

# RISK ASSESSMENT IN SMALLPOX BIOTERRORIST AGGRESSION

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## 1. Abstract

As many specialists pointed out, a bioterrorist attack using a smallpox virus becomes an increasing probability. Global susceptibility of the population, high transmissibility, lack of specific treatment, difficult and late clinical diagnosis of first cases, and impressive and severe clinical pictures are important factors of risk assessment in smallpox terrorist aggression.

Airborne, the major way of spreading, intensive and long-distance traveling, and absence of bioprevention measures increase dramatically the epidemic extension. Under these circumstances, the capacity to limit aggression is rapidly overcome. So, risk assessment is one of the most important steps of bioprevention strategy of smallpox aggression.

## 2. Introduction

“The September 11, 2001 attacks on the World Trade Center and Pentagon changed forever our collective thinking with regard to our vulnerability to terrorist attacks” [7]. Less than one month later on October 4, 2003, a criminal anthrax epidemic lasting almost two months demonstrated the reality of large impact of present-day bioterrorism. Several scenarios were imagined on the possible future bioterrorist attacks. Among potential agents variola virus was estimated as one of the most probably used [2, 5, 7].

### 2.1. SMALLPOX: A FORGOTTEN DISEASE?

In 1980, World Health Organization (WHO) certified smallpox eradication worldwide and officially variola virus storage was restricted to two WHO reference laboratories: the Center for Disease Control and Prevention (CDC) in Atlanta, USA and State Research Center for Virology and Biotechnology “Vector” at Koltsovo, in Novosibirsk, Russia. All other

laboratories in the world were required to destroy their remaining variola virus stocks. In 1996, WHO General Assembly decided to destroy the stocks in 1999. But in 1999, the destruction was postponed until 2002. An advisory Committee of variola virus research proposed a program of work and indefinite postponement was admitted, so nowadays live smallpox virus stocks exist officially [16]. Immense stockpiles of variola virus were held by former Soviet Union at Sergiev Posad; the secret plant, as Dr. Alibek said, still exists and by Dr. Henderson's opinion remains as a focus of concern [9]. The black market trade in weapons of mass destruction is probably the only way of acquiring the virus. But this possibility exists and bioterrorism has no logic limits.

## 2.2. WHY SMALLPOX?

According to the specialists, smallpox is a "very potential bioterrorism choice" as:

1. At present, there is a high and global receptivity to variola virus. After eradication and more than 30 years no vaccination was performed and average protection postvaccination is about 5–7 years. A stock of 200 million doses of prepared vaccine was saved for use in case of accidental outbreak. In the last 5 years many countries prepared necessary stockpile of vaccine against smallpox. But WHO does not recommend vaccination of individuals before the smallpox epidemic occurs because of side effects. Vaccinia immune globulin recommended for the treatment of serious side effects is in very limited quantity so that stockpiles of this globulin were suggested to be made along with smallpox vaccine [6].
2. Contagiousness of smallpox is higher than 80%. The first generation of cases would rapidly spread in highly susceptible population, expanding each generation of cases, by a factor of 10 times or more during winter or spring [9]. As was recently demonstrated by pandemic spreading of severe acute respiratory syndrome (SARS), this rapid extension of smallpox could be a global disaster. Long-distance traveling of undetected human sources could represent the major way of pandemic spreading of smallpox also.
3. Clinical picture of smallpox has always had strong psychological impact in "civilian population", so this impact is expected to happen. Because of lack of immunoprotection a high proportion of severe clinical pictures involving long hospitalization is estimated. Unpredictable medical difficulties will be arisen by the incapacity of medical authorities to cover these huge requirements. Mild cases will be home-isolated increasing epidemic risk and spreading [14, 15].

4. There is no specific antiviral treatment for smallpox. Thiosemicarbazones and rifampicin previously reported having therapeutic benefits proved to be ineffective [9]. Cidofivir, a nucleotide analog of DNA polymerase inhibitor, experimented in cytomegalovirus infection treatment suggested to be used in postexposure treatment rather for treatment of the diagnosed smallpox [9, 11].
5. The reported mortality of the smallpox was higher than 30%. Hemorrhagic and malignant forms are uniformly fatal [9, 14].
6. A violent psychosocial reaction is likely to appear at the beginning of the epidemic “smallpox fear.” This psychological impact is more stronger in the population than in some other severe transmissible diseases.

Medical (clinical) impressive aspects, antiepidemic restrictive measures, current difficulties, and social perturbances could determine a psychosocial crisis followed by a real civilian panic [13].

### 3. Risk Assessment in Smallpox Bioaggression

The main areas of risk in smallpox bioaggression are presented in Figure 1. All these areas are influencing in between them in realizing very strong psychosocial perturbances that could degenerate in a strong panic of civilian population.

It is well known that one of the main targets of bioterrorist attack is to produce impressive psychosocial effects followed by socioeconomic perturbances and social disorganization.

This psychosocial impact influences in many aspects of clinical and epidemic side effects by magnifying difficulties of medical and anti-epidemic intervention [13].

