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REVIEW ARTICLE

The Initial Hospital Response to an Epidemic

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The last decades have been characterized by the appearance of a substantial number of newly recognized or novel infectious agents and by the re-emergence of infectious diseases with a global impact. The objective of this article is to briefly describe the model of hospital response for early diagnosis and prompt management of patients with highly contagious infectious diseases. We reviewed the main components of hospital preparedness in response to clustering of highly contagious diseases. A model for the initial hospital response to an epidemic in our referral Institute is discussed. Prompt recognition and identification is the initial and indispensable step in facing any communicable diseases, regardless of whether it is a prevalent, a newly emerging one or deliberately released. The importance of developing and implementing nontraditional methods of public health surveillance and a system that allows a wide and immediate dissemination of information and exchange of views on risk assessment and risk management are highlighted. Case identification and laboratory capabilities and isolation procedures are the essential components for an initial hospital response. The recent bioterrorist events and the worldwide outbreaks of highly contagious infectious diseases have evidenced the need for institutional preparedness at each hospital and for identification of referral centers for patient isolation and of laboratories with adequate capabilities. Moreover, hospitals should develop a plan for coordinating all hospital components to respond to critical situations deriving from the admission of patients with highly contagious infectious diseases. © 2005 IMSS. Published by Elsevier Inc.

Key Words: Hospital, Preparedness, Emerging infectious diseases, Surveillance, Communication.

Introduction

The last decades have been characterized by the appearance of a substantial number of newly recognized or novel infectious agents and by the re-emergence of infectious diseases with a global impact (1). Among them are included novel agents such as HIV and the human variant Creutzfeldt-Jakob Disease (2), re-emerging organisms such as those responsible for outbreaks of viral hemorrhagic fevers (VHF) in Africa (3–5), as well as those related to bioterrorism such as the deliberate release of anthrax in the U.S. (6). Moreover, expanding international travel has enhanced the movement and the speed of diffusion of infectious agents, as dramatically

demonstrated by the epidemic observed in 2003 due to the novel SARS-associated coronavirus (7,8).

Agents with a potential severe and pandemic impact such as the avian influenza virus H5N1 currently circulating in Asia are under surveillance (9–11). Almost all of these infectious diseases have a significant link to the hospital setting that often represents the case of resonance for community epidemic events. Hospitals serve as important settings for identification of these threatening agents and play important roles in addressing these threats.

The objective of this article is to briefly describe the model of hospital response for early diagnosis and prompt management of patients with highly contagious infectious diseases, their recognition in case of clustering among hospitalized patients, and the infection control procedures to minimize the risk for the healthcare workers and the spread to the community. Moreover, the model of a referral hospital for the management of highly contagious diseases will be presented.

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Steps towards a Correct Hospital Response to an Epidemic

Recognition and Surveillance

Prompt recognition and identification is the initial and indispensable step in facing any communicable disease, regardless of whether it is a prevalent, a newly emerging one or deliberately released. Whether in the community or in the hospital setting, early detection of the occurrence of any communicable or infectious diseases rests on the primary healthcare worker who recognizes the first unusual patients. Indeed, before any response can be mounted, the event has to be detected, recognized and then identified as requiring special action. Detection requires clinical awareness, timely surveillance and often cleverness.

The importance of developing and implementing nontraditional methods of public health surveillance has been recently highlighted in view of the increasing concern related to the emergence and re-emergence of naturally occurring or deliberately delivered transmissible diseases.

Several surveillance systems have been proposed. Advantages and disadvantages of these different systems have been previously reviewed (12–16).

Apart from ongoing surveillance systems, several of the recent outbreaks were first suspected and brought to the attention of the public health officials by astute clinicians who identified a cluster of cases among in-patients and an epidemiological or microbiological or clinical link between these cases.

Several recent major outbreaks have been brought to the attention of public health authorities when unusual clustering of illness was recognized in hospitalized patients. This was the case of the recognition of unusual incidence of *Pneumocystis jiroveci* pneumonia among in-patients that prompted the identification of the HIV/AIDS epidemic in the early 1980s (17).

After the 1976 outbreak of Legionella infections in Philadelphia (18), several outbreaks were identified, thanks to the recognition of unusual clustering, including an outbreak occurring on a passenger cruise ship (19).

In the outbreak of Hantavirus pulmonary syndrome in 1993 in the southwestern U.S. (20), a clustering of cases was observed by the Indian Health Service, and physicians were requested to report cases meeting the clinical case definition that was adopted.

