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Biopreparedness

M1 Infectious Diseases Sequence

Sandro Cinti

Spring 2009

University of Michigan
Medical School

What is Bioterrorism?

- Bioterrorism is the malevolent use of viruses, bacteria, fungi or toxins to produce death or disease in humans, animals or plants.

Any Examples of Bioterrorism?

- 1360 – Plague victims' bodies thrown over besieged city's walls
- 1763 – Europeans give smallpox infected blankets to Native Americans
- 1984 – Bhagwan Shree Rajneesh contaminates food with Salmonella to win election
- 1994 – Shoko Assahara group attack Tokyo subway with sarin gas
- 2001 – Anthrax

The 1979 Sverdlovsk Anthrax Outbreak

PD-INEL UCLA Department of Epidemiology

Other images of Sverdlovsk facility removed

See: http://www.semp.us/publications/biot_reader.php?BiotID=324

Why use biological weapons?

Why Use Biological Weapons?

- Cheap-800 X less than nucs
- Easy to acquire
  - Dual use
  - Web-based information
- High Fatality
  - 100 kg anthrax could kill 3 million (OTA report, 1993)
- High Panic factor

What makes a good bioweapon?

HHS AND USDA SELECT AGENTS AND TOXINS
7 CFR Part 331, 9 CFR Part 121, and 42 CFR Part 73

HHS SELECT AGENTS AND TOXINS

Abrin
Cercopithecine herpesvirus 1 (Herpes B virus)
Coccidioides posadasii
Conotoxins
Crimean-Congo haemorrhagic fever virus
Diacetoxyscirpenol
Ebola virus
Lassa fever virus
Marburg virus
Monkeypox virus
Reconstructed replication competent forms of the 1918 pandemic influenza virus containing any portion of the coding regions of all eight gene segments (Reconstructed 1918 Influenza virus)
Ricin
Rickettsia prowazekii
Rickettsia rickettsii
Saxitoxin
Shiga-like ribosome inactivating proteins
South American Haemorrhagic Fever viruses
- Flexal
- Guanarito
- *Junin*
- Machupo
- Sabia

Tetrodotoxin
Tick-borne encephalitis complex (flavi) viruses
- Central European Tick-borne encephalitis
- Far Eastern Tick-borne encephalitis
- Kyasanur Forest disease
- Omsk Hemorrhagic Fever
- Russian Spring and Summer encephalitis

Variola major virus (Smallpox virus) and
- Variola minor virus (Alastrim)

Yersinia pestis

OVERLAP SELECT AGENTS AND TOXINS

Bacillus anthracis
Botulinum neurotoxins
Botulinum neurotoxin producing species of *Clostridium*
Brucella abortus
Brucella melitensis
Brucella suis
Burkholderia mallei (formerly *Pseudomonas mallei*)
Burkholderia pseudomallei (formerly *Pseudomonas pseudomallei*)
Clostridium perfringens epsilon toxin
Coccidioides immitis
Coxiella burnetii
Eastern Equine Encephalitis virus
Francisella tularensis
Hendra virus
Nipah virus
Rift Valley fever virus
Shigatoxin
Staphylococcal enterotoxins
T-2 toxin
Venezuelan Equine Encephalitis virus

USDA SELECT AGENTS AND TOXINS

African horse sickness virus
African swine fever virus
Akabane virus
Avian influenza virus (highly pathogenic)
Bluetongue virus (Exotic)
Bovine spongiform encephalopathy agent
Camel pox virus
Classical swine fever virus
Cowdria ruminantium (Heartwater)
Foot-and-mouth disease virus
Goat pox virus
Japanese encephalitis virus
Lumpy skin disease virus
Malignant catarrhal fever virus (Alcelaphine herpesvirus type 1)
Menangle virus
Mycoplasma capricolum/ M.F38/M. *mycoides* Capri (contagious caprine pleuropneumonia)
Mycoplasma mycoides mycoides (contagious bovine pleuropneumonia)
Newcastle disease virus (velogenic)
Peste des petits ruminants virus
Rinderpest virus
Sheep pox virus
Swine vesicular disease virus
Vesicular stomatitis virus (Exotic)

