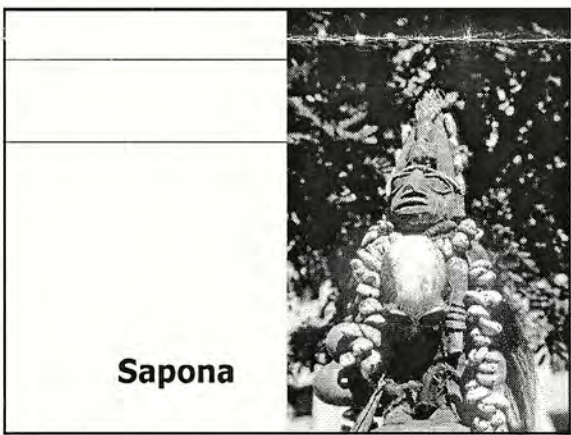
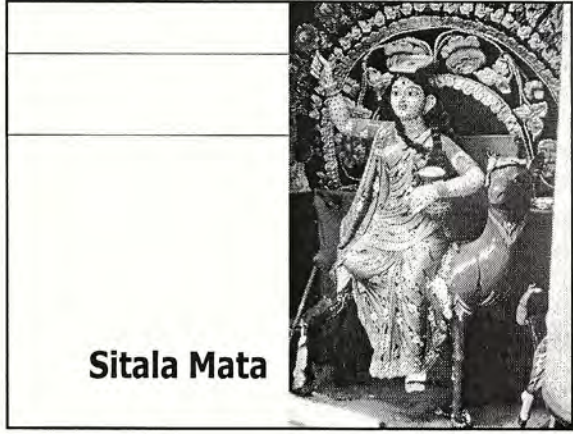
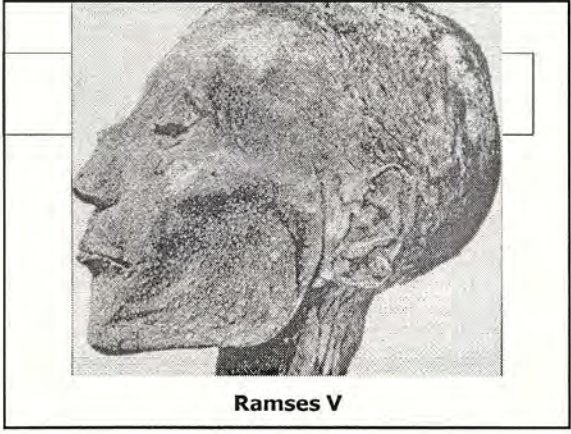


- 25 years ago - An international commission declared eradication / 16 years ago - completed the Final Red Book / 2 labs
- Member Expert in disease - but smallpox is back & thus a most serious bio weapon threat.
- Today - cover three themes
 - ① Reminders of what smallpox represents
 - ② Brief recap of the eradication campaign succeeded primarily because of...
 - ③ Discuss threat & what we are doing about it.

