerging and re-emerging infections or deliberately released biological agents [3,4]. Smallpox [5] and haemorrhagic fever viruses (VHF) [6] pose the greatest concern because of their potential ease of dissemination or transmission, major public health impact (e.g., high mortality), panic and social disruption [4].

This report describes the model of response for the Istituto Nazionale per le Malattie Infettive Lazzaro Spallanzani (INMI), Rome, Italy in managing patients suspected of or affected by smallpox or VHF either in the context of an intentional release or natural occurrence.

The Institute

Since its foundation in 1936, the Lazzaro Spallanzani hospital has been devoted to the prevention, diagnosis and care for infectious diseases. Over the years, its focus has changed in relation to the evolving patterns of infection threat. In particular, the hospital was heavily involved in the control of hepatitis B and C epidemic in the '70s, and the human immunodeficiency virus (HIV) and tuberculosis spread in the mid '80s and early '90s.

In 1982, after smallpox vaccinations in Italy were discontinued, the Italian Ministry of Health identified the Lazzaro Spallanzani hospital as the place that would receive suspected cases and a negative-pressure Gelman's containment bed isolator was purchased. The isolator was rigid, uncomfortable and unacceptable to patients, although it gave the nursing and medical staff a high degree of protection. However, not all routine nursing and medical procedures could be carried out due to this rigid physical barrier and it was also not practical to perform mechanical ventilation or haemodialysis.

In 1994, a new three floor hospital complex was completed for a total of 256 beds in 7 wards, 48 beds in day hospital care, and 20 intensive care beds.

The building has an air conditioning system that is able to provide up to 12 air changes per hour to all single and double rooms. In addition, the system also allows changes from negative to positive room pressure and vice versa, enabling the rooms to be used for airborne isolation or as a protective environment. All rooms have

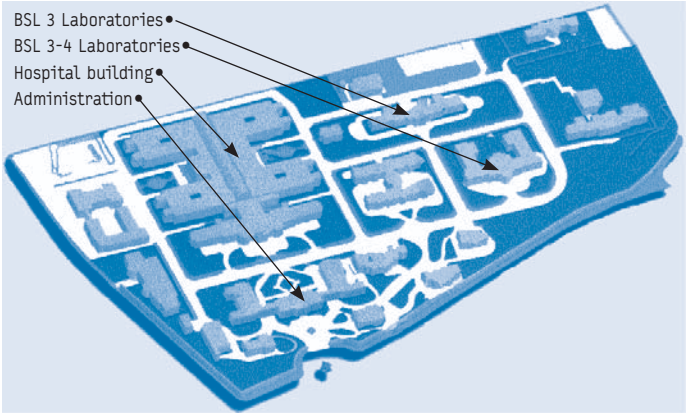
Instituto Nazionale per le Malattie Infettive Lazzaro Spallanzani, Rome, Italy

private baths, TV, telephone line and a fully-equipped anteroom with well-sealed doors, and HEPA filter on the incoming and outgoing air flow.

Five biosafety level (BSL) 3, one cabinet BSL 4 laboratories, and a BSL 3-like autopsy suite are available [FIGURE 1. Hospital map].

FIGURE 1

Map of the Istituto Nazionale per le Malattie Infettive Lazzaro Spallanzani, Rome, Italy



In 1995, INMI was identified by the Italian Ministry of Health as the national referral centre for the management of patients affected by naturally occurring highly transmissible infectious disease (i.e. VHF) and in late 2001 as the national referral centre in the case of deliberately release of biological agents.

Recently, INMI has organised an effective multidisciplinary European network of isolation facilities, physicians and other health professionals with expertise in the management of these facilities and infections. EUNID (European Network of Infectious Diseases physicians) consists of representatives from all member states and applicant countries, which have or are planning highly secure isolation facilities. One of EUNID's primary objectives is to establish an inventory of European high isolation facilities and the healthcare workers involved in the management of patients needing these facilities.

Patient transportation and admission

For transportation of patients suspected to be affected by VHF or smallpox, two fully equipped ambulances are available with a sealed negative pressure section that is completely isolated from two other sections (one for the driver and the other for the external staff control) [FIGURE 2]. The air is expelled outside through HEPA filters. The isolation section is minimally furnished and stripped of unnecessary devices; needed sharps can easily be removed and the interior is easy to decontaminate. All resuscitation equipment, including ventilator and mechanical aspirators, is available inside the ambulance. Ambulances are also equippe with mobile phones and internet access.

