

# Overview of Smallpox

2002

# Smallpox as a Bioterrorism Agent

- Last reported case in Minnesota in 1947
- Eradicated in 1977
- Intelligence reports indicate virus has been stolen
- Potential for use as bioweapon
- High (30%) case fatality rate
- Small infectious dose (10-100 organisms)
- Much secondary spread; 10 to 20-fold increase each generation

# Variola Virus

- **Orthopoxvirus**
- **Infects only humans in nature**
- **Rapidly inactivated by UV light, chemical disinfectants, heat**

# Smallpox Clinical Presentations

- **Variola major**
  - Severe illness
  - Case fatality rate of >30%
  
- **Variola minor**
  - Less severe
  - Case fatality of <1%

# Clinical Presentations of Variola Major

- **Ordinary (>90% of cases in unvaccinated people)**
- **Modified (mild; occurs in previously vaccinated people)**
- **Flat (uncommon; usually fatal)**
- **Hemorrhagic (uncommon; usually fatal)**

## Modified Smallpox

- Occurs in previously vaccinated persons
- Prodrome may be less severe
- No fever during evolution of rash
- Skin lesions evolve more quickly
- Rarely fatal
- More easily confused with chickenpox



- **Severe prodrome**
- **Fever remains elevated throughout course of illness**
- **Extensive enanthem**
- **Skin lesions soft and flat, contain little fluid**
- **Most cases fatal**



# Hemorrhagic Smallpox

- Prolonged severe prodrome
- Fever remains elevated throughout course of illness
- Early or late hemorrhagic signs
- Bleeding into skin, mucous membranes, GI tract
- Usually fatal





# Smallpox Complications

- **Bacterial infection of skin lesions**
- **Arthritis**
- **Respiratory**
- **Encephalitis**
- **Death**
  - **30% overall for ordinary smallpox**
  - **40%-50% for children <1 year**
  - **>90% for flat and hemorrhagic smallpox**

# Smallpox Prodrome

- Incubation period 12 days (range 7-19 days)
- Prodrome
  - abrupt onset of fever  $>101^{\circ}\text{F}$
  - malaise, headache, muscle pain, nausea, vomiting, backache
  - lasts 1-4 days

# Smallpox Rash

- **Enanthem (mucous membrane lesions) appears approx. 24 hours before skin rash**
- **Minute red spots on the tongue and oral/pharyngeal mucosa**
- **Lesions enlarge and ulcerate quickly**
- **Virus titers in saliva highest during first week of exanthem**

# Smallpox Rash

- **Exanthem (skin rash) appears 2-4 days after onset of fever**
- **First appears as macules, usually on the face**
- **Lesions appear on proximal extremities, spread to distal extremities and trunk**
- **Vesicles often have a central depression (“umbilication”)**
- **Pustules raised, round, firm to the touch, deeply embedded in the skin**

# Smallpox Rash

- Lesions in any one part of the body are in same stage of development
- Most dense on face and distal extremities (centrifugal distribution)
- Lesions on palms and soles (>50% of cases)



**Day 2 of rash,  
papules  
apparent**



**Day 3, rash  
more  
discrete and  
raised above  
the skin  
surface.  
Fluid  
beginning to  
accumulate  
in papules to  
form  
vesicles**



**Day 4,  
vesicles  
are more  
distinct  
and feel  
firm to the  
touch.**





**Day 5, fluid in vesicles becomes cloudy, rash now pustular. Fever usually rises and patient feels more ill.**



**Day 7,  
rash  
definitely  
pustular**



**Days 8-9,  
pustules  
increase in  
size, are  
firm to the  
touch and  
are deeply  
embedded  
in the skin.**



**Days 10-14,  
scabs form.  
The scabs  
contain live  
virus. Until  
all scabs fall  
off, patient  
may infect  
others.**