Smallpox
the death and resurrection of a virus

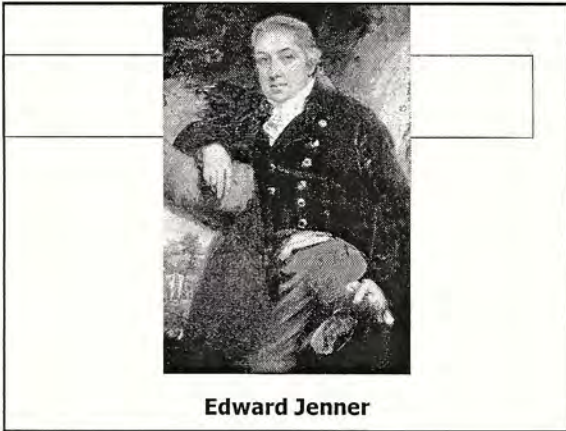
D.A. Henderson MD, MPH

Yale School of Medicine
April 7, 2004

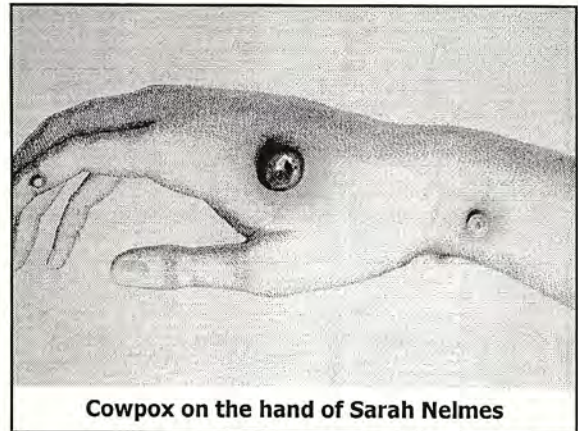


"That disease was the most terrible of all the ministers of death. The horror of the Plague...visited our shores only once or twice within living memory but the smallpox was always present, filling the churchyards with corpses...and making the eyes and cheeks of the betrothed maiden objects of horror to the lover."

Macauley



Edward Jenner



Cowpox on the hand of Sarah Nelmes

Deaths in the 20th Century

Due directly or indirectly to armed conflict:

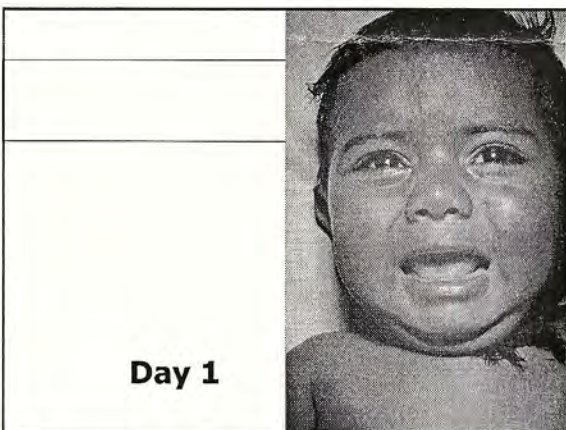
100,000,000

Due to smallpox

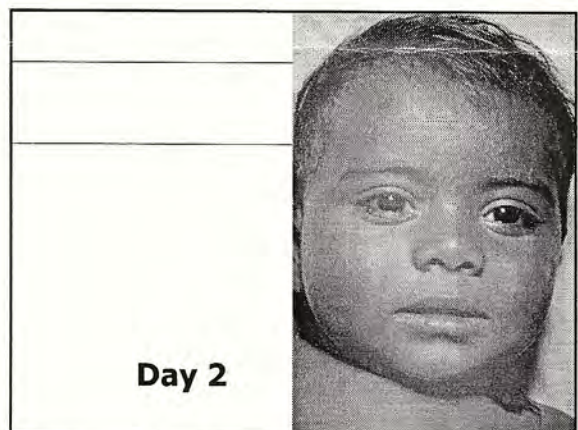
300,000,000+

Smallpox -- characteristics

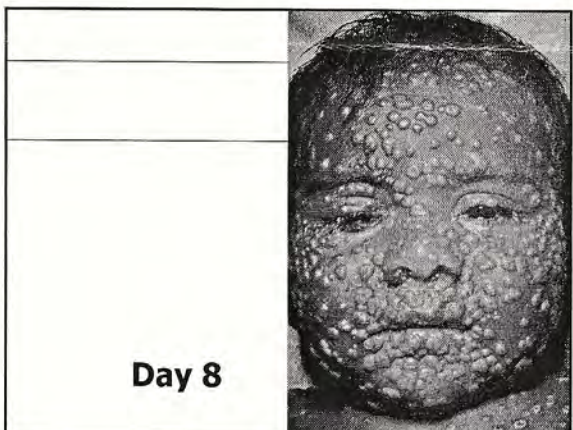
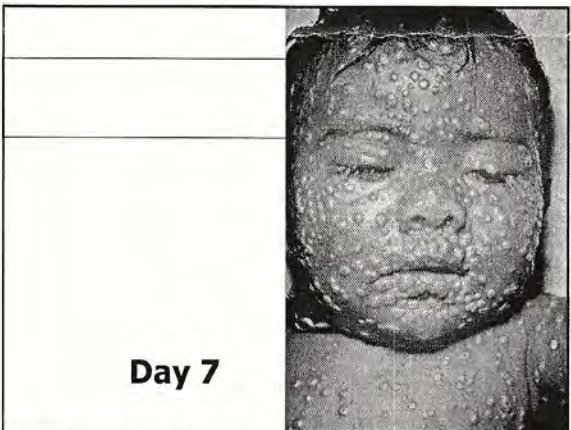
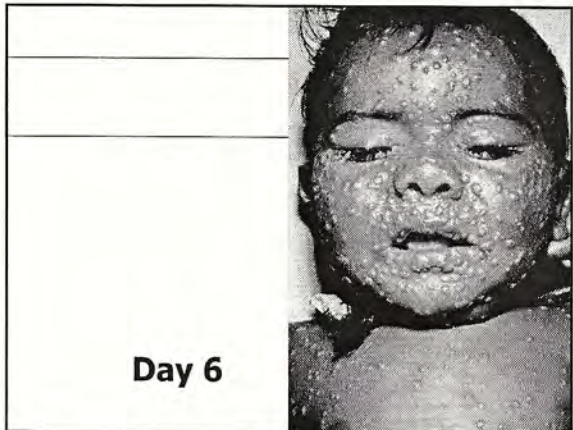
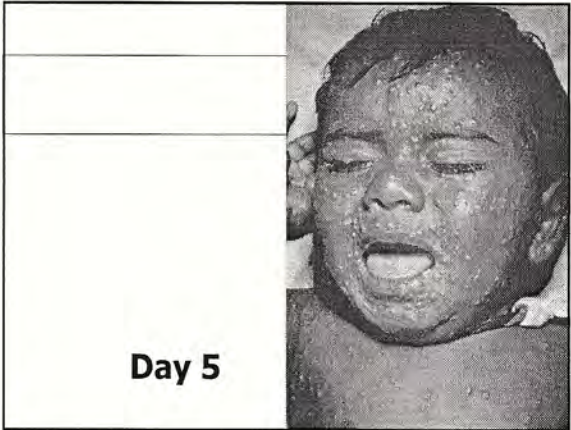
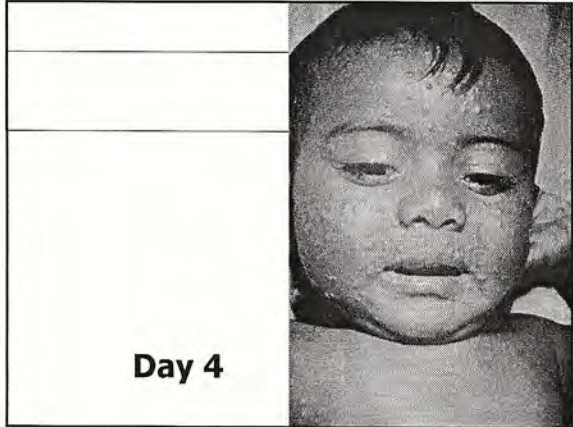
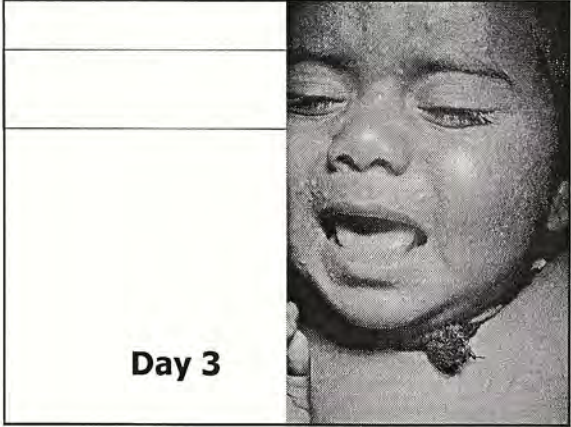
- Incubation period is 10-12 days
- Severe flu-like symptoms then rash
- Case fatality rate --30 %
- No therapy available

