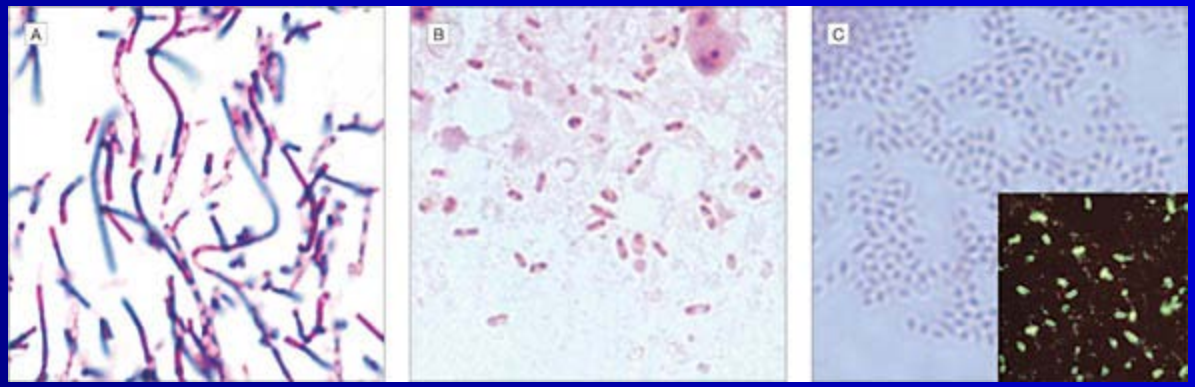
Smallpox



CDC, AFIP

Smallpox
Overview

- Two strains: variola major and variola minor
  - Variola minor – milder disease with case fatality typically 1% or less
  - Variola major – more severe disease with average 30% mortality in unvaccinated

- Person-to-person transmission

Smallpox
Overview

- Killed approximately 300,000,000 persons in 20th century
- Routine smallpox vaccination in the U.S. stopped in 1972
- WHO declared smallpox eradicated in 1980
- Vaccine has significant adverse effects
- No effective treatment

Smallpox
Overview

- Person-to-person transmission
- *Average* 30% mortality from variola major in unvaccinated
- A single case is considered a global public health emergency

Smallpox
Transmission

- Infectious dose extremely low
- Spread primarily by droplet nuclei >aerosols > direct contact
- Maintains infectivity for prolonged periods out of host
  - Contaminated clothing and bedding can be infectious

Smallpox
Transmission

- Transmission does not usually occur until after febrile prodrome
  - Coincident with onset of rash
  - Slower spread through the population than chickenpox or measles
  - Large outbreaks in schools were uncommon
- Less transmissible than measles, chickenpox, influenza

Smallpox Transmission

- Secondary cases primarily household, hospital, and other close contacts
- Secondary attack rate 37-87% among unvaccinated contacts
- Patients with severe disease or cough at highest risk for transmission
- Greatest infectivity from rash onset to day 7-10 of rash
  - Infectivity decreases with scab formation and ceases with separation of scabs

Smallpox
Case Definition

- Clinical case definition
  - An illness with acute onset of fever ≥101° F followed by a rash characterized by vesicles or firm pustules in the same stage of development without other apparent cause
- Laboratory criteria for confirmation (Level C/D* lab)
  - Isolation of smallpox virus from a clinical specimen, **OR**
  - Identification of variola in a clinical specimen by PCR or electronmicroscopy

