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REVIEW

Bioterrorism: practical aspects

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Although biological weapons have been used since ancient times, general fear and the concerns of Western governments over the possibility of bioterrorist attacks have meant that this subject has received unparalleled attention in the past decade. The main characteristics of a biological weapons attack are high yield at low cost, extensive socioeconomic repercussions and press coverage, the potential to generate panic in the population, and ease of creating and hiding the weapon. Biological agents may be released openly, announcements or warnings may be given, they may be distributed selectively, or they may be hidden before release. The United States Center for Disease Control has described more than 150 agents as potential biological weapons, classifying them in 3 groups according to risk, impact on public health, impact on the economy, and availability or ease of manufacture. This review summarizes the epidemiologic, diagnostic, clinical, therapeutic, and prophylactic aspects of bioterrorism. [Emergencias 2010;22:130-139]

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Introduction

A bioterrorist attack consists of the intentional dissemination of microorganisms, or of substances of biological origin, that are pathogenic for human beings, in order to cause panic or economic and / or health damage by causing death or disease in humans, animals or plants[1].

One of the growing concerns of many governments in the last decade is the potential use of biological weapons and bioterrorism. The first historical references date back to the sixth century BC when the Assyrians used the fungus *Calviceps purpurea* to pollute and poison the water supply of their enemies[2]. In medieval times, to contaminate the water supplies of a besieged city, cadavers or contaminated sheets were used for the spread of disease[3]. About the year 1346, the Tartars catapulted corpses of plague victims into the Kaffa city during its siege and conquest[2,4].

The potential effects of a well designed biological attack can be devastating for a community, causing morbidity and mortality, depletion of regional health resources and disarray of the system due to the fear and terror generated in the population. Unlike biological warfare that seeks to cause the greatest possible number of enemy casualties, in a bioterrorist attack the goal is to instil fear and uncertainty in the society. Bioterrorism is a form of "asymmetric threat" where an act causing a small number of casualties can have a major social impact or even world political and economic repercussions[1,5]. This effect on the population was manifest in a particular way in the USA and had world-wide impact in October 2001: envelopes contaminated with anthrax endospores were sent through the U.S. postal system, causing disease in 22 people and death in 5 people[3,5,6].

Although the morbidity and mortality caused by bioterrorist attacks is currently low, the potential of a biological weapon is tremendous. To illustrate this potential, if a plane at 6,600 feet were to disseminate 50 kg of Bacillus anthracis spores in an aerosol form over a town with 500,000 inhabitants under adequate weather conditions, 220,000 people would be infected; if *Francisella tularensis* (biovar *tularensis*) were used, only 5 kg would be necessary to obtain similar results[7,8]. The American Agency for Technology Assessment has estimated that the spread of 100 kg of anthrax over Washington could kill between 1 and 3 million people, while similar calculations show that detonation of a 1-megaton nuclear head in the same city would cause the death of 759,000 - 1.9 million people (NATO and Carus, W. S. Center for counterproliferation research, Washington DC. National Defense University. 1999).

A given organism may be considered a potential bacteriological weapon depending on certain intrinsic and extrinsic characteristics (Table 1). An adequate combination of both modulate the morbidity and mortality potential of the biological agent that may cause a catastrophe. The strategies used to optimize the harmful effects of these agents of biological warfare are known as "weaponization". They include genetic modifications to increase antimicrobial resistance or to overcome the human immune system. Other modifications are aimed at prolonging stability in the environment, enhancing infectivity and / or altering host resistance by altering membrane proteins[3].

In 1972 the Biological and Toxin Weapons Convention Treaty outlawed research and development of biological weapons worldwide. Since then there has accumulated evidence of violations of the treaty by numerous governments[3].

In recent years, growing concern about possible bioterrorist attacks has been reflected in the increased number of publications with the terms "bioterrorism" or "biodefense" in the title. Using these two words as search items in the medical literature of the world's largest database PubMed, National Center for Biotechnology of the U.S. National Library of Medicine, we found 142 hits in the last 10 years, of which 108 are from the latest five years (accessed in January 2008).