In the large outbreak of *Escherichia coli* O157:H7 infections in the state of Washington, recognition by the hospitalization of multiple patients with hemolytic-uremic syndrome was crucial, and public health surveillance through state-mandated reporting of *E. coli* O157:H7 infection as was carried out in the state of Washington was critical for prompt outbreak recognition and control (21).

Hospital administrators should be aware of the need for establishing hospital surveillance aimed at early detection

of cases and clusters of severe unexplained infections that might signal the emergence or re-emergence of public threat. Focus of this kind of surveillance is represented by transmissible diseases clustering and by novel or unusual illnesses, even as sporadic case. Unusual illness may (a) occur in patients presenting with signs or symptoms that do not fit any recognizable clinical picture, (b) be of known etiology but not usually expected to occur in a specific geographical area or setting where it has been observed, (c) show unexpected behavior, e.g., failure to respond to standard therapy, or (d) be of unknown etiology.

An outbreak is said to occur where the number of cases observed is greater than the number expected over a given time period, and cases are linked by epidemiological or microbiological features.

Whenever hospital health professionals are involved with cases of an unusual illness, reporting to national authorities should follow local regulations. Certain prescribed diseases, including cholera and yellow fever, are subject to the International Health Regulations reporting guidelines. The local health authority forwards the initial report to the next superior jurisdiction.

A system that allows a wide and immediate dissemination of information and exchange of views on risk assessment and risk management is crucial for timely public health action. In this regard, an important lesson derived from the multi-country outbreak of SARS. The disease originated in November 2002 from Guangdong province in China and emerged only after some months when the World Health Organization (WHO) launched an international alert in February 2003. Soon after the alert, as a direct result of globalization, several countries and regions notified of cases of SARS.

As of July 2003, when the WHO announced the containment of the epidemic, a total of 8,500 cases and 916 deaths had been reported; the major impact was sustained by southeast Asian countries and Canada. The severe consequences of the few months lost because of delayed notification have been stressed by the exceptional results obtained after the international community become aware of the SARS threat. Indeed, the prompt identification of a novel coronavirus as the etiologic agent of SARS and the implementation of hospital-based, national and international control measures demonstrated the power of coordinated integration of efforts and capabilities and of shared information.

As the first epidemic ended, scattered new cases have been promptly reported, and a surveillance system proposed to promptly highlight a possible re-emergence of the disease (22–25).

In the last years a great opportunity derived from the exploitation of the speed and ubiquity of the Internet to serve as an early warning system for the detection of emerging disease outbreaks. Several web sites are available to help health professionals and consumers find current, accurate information on the topic and should be consulted daily by dedicated hospital personnel (26–28). In fact, the World

Wide Web provides a plethora of information on infectious diseases; unfortunately, not all of it is reliable.

Examples of widely used, timely and reliable Web sites are those from the WHO and the U.S. Centers for Disease Control and Prevention, Atlanta, GA (CDC). A useful tool is represented by the International Society for Infectious Diseases Web site, Program for Monitoring Emerging Diseases (ProMED).

ProMED receives reports on outbreaks or unusual cases of infectious diseases, whether natural or intentionally released, that affect humans, animals and plants. Reports are carefully screened for validity and are placed in an appropriate context by commentary and references from a panel of expert moderators. Reports are then posted to the Web and available to users free of charge (29).

Another pillar of international infectious diseases control is the European Network for the Surveillance and Control of Communicable Diseases and its Early Warning and Response System (EWRS <http://webgate.cec.eu.int/ewrs/>). The EWRS is a telematic system linking the designated authorities in Member States and the Commission, to alert public health authorities on outbreaks with greater than national dimensions, so that a co-ordinated European Union (EU) action may be required.

The Decision No. 2119/98/EC of the European Parliament and of the Council of 22 December 1999 on the early warning and response system for the prevention and control of communicable makes it clear that all events that could lead to outbreaks of EU-wide significance should be reported under the EWRS irrespective of whether or not a disease-specific network at EU level has been set up. Depending on the specific situation, the Commission and Member States agree on the appropriate action to be taken individually or together. The system allows for immediate exchange of views on risk assessment and risk management crucial for timely public health action (30).