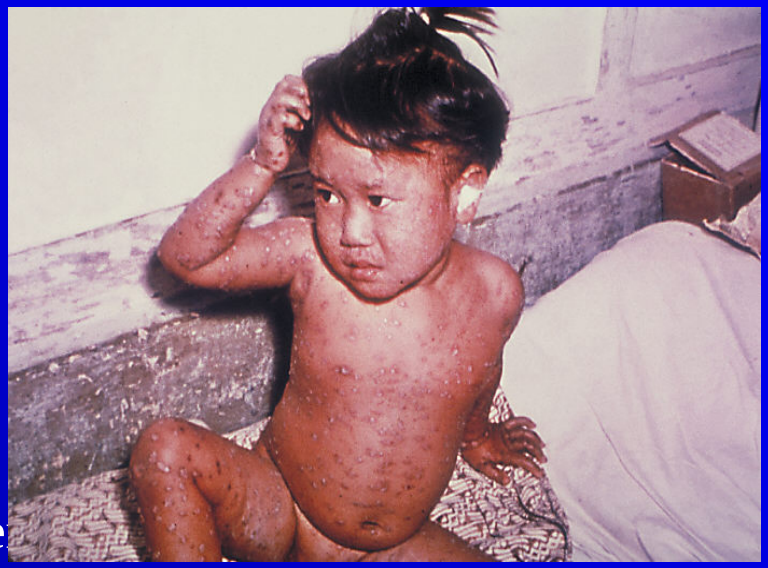
*initial confirmation of outbreak requires testing in level D lab (I.e., CDC)

Smallpox
Case Classification

- Case classification
  - Confirmed: laboratory confirmed
  - Probable: meets clinical case definition & has an epi link to another confirmed or probable case
  - Suspected:
    - Meets clinical case definition but is not laboratory-confirmed and does not have an epi link **OR**
    - Atypical presentation not lab confirmed but has an epi link to a confirmed or probable case

Smallpox
Clinical Features

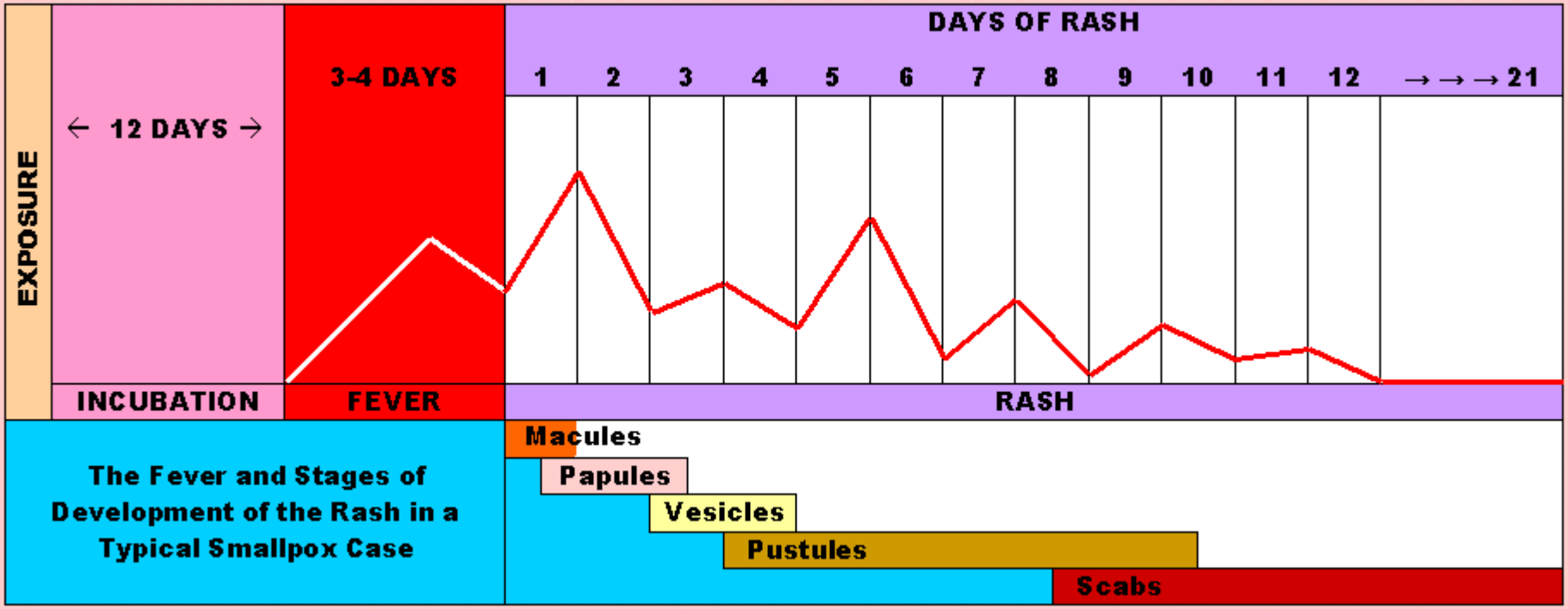
- Prodrome (incubation 7-19 days)
  - Acute onset of fever, malaise, headache, backache, vomiting, occasional delirium
  - Transient red rash
- Exanthem (2-3 days later)
  - Preceded by enanthem on oropharyngeal mucosa
  - Begins on face, hands, forearms
  - Spread to lower extremities then trunk over ~ 7 days
  - Synchronous progression: flat lesions → vesicles → pustules → scabs