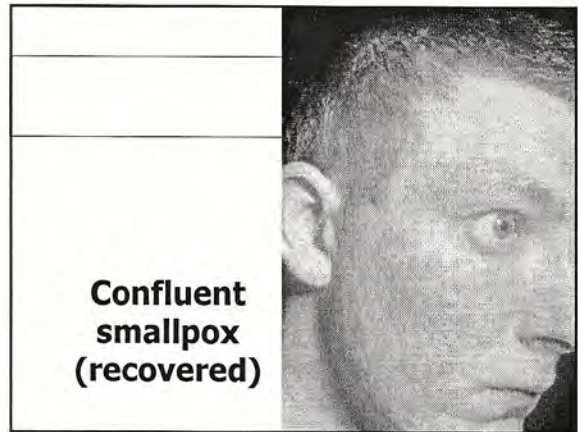
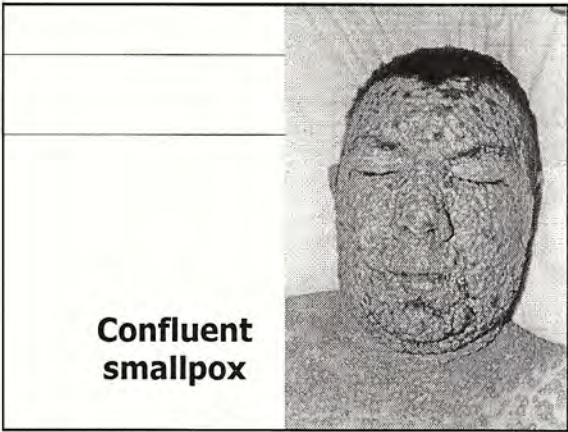
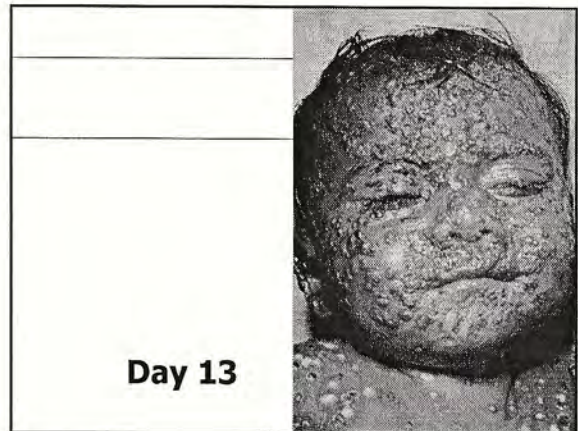
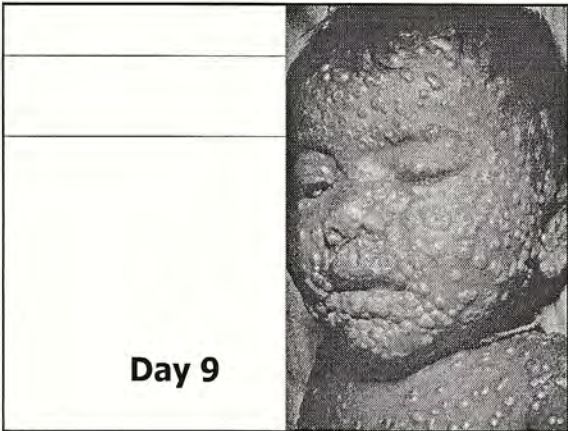