A non-negligible issue of the outbreak management attains to communication to public opinion through media. Indeed, outbreaks are frequently marked by uncertainty, confusion and a sense of urgency. The overriding public health goal is to bring the outbreak under control as quickly as possible, with as little social disruption as possible.

Effective outbreak communication is one tool to achieve that goal. Unfortunately, examples abound of communication failures that have undermined public trust and compliance, as well as unnecessarily prolonged economic, social and political turmoil (31,32). As part of hospital preparedness and management planning, an outbreak communication plan should be ready from the start.

The WHO believes it is now time to acknowledge that communication expertise has become as essential to outbreak control as epidemiological training and laboratory and recently issued specific guidelines to manage public and media outbreak communication (33).

Initial Management of Hospitalized Cases

The case definition developed by health authorities at the beginning of an alert represents the first tool that a hospital should adopt in order to implement timely and appropriate diagnostic, clinical and infection control measures.

Of intuitive primary importance in this regard is the role of hospital emergency departments that may be the first link where suspected patients related to an alert can refer, as well as the first to recognize unusual illness (16,34,35).

Moreover, high-quality clinical microbiology laboratories capability should be available on site or identified as referral labs for the timeliness of diagnosis, and early detection of infectious disease outbreaks should be addressed. Proper specimen collection, transport, nucleic acid processing, molecular assay diagnostic reagent and equipment development, and standardization for sensitive and rapid detection of bioagents in blood and other clinical samples should be addressed. Combinations of appropriate diagnostic technologies (culture, immunoassay, and molecular assay) can provide rapid diagnostic response capabilities to microbial threats with antimicrobial resistant organisms, new emerging infectious disease agents, and possible agents of bioterrorism (36–38).

Decisional algorithms for the diagnostic management of suspected, probable or confirmed cases should be developed taking into account available knowledge. Concerns that unusual or eradicated diseases might reappear and limited clinical experience with their diagnosis prompted many clinicians to design clinical algorithms. An algorithm is a step-by-step instruction for solving a problem. Several algorithms have been proposed for emerging and re-emerging highly contagious infectious diseases.

In the case of smallpox, Seward et al. used clinical features of classic smallpox to classify persons presenting with suspected smallpox rashes into three categories: those with high, those with moderate, and those with low risk of having smallpox. The classification guides subsequent diagnostic strategies, limiting smallpox laboratory testing to high-risk persons to minimize the number of false-positive test results. In their experience at CDC, the algorithm worked well to guide clinical and public health responses to suspected smallpox cases and was recommended elsewhere (39).

For inhalational anthrax (IA), an algorithm seems more difficult to design because the decision criteria should be based on the limited knowledge of the clinical presentation in the reported cases for the literature. Hupert et al. proposed a method to screen for IA by quantifying differences in clinical presentation between IA anthrax and common viral respiratory tract infections. Review of case reports of IA and epidemiologic studies of influenza and other viral respiratory infections were used for this purpose. In their study, IA had characteristic clinical features distinct from those seen in common viral respiratory tract infections.

Screening protocols based on these features might, therefore, improve rapid identification of patients with presumptive IA in the setting of a large-scale anthrax attack (40).

On the other hand, Mayer et al. proposed to modify the CDC-issued interim guidelines for clinical evaluation of persons with possible IA (41) on the basis of the epidemiological, clinical, laboratory, and radiologic findings of the 11 patients with bioterrorism-related IA during their first visit to a physician. Whereas the CDC guidelines would not have identified 10/11 of these patients, the proposed extensions of the guidelines retrospectively identified 8/11 of the patients with IA (42). In a recent article, Howell et al. compared the two methods proposed to screen for IA, applying them to the emergency department charts of patients who presented with possible signs or symptoms of IA at a hospital. Applying the Mayer criteria would have identified both patients with IA and would have generated fewer charges than applying the Hupert criteria (\$13,325 vs. \$126,025 USD) (43).

In the early phase of the SARS epidemic, given the non-specific presentation of the disease and lack of diagnostic methods, case definitions were proposed that combined epidemiological and clinical features (44,45). When a diagnostic tool became available, this was incorporated in a panel of laboratory assays to be used in case of high suspicion of SARS (46).

A similar approach that takes into account a complete panel of classic lab methods and biomolecular assays should be adopted in case of diseases characterized by a syndromic presentation, such as respiratory and diarrheal illnesses (47).

An epidemiological (mostly the geographical area of interested by the outbreak), clinical and laboratory-based case definition should be adopted for the purpose of surveillance and management of VHF suspected cases, as well as contacts (48).