USDA PLANT PROTECTION AND QUARANTINE (PPQ) SELECT AGENTS AND TOXINS

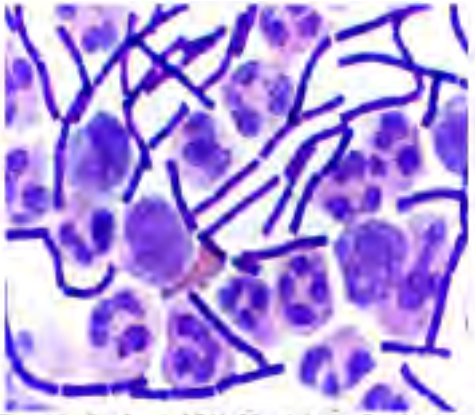
Candidatus Liberobacter africanus
Candidatus Liberobacter asiaticus
Peronosclerospora philippinensis
Ralstonia solanacearum race 3, biovar 2
Schlerophthora rayssiae var zeae
Synchytrium endobioticum
Xanthomonas oryzae pv. oryzicola
Xylella fastidiosa (citrus variegated chlorosis strain)

2/23/06

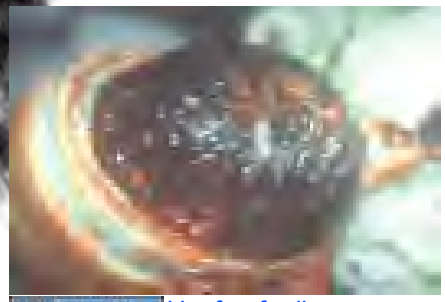
Category "A" Biological Agents

- Variola major (Smallpox)
- *Bacillus anthracis* (Anthrax)
- *Yersinia pestis* (Plague)
- *Francisella tularensis* (Tularemia)
- Botulinum toxin (Botulism)
- Filoviruses and Arenaviruses (Viral hemorrhagic fevers)

Anthrax- *Bacillus anthracis*



Cutaneous



Inhalational

Gastrointestinal

Anthrax

- Spore former
- Not transmissible person-person
- Inhalational-high mortality (50-90%)
  - 2-3 IV antibiotics
- Prophylaxis- ciprofloxacin, doxycycline-60 days

Tularemia

PD-INEL Source Undetermined

PD-GOV CDC

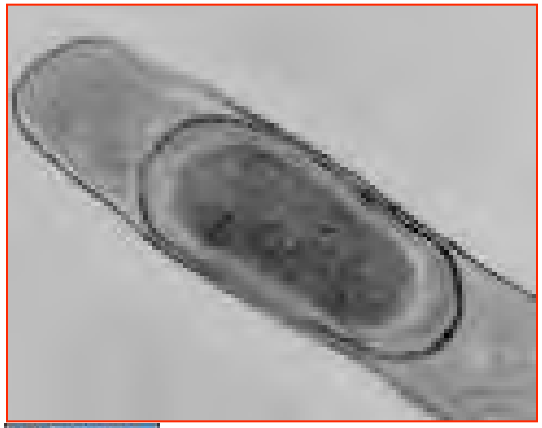
Cutaneous

PD-INEL Cornell University Medical College

- G(-) Coccobacillus
- 1-2 organisms can cause infection
- Not person-person spread
- Tx-aminoglycosides, cipro, doxycycline

Botulinum Toxin

- Made by the bacterium *Clostridium botulinum*
- Most toxic substance on earth - food poisoning (0.1 ug lethal dose)
- Weaponizable and aerosolizable (air & food supplies)
- *BoTox* also used to medically, anti-wrinkle
- Secreted protein neurotoxin causing flaccid paralysis
- Death due to asphyxiation



PD-INEL Source Undetermined

C. botulinum

Image of Botox injection removed

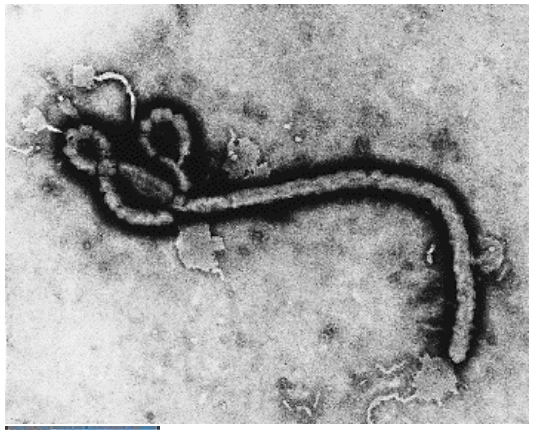
Image available here: www.stylelist.com/blog/tag/anti-aging/