Since October 2001, Europe has set up different epidemiological monitoring and response to emergent infectious diseases[9]. After the creation in 1998 of the Network of Epidemiological Surveillance and Communicable Disease Control, there emerged, in 2002, the DG-SANCO (Directorate General for Health and Consumer Protection of the European Commission) which coordinates activities between the different member states and includes European networks, including: EURONET-P4 (European Union Response Network for P4 Virus Infections), ENIVD (European Network for Diagnostics of Imported Viral Diseases) and GHSAG (Global Health Security Actin Group Laboratory Network) (http://europa.eu.int/comm/etwo/ph_threats/com/comm_diseases_networks_en.htm).

Among the tasks of the monitoring system is early detection and adoption of prophylactic measures and control in the event of a bioterrorist attack. In addition, the World Health Organization (WHO) has a Department of Communicable Disease Surveillance and Response, CSR) and a Global Outbreak Alert and Response Network, GOARN). One of the most recent measures, taken in April 2004 by the European Parliament and Council was legislation creating an independent agency, the European Centre for Disease Prevention and Control, ECDC) based in Stockholm as of May 2005[1].

In Spain, apart from epidemiological monitoring networks, there are local and central rapid response units for situations of health emergencies, based at the Carlos III Health Institute (created by the Ministry of Health in 2003)[1]. It is the responsibility of the emergency services to be prepared to provide an appropriate response in the event of a bioterrorist attack[10].

Table 1. Key features and factors that allow a biological agent to be used as a biological weapon.

Features of a biological agent
– Resistance and stability in the environment.
– High virulence and low infective dose.
– High morbidity and mortality, with or without treatment.
– Possibility of person to person transmission.
– Possibility of dissemination (vectors, pets, etc.)
– Unusual treatment or no treatment available.
– Potential to cause serious public health impact.
– Ability to generate panic and social disruption.

Extrinsic characteristics
– Climatic and environmental conditions.
– Lack of simple, rapid, low-cost detection/diagnostic techniques.
– Ability to obtain and produce the pathogen.
– Difficulty in obtaining effective treatment quickly and on a large scale.
– Existence of previous research and easy access to documentation.
– Level of public health development and existence of surveillance systems
– Immunological status of the target population.
– Lack of universal effective vaccination.

Characteristics of Biological weapons

Biological weapons constitute an instrument for blackmail by a terrorist organization (TO) for a number of reasons:

– They offer high return, with low cost and high social, economic, health and media impact. According to the UN, in a large-scale operation against civilians, the cost of generating such victims would be about $ 2,000 per square mile if the weapons used were conventional, $ 800 with nuclear weapons, $ 600 with nerve gas and only 1 dollar if biological weapons were used.

– A weapon that is "unseen" by the target population generates more panic.

– They are relatively easy to produce and to hide[11].

– Spraying in aerosolized form is not unduly complicated[11].

– The target population itself requires a large amount of resources to deal with the attack.

The main forms of media coverage are:

– The agent is self-evident.

– The attack is announced beforehand by the TO.

– The selective use of letters, packages or property treated with aerosol.

– Covert, with a hidden source of dispersion.

All dissemination methods depend on the biological agent, intended objectives, the intended scale of the attack, etc.. Among others, there are: aerosols, dust clouds, food and water pollution, fomites and other objects, vectors such as mosquitoes or fleas, etc. If the agent can be transmitted person-person or there are transmission vectors, the effects can be multiplied[11,12].

Classification

More than 150 agents have been described as potential bioterrorist weapons[13]. The CDC has three categories of such agents: A, B and C[14,15] which are detailed in Table 2.

