

Smallpox - Priority concerns → Decision to produce vaccine & vaccination program
 Anthrax
 Those who say - no need to be concerned now - ~~they~~ ^{should not be concerned now about with it}
 - should we ~~delay~~ ^{relax} our efforts vaccination programs
 To better understand - why the emphasis on smallpox - need to know something of its history
 Vaccine - vaccination and response policy

Smallpox: then and Now

University of Minnesota
 D.A. Henderson M.D., M.P.H.
 June 10, 2003



Ali Maalin - 26 October 1977



Ramses V

Deaths in the 20th Century

Due directly or indirectly to armed conflict:

100,000,000

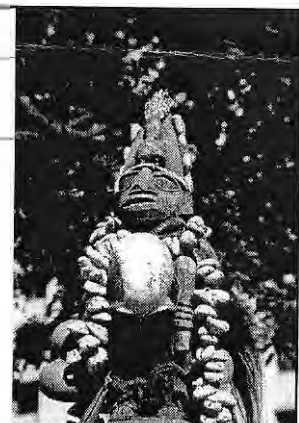
Due to smallpox

300,000,000+

Sitala Mata



Sapona

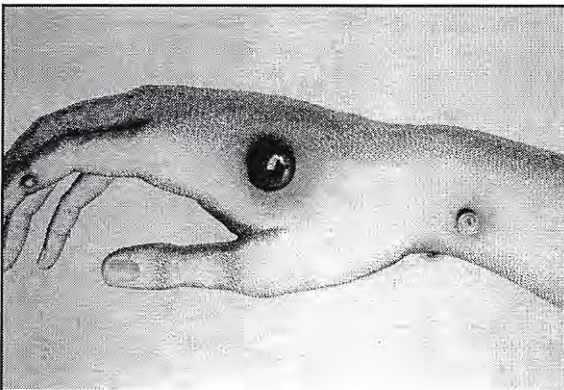


"That disease was the most terrible of all the ministers of death. The horror of the Plague...visited our shores only once or twice within living memory but the smallpox was always present, filling the churchyards with corpses...and making the eyes and cheeks of the betrothed maiden objects of horror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