**Day 20, scabs  
have fallen off  
and  
depigmented  
areas evident.  
Skin may return  
to normal  
appearance,  
however scars  
may remain on  
the face.**



# Smallpox Differential Diagnosis

- **Varicella (chickenpox)**
- **Vaccinia**
- **Monkeypox**
- **Cowpox**
- **Herpes zoster**
- **Drug-induced rashes**
- **Erythema multiforme**
- **Coxsackie virus**
- **Herpes Simplex Virus**
- **Secondary syphilis**
- **Molluscum contagiosum (esp. HIV patients)**
- **Scabies and insect bites**
- **Impetigo**
- **Contact dermatitis**

# Smallpox (Variola)

- **Febrile prodrome**
- **Centrifugal distribution (most dense on face, then extremities, less on trunk)**
- **Synchronous lesions (appear during a 1-2 day period and evolve at the same rate)**
- **Rash maculopapular, then vesicular, and later pustular**
- **Lesions firm to touch, deeply embedded in skin**
- **Lesions on palms and soles**



# Chickenpox (Varicella)

- **Fever with onset of rash**
- **Centripetal distribution (greater concentration of lesions on the trunk rather than the face and extremities)**
- **Lesions appear in crops every few days and develop at different stages: papules, vesicles, pustules, and scabs**
- **Lesions are more superficial and will burst if probed**
- **Not on palms and soles**



**Day 1-2,  
difficult to  
distinguish  
rash**



**Lesions same stage and deeply embedded in skin**

**Lesions in different stages and more superficial**



SMALLPOX

Day 7

CHICKENPOX



**Scabs not yet formed**

**Most lesions have formed scabs**

# Smallpox Major Criteria

- **Febrile prodrome 1-4 days before rash onset; fever of >101 F, and at least 1 additional symptom\***
- **Rash lesions deep, firm/hard, round and well circumscribed**
- **On any one part of the body lesions in same stage of development**

**\*Prostration, headache, backache, chills, vomiting or severe abdominal pain**

# Smallpox Minor Criteria

- **Greatest concentration of lesions on face and distal extremities**
- **Lesions first appeared on oral mucosa/palate, face, forearms**
- **Patient appears toxic or moribund**
- **Lesions evolve from macules to papules to pustules over days**
- **Lesions on palms and soles**

# Risk of Smallpox by Clinical History and Examination

- **High risk**
  - febrile prodrome and
  - classic smallpox lesions and
  - same stage of development
- **Moderate risk**
  - febrile prodrome and
  - 1 major OR  $>$  4 minor criteria
- **Low risk**
  - no febrile prodrome or
  - febrile prodrome and  $<$  4 minor criteria



# Chickenpox (varicella)



## IMAGES OF CHICKENPOX (VARICELLA)



## DIFFERENTIATING CHICKENPOX FROM SMALLPOX

Chickenpox (varicella) is the most likely condition to be confused with smallpox.