Table 2. Classification of biological agents A, B and C according to the Atlanta Center for Disease Control (CDC)

Category	Agent	Clinical picture
A	*Bacillus anthracis*	Anthrax
	Clostridium botulinum	Botulism (botulinum toxin)
	Yersinia pestis	Plague
	Variola mayor	Smallpox
	Francisella tularensis	Tularemia
	Filoviruses: Ebola virus	Haemorrhagic fever
	Marburg virus	
	Arenavirus: Lassa virus	
	Machupo virus	
B	*Brucella sp*	Brucellosis
	Clostridium perfringens	Poisoning (epsilon toxin)
	Salmonella sp	Safety Threat food and
	Escherichia coli O157:H7	water
	Shigella	(Infection)
	Vibrio cholerae	
	Cryptosporidium parvum	
	Burkholderia mallei	Glanders
	Burkholderia pseudomallei	Melioidosis
	Chlamydia psittaci	Psittacosis
	Coxiella burnetii	Q fever
	Ricinus communis	Poisoning
	(Castor beans)	(ricin toxin)
	Staphylococcus aureus	Poisoning (enterotoxin B)
	Rickettsia prowazekii	Typhus
	Alphaviruses:	
	Venezuelan equine encephalitis	viral encephalitis
	Eastern equine encephalitis	
	Western equine encephalitis	
C	*Nipah Virus*	Emerging Infectious
	Hantavirus	Diseases
	SARS etc.	

SARS: severe acute respiratory syndrome.

Diseases/category A agents

These are top priority agents - organisms that pose a risk to national security because:

– They can be easily spread or transmitted from person to person.

– They have a high mortality rate and very high potential to cause serious impact on public health.

– They could cause panic in the civilian population and give rise to serious social unrest.

– They require special action to achieve levels of readiness in the health system.

A summary of the agents in this category with some of their characteristics is given in Table 3. Because of its importance and recent use as a bioterrorist weapon, we will briefly elaborate on anthrax (*Bacillus anthracis*).

Anthrax is an acute disease caused by *Bacillus anthracis.* Historically, human anthrax is a disease contracted through contact with animals or food contaminated by a spore or endospore (infective form) of *B. anthracis.* In the environment the endospore can be found in soil and plants, and remains viable for decades, infecting animals, normally herbivores[7].

Since World War II, anthrax is considered as the prototype agent of bioterrorism by some authors. The endospores can be used as a biological weapon because of their resistance in the environment and small size. Coating with an additive facilitates suspension in the air and consequent inhalation, as well as increasing contagious capacity. The potential as a weapon was revealed in 1979 during an accident in which endospores were dispersed into the atmosphere from a biological weapons facility in Sverdlovsk, Russia. Despite early chemoprophylaxis, there were at least 77 cases of anthrax in an area of 4 square km, with 66 deaths[16]. In 2001, there were 22 confirmed cases of anthrax in the U.S., 11 due to inhalation and 11 by cutaneous route[6].

The causative agent of anthrax, belongs to the genus Bacillus, is elongate with concave edges (1 -1.5 μm wide x 3-10 μm in length), aerobic, Gram +, sporogenic, immobile and non-hemolytic in blood agar. The spore measures 1 micron, is resistant to dehydration, heat, ultraviolet radiation and many disinfectants. It contains three proteins that produce two lethal exo-toxins (edema toxin and lethal toxin)[17]. Three different clinical pictures have been observed:

Inhalation Anthrax: Incubation period: 2-43 days, the endospores can remain dormant in the respiratory tree for weeks. The clinical picture begins with a prodrome of malaise and dry cough, after 24 hours this is followed by a flu-like symptoms, including fever, malaise, fatigue, cough, dyspnea, headache, anorexia, and chest pain. This phase lasts from hours to about three days and if left untreated, patients develop sudden increased fever, severe dyspnea, profuse sweating, evolving to shock and death. Untreated mortality is 90%[17]. After inhalation, the endospores in the lower respiratory tract are ingested by macrophages and transported to the hilar and mediastinal lymph nodes, where they germinate and produce necrotizing hemorrhagic mediastinitis[7]. Chest radiography typically shows mediastinal enlargement (70%), interstitial infiltrates (70%) and pleural effusion (80%). No cases of person-to-person transmission of inhalational anthrax have been described[17].

Cutaneous anthrax: This represent 95% of natural cases of Anthrax. After contact, the bacteria incubate during 1-5 days[17]. The wound is shaped like a small papule or macule and is painless. On the second day it turns into a vesicle from 1 to 3 cm and then an ulcer. After 2 to 6 days it shows the typical black scab with surrounding edema; the scab falls off after 1 to 3 weeks with 80% of cases being cured. Any fever is due to infection of the lesion or systemic spread of bacteremia (20% of cases). Without antibiotic treatment, mortality is 20%, but less than 1% in treated cases[17].