Cosmetic improvements are NOT bioterrorism

Hemorrhagic Viruses

- Ebola, Marburg, Yellow Fever, Lassa
- Viral syndrome with hemorrhagic complications
- High fatalities with Ebola (80%)
- No treatments, few vaccines (YF)
- Person-person spread

PD-INEL Dr. Lyle Conrad, Joel G. Breman, CDC PHIL #7201



PD-INEL Source Undetermined

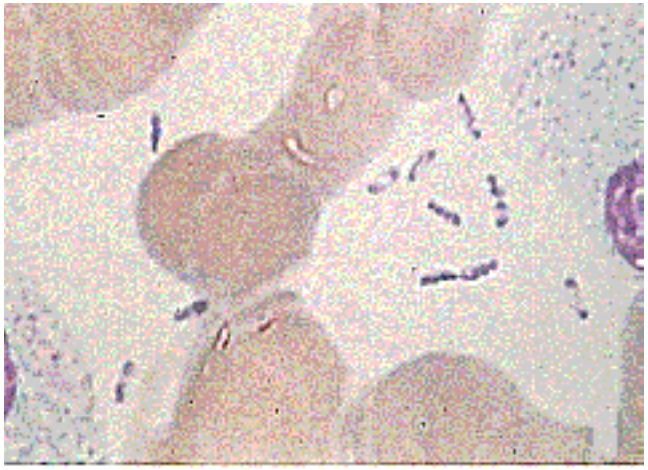
Plague-*Yersinia pestis*

PD-GOV World Health Organization, CDC PHIL #463

PD-GOV CDC PHIL #2047

PD-INEL Source Undetermined

Bubonic



PD-INEL Source Undetermined

Septicemic Plague

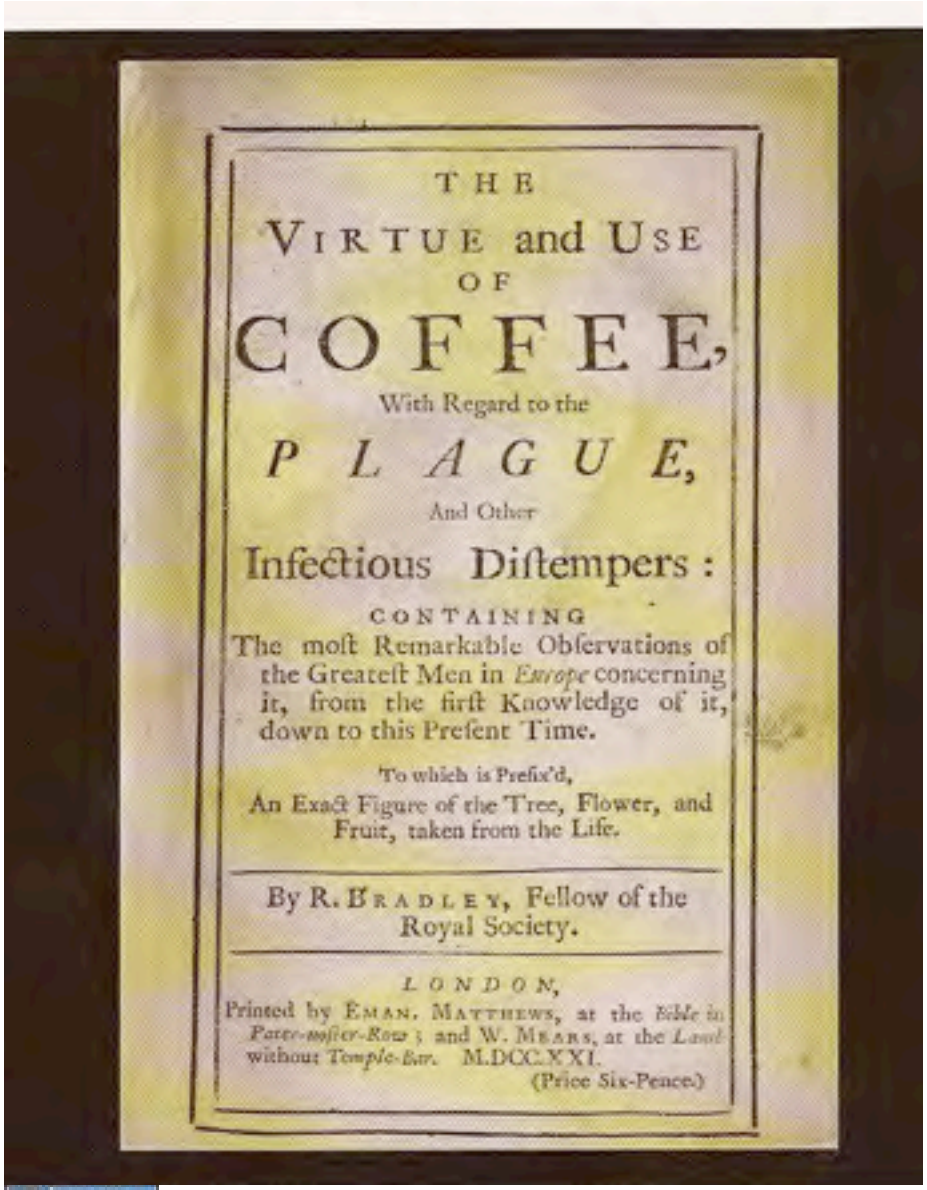
PD-INEL Source Undetermined

PD-INEL Source Undetermined

Pneumonic Plague

- Most likely form in BT
- Mortality 80-90%
- Person-person transmission
- Tx- Streptomycin, IV ciprofloxicin or doxycycline
- Prophylaxis- oral cipro or doxy

PD-INEL Source Undetermined



THE

VIRTUE and USE

OF

COFFEE,

With Regard to the

PLAGUE,

And Other

Infectious Diſtempers:

CONTAINING

The moſt Remarkable Obſervations of the Greateſt Men in *Europe* concerning it, from the firſt Knowledge of it, down to this Preſent Time.

To which is Preſix'd,

An Exact Figure of the Tree, Flower, and Fruit, taken from the Life.

By R. BRADLEY, Fellow of the Royal Society.

LONDON,

Printed by EMAN. MATTHEWS, at the *Bible* in *Paternoſter-Row*; and W. MEARS, at the *Lamb* without *Temple-Bar*. M.DCC.XXI.

(Price Six-Pence.)

PD-EXP 18th century London newspaper

How would BT agents be disseminated?

- Food
- Water
- Zoonotic
- Aerosol

How would a BT attack be detected?

Clues to a BT Attack

- A large number of ill persons presenting at the same time with a similar disease, especially the following syndromes:
  - Flaccid paralysis (botulinum toxin)
  - Hemorrhagic fevers (Ebola, Lassa fever)
  - Vesicular/pustular rash with considerable mortality (smallpox)
  - Influenza-like illness associated with a widened mediastinum on chest X-ray and/or meningitis (anthrax)
  - Pneumonia with painful lymphadenopathy (plague)

Clues to a BT Attack

- Illness in animals and humans concurrently
- A large number of unexplained deaths, especially in young healthy adults
- A single case of an uncommon organism (e.g., smallpox, pulmonary anthrax, Ebola)
- Multiple disease entities presenting in one patient
- An unusual disease presentation (e.g., pneumonic instead of bubonic plague)