In the U.S., the CDC provides support to local health care institutions, including hospitals, in case of national and international needs. With a similar aim, in Spring 2004 the Council and the European Parliament adopted enabling legislation to create a European Centre for Disease Prevention and Control (ECDC). This new EU agency will provide a structured and systematic approach to the control of communicable diseases and other serious health threats that affect European Union citizens. The ECDC will also mobilize and significantly reinforce the synergies among the existing national centres for disease control (49).

Hospital Isolation Measures

Whenever the alert is done, the hospital infection control unit should be promptly notified in order to organize an appropriate response and management.

A crucial step in the containment of an outbreak in a hospital is the implementation of proper isolation procedures. Each health care institution should have issued protocols to implement standard as well as transmission-based

precautions, as recommended by health care-associated infection control guidelines (50).

These protocols should be reinforced all over the hospital in the case of national and international alert, also through educational initiatives, and integrated with specific recommendations issued by International Health authorities. For example, a new addition to the recommendations for Standard Precautions is called Respiratory Hygiene/Cough Etiquette, and grew out of observations during the SARS epidemic for a better control of droplet transmission of communicable diseases in the hospital setting with particular regard to the emergency and triage areas (51,52).

Finally, surveillance of healthcare and laboratory workers exposed to highly transmissible patients or specimens and post-exposure protocols must be issued as an essential component of hospital response. In this context, the WHO has recommended the implementation of a SARS alert system in the post-epidemic period that involves surveillance of clustered cases of pneumonia among healthcare workers (HCW). This proposal is based on the consideration that occupational transmission among HCW has been a striking feature of the SARS outbreak (24).

Similar recommendations were also issued by the CDC (53). A plan for referral of suspected or confirmed cases of highly contagious and public threatening infectious diseases to a hospital provided with a higher infection control capability should be implemented, when necessary.

A model for the initial hospital response to an epidemic in a referral center "Lazzaro Spallanzani" National Institute for Infectious Diseases, Rome, Italy has been identified by the Italian Ministry of Health as the national referral center for the management of patients affected by highly transmissible infectious disease, including naturally transmitted diseases and cases of deliberate release of biological agents (54).

The Institute consists of a modern three-floor acute care hospital complex and two buildings where research and laboratory facilities are located. The hospital has 256 beds in seven wards, 48 beds in day hospital care, and 20 intensive care beds. All wards are provided with single or double rooms, with an air conditioning system that is able to provide up to 12 air changes per hour. All rooms have private baths and a fully equipped anteroom and are equipped with well-sealed doors and HEPA filter on the incoming as well as exhausted air flow. The anterooms contain supplies for routine patient care, protective barriers for personnel and hand washing facility. Moreover, the system also allows changes from negative to positive room pressure and vice versa, in order to use the rooms for airborne isolation or as a protective environment. All rooms are potentially suitable for isolation or cohorting according to adopted airborne, droplet and/or contact precautions.

In addition, a high isolation unit has been created for the management of sporadic cases of highly contagious infectious diseases such as VHF or smallpox. The unit consists of

two private rooms and a biosafety level (BSL) 3 laboratory. Inside the hospital building, imaging and pathology services provide support to clinical activities. Both laboratory facilities are separate from the hospital and are provided with a total of four BSL 3 and one cabinet BSL 4 laboratories.

The Institute preparedness plan states that dedicated personnel should consult the above-mentioned Web sites daily for infectious disease news worldwide. An infection control team is active to provide support for the management of emergencies, when necessary.

In case of admission of patients with suspected or documented highly contagious infectious diseases referred to our Institute from the airport, ports or other hospitals, a dedicated pathway with a separate entrance from daily hospital activities has been designed.

The Institute is equipped with two high-containment ambulances for transportation of highly contagious patients, with a sealed negative pressure section for the patient area and HEPA filters for air exhausting. Two stretcher isolators (Vickers Medical Containment Stretcher Transit Isolator®, Isolators Ltd., Shropshire, UK) are also available for transportation of patients with highly infectious diseases. The self-contained isolation system consists basically of a light-weight stretcher onto which is attached a demountable framework supporting a transparent plastic envelope. The plastic envelope has a negative pressure differential with respect to the atmosphere, which is maintained by an air supply system in order to avoid the exit of potentially contaminated air.