CDC

Lesions most abundant on face and extremities, including palms/soles

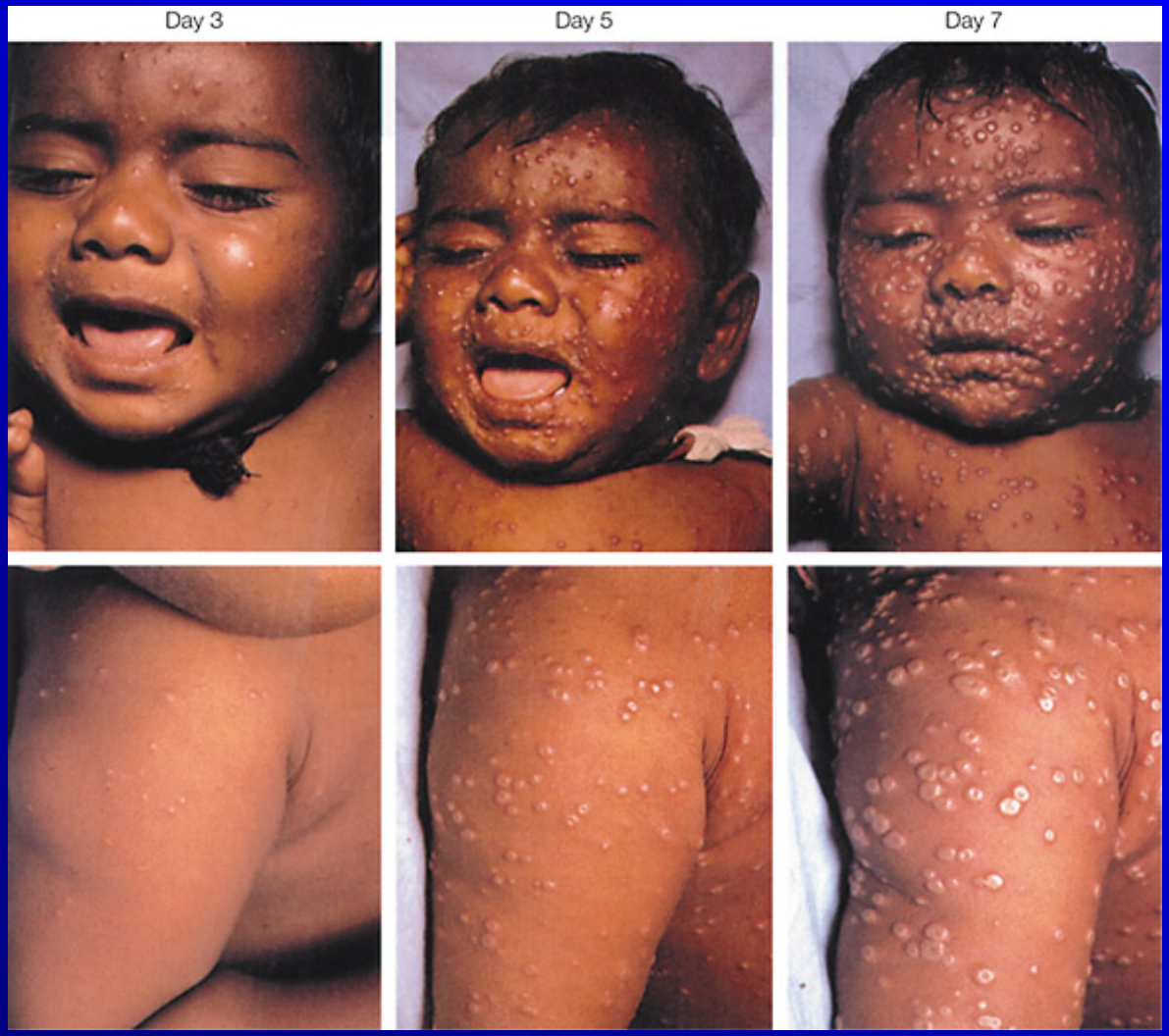
Smallpox
Clinical Course



WHO

Smallpox

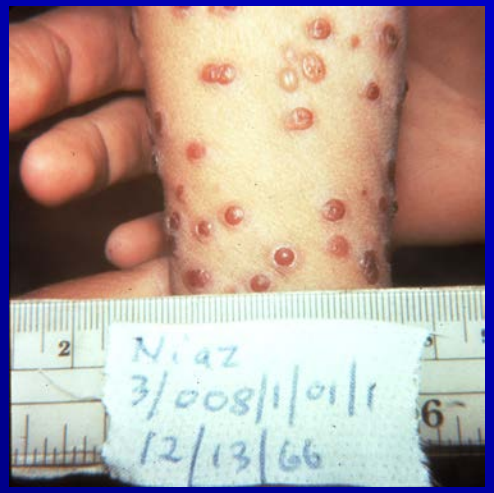
Clinical Progression



WHO

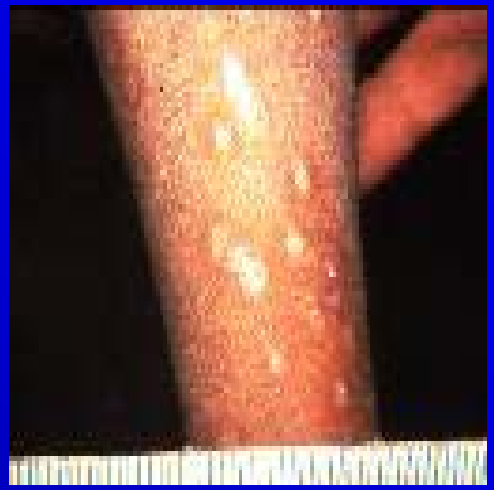
Smallpox

Clinical Progression



Day 10

Day 14



Day 21

Thomas, D.

Smallpox
Clinical Types

- Ordinary smallpox: 90% of cases
  - Case-fatality average 30%
  - Occurs in non-immunized persons

- Modified smallpox
  - Milder, rarely fatal
  - Occurs in 25% of previously immunized persons and 2% of non-immunized persons
  - Fewer, smaller, more superficial lesions that evolve more rapidly