Clues to a BT Attack

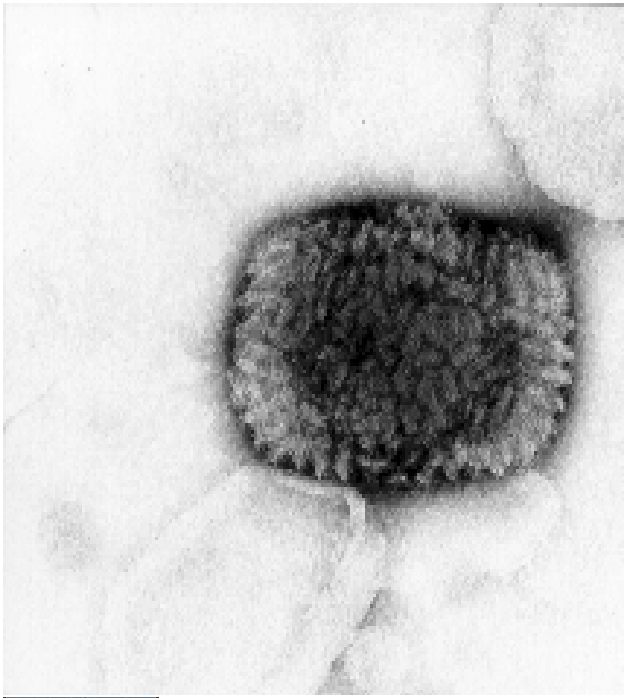
- An unusual geographic distribution (e.g., Ebola in the U.S.)
- An unusual seasonal pattern (e.g., influenza in summer)
- An illness that fails to respond to usual antimicrobials or vaccines (e.g., engineered antibiotic/vaccine resistant anthrax)
- Clusters of a similar illness in non-contiguous areas, domestic or foreign

36 yo female with rash and fever

PD-INEL Source Undetermined

Smallpox: Overview

- **1980 - Global eradication**
- **Humans were only known reservoir**
- **Person-to-person transmission (aerosol/ contact)**
- **Up to 30% mortality in unvaccinated**



PD-INEL Source Undetermined

Smallpox: Clinical Features

- Prodrome (incubation 7-17 days)
  - **Acute onset of fever, malaise, headache, backache, vomiting, occasional delirium**
  - **Transient erythematous rash**
- Exanthem
  - **Begins face, hands, forearms**
  - **Spread to lower extremities then trunk over ~ 7 days**
  - **Synchronous progression: macules --> vesicles --> pustules --> scabs**
  - **Lesions on palms /soles**

Smallpox Enanthem

Day 3

PD-INEL World Health Organization

Day 4

PD-INEL World Health Organization

Day 5

PD-INEL World Health Organization

Day 7

PD-INEL World Health Organization

Day 8-9

PD-INEL World Health Organization

Day 10-14

PD-INEL World Health Organization

PD-1NEL World Health Organization

PD-INEL CDC PHIL # 131

PD-INEL Source Undetermined

	SMALLPOX	CHICKENPOX
FEVER	2–4 days before the rash	At time of rash
RASH		
Appearance	Pocks at same stage	Pocks in several stages
Development	Slow	Rapid
Distribution	More pocks on arms & legs	More pocks on body
On palms & soles	Usually present	Usually absent
DEATH	More than 10%	Very uncommon