Gastrointestinal anthrax: This appears after consumption of infected food, raw or undercooked. There are two forms: oropharyngeal and abdominal. After 1-7 days of incubation, fever begins with nausea, vomiting, loss of appetite, pain and diarrhea. The disease evolves rapidly to bloody diarrhea, acute abdomen, shock and death after 2-5 days of the onset of symptoms. Early diagnosis is difficult and mortality is above 50%[17].

Meningitis can be a complication of any form of Anthrax and is usually fatal. Cerebrospinal fluid (CSF) is frequently hemorrhagic with polymorphonucleii, elevated proteins, reduced blood sugar and decreased gram + bacilli[17].

Cutaneous Anthrax is easily diagnosed when the necrotic scab appears. Early diagnosis of the other forms of the disease is more difficult[17]. An athrax attack is suspected when faced with many simultaneous cases with symptoms of severe lung disease. If possible, one should take blood and biological samples for lab culture (CSF, pleural effusion and pleural biopsy, bronchial and skin samples) before the administration of antibiotics, since the results of these tests are the most useful diagnostic method. Positive cultures are obtained within 24 hours. The gram-positive bacillus, pre-identified as belonging to the genus Bacillus in the context of meningitis, pneumonia or sepsis should be assessed as a possible Anthrax and should be sent to a reference laboratory for investigation of the strain and whether it has been manipulated. Anthrax is not ruled out by testing sputum and nasal smear[18]. Fever and widened mediastinum in imaging are highly suggestive of anthrax.

Direct immunofluorescence is used for quick identification of *B. anthracis.* Culture or PCR provides diagnostic confirmation. Serological techniques serve only in retrospect.

For the (CDC) definition of a case, the following criteria are used:

Possible: Not applicable.

Probable: Clinical symptoms compatible with anthrax, without isolation of *B. anthracis* or other diagnostic test confirmation, but with a positive laboratory test. Clinical symptoms compatible with previous and confirmed epidemiological environmental exposure without laboratory test results.

Confirmed: Clinical symptoms compatible with anthrax and confirmed by laboratory tests.

Deliberate: More than one confirmed case of inhalation Anthrax, or more than one case of cutaneous Anthrax without natural epidemiological factors, or more than 2 suspected cases of Anthrax linked in time and space, especially groups of patients in the same direction of the wind.

According to the CDC and the American Society of Infectious Diseases, a patient with suspected of anthrax and with symptoms requires immediate treatment, without waiting for confirmatory laboratory test results. Although the treatment of choice is penicillin, this is not indicated in the case of suspected intentional infection, since it is not difficult to select resistant strains in the laboratory. So far, there are reports of resistance to quinolones, and ciprofloxacin as the treatment of choice[19,20] (Table 3).

Chemoprophylaxis (also for cutaneous or inhalation anthrax in the context of multiple victims where intravenous administration is not feasible) consists of oral ciprofloxacin 500 mg every 12 h (10-15 mg / kg / dose for children) or oral doxycycline 100 mg every 12 h (2.2 mg / kg / dose for children). This must continue for 60 days or until the confirmation of non-exposure. Postexposure vaccination can reduce the number of days required to medical prophylaxis.

It has been shown that antibiotic treatment one day after inhaling a lethal dose of *B. anthracis* aerosol reduces mortality considerably[21].

Currently there is an anthrax vaccine consisting of a sterile, filtered non-infectious suspension of an attenuated strain of *B. anthracis.* Although it is well tolerated and effective, it requires several administrations and the duration of protection is low (88% protection in 100 weeks). In Spain, this vaccine is only available at a military level. Now work is under way on a new vaccine with recombinant protective antigen. Vaccination of personnel at risk is recommended (laboratory and military workers) and of the target population after an attack[17].