Day 1



Day 2

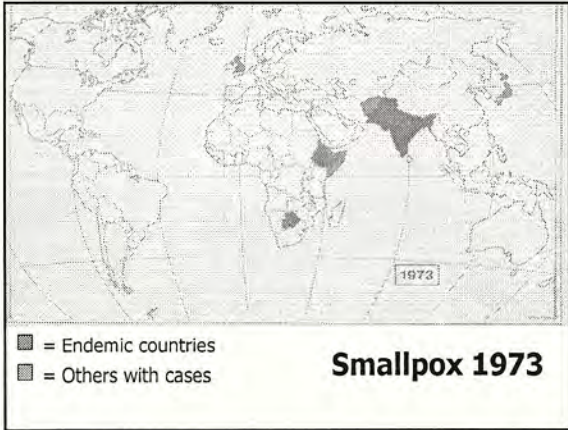
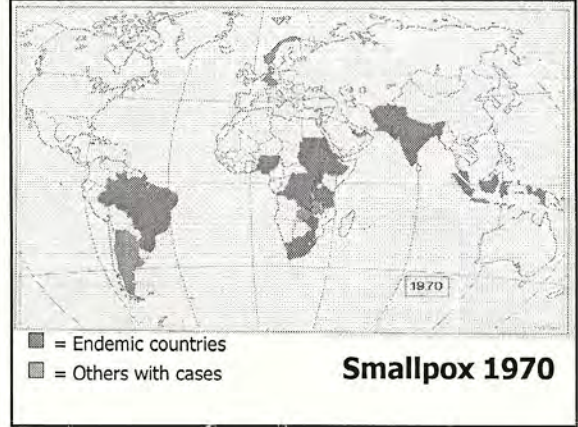
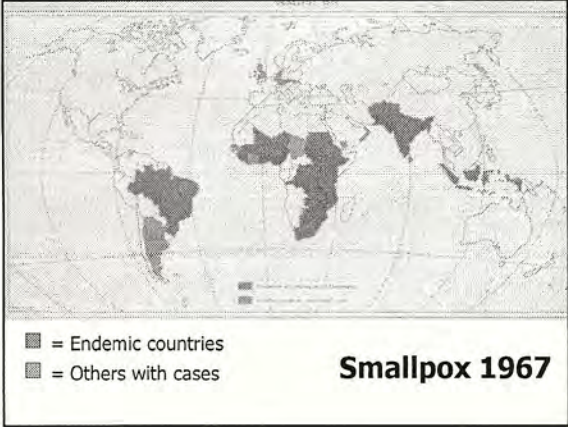


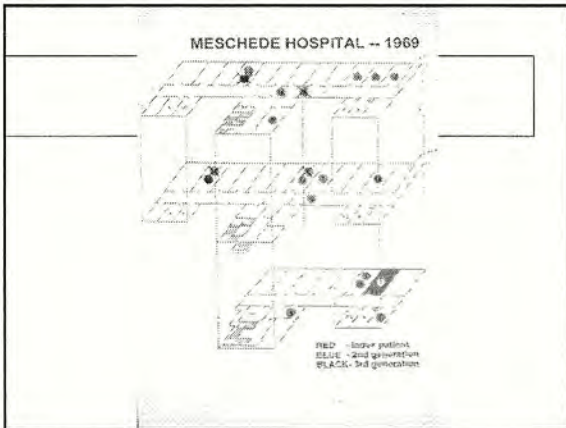
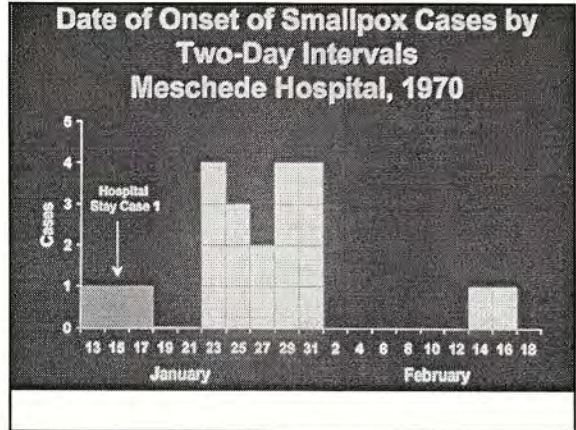
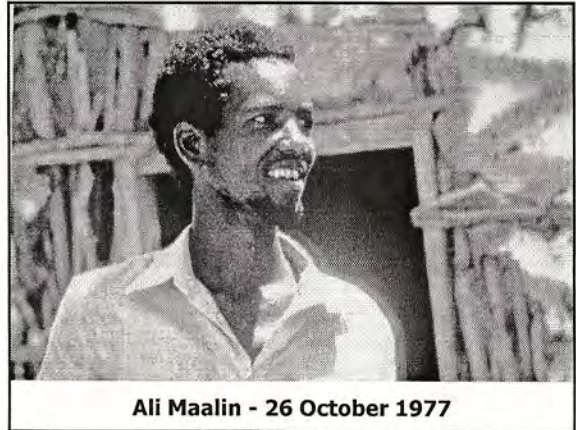
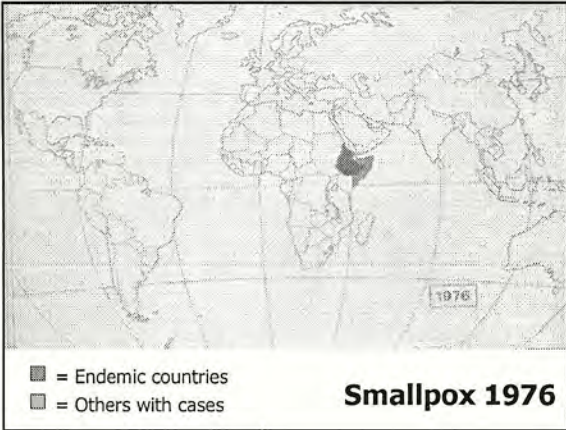