Smallpox
Clinical Types

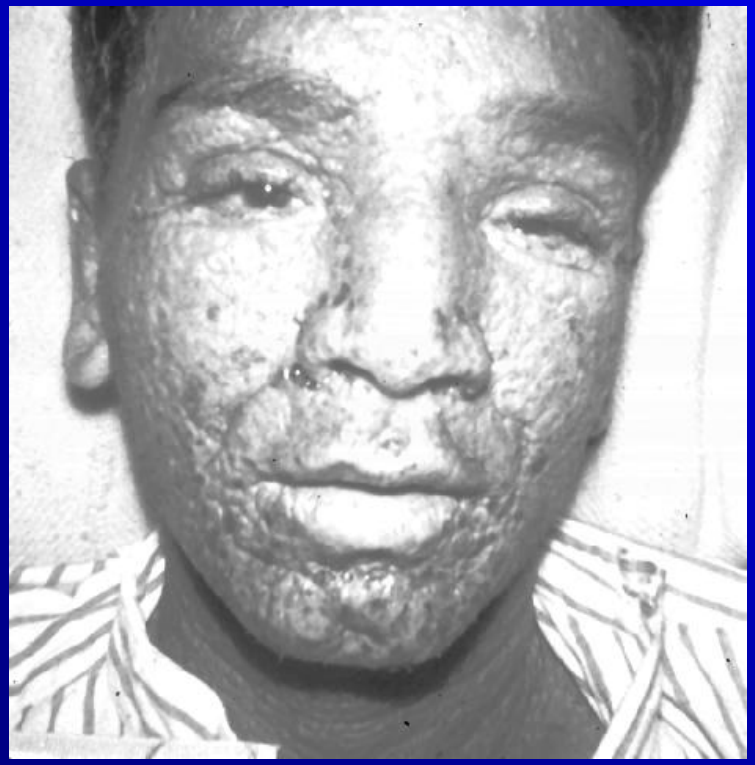
- Hemorrhagic smallpox: <3% of cases
  - Immunocompromised persons and pregnant women at risk
  - Shortened incubation period, severe prodrome
  - Dusky erythema followed by petechiae & hemorrhages into skin and mucous membranes
  - Almost uniformly fatal within 7 days

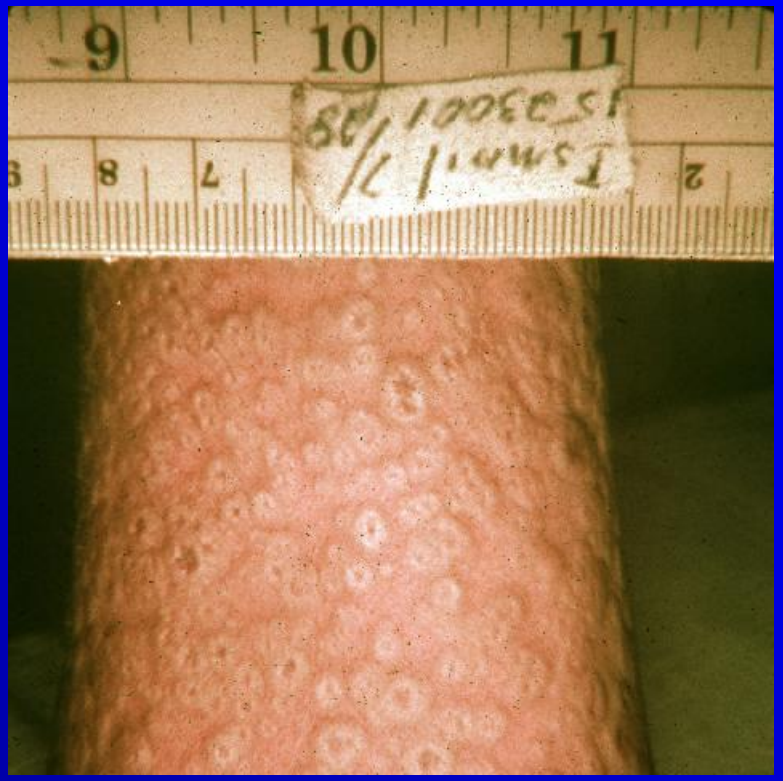
Smallpox
Clinical Types

- Malignant or flat-type smallpox: 7% of cases
  - Slowly evolving lesions that coalesce without forming pustules
  - Associated with cell-mediated immune deficiency
  - Usually fatal

- Variola sine eruptione
  - Occurs in previously vaccinated persons or infants with maternal antibodies
  - Asymptomatic or mild illness
  - Transmission from these cases has not been documented

Malignant Smallpox





Thomas, D.