For infection control, decontamination and inactivation of spores is required[22]. Patients do not require isolation measures; only cutaneous anthrax can be transmitted by direct contact in the first few days, so standard precautions constitute a sufficient barrier. There is no need for contact immunization or prophylaxis, only in those exposed[17]. Disclosure of cases is mandatory to epidemiology services and the health authorities.

Diseases / Category B agents

These occupy second place in terms of priority and are characterized by being moderately easy to disseminate; they are associated with moderate morbidity and low mortality rates but require specific advances in diagnostic capacity and disease surveillance on the part of the health system. As an example of bioterrorist attack with a category B agents, in 1984 the members of a religious cult intentionally used Salmonella typhimurium to contaminate food in several restaurants in Oregon, causing an outbreak with 751 cases, none fatal[3,23].

Diseases / Category C Agents

These occupy third place in terms of priority; they consist of emergent natural pathogens against which the general population has no immunity and agents that could be created or modified by genetic engineering. This is the case with the coronavirus of severe acute respiratory syndrome (SARS), which is susceptible to bio-engineering and used for mass dissemination in the future. These agents are characterized by ease of production and dissemination, with high rates of morbidity and mortality and enormous repercussions for public health. There is no agreed list of agents currently included in category C[3].

Evidence of suspected bioterrorist attack

There are certain parameters that differentiate outbreaks of infectious diseases, including temporal patterns of occurrence of the disease, number of cases, incubation period, clinical presentation, the strain or biovar (serotype), antimicrobial resistance, morbidity and mortality, economic impact, location and geographic distribution, seasonal distribution, potential zoonotic infectivity, residual toxicity, prevention and therapeutic potential, route of exposure, the weather and the connection with belligerent activities of possible terrorist groups[24].

The reasons to suspect a bioterrorist attack include: multiple and simultaneous occurrence (within hours or days) of patients with the same clinical picture (temporal grouping); claim or evidence of notice from a TO; suspicious acute clinical pictures in young people with good health, failure to respond to routine treatment, unusual resistance to antibiotics, evolution of the disease in an atypical way or worse, cases of diseases with unusual geographic or seasonal distribution (anomalous), simultaneous occurrence of clustered cases in non-contiguous areas (temporal grouping + anomalous distribution), and cases of people in the same environment (common ventilation systems) (temporal clustering + anomalous distribution + common link)[1,25,29].

Ten steps for managing a bioterrorist attack

Table 4 summarizes the initial sequence of events and an example of management procedure[2,14,25-27]. The following section describes a modified 10-step method based on that described in Bluebook 6th edition[2,25-27].

1. *Maintain a certain degree of suspicion:* Unlike an act of terrorism that is conventional or involves chemicals, an attack with biological weapons is not necessarily obvious. There is an incubation period, which favors a dispersed distribution of victims in time and space, and this complicates the