Two stretcher isolators (Vickers Medical Containment Stretcher Transit Isolator®) are also available, specifically designed for the isolation and transportation of patients believed to be affected by highly infectious diseases. The self-contained isolation system consists basically of a lightweight stretcher onto which a demountable framework is attached enveloped by a transparent plastic [FIGURE 3]. The plastic envelope has negative air pressure, which is maintained by an air supply system in order to avoid the exit of potentially contaminated air. Thus, patients can be transported by the stretcher isolator directly into the ambulance's isolated negative pressure section.

To ensure competent use, continual education and training of selected personnel is required.

In case of admission of patients with suspected or documented VHF referred to the INMI from the airport, ports or other hospitals, a dedicated pathway with a separate entrance from daily hospital activities has been designed.

Isolation procedures are implemented at admission, where a triage area with a negative air pressure room is dedicated to patients presenting syndromes of a suspected airborne infection.

FIGURE 2

Fully equipped ambulance with a sealed negative pressure section for transportation of patient believed to be suffering from highly infectious diseases, Rome, Italy

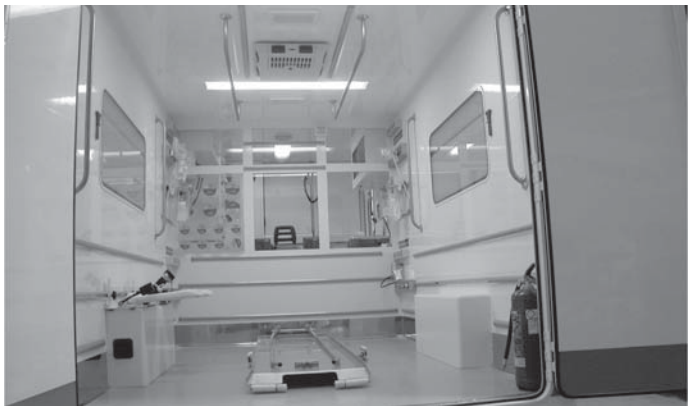
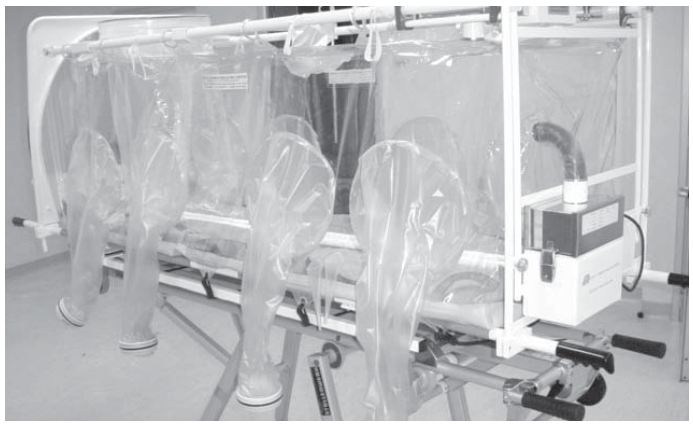


FIGURE 3

Stretcher isolator specifically designed for the isolation and transportation of patients believed to be suffering from highly infectious diseases, Rome, Italy



Care facilities

Currently, 42 single and 59 double rooms on 5 wards, and 42 beds in day hospital care are in use. However, the remaining facilities can be activated in case of a crisis according to the National Response Plan.

All single or double rooms of the Institute are potentially suitable for isolation or cohorting according to adopted airborne, droplet and/or contact precautions. The anterooms contain supplies for routine patient care, protective barriers for personnel and hand washing facility.

Moreover, there are two special adjacent single rooms in a ward dedicated for sporadic cases of VHF or smallpox. Next to to the rooms, there is a BSL3 laboratory, available for bloodfilm examinations to rule out malaria, basic blood testing, bacteriological cultures and preparation-inactivation of biological samples for molecular biological testing. Intravenous ribavirin is also available for the treatment of patients with suspected VHF while laboratory confirmation is pending. In case such patients are admitted, the other patients in the ward can be easily transferred to other wards in the institute. A step-by-step gradual floor-to-floor evacuation plan has been prepared, if needed.

In the last three months of 2001, following the deliberate release of anthrax in US, 201 individuals were referred to our admissions unit who reported being contaminated by suspected dust. However, no exposed individuals were admitted and no anthrax spores were detected.

At the beginning of the SARS epidemic when limited data on the route of the SARS-Coronavirus transmission were available, the high isolation unit was used for the two initial suspected SARS cases we cared for. During this epidemic, 72 subjects were referred to our admissions unit with SARS-

like symptoms. Eight of them were admitted in a dedicated hospital ward as suspected cases. One of them satisfied the WHO criteria for SARS [7].