Smallpox
Complications

- Encephalitis
  - 1 in 500 cases Variola major
  - 1 in 2,000 cases Variola minor
- Corneal ulceration
  - Blindness in 1% of cases
- Infection in pregnancy
  - High perinatal fatality rate
  - Congenital infection

Smallpox
Medical Management

- Respiratory and contact isolation for hospitalized cases
  - Negative pressure room; HEPA-filtered exhaust
  - All health care workers employ aerosol and contact precautions regardless of immunization status
- No specific therapy available
- Supportive care: fluid and electrolyte, skin nutritional

Smallpox
Medical Management

- Antibiotics for secondary infection
- Antiviral drugs under evaluation
- Notify Public Health and hospital epidemiology immediately for *suspected* case

Smallpox

Outbreak Management

- Case identification, isolation, and immunization
- Rapid identification of contacts
- Immediate vaccination or boosting of ALL potential contacts including health care workers (ring vaccination)
  - Vaccination within 4 days of exposure may prevent or lessen disease
  - Isolation with monitoring for fever or rash
    - 18 days from last contact with case
    - Respiratory isolation if possible for febrile contacts

Smallpox

Outbreak Management

- Priority groups for vaccination in a smallpox outbreak include persons involved in the direct medical or public health evaluation of confirmed, probable, or suspected smallpox patients

- Passive immunization (VIG)

  - Potential use for contacts at high risk for vaccine complications
    - Pregnancy, skin disorders, immunosuppression
    - VIG not readily available

More on CDC's response plan...

Smallpox
Definition of a Contact

- Contact: A person who has had contact with a suspected, probable or confirmed case of smallpox
  - Cases should be considered infectious from the onset of fever, until all scabs have separated

- Close contact: face-to-face contact (≤6ft) with a smallpox case

Smallpox Outbreak Management
Pre-release Vaccination

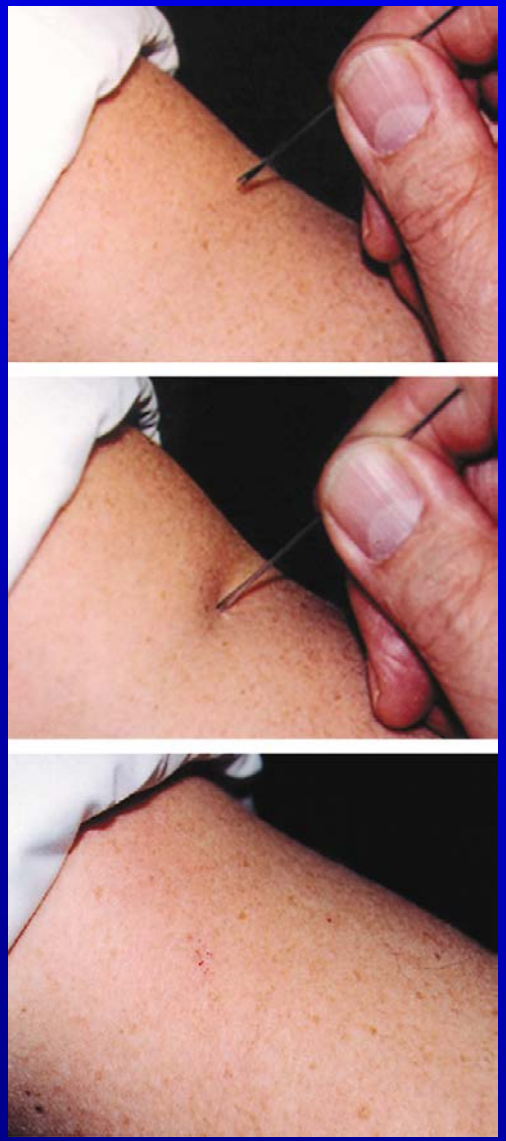
- Select individuals vaccinated to enhance smallpox response capacity
- Smallpox Response Teams
  - Designated public health, law enforcement, and medical personnel in each state/territory
  - Investigate, evaluate, and diagnose initial suspect cases of smallpox
- Select personnel at acute care health care facilities (Smallpox Health Care Teams)