Table 3. Summary of Category A agents

Disease	Anthrax	Tularemia	Plague	Botulism	Smallpox	Hemorrhagic fevers
Causative agent	*Bacillus anthracis*	*Francisella tularensis*	*Yersinia pestis*	Toxin *Clostridium botulinum*	*Variola mayor*	*Filovirus* (Ebola & Marburg virus) *Arenavirus* (Lassa and Machupo virus)
Historical events/use as weapon B	1979 Accident in USSR with 66 deaths	World War II	Tartar siege of Kaffa in 1346	Experimentation on Japanese prisoners 1930	USSR program of manipulation	Development as a weapon by numerous countries
Microbiological characteristics	Aerobic. Gram +, Sporagenic	Aerobic. Cocobacillus Gram–, Crop danger	Anaerobic, Gram-bipolar	Anaerobic, Gram+, Sporagenic. 4 groups, 7 toxins (A-G)	Double-strand DNA. Poxviridae family	Small RNA virus, lipid enveloped
Reservoir	Soil	Lagomorphs and ticks	Rodents	Soil	Eradicated 1980 Only 2 world reservoirs (?)	Animals, insects, etc.
Resistance in the environment	Decades	Several weeks	Short	Short, 1% degradation per minute	>1 year in clothing/dust	Short in general
Possible dissemination in BT attack	Aerosol spores	Aerosol or contaminated water	Direct aerosol	Aerosol or contaminated food	Aerosol or infected terrorist	Aerosol or insects
Inhalation infective dose	8-50 thousand spores	5-10 bacterial units (BU)	100-20,000 BU	DL50 = 0,003 µg/kg inhaled		Variable
Suspicion	High nº cases respiratory symptoms	Outbreak of atypical pneumonia	Outbreak of complicated pneumonia	Patients with paralysis	Outbreak of characteristic rash	Outbreak of haemorrhagic fever in non-endemic country
Clinical picture	Inhalation (expected in TO attack) Cutaneous (natural event) GI (food) and Meningitis (complication)	Ulceroglandular (common, natural from) glandular (oculoglandular) ENT symptoms typhoid (GI) & pneumonia	Bubonic plague (common, natural form) primary septicaemia & primary pneumonia	Inhaled: descending symmetric flaccid paralysis, Alimentary: nausea vomiting & diarrhoea followed by constipation and paralysis	Common (severe prodrome & rash), haemorrhagic, medium, malignant & *sine erupcione*	In general: fever, breathing difficulties, capillary and coagulation alterations, bleeding, renal failure and shock
Incubation period	Inhaled 2-23 days Cutaneous 1-5 days GI 1-7 days	3-5 days (Range 1-21)	1-8 days	12-72 hours	10-12 days (range 4-19)	1-21 days depending on the agent
Mortality if untreated	20-90% depending on clinical picture	Inhaled: 30-60%	Inhaled: 40-85%	High dose 100%	Unvaccinated 30%	1-72% depending on the agent
Mortality if adequately treated	1-50% depending on clinical picture	1-4%	Less than 10%	Depends on when the antidote is administered	3% with prior vaccination	Variable
Diagnosis	Clinical picture + culture or PCR	Epidemiology + + clinical picture + serology	Clinical picture + culture or PCR	Clinical picture +24h sample ELISA or mouse bioassay	Egg culture or monoclonal cells	Clinical picture + lab tests: ELISA or PCR
Treatment 1st choice	Ciprofloxacin 400 mg IV/12 h (children 10-15 mg/kg IV/12h))	Aminoglycoside standard dose 10-12 days	Aminoglycoside standard dose 10-12 days	Specific antitoxin A & B, single dose is sufficient	Early vaccination reduces mortality 50%	Rivoflavin alone or with interferon
Treatment 2nd choice	Doxycycline 100 mg IV/12 h (children 2,2 mg/Kg IV/12h)	Ciprofloxacin 400 mg IV/12 h (children 10-15 mg/kg IV/12h)	Ciprofloxacin 400 mg IV/12 h 4 (children 10-15 mg/kg IV/12h)	The antitoxin against one type is ineffective against others	Zydovudine, untested in humans	Potent in vitro activity of Albumin-interferon–α/β

(Continued)

Table 3. Summary of Category A agents (Continued)

Disease	Anthrax	Tularemia	Plague	Botulism	Smallpox	Hemorrhagic fevers
Other measures	ICU	Normal hospitalization in the absence of complications	Hospital bed with isolation, Consider ICU	Mechanical, ventilation ICU	Hospital bed with isolation	Strict isolation in general
Transmission Person to person	Only cutaneous by direct contact	Not documented	Yes	No	Yes, very high	Yes, in most cases
Prophylaxis in in cases of suspected exposure	Ciprofloxacin (500 mg/12 h) or Doxycycline (100 mg/12 h) 60 days oral route	Doxycycline (100 mg/12 h) or Ciprofloxacin (500 mg/12 h) 14 days oral route	Doxycycline (100 mg/12 h) or Ciprofloxacin (500 mg/12 h) 7 days oral route	Early antitoxin	Early vaccination	Ribavirin
Vaccination	Available but short-lasting. New vaccine with recombinant antigen in experimental phase	Vacuna viva attenuated, partial protection	Current vaccines ineffective against pneumonic plague. New experimental bio-engineered vaccines (effective in mice)	Pentavalent (A-E) vaccine, experimental phase, requires numerous administrations	Vaccination effective but with risks, not indicated in pregnancy, immunodepression and severe excema	Currently no effective vaccines on the market except for yellow fever. Many in experimental phase
Control of infection	Deactivation of spores in environment	Control of the focus	Control of the focus	Decontamination within 2 hours	Strict quarantine of contacts	Isolation and focus control. Quarantine
Isolation of patients	Standard measures. Strict in pneumonic cases	Standard measures	Isolation respiratory cases	Standar measures	Strict isolation in negative pressure rooms	Some, even strict isolation in negative pressure rooms
Importance	Rapid evolution with high mortality	Ineffective dose extremaly low	Person to person dissemination	100,000 times more toxic than sarin gas	Less than half the world population is currently immunized	Heterogeneous group, unknown by our faculty staff
Observations	Difficult to initiate treatment in time	High risk culture, low performance		The antitoxin does not neutralize the toxin once bound to axon	Risk of infected terrorists spreading the disease	Laboratory manipulated samples, with level 4 biosafety