Isolation precautions, education and training, and personal protective equipment

At INMI, isolation precautions have been updated several times in the last 20 years as it is Italy's national referral institution.

In the mid 1980's, universal precautions to prevent transmission of HIV were implemented. In the following years isolation procedures were strengthened to cope with the re-emergence of tuberculosis, possible cases of emerging infections such as Ebola virus, and the threat of bioterrorism. More recently with the advent of the SARS threat, the hospital protocols, largely based on the Hospital Infection Control Practices Advisory Committee guidelines on isolation precautions in hospitals [8], have been further reinforced. Healthcare workers have been strongly recommended to comply with the required precautions, wearing disposable personnel protective equipment (PPE) consisting of masks or respirators, gloves, gown, head and shoe covers, and eye protection before entering the patient's room. These have to all be discarded in the anteroom. Multiple educational and training sessions, including simulations focused on adherence to infection control protocols, have been developed for healthcare and laboratory personnel. Special efforts have been made to stress the importance of seal checking when wearing disposable respirators, and the safe removal of PPE [9,10]. Tests of respirator fit has been carried out for all health care workers. Protocols for the surveillance and management of health care workers potentially exposed to highly transmissible agents have been issued and updated, including post-exposure treatment when available.

Available PPE recommended for the management of highly contagious patients consists of Tyvek™ tissue full-body suits with thermo activated closure, full face mask with P3 filtered respirators (EU standard EN 149:2001), and latex obstetric gloves to be used in double gloving. Needle stick prevention devices are also provided.

All materials used for patients and disposable items worn by staff, in accordance with the Italian Ministry of Health recommendations, must be placed into a secure waste bag and then packaged into a rigid container before leaving the isolation rooms. The containers are then destroyed by incineration.

In case of patient death, autopsy is discouraged. The corpse must first be wrapped in linens permeated with disinfectants and then double bagged in sealed impermeable body bags before being transported for burial or cremation. All unnecessary handling of the body should be avoided.

In Italy, immunisation of healthcare workers against smallpox has not yet been implemented. The Italian Ministry of Health will activate immunisation program within the National Response Plan.

Transport, and processing of biological samples

Packaging and transportation of biological samples that are sent to INMI by external facilities, or which is sent by INMI to a WHO-reference laboratory, is done according to WHO guidelines [11,12]. Tubes and sample vessels are made of non-breakable material, and are tightly closed before being packaged and forwarded to the laboratory. Secondary packaging is consists of a waterproof plastic envelope. A complete patient information sheet, including all useful information for laboratory personnel and suspected diagnosis is inserted in an external pocket of the secondary envelope. Usually a single secondary envelope is used for several samples from one patient, but different secondary envelopes are used for different patients. Several secondary envelopes are grouped in a rigid impermeable plastic container that is transported to the laboratory by dedicated personnel. Collection of samples is preceded by informal direct contact between clinicians and laboratory personnel, in order to optimise sample collection and diagnostic assays.

When a class A viral agent is suspected, preliminary blood tests are carried out in the laboratory juxtaposed to the high isolation unit to rule out malaria, as well as blood counts, transaminases and other urgent determinations. The biosafety level for sample handling is based upon to the pathogen's classification, which is divided into 4 risk groups [13,14]. For level 3 pathogens, when cultivation of the microorganism is not required, samples can be initially processed in a level 2 laboratory, adopting level 3 procedures. In case of microorganism cultivation, the appropriate cell line panel or bacterial culture medium is inoculated with each patient's sample in a BSL 3 laboratory. Samples from patients suspected to be infected with class 4 VHF or variola virus are handled under level 4 procedures, in the BSL 4 facility for both aliquotation and initial assay set up. Viral cultures are maintained in a level 4 facility throughout the entire observation time, but other assays are continued under lower biosafety levels when they undergo a treatment known to inactivate pathogen infectivity, such as heat treatment, fixation, solvent exposure and protein or nucleic acid extraction. The methods currently available for the detection of class A viral agents, as well as methods to detect other viruses important for differential diagnosis are included in the table. This list is continuously updated according to the specific literature available from the international community. In addition, the immune response to suspect pathogens are tested by antibody tests, in both acute and convalescent serum sample pairs. Both commercial and in-house assays, including indirect immunofluorescence and enzyme-linked immunoassays are used.