ACIP, June 2002

Smallpox Vaccine

- Made from live *Vaccinia* virus
  - ~ 200 million doses in U.S. stores
- Intradermal inoculation with bifurcated needle (scarification)
  - Pustular lesion or induration surrounding central lesion (scab or ulcer) 6-8 days post-vaccination
  - Low grade fever, axillary lymphadenopathy
  - Scar (permanent) demonstrates successful vaccination ("take")
  - Immunity not life-long

Smallpox Vaccine
Administration

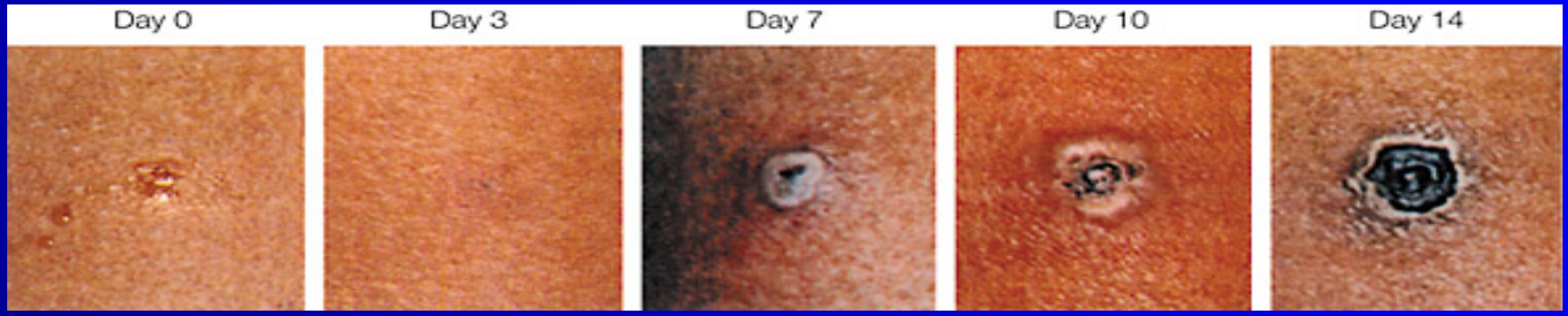


Vaccine admin instructions

JAMA 1999;281:1735-45

WHO

Smallpox Vaccine
"Take"



WHO

Smallpox Vaccine Complications

- More common in children and primary vaccinees
- Most common: secondary inoculation
  - Skin, eye, nose, genitalia
  - 50% of all complications
  - 529/million (30% in one study were contacts)
- Severe reactions less common
- Primary vaccination ~ 1 death/million
- Revaccination ~ 0.2 deaths/million

Smallpox Complication Rates for Primary Vaccination

- Less common
  - Post-vaccination encephalopathy (7-42.3/million)*
  - Post-vaccination encephalitis (12.3/million)
    - 25% fatal; 23% neurological sequelae
  - Progressive vaccinia/vaccinia necrosum (1.5/million)
  - Generalized vaccinia (241.5/million): severe in 10%
  - Eczema vaccinatum (38.5/million)
  - Fetal vaccinia - rare

Sourced: MMWR June 22, 2001 / 50(RR10);1-25. Vaccinia (Smallpox) Vaccine Recommendations of the Advisory Committee on Immunization Practices (ACIP), 2001