References in the table [3, 7, 8, 10, 15, 17, 21, 22, 33, 36, 40-52]. ICU: intensive care unit; B: Bacteriological, BT: Bioterrorism, GI: Gastrointestinal. USSR: Union of Soviet Socialist Republics.

the task of locating the original focus. Moreover, in many diseases caused by these agents, early treatment is vital. It is therefore essential to maintain a certain level of suspicion for early detection.

2. *Apply self-protection measures:* Use common self-protective measures. Although the M-40 series of masks are indicated (one-piece silicon-sealed rubber with 2 rigid lenses and a filter device), these masks are often not available. An alternative is the surgical mask, which offers adequate protection against aerosols of biological agents. Empirical chemoprophylaxis before and after exposure is recommended, with vaccination of the staff once the agent has been identified.

3. *Assess the patient,* and use the ABCD of advanced life support. Include physical examination, with emphasis on respiratory, neuromuscular and dermatologic examination, as well as history and detailed epidemiological data reflecting recent travel, food consumed in public, exposure to vectors, occupation and leisure activities, nearby people that have similar symptoms, etc.

4. *Proper decontamination if applicable:* in health centers, it is sufficient to change clothing and wash the patient with a normal disinfectant. In an outbreak, decontamination solutions such as the hypochlorite are effective against most chemical agents.

5. *Establish a diagnosis:* for the diagnosis, clinical and epidemiological criteria should be taken into account together with laboratory testing. Laboratory samples can be obtained from nasal and oropharyngeal swabs for PCR and culture; blood and sputum for culture, serum for serological tests, biopsies or scrapings of lesions, and environmental samples from sites suspected to harbour the agent. While waiting for laboratory results, the physician should establish a suspected clinical

Table 4. Initial sequence of events and examples of procedures to be followed

Initial sequence of events
– Dispersion of the agent, in a patent or covert way.
– Primary contagion, can take many forms (inhalation, food, contact, etc.) and can be abrupt or gradual.
– Incubation period, the longer the larger the number of victims until focus is detected[14].
– Transmission from person to person: if the agent has this capability it requires measures of isolation that are scarce and costly[14].
– Increased mobility of the population favours dissemination; quarantine will be required in some cases.

An example of procedure to be followed[2,25-27]
– Report suspected biological incident to the health authorities.
– Protect and alert own staff.
– Carry out epidemiological surveillance and screening in health centers and rule out other hypotheses, such as emerging diseases.
– Define the population at risk.
– Make an initial assessment of the extent and spread of the outbreak.
– Attempt to control the initial dispersion of the agent and the population.
– Decide on resources and whether these are sufficient, establish operational measures, pre-alert other resources.
– Implement a system of informing the public with clear recommendations.
– Elaborate prevention and surveillance measures to contain the outbreak.

and epidemiological diagnosis, initiate preventive measures and alert the epidemiological surveillance services.

6. *Provide appropriate treatment:* with a suspected diagnosis, empirical therapy should be initiated without waiting for laboratory results. Select a wide-spectrum antibiotic to which the suspected agent has least resistance (consider tetracycilins and fluoroquinolones). Consider prophylactic treatment for the population at risk[18].