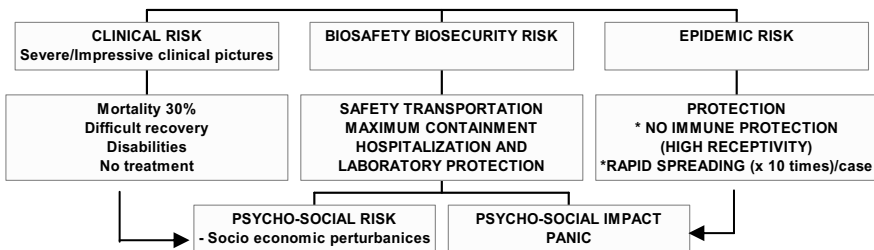


Figure 1. Risk areas in smallpox bioaggression.

### 3.1. CLINICAL RISK ASSESSMENT

Clinical risk assessment is considered to be important. During the progression of the disease it has to take into account the following gravity factors in risk evaluation [5, 9, 14].

- Smallpox is an exclusively human disease and nowadays any case is an alleged manipulation of variola virus.
- The illness is expected to be very severe in the majority of cases as the population under 40 years has no variola, “immunologic specific memory” (the vaccination was stopped in many countries before 1977).
- There is no etiologic treatment in smallpox. So the hospitalization will be of long duration overcoming hospital capacities in an epidemic situation.
- Severe malignant and hemorrhagic forms are fatal always so mortality is overcoming 30% in smallpox. Immunodeficient patients, pregnancy, and chronic cardiac diseases are predisposing conditions to severe forms.
- Clinical recognition of the illness is difficult in the first stage in the absence of epidemic information/suspicion. First cases will have high epidemic potential.
- Laboratory confirmation is also late in the first cases because routine laboratory investigation does not include such a potential etiology.

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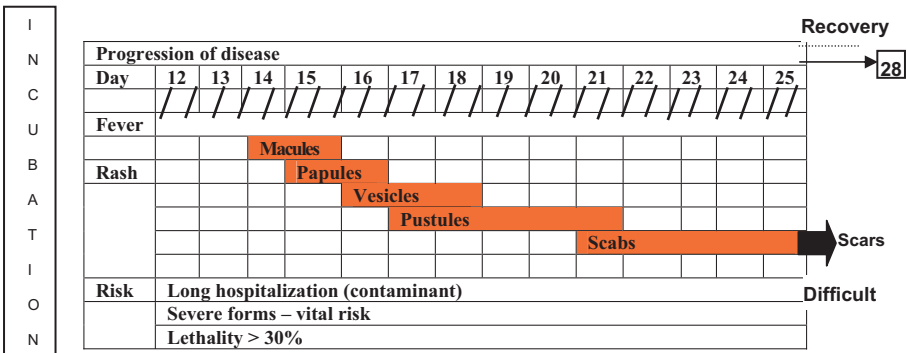


Figure 2. Smallpox – clinical risk assessment.

Figure 2 shows the risk during the progression of disease. Starting from the 10th day after contamination, the patient represents an important source of infection by respiratory droplets and later by the content of vesicles and pustules and at the end by scabs. The hospitalization in smallpox is compulsory in all the period of contagiousness that means minimum 3–4 weeks. In epidemic situation hospital capacities are overcome.

As the febrile onset is not specific, clinical presumption is late, when characteristic vesicles and pustules develop. In malignant forms, the diagnostic confusion is more frequent so first cases in absence of epidemic suspicion are “sacrificed patients” [9].

Laboratory identification of the virus in oropharyngeal exudate is possible by modern techniques (electron microscopy, immunoenzymatic detection, and molecular techniques) in less than 24 hours. Routine laboratory investigation does not include variola virus detection without any particular requirement. The confirmation of the first cases is late when virus detection is recommended from vesicles content (5–7 days of the progression of the disease) [3, 15].

No antiviral treatment is efficient in smallpox. The progression of the disease depends on the capacity of response of the patient. The estimated severity of the disease determines important vital risk. The historical known mortality of 30% is expected to be higher in absence of immune specific background [9].

Clinical factor will contribute substantially to increase associated psychosocial risk. Socioeconomic perturbances will increase psychosocial impact leading to “psychological mass reaction.” Risk assessment of psychosocial reaction is as well important as medical risk.

*Epidemic risk assessment* is dominated by the high capacity of spreading of the disease in modern opportunities of dissemination and lack of any immune protection [2, 10].

The interdependence of the particular epidemic factors in smallpox is presented schematically in Figure 3.

As global extension of SARS demonstrated recently, long-distance traveling nowadays represents a major risk activation of rapid spreading of high-risk respiratory diseases.