*Vaccines 3rd Ed. Plotkin SA, Orenstein WA. W.B. Saunders, Phila. 1999

Smallpox Vaccine
Pre-exposure Contraindications

- Immunosuppression
  - Agammaglobulinemia
  - Leukemia, lymphoma, generalized malignancy
  - Chemo- or other immunosuppressive therapy
  - HIV infection
- History or evidence of eczema
- Household, sexual, or other close contact with person with one of the above conditions
- Life-threatening allergy to polymixin B, streptomycin, tetracycline, or neomycin
- Pregnancy

Distinguishing Smallpox from Chickenpox:
Similar Epidemiologic Features

- Incubation period 14 (10-21) days

Delete hyphens in “Person-to-person”

- Person-to-person transmission

- Seasonal transmission of disease highest during winter and early spring

Distinguishing Smallpox from Chickenpox:

Epi Features that Differ

- Chickenpox (varicella)
  - Most cases occur in children
  - Expected case fatality rate 2-3/100,000
  - Secondary attack rate of 80% among susceptible household contacts
- Smallpox (variola)
  - Most of the population expected to be susceptible
  - Expected case fatality rate averages 30%
  - Secondary attack rate ~60% in unvaccinated family contacts

Distinguishing Smallpox from Chickenpox: Clinical Features that Differ

- Chickenpox (varicella)
  - Lesions superficial
  - Rash concentrated on trunk
  - Lesions rarely on palms or soles
  - Lesions in different stages of development
  - Rash progresses more quickly
- Smallpox (variola)
  - Lesions deep
  - Rash concentrated on face & extremities
  - Lesions on palms & soles
  - Lesions in same stage of evolution on any one area of body
  - Rash progresses slowly

CDC

Smallpox Surveillance

- Pre-event
  - Development of a listing of surveillance partners, points of contact, and mechanisms for reporting
  - Establishing sentinel surveillance for generalized febrile vesicular-pustular rash in health care settings
- Post-event:
  - Once a confirmed case of smallpox is identified in your jurisdiction, active surveillance for suspected, probable, and confirmed cases should be initiated

Smallpox Surveillance, cont.

- Contact tracing, interviewing, and vaccination
  - Monitored for vaccine “take”
  - Non-symptomatic contacts monitored for fever or rash
    - 18 days beyond last contact **OR**
    - 14 days beyond successful vaccination
- Followup
  - Laboratory results & epi links
  - Case outcomes/complications
  - Vaccine adverse events (for VAERS)

Smallpox
Summary of Key Points

- Smallpox is transmitted person to person; standard and airborne precautions should be initiated in all suspected cases until smallpox is ruled out.

- Smallpox cases should be considered infectious from the onset of fever until all scabs have separated.

Smallpox
Summary of Key Points

- Vaccine-induced immunity wanes with time; therefore most people today are considered susceptible to smallpox infection.
- In a smallpox outbreak, vaccination is indicated for all case contacts, including health care workers and case investigators.
- Smallpox surveillance includes pre-event rash surveillance, post-event surveillance for active cases, and follow-up of cases, contacts, and vaccine recipients.

Smallpox
Summary of Key Points

- Epidemiologic features that differentiate smallpox from chickenpox include a higher case fatality and a lower attack rate.

- Clinical features differentiating smallpox from varicella include differences in lesion progression and distribution, illness course and presence of a febrile prodrome.

Resources

- Centers for Disease Control & Prevention
  - Bioterrorism Web page: http://www.bt.cdc.gov/
  - CDC Office of Health and Safety Information System (personal protective equipment)

    http://www.cdc.gov/od/ohs/

- USAMRIID -- includes link to on-line version of Medical Management of Biological Casualties Handbook http://www.usamriid.army.mil/

Resources

- Office of the Surgeon General: Medical Nuclear, Biological and Chemical Information

  http://www.nbc-med.org

- St. Louis University Center for the Study of Bioterrorism and Emerging Infections

  http://bioterrorism.slu.edu