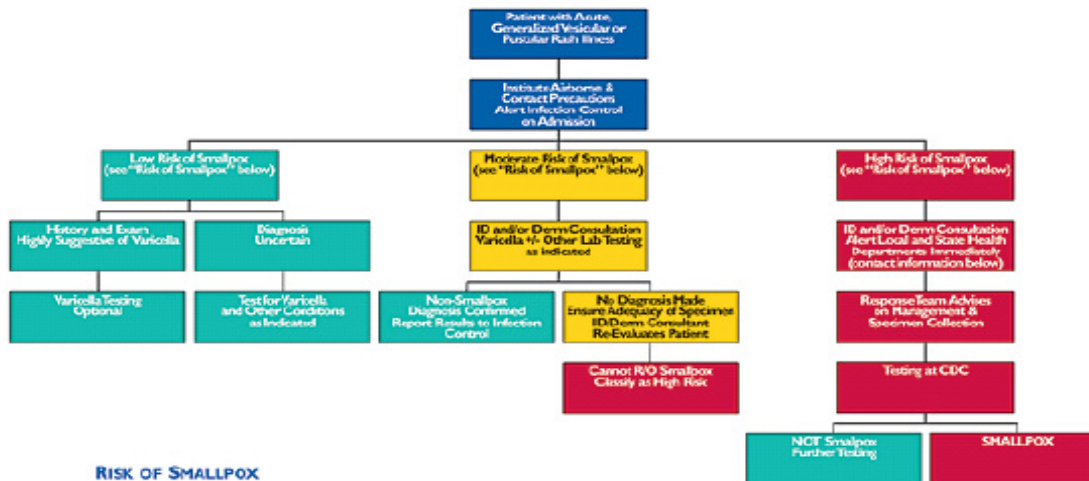
**In chickenpox:**

- No or mild prodrome
- Lesions are superficial vesicles: "dewdrop on a rose petal" (see photo at top)
- Lesions appear in crops; on any one part of the body there are lesions in different stages (papules, vesicles, crusts)
- Centripetal distribution: greatest concentration of lesions on the trunk, fewest lesions on distal extremities. May involve the face/scalp. Occasionally entire body equally affected.
- First lesions appear on the face or trunk
- Patients rarely toxic or moribund
- Rapid evolution: lesions evolve from macules → papules → vesicles → crusts quickly (<24 hours)
- Palms and soles rarely involved
- Patient lacks reliable history of varicella or varicella vaccination
- 50-80% recall an exposure to chickenpox or shingles 10-21 days before rash onset

Photo Credits: Dr. Thomas Mack, Dr. Barbara Wilson, Dr. Scott A. Norman, Dr. Patrick Algren, World Health Organization, American Academy of Pediatrics, American Academy of Dermatology

# EVALUATING PATIENTS FOR SMALLPOX

## ACUTE, GENERALIZED VESICULAR OR PUSTULAR RASH ILLNESS PROTOCOL



### RISK OF SMALLPOX

- High Risk of Smallpox → Report Immediately**
1. Febrile prodrome (defined below) **AND**
  2. Classic smallpox lesion (defined below & photo at top right) **AND**
  2. Lesions in same stage of development (defined below)
- Moderate Risk of Smallpox → Urgent Evaluation**
1. Febrile prodrome (defined below) **AND**
  2. One other **MAJOR** smallpox criteria (defined below) **OR**
  1. Febrile prodrome (defined below) **AND**
  2. ≥4 **MINOR** smallpox criteria (defined below)
- Low Risk of Smallpox → Manage as Clinically Indicated**
1. No febrile prodrome **OR**
  1. Febrile prodrome **AND**
  2. <4 **MINOR** smallpox criteria (defined below)

There have been no naturally occurring cases of smallpox anywhere in the world since 1977. A high risk case of smallpox is a public health and medical emergency.

**Report ALL HIGH RISK CASES immediately (without waiting for lab results to:**

1. Hospital Infection Control \_\_\_\_\_ ( ) \_\_\_\_\_
2. \_\_\_\_\_ health department ( ) \_\_\_\_\_
3. \_\_\_\_\_ health department ( ) \_\_\_\_\_

### MAJOR SMALLPOX CRITERIA

- **FEBRILE PRODROME:** occurring 1-4 days before rash onset; fever ≥101°F and at least one of the following: prostration, headache, backache, chills, vomiting or severe abdominal pain.
- **CLASSIC SMALLPOX LESIONS:** deep-seated, firm/hard, round well-circumscribed vesicles or pustules; they evolve, lesions may become umbilicated or ~~umbilicated~~
- **LESIONS IN SAME STAGE OF DEVELOPMENT:** on any one part of the body (e.g. the face, or arm) all the lesions are in the same stage of development (i.e., all are vesicles, or all are pustules)