Characteristics of Smallpox Favoring Eradication

- Man -- the only host
- Virus spread -- only during rash; face-to face contact
- Permanent immunity after recovery
- Transmission stops spontaneously in remote areas
- Vaccine is heat-stable and easy to administer
One dose provides long-lasting protection

WHO program





"On May 8, 1980, WHO announced that smallpox had been eradicated from the planet... Soon after the WHO announcement, smallpox was included in a list of viral and bacterial weapons targeted for improvement in the 1981-85 Five-Year Plan.... Where other governments saw a medical victory, the Kremlin perceived a military opportunity...the Soviet military command issued an order to maintain an annual stockpile of 20 tons."

Alibek, 1998

Susceptibility of US Population to Smallpox -- 2004

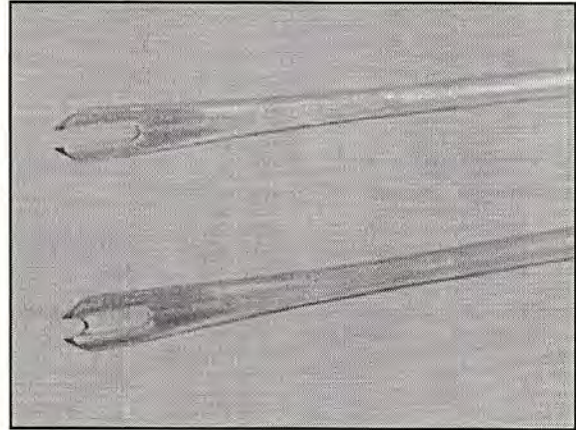
- Vaccination stopped in 1972
- Persons under 33 years have not been vaccinated -- 45% of population
- Persons vaccinated only once pre-1972 have little or no immunity
- Population-- >75% are fully susceptible

Epidemic Response Capability September 18, 2001

- Vaccine manufacturers
 - U.S. None
 - World None
- Vaccine in storage
 - U.S. 15 million doses
 - World ? 80 million doses
- Ready for emergency shipment
 - 90,000 doses of vaccine
 - Limited quantities -- needles, VIG

Smallpox Vaccine Reserve--2004

	<u>No. of doses</u>
■ Wyeth DryVax	15 million
■ Calf-lymph - 1978	
■ Aventis Pasteur	85 million
■ Calf-lymph - 1958	
■ Acambis/Baxter	209 million
■ Vero cell - 2002	
In emergency – dilution of vaccine 1:5 is possible	



MVA – A Next Generation Vaccine?