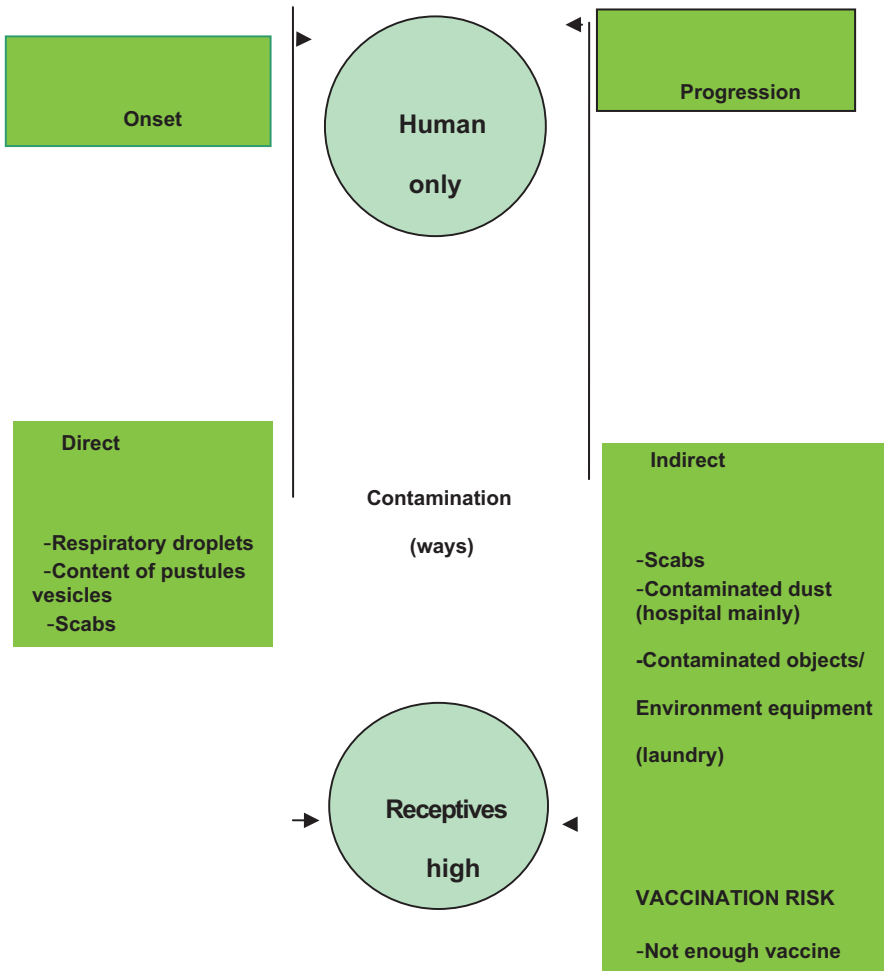


Figure 3. Epidemic risk factors in smallpox.

	Biosafety risk	Under the risk	Risk of contamination*
R	Hospital ↓	- Patients	- Clinical investigation - Procedures (therapeutic) - Sampling
		- Personnel - Environment	- Death – manipulation - Waste- management
I	Sampling ↓ Transportation/ Manipulation ↓		- Laundry
S			
K	Laboratory maximum containment (BL4)	- Personnel - Environment	- Procedures - investigation - Equipment - dedicated Environment/negative pressure

Figure 4. Smallpox: biosafety risk (extreme biosafety measures).

\* Accidentally.

Air-conditioning plane systems activate the spreading of virus by respiratory route. Virus dispersion in the modern huge “crowded” plains is very “efficient” in contaminating hundreds of people at once. Potential sources (unknown contaminated persons) play a huge spreading risk.

Starting from a “first contaminated person” all the contacts incubating the smallpox become “secondary bioterrorists.” Assuming a transmission rate of 20 cases by the “secondary bioterrorists” and a rate of 50 by the active, initial bioterrorist, a total of 1,000 cases would be prevalent before the earliest possible identification of the first wave of disease. Assuming that the first wave were misdiagnosed or diagnosed late the next wave would see 20,000 such cases, followed by 400,000 cases, 8 million cases, and so on [3].

Few physicians have enough experience, essential to establish a quick and accurate clinical diagnosis. But the high rapid detection and isolation of the first cases is crucial in limiting the risk of second-generation cases and in this context the professional training in urgent required today [3, 8, 12].

Preventing smallpox by vaccination is a long-debated decision. Well-known reverse reaction mentioned in Figure 3 is a major limiting risk factor in a mass vaccination campaign in the present situation. As WHO specialists recommended important stockpiles of specific globulin have to be prepared for the moment when the vaccination will be considered necessary [4, 15].

*Biosafety biosecurity risk.* Maximum security measures are recommended for special designated hospitals for isolation and quarantine for protection of personnel and environment. Negative air pressure, fully isolating equipment for personnel, and continuing disinfection measures are recommended for limiting the risk of contamination (Figure 4). Laundry and waste is sterilized and strictly surveyed for safety transportation before incineration [11].

Sample transportation and laboratories manipulating variola virus require maximum containment (BL4 biosafety) [3, 11].

Smallpox became a symbol of the victory of the humanity against infectious diseases. Risk assessment of smallpox estimated by many specialists after 2001 is an alarming scenario to prevent a global catastrophe, because epidemic extension of very aggressive diseases has no borders [1, 3, 14].

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