Bioterrorism is the use or threatened use of biological agents against a person, group, or a larger population in order to create fear or illnesses for purpose of intimidation, gaining an advantage, interruption of normal activities, or for ideological objectives.
7 TYPES OF SMALLPOX

- No rash – *Variola sine eruptione*
- Modified
- Discrete
- Semi-confluent
- Confluent
- Flat
- Hemorrhagic – early and late
Smallpox - March 25, 2002

Smallpox

**VARIOLA SINE ERUPTIONE**

- Fever 39° C
- Headache, backache
- Recovery in 48 hours

- Requires laboratory studies
- Virus isolation up to day 3
- Neutralizing Antibody
- No rash
- Not thought to be infectious
Areas of normal skin between pustules, even on face
• Pustules confluent on face but discreet elsewhere
Smallpox - March 25, 2002

SMALLPOX - CONFLUENT

• Confluent rash on face and forearms
SMALLPOX - FLAT

• Pustules confluent or semiconfluent – appear flat
Fig. 32. Malignant. Flat soft vesicles, some with adherent roofs, simulating haemorrhage, ninth to tenth day.
HEMORRHAGIC SMALLPOX

- Widespread hemorrhage into skin
- Two types (early and late) both 98% case fatality
SMALLPOX Proportion by Rash Type Among Unvaccinated Persons

*Rao, Smallpox in Bombay, Kothari, Bombay, 1972 (6942 cases)
THE FEVER AND STAGES OF DEVELOPMENT OF THE RASH IN A TYPICAL SMALLPOX CASE

- Macules
- Papules
- Vesicles
- Pustules
- Scabs

INFECTIOUS XXXXXXXXXXX
INCUBATION PERIOD

• Usual incubation period (interval between exposure/infection and first symptoms) is 10-14 days
• Can be as short as 7 days and as long as 19 days
PRE-ERUPTION PRODROME

- Sudden onset of high fever (38.5-40.5°C or 101.3 -104.9°F) and malaise
- Toxic during first two days
- Fever drops and patient feels better when rash appears
### PRODROMAL SYMPTOMS

6942 CASES OF VARIOLA MAJOR

Rao, Smallpox in Bombay, Kothari, Bombay, 1972

<table>
<thead>
<tr>
<th>SYMPTOM</th>
<th>PERCENT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fever</td>
<td>100</td>
</tr>
<tr>
<td>Headache</td>
<td>90</td>
</tr>
<tr>
<td>Backache</td>
<td>90</td>
</tr>
<tr>
<td>Chills</td>
<td>60</td>
</tr>
<tr>
<td>Vomiting</td>
<td>50</td>
</tr>
<tr>
<td>Pharyngitis</td>
<td>15</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>10</td>
</tr>
<tr>
<td>Delirium</td>
<td>15</td>
</tr>
<tr>
<td>Abdominal Pain</td>
<td>13</td>
</tr>
<tr>
<td>Convulsions</td>
<td>7</td>
</tr>
</tbody>
</table>
MACULES

- Minute red spots (first of tongue and palate)
- Lesions of the face and forehead ("herald spots")
- Proximal part of extremities
- Distal parts extremities
- All in 1-2 days
- Difficult to see on dark skinned people
Fig. 116. Early maculo-papular rash on the scalp, variola minor.
PAPULES

- Day 2 of rash
- Pharyngeal lesions evolve quickly to papules, vesicles, and break down (virus present)
- Raised above the skin
- Fluid accumulating
VESICLES

- Day 4 and 5
- Accumulation of fluid
- Over next 24-48 hours, clear fluid becomes cloudy and begins to thicken
- Vesicular fluid becomes pus
- Most lesions are pustules by day 7
- Reach maximum size by day 11
- As fluid absorbed, lesions become flatter
- Feel like hard peas in skin
UMBILICATED LESIONS

PUSTULES TURNING INTO SCABS
SCABS ON FEET
SCABS BEGIN TO FALL OFF

- Scabs form as pustular fluid is absorbed
- Because scabs contain viable virus, patients are infectious until all scabs separate
- In calloused areas (palms and soles) scabs are deeply embedded and may take 2-3 weeks to fall
COMPLICATIONS

• Bacterial infection of the skin, e.g., boils, impetigo (2-5% in dirty environment); blood stream infection (septicemia)
• Corneal ulceration and blindness: corneal opacity (4.4%), corneal ulcer (1%)
• Bones and joints
• Bronchitis and pneumonia probably due to secondary infection
• Encephalitis: 1 in 1000 cases
SEQUELAE