TABLE

Capability of INMI to detect class A viruses, including viral agents important for differential diagnosis, Rome, Italy

	PCR	SEQ	VI	EM	IFA	EIA	NT	CF	IB
Class A viruses									
Filoviruses: Ebola, Marburg	X	X	X	X					
Arenaviruses: old and new world viruses	X	X	X	X					
Bunyaviruses: CCHF	X	X	X	X			X		
Orthopoxviruses	X	X	X(*)	X					
Other viruses									
HSV	X	X	X	X		X		X	
VZV	X	X	X	X	X	X		X	
Flaviviruses: Dengue, Yellow fever	X	X	X	X	X	X	X		
Hantaviruses	X	X	X	X	X				X

(*) Only for differential diagnosis. If virus isolation consistent with smallpox

PCR: Polymerase chain reaction
SEQ: Sequencing
VI: Virus isolation
EM: Electron microscopy
IFA: Immunofluorescence assay
EIA: Enzyme Immuno assay
NT: Neutralization test
CF: Complement fixation
IB: Immuno-Blot

In the BSL 3/4 laboratories, all solid waste and residual biological specimens are autoclaved before disposal. Liquid waste is chlorinated before entry into the hospital sewage system.

Finally, in the last two years INMI was alerted twice for a possible referral of a patient with suspected VHF. The first case was a suspected Guanarito virus infection after travelling in Venezuela. RT-PCR assays for the New World Arenavirus were negative. The second case was a missionary who fell sick after travelling in Central Africa and Lassa fever was suspected. Multiple RT-PCR assays for VHF viruses were negative and VHF infection was ruled out.

Conclusion

The present work is aimed at presenting the model of preparedness and response of INMI within the scenario of public health threats due to emerging and re-emerging infections, or to deliberately released biological agents.

The efficiency of our system to deal with highly transmissible and threatening infectious diseases has not been extensively tested. Only a few individuals with suspected anthrax exposures or SARS-Coronavirus infection have been cared for in recent years and, although

essential, training simulations do not represent real practice.

Thus, it could be argued that an apparently perfect-looking system could be over-stretched, and the clearest and best laid-out guidelines not complied with, when a patient or several patients with suspected VHF or smallpox are hospitalised.

However, in the past two decades INMI has efficiently dealt with the impact of the HIV epidemic and has cared for several patients with multi-drug resistant tuberculosis. Moreover, experiences from hospitals in other countries have demonstrated that a well-prepared system can manage sporadic cases of VHF [15-19]. Within this scenario, the anthrax and SARS emergencies we have dealt with represent important tests with substantially positive results. Based upon this, due to our consistent application of infection control practices, we feel sufficiently prepared to adequately care for these patients and to protect public health.

A key point to be addressed in the near future is the surge capacity. This is a healthcare system's ability to rapidly expand beyond normal services to meet the increased demand for qualified personnel, medical care, and public health in the event of the release of biological agents or other large-scale public health emergencies or disasters. To build an effective surge capacity, INMI is currently developing innovative educational programs to create and maintain the readiness of an appropriately trained workforce. Its goal is to help healthcare workers change their focus from the traditional clinical oriented view of infectious disease treatment to a more integrated, problem solving, infection control management approach that should be relevant during a large scale emergency response situation.

Finally, we strongly believe that uniting as is the case for INMI, the people and facilities involved with clinical care and those that promote public health in a single institution, enhances cooperation, encourages the interchange of information and provides high quality clinical care to all patients.

Acknowledgment

Performed within the Ministero della Salute Ricerca Finalizzata 01.102 e Ricerca Corrente IRCCS. The authors wish to thank Dr. Andrea Stoler for the editing of the manuscript.

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ORIGINAL ARTICLES

Surveillance report

SUSPECTED SARS PATIENTS HOSPITALISED IN FRENCH ISOLATION UNITS DURING THE EARLY SARS EPIDEMIC: THE FRENCH EXPERIENCE

B Issartel[1], O Lesens[2], C Chidiac[1], Y Mouton[3], D Christmann[2], D Peyramond[1] and members of the French SARS study group*

During the SARS epidemic, many patients were screened according to WHO criteria but never went on to develop SARS. In May 2003, early in the epidemic, we conducted a retrospective study to describe suspected SARS patients hospitalised in France and compared them with documented cases of patients with SARS to evaluate the screening strategy. A total of 117 patients were studied. Only 3.4% had been in close contact with a SARS patient but 73.5% came from an affected area. 67.5% had fever and respiratory symptoms on their admission to hospital. 49.6% had fever and non specific symptoms. Clinical symptoms that were significantly more common among patients with SARS were fever, myalgia, dyspnoea, and nausea or vomiting. Presumed viral fever and respiratory tract infection were the most common diagnosis. Symptoms cannot be distinguished from an early stage of SARS confirming the usefulness of the WHO case definitions in isolation decision to avoid further transmission

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Euro Surveill 2005;10(3):39-43 Published online Mar 2005

Key words: diagnosis, infection control, patient care management, SARS virus, screening