7. *Control the infection:* standard precautions provide adequate protection against most diseases. However, special measures are required against some diseases such as smallpox, pneumonic plague and certain hemorrhagic fevers. We should ensure that the original source/s of the disease are inactive.

8. *Alert the authorities:* the physician detecting a suspected outbreak must report it immediately to epidemiological surveillance systems.

9. *Assist in epidemiological investigations and treat psychological effects:* work with those responsible for epidemiological investigations. Support and psychological treatment victims and their families and manage from here sight of the general population.

10. *Maintain continuous education and disseminate knowledge:* most healthcare personnel lack experience in such situations and their knowledge is theoretical. It is essential to maintain adequate training and preparation in this field despite the low probability of such an attack, given its potential impact and serious consequences. In this regard, Natalie E. Ferguson in 2003 published an important classification of information sources and websites on bioterrorism that has been used for this review, and we recommend that readers consult it[30].

Preparation for an adequate response

A Although no large-scale bioterrorist attacks have been reported and the possibility is remote according to some authors, the United States has accelerated its program of defense against biological weapons[31].

In 2003, Ashford et al.[32] showed that in the cases considered as possible terrorist acts between 1988 and 1999 worldwide, the time lapse between the start of the outbreak and identification of the problem was from 0 to 26 days, and that public declaration after identification was delayed for as long as 6 days. This study confirms the importance of role of primary and emergency care teams in early detection and control of the attack.

Good preparation for a possible attack[14,15] includes an effective communication system and should focus on:

1. Create effective epidemiological monitoring networks[14].

2. Provide primary care teams and emergency services with basic material resources[10,14,33,34] and appropriate training.

3. Geographical regionalization of resources and infrastructure[35].

Among other measures, stocks of medication and vaccines against major agents should be established[14,31]. There seems to be consensus on the effectiveness of this in the event of a catastrophe. However, the distribution by hospitals or regionalized storage of material resources such as ventilators and electromedical equipment poses questions that each health system should resolve according to their economic resources and needs, always under the premise of "helping the greatest number of the population possible with the resources available." This can lead to unpopular decisions[36].

4. Create a network of reference laboratories according to this regionalization[14].

5. Create reference hospital units with negative air pressure for admission of contaminated patients and a transport network with adequate isolation to these centers[37].

6. Implement a good communication system[38].

7. Training with computer systems based on

statistical programs for the detection of bioterrorist attacks and evolution simulators[39].

The advantage of this effort is twofold, since these resources are the same as those needed to address outbreaks of emerging infectious diseases and other types of disease[14]. Epidemic outbreaks of emerging diseases can cause considerable economic impact and even civil panic, similar to that caused by a bioterrorist incident. These effects were observed in spring 2003 during the SARS outbreak, in 1996 with bovine spongiform encephalopathy, and in 1981 with the so-called Toxic Oil Syndrome.

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Bioterrorismo: aspectos prácticos

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Aunque las armas biológicas han sido utilizadas desde la antigüedad, el temor y la preocupación de los gobiernos occidentales ante la posibilidad de un ataque bioterrorista ha cobrado una inusual importancia en la última década. Las principales características de un ataque biológico son: alta rentabilidad para sus fines con un bajo coste, gran repercusión socio-económica y mediática, capacidad de generar pánico entre la población y que el ajuste es relativamente fácil de producir y ocultar. Las principales formas de liberación del agente son: manifiesta, anunciada, selectiva y encubierta. Existen más de 150 agentes descritos como posibles armas biológicas que son clasificados por el CDC en tres categorías en función del riesgo epidemiológico, el impacto sobre la salud pública, el impacto sobre la economía y de la disponibilidad y facilidad de producción. En el texto se resumen las principales características epidemiológicas, diagnósticas, clínicas, terapéuticas y profilácticas de los principales agentes biológicos susceptibles de ser utilizados como arma biológica. [Emergencias 2010;22:130-139]

Palabras clave: Bioterrorismo. Ataque biológico. Biodefensa. Armas biológicas.