• Pock Marks
  – Scarring
  – “Not-marriageable”
  – Epidemiologic importance – scar survey

• Blindness (Hughes et al, Bangladesh)
  – Corneal Opacities 2.1%
  – Blindness 0.9%

• Limb Deformities
MORTALITY RISK FACTORS

- Type of Virus (Major vs. Minor)
- Case Type
- Age
- Vaccination Status
- Environmental sanitation (soap and water)
- Treatment (antibiotics)
- Antivirals
<table>
<thead>
<tr>
<th>STRAIN</th>
<th>MILD</th>
<th>MODERATE</th>
<th>SEVERE</th>
<th>CASE FATALITY</th>
</tr>
</thead>
<tbody>
<tr>
<td>Variola Minor Minor</td>
<td>Most</td>
<td>Some</td>
<td>Few</td>
<td>1 %</td>
</tr>
<tr>
<td>Variola Major</td>
<td>30%</td>
<td>60%</td>
<td>10%</td>
<td>5-30%</td>
</tr>
</tbody>
</table>
SMALLPOX CASE FATALITY RATES* BY CASE TYPE

**Rao, Smallpox in Bombay, Kothari, Bombay, 1972, 6942 cases

Deaths per 100 Cases

Modified | Discrete | Semi Confluent | Confluent | Flat | Hemorrhagic

0 | 10 | 30 | 60 | 90 | 100
AGE-SPECIFIC CASE FATALITY UNVACCINATED

SMALLPOX CASE FATALITY*
INFANT IMMUNIZATION AND AGE OF INFECTION

Deaths per 100 Cases

- 0-4: 45
- 5-14: 0
- 15-29: 0.7
- 30-49: 54.2
- >=50: 50

Legend:
- Immunized in Infancy
- Not Immunized in Infancy

Smallpox - March 25, 2002
EPIDEMIOLOGY OF SMALLPOX

- Smallpox has limited infectivity (compared to measles)
- Transmission primarily by droplets
- Transmission primarily among close contacts (within 6 feet)
- Occasional cases where lesions occur in nasopharynx, cough aerosolizes small particles
### Herd Immunity Thresholds for Selected Vaccine-Preventable Diseases†

<table>
<thead>
<tr>
<th>Disease</th>
<th>$R_o$</th>
<th>Herd Immunity</th>
<th>Immunization Levels</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>1999</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>19-35 months</td>
</tr>
<tr>
<td>Diphtheria</td>
<td>6-7</td>
<td>85%*</td>
<td>83%*</td>
</tr>
<tr>
<td>Measles</td>
<td>12-18</td>
<td>83-94%</td>
<td>92%</td>
</tr>
<tr>
<td>Mumps</td>
<td>4-7</td>
<td>75-86%</td>
<td>92%</td>
</tr>
<tr>
<td>Pertussis</td>
<td>12-17</td>
<td>92-94%</td>
<td>83%*</td>
</tr>
<tr>
<td>Polio</td>
<td>5-7</td>
<td>80-86%</td>
<td>90%</td>
</tr>
<tr>
<td>Rubella</td>
<td>6-7</td>
<td>83-85%</td>
<td>92%</td>
</tr>
<tr>
<td>Smallpox</td>
<td>5-7</td>
<td>80-85%</td>
<td>___</td>
</tr>
</tbody>
</table>

*4 doses

Airborne transmission of smallpox

Meschede, Germany 1972

Index case five days in room

Visitor 15 minutes in hospital

Smoke studies in triangle

Sick nurse never left room

Smallpox - March 25, 2002
<table>
<thead>
<tr>
<th></th>
<th>SMALLPOX</th>
<th>CHICKENPOX</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>FEVER</strong></td>
<td>2 to 4 days before rash</td>
<td>At time of rash</td>
</tr>
<tr>
<td><strong>RASH</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Appearance</td>
<td>Pocks in same stage</td>
<td>Pocks in several stages</td>
</tr>
<tr>
<td>Development</td>
<td>Slow</td>
<td>Rapid</td>
</tr>
<tr>
<td>Distribution</td>
<td>More pocks on arms and legs</td>
<td>More pocks on body</td>
</tr>
<tr>
<td>On Palms and Soles</td>
<td>Usually present</td>
<td>Usually absent</td>
</tr>
<tr>
<td><strong>DEATH</strong></td>
<td>Usually 1 in 10 die</td>
<td>Very uncommon</td>
</tr>
</tbody>
</table>
## DIFFERENTIAL DIAGNOSIS