- Non-replicating attenuated vaccinia strain (Modified Vaccinia Ankara)
- Vaccination by IM –either 2 doses or 1 dose followed by NYCBH vaccinia
- Contract awarded for development and initial manufacturing
- Phase 1 trials are in progress

Options for Vaccination Before an Event

- **Vaccinate no one**
- **Vaccinate those at highest risk, candidates:**
 - Health care workers
 - First responders
 - Truck drivers
 - Essential personnel
- **Vaccinate anyone desiring to be vaccinated**
 - Recommend vaccination
 - Recommend against vaccination
- **Make vaccination compulsory**

A Balance of Risks

- Probability that smallpox will be used as a weapon
- Frequency of adverse reactions
- Likely effectiveness of outbreak control

Smallpox Vaccine Expected Adverse Events

- **Life-threatening complications (per million)**
 - Post-vaccinal encephalitis (3)
 - Progressive vaccinia (1)
 - Eczema vaccinatum (12)
- **Less serious**
 - Generalized vaccinia
 - Accidental inoculation
 - Rash and fever
- If 100 million vaccinated, 100+ deaths might occur (1960's data)

Smallpox vaccine Military Experience to date*

- Numbers are still small – 493,000
 - None hospitalized; 10 missed 1+days of work
- **Post-vaccinal encephalitis - 1**
- **Progressive vaccinia - 0**
- **Eczema vaccinatum - 0**
- Generalized vaccinia - 33
- Infection in contacts - 29

*Note: September 11, 2003

Smallpox vaccine Cardiac complications

- Myopericarditis 56*
 - Onset 7 to 17 days
 - Fever, chest pain, EKG changes, enzymes increased
 - Recovery
- Ischemic events (civilian) 10*
 - Angina, myocardial infarct
 - Difficult to distinguish from normal background
 - Almost certainly coincidental

*Note: data are provisional

Outbreak control

- Smallpox doesn't spread readily
- Patient transmits only after symptoms
- Vaccine protects even when given 3-4 days after infection

Spread of Infection

Spread of disease is slow

- **Household spread --Secondary attack rates**

Measles	76%
Chickenpox	74%
Smallpox	58%
- **Community spread --measles and chickenpox spread before symptoms; smallpox does not**

Epidemiology of Smallpox

Transmission Patterns in Europe: 1958-1973

- **Outbreaks: 34**
- **Cases: 573**
 - Transmission in hospital: 277 (48%)
 - Transmission in home: 143 (25%)
- **Hemorrhagic and malignant cases – a threat to hospitals**
 - Bradford, UK (1961) Hemorrhagic smallpox 10 cases
 - Germany (1970) Malignant smallpox 16 cases
 - Yugoslavia (1972) Hemorrhagic smallpox 38 cases

Surveillance and Containment

Steps in Containment -- I

- Isolate patient
- Vaccinate all persons who had been in a room with the patient since he/she became febrile (primary contacts)
- Place primary contacts under surveillance with daily temperatures
 - If contact develops fever, isolate at home or special facility until diagnosed
- Vaccinate all household members of primary contacts (secondary contacts)

Surveillance and Containment

Steps in containment -- II

- Make vaccine available on request to those in the area
- Not generally desirable:
 - Compulsory vaccination
 - Quarantine of city or groups of people
 - Closure of airports, suspension of transport

Preparatory steps -- in progress

- Vaccine –
 - Stockpiled--available anywhere in 12 hours
- Each metro region to have plan to make vaccination widely available over 7 days
- Each metro region to have plan to accommodate 500+ patients per million pop.
- Every ER to have negative pressure rooms for examining rash and fever patients

Vaccination Program in Transition

Current, erroneous beliefs

- Smallpox is no longer a threat
- Complication rates are very high
- For health care personnel, vaccination after beginning of an outbreak will suffice
- The responsibility for vaccination rests entirely with the government and the individual

- Are we now better prepared than on 9/11 ?

- Are we fully prepared ?

- How long must we sustain our efforts ?