### MINOR SMALLPOX CRITERIA

- Centrifugal distribution: greatest concentration of lesions on face and distal extremities
- First lesions on the oral mucosa/palate, face, or firearms
- Patient appears toxic or moribund
- Slow evolution: lesions evolve from macules to papules → pustules over days (each stage lasts 1-2 days)
- Lesions on the palms and soles

# Smallpox (variola)



## IMAGES OF SMALLPOX



## COMMON CONDITIONS THAT MIGHT BE CONFUSED WITH SMALLPOX

CONDITION	CLINICAL CLUES
Varicella (primary infection with varicella-zoster virus)	Most common in children <13 years; children usually do not have a viral prodrome
Disseminated herpes zoster	Immunocompromised or elderly persons; rash looks like varicella, usually begins in dermatomal distribution
Impetigo (Streptococcus pyogenes, Staphylococcus aureus)	Many-colored crusted plaques with bullae are classic but may begin as vesicles; regional not disseminated distribution
Drug eruptions	Exposure to medications; rash often generalized
Contact dermatitis	Rhyming contact with possible allergens; rash often localized in pattern suggesting external contact
Erythema multiforme minor	Target "bull's eye" or iris lesions often follow recurrent herpes simplex virus infections; may involve hands & feet (including palms & soles)
Erythema multiforme (incl. Stevens-Johnson Syndrome)	Major form involves mucous membranes & conjunctivae; may be suggestive to air vesicles
Enteroviral infection (eg. Hand, Foot and Mouth disease)	Summer & fall; fever & mild pharyngitis 1-2 days before rash onset; lesions initially maculopapular but evolve into wheal-pruritic tender flat oval vesicles; peripheral distribution (fingers, toes, mouth or disseminated)
Disseminated herpes simplex	Lesions indistinguishable from varicella; immunocompromised host
Sabies; insect bites (incl. fleas)	Rhyming is a major symptom; patient is not febrile & is otherwise well
Multibacilar contagionum	May disseminate in immunosuppressed persons

For more information, please go to the CDC website <http://www.cdc.gov/vp/smallpox/> and <http://www.hhs.gov/cdc/nczod/epidemiology/>





# **POSSIBLE CASE OF SMALLPOX**

**REPORT TO MDH IMMEDIATELY:**

**1-877-676-5414 or 612-676-5414**

# Smallpox Clinical Treatment

- **Strict airborne and contact isolation**
- **Supportive care is the mainstay of smallpox therapy**
  - **Ensure adequate fluid intake**
  - **Alleviate pain, fever**
  - **Aggressive treatment of secondary infections**
- **Antiviral therapy is experimental (Cidofovir)**
- **Vaccination of contacts up to 4 days post-exposure can prevent/attenuate clinical symptoms**

# Infection Control

- **Strict adherence to Standard, Airborne, and Contact Precautions**
- **Airborne:**
  - **Closed door, negative pressure rooms with  $> 6$  air exchanges per hour. Exhaust outside or through HEPA filtration.**
  - **Caregivers must wear NIOSH respiratory protection when entering rooms (N95 masks preferred because PAPRs difficult to clean).**

# City Smallpox Hospital, Roseville MN



# Smallpox Information on the Web

- American Academy of Dermatology:  
[www.aad.org/BioInfo/smallpx.html](http://www.aad.org/BioInfo/smallpx.html)
- CDC smallpox: [www.bt.cdc.gov/agent/smallpox/index.asp](http://www.bt.cdc.gov/agent/smallpox/index.asp)
- Center for Civilian Biodefense Strategies: [www.hopkins-biodefense.org](http://www.hopkins-biodefense.org)
- Center for Infectious Disease Research and Policy:  
[www.umn.edu/cidrap/](http://www.umn.edu/cidrap/)
- IDSA Website. [www.idsociety.org/BT/ToC.htm](http://www.idsociety.org/BT/ToC.htm)
- MDH: [www.health.state.mn.us/bioterrorism/professionals.html](http://www.health.state.mn.us/bioterrorism/professionals.html)