<table>
<thead>
<tr>
<th>CONDITION</th>
<th>VARIOLA MAJOR, United Kingdom</th>
<th>VARIOLA MINOR, SOMALIA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chickenpox</td>
<td>41</td>
<td>20</td>
</tr>
<tr>
<td>Syphilis</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Erythema Multiforme</td>
<td>7</td>
<td></td>
</tr>
<tr>
<td>Allergic Dermatitis</td>
<td>7</td>
<td>1</td>
</tr>
<tr>
<td>Drug Rash</td>
<td>6</td>
<td>1</td>
</tr>
<tr>
<td>Vaccinia</td>
<td>5</td>
<td>1</td>
</tr>
<tr>
<td>Septicemia</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>Herpes</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Measles</td>
<td>2</td>
<td></td>
</tr>
</tbody>
</table>
EVOLUTION OF SMALLPOX RASH

• A major diagnostic characteristic of smallpox is that lesions in a given area are similar in appearance and feel.

• Lesions appear first on the head and evolve distally:
  – Pharynx, Palate
  – Face
  – Proximal Extremities
  – Hands and Feet
SMALLPOX
CHICKENPOX
## SMALLPOX ERADICATION STRATEGIES

<table>
<thead>
<tr>
<th>STRATEGY</th>
<th>METHOD</th>
<th>MEASURE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Traditional</td>
<td>Isolation of Cases</td>
<td></td>
</tr>
<tr>
<td>Outbreak Response</td>
<td>Quarantine &amp; Vaccination</td>
<td>Number of Cases</td>
</tr>
<tr>
<td>Vaccination</td>
<td>Routine Vaccination</td>
<td>Number of vaccinations</td>
</tr>
<tr>
<td>Campaign Vaccination</td>
<td>Campaigns &amp; Survey</td>
<td>Vaccination coverage</td>
</tr>
<tr>
<td>Surveillance Containment</td>
<td>Active Search Containment</td>
<td>Number of infected villages</td>
</tr>
</tbody>
</table>
1. In the fall of 1966 with little vaccine available, a smallpox outbreak in Ogoja, Nigeria was stopped by vaccinating infected villages.

2. Bill drew a series of spot maps of infected villages. Maps showed entry from north and spreading to the south. He asked me, if I stop the first will I stop the others?

3. An outbreak occurred in Abakaliki with 95% coverage. Smallpox found its way into a faith community that refused vaccination.

4. Bill noted that smallpox transmission was high in the dry season, and low in rainy season (What if we focus surveillance on the period of low transmission?)

William Foege MD, MPH
Fig. 3. Average number of reported smallpox cases in West and Central Africa by month, 1960-67. Source: World Health Organization.

Bull WHO 1975; 52: 209-222
Search and Containment Strategy

• Principal global eradication strategy was search for cases and containment of spread by locating and vaccinating contacts

• Search and containment continues to be the most efficient strategy
LAST CASES OF SMALLPOX**

Rahima Banu – 16 October 1975
Variola Major-Bangladesh

Ali Maow Maalin – 26 October 1977
Variola Minor-Somalia

** Two laboratory acquired cases occurred in UK in 1978
DANGEROUS ASSUMPTION

BIOTERRORISM

SMALLPOX WILL

BEHAVE AS

ENDEMIC

SMALLPOX
BIOTERRORISM REINTRODUCTION SP INTO WORLD

• UNITED STATES
  – Preparedness
  – Infrastructure
  – Vaccine Supply
  – Plan
  – Media

• WORLD
  – Limited Vaccine
  – Limited Capacity
  – 100 million cases, 20 million deaths
FACES OF SMALLPOX
HOSPITAL RISKS

• Delayed recognition in crowded emergency rooms
• Transmission to staff, other patients and visitors
• Aerosol spread
• Fomite contamination, e.g., laundry
• Atypical presentation delaying diagnosis
PEDIATRIC EMERGENCY

- 18 months
- 4 day history of high fever (>103)
- 1 day history of rash
ADULT EMERGENCY

• 30 year old women
• 4 day history of fever
• Contact with chicken pox
• Developed rash on face
ADULT EMERGENCY

• 40 year old female
• History of high fever
• Bleeding into skin
• Unconscious