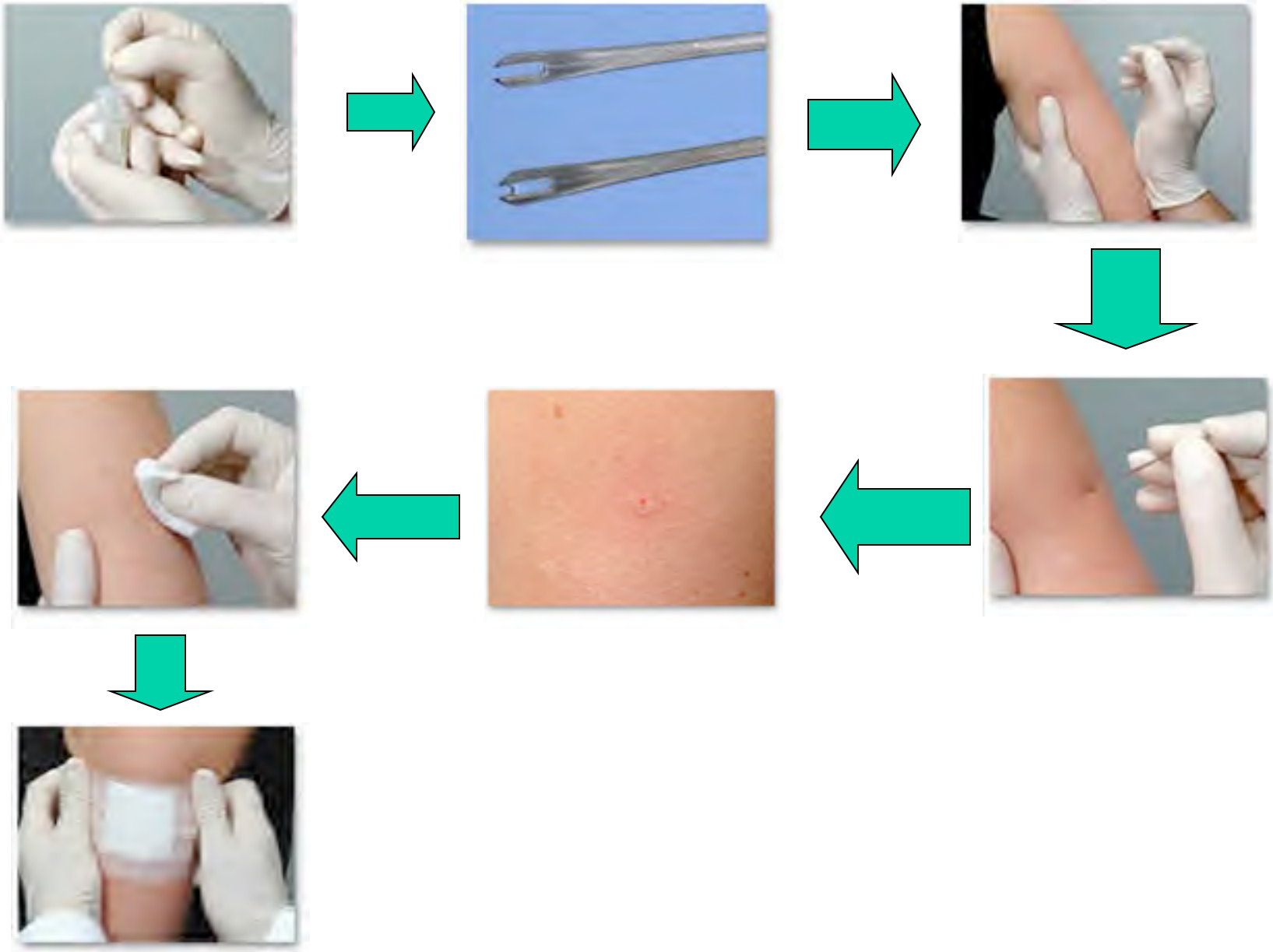
Source Undetermined

PD-INEL World Health Organization

PD-INEL World Health Organization

- Smallpox vaccine production using cows

FAIR USE Source Undetermined



Day 4 (8-13-02)

Day 6 (8-15-02)

Day 8 (8-17-02)

Day 10 (8-19-02)

Day 12 (8-21-02)

Day 14 (8-23-02)

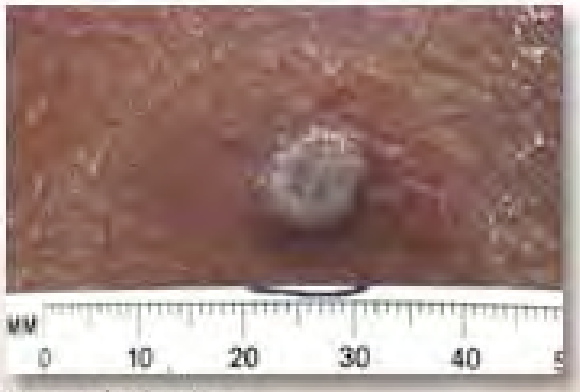
Day 18 (8-27-02)

Day 20 (8-29-02)

Normal Reactions

Normal reactions include a wide spectrum of cutaneous presentations:

Normal Reaction



Normal Reaction

Normal with Lymphangitis

Normal with Satellite Lesions

PD-INEL Source Undetermined

Staph Infection at Site

Dr. V. Fulginiti

Erythema Multiforme

PD-INEL Dr. V. Fulginiti

PD-INEL Dr. V. Fulginiti

PD-INEL Dr. V. Fulginiti

PD-GOV Arthur E. Kaye CDC ID#:3286

PD-GOV Arthur E. Kaye; J. Michael Lane, M.D. CDC PHIL #3318

Accidental Inoculation


PD-INEL Dr. H. Kempe


PD-INEL Dr. V. Fulginiti


PD-INEL Dr. V. Fulginiti

To sites of acne


PD-INEL Dr. V. Fulginiti


PD-INEL Dr. V. Fulginiti

Diaper implantation

Eczema Vaccinatum

PD-INEL Dr. H. Kempe

PD-INEL Dr. H. Kempe

PD-GOV Arthur E. Kaye CDC PHIL #3305

Generalized Vaccinia





Progressive Vaccinia

Child with Hypogam

Child with Hypogam

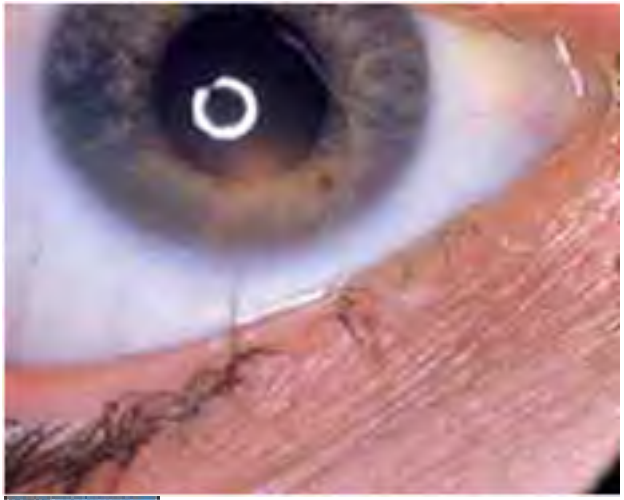
Lymphosarcoma

Child with SCID

Child with SCID

Lymphoma

Vaccinia Keratitis



PD-INEL Dr. V. Fulginiti

PD-INEL Dr. V. Fulginiti

Congenital Vaccinia

PD-INEL Source Undetermined

PD-INEL Source Undetermined

3rd Trimester has the highest risk

Contraindications to Vaccination

- Pregnancy
- Immunodeficiency
- Eczema or Atopic Dermatitis
- Active Skin Conditions
- Active Eye Disease
- Allergy to Components
- Heart Problems

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Slide 9: UCLA Department of Epidemiology, School of Public Health, http://www.ph.ucla.edu/epi/bioter/sverd/sverd_fig3.html
Slide 13: USDA, HHS, http://www.selectagents.gov/resources/List%20of%20Select%20Agents%20and%20Toxins_111708.pdf
Slide 15: U.S. Air Forces in Europe, http://www.usafe.af.mil/direct/sg/anthrax/Pictures/anthrx22.jpg, Sources Undetermined (All other Images)
Slide 17: Lesion: Source Undetermined, Thumb: CDC, http://www.cdc.gov/Tularemia/Tul_Signssymptoms.html X-Ray: Cornell University Medical College
Slide 18: C. botulinum: Source Undetermined; Image of botox injection is available here: www.stylelist.com/blog/tag/anti-aging/
Slide 19: Dr. Lyle Conrad, Joel G. Breman, CDC PHIL #7201; Source Undetermined
Slide 20: (From left to right) Source Undetermined; World Health Organization, CDC PHIL #463; CDC PHIL #2047; Source Undetermined
Slide 21: Sources Undetermined
Slide 22: Source Undetermined
Slide 23: 18th century London newspaper
Slide 31: Source Undetermined
Slide 32: Source Undetermined
Slide 35: World Health Organization, http://www.who.int/emc/diseases/smallpox/slideset/ (All images)
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Slide 38: World Health Organization, http://www.who.int/emc/diseases/smallpox/slideset/ (All images)
Slide 39: CDC PHIL # 131, http://emergency.cdc.gov/agent/smallpox/smallpox-images/smallpox1.htm
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Slide 43: Source Undetermined
Slide 44: CDC, http://emergency.cdc.gov/training/smallpoxvaccine/reactions/download_pocket_guide.htm
Slide 45: Logical Images (All Images), http://emergency.cdc.gov/training/smallpoxvaccine/reactions/tl_view.htm
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Slide 53: Dr. V. Fulginiti; Dr. V. Fulginiti
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