Isolation procedures are implemented from the time of admission, where a triage area with a negative air pressure room is dedicated to patients presenting syndromes of a suspected airborne infection, and Respiratory Hygiene/Cough Etiquette recommendations are already ongoing.

At Spallanzani Institute, hospital isolation measures and universal precautions have been implemented since the mid-1980s, after the spread of HIV. The hospital infection control protocols, largely based on the Hospital Infection

Control Practices Advisory Committee guidelines on isolation precautions in hospitals (50), have been further reinforced, strengthened and updated in the following years to deal with the re-emergence of tuberculosis and the management of SARS, anthrax, and VHF crisis (55,56).

Disposable personnel protective equipment (PPE) consisting of masks or respirators, gloves, gowns, hair and shoe covers, and eye-wear are available. PPE recommended for the management of highly contagious patients are Tyvek tissue full-body suits with thermo-activated closure, full face mask with P3 filtered respirators, and latex obstetric gloves to be used in double gloving.

Multiple educational and training sessions on adherence to infection control protocols have been developed for health care and laboratory personnel.

Transport, collection and handling of samples follow biosafety level procedures, according to WHO (57).

In addition to routine microbiological tests (i.e., serological commercial and in-house assays, direct identification, and culture), several multi-diagnostic panels based on modern biomolecular technology have been developed, and electron microscopy is available (Table 1).

For example, respiratory clinical specimens can be timely analyzed by PCR or RT-PCR for the presence of different viruses (influenza A and B, metapneumovirus, adenoviruses, parainfluenza 1, 2 and 3, RSV, rhinovirus), including old and novel coronaviruses (coronaviruses OC43, 229E, NL63, New Haven and HKU1), as well as *Chlamydia*, *Mycoplasma pneumoniae* and *Legionella pneumophila* (58).

Conclusions

The recent bioterrorist events and the worldwide outbreaks of highly contagious infectious diseases have evidenced the need for institutional preparedness at each hospital, for identification of referral centers for patient isolation and of laboratories with adequate capabilities. Moreover, hospitals

Table 1. Diagnostic capability for relevant viral imported diseases at the National Institute for Infectious Diseases L. Spallanzani, Rome, Italy

Viruses	IFA	EIA	NT	PCR	SEQ	VI	WB	CF
Arenaviruses: Old & New World				–	–	–		
CCHF				–	–	–		
Dengue	–			–	–	–		
Filoviruses: Ebola & Marburg				–	–	–		
Hantavirus				–	–	–	–	
Old World Orthopoxviruses			–	–	–	–		
Polioviruses 1,2,3			–	–	–	–		–
SARS CoV	–	–	–	–	–	–		
West Nile Virus	–		–	–	–	–		
Japanese Encephalitis	–		–	–	–	–		
Tick-Borne Encephalitis	–		–	–	–	–		
Yellow Fever Virus	–		–	–	–	–		

IFA, immunofluorescence assay; EIA, enzyme immunoassay; NT, neutralization test; PCR, polymerase chain reaction; SEQ, sequencing; VI, virus isolation; WB, Western blot; CF, complement fixation; EM, electron microscopy.

should develop a plan for coordinating all hospital components to respond to critical situations deriving from the admission of patients with highly contagious infectious diseases. In our article, we reviewed the main components of hospital preparedness in the initial response to sporadic or clustered highly contagious diseases, and illustrated the model of the “Spallanzani” Institute for coping with the challenge posed by emerging and re-emerging agents.

Reporting to public health authorities by hospital doctors, infection control professionals and lab personnel of unusual infectious diseases, either sporadic or unusual clustering of illness in hospitalized patients, may serve as an early alert for prompt public health action and management in case of an epidemic risk.

Moreover, active surveillance and participation in sentinel hospital networks should be encouraged by public health authorities in order to strengthen the capability to promptly identify community and hospital-acquired epidemics.

Additionally, healthcare settings represent the frontline for reducing the emergence and spread of infectious diseases through the application of strict infection control practices, patient and HCW education, and provision of preventive measures.

Finally, in the near future the surge capacity that is a health care 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 large-scale public health emergencies or disasters, should be strengthened. Therefore, a host of issues including education, communication, and institutional response require innovative solutions. For this purpose, innovative educational programs to create and maintain the readiness of an appropriately trained workforce are necessary in order to help HCWs change their focus from the traditional clinically oriented view of infectious disease treatment to a more integrated, problem solving, infection control management approach.

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