Macauley



Edward Jenner

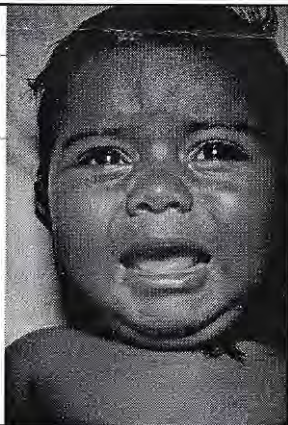


Cowpox on the hand of Sarah Nelmes

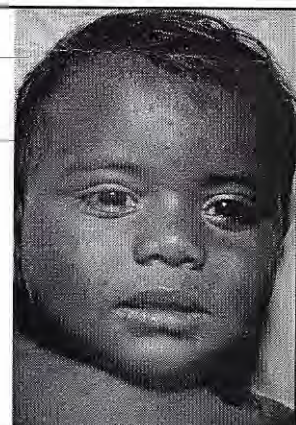
Smallpox -- characteristics

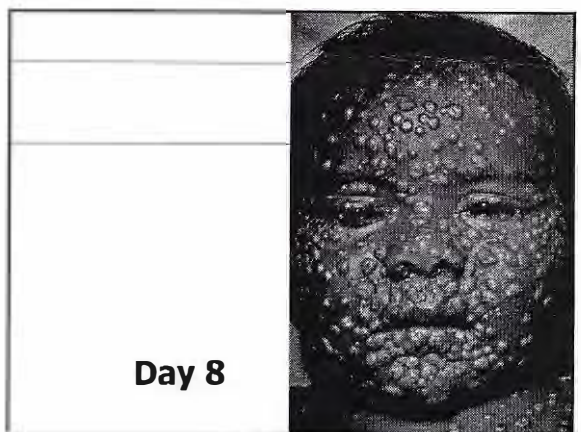
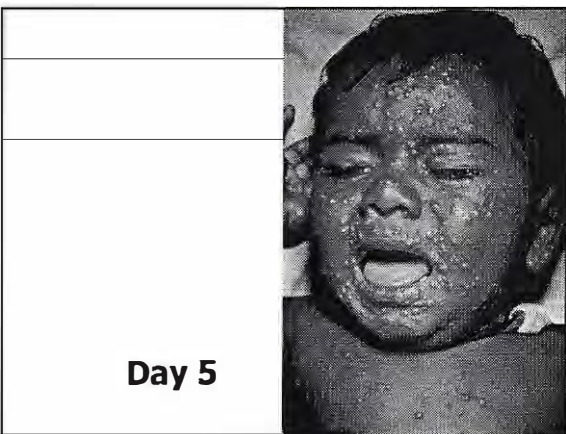
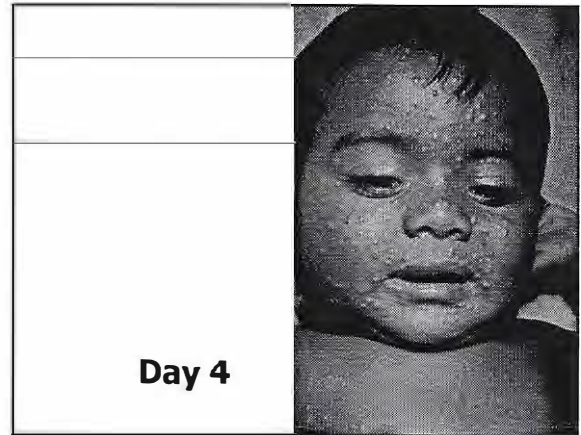
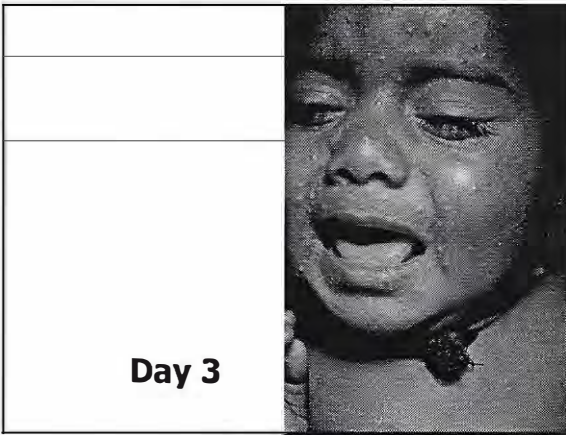
- Time -- infection to illness is 12 days
- Fever, flu-like symptoms then rash
- No anti-viral therapy available
- Case fatality rate --30 %

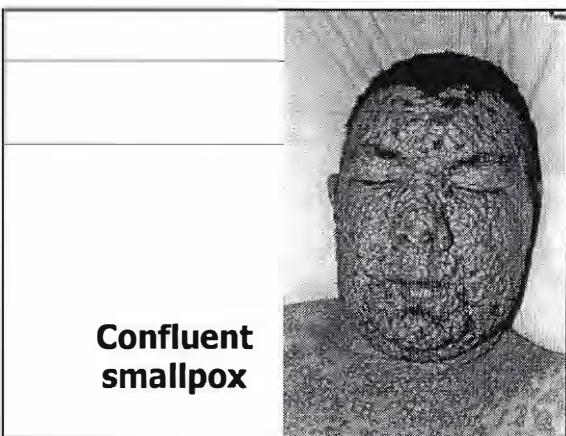
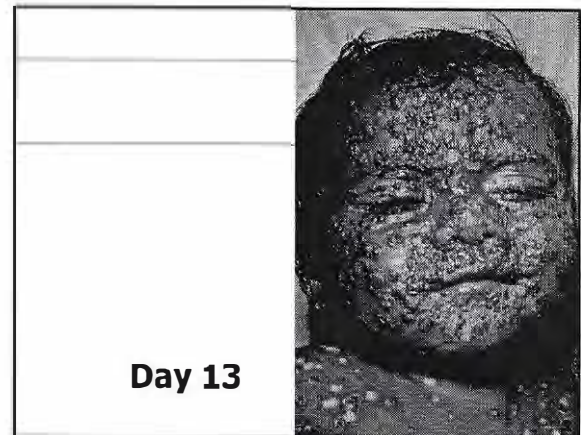
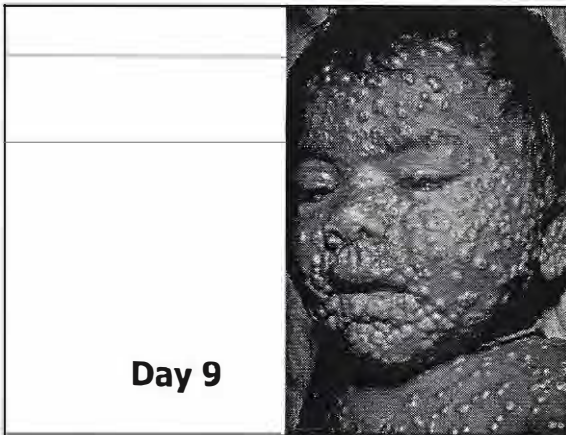
Day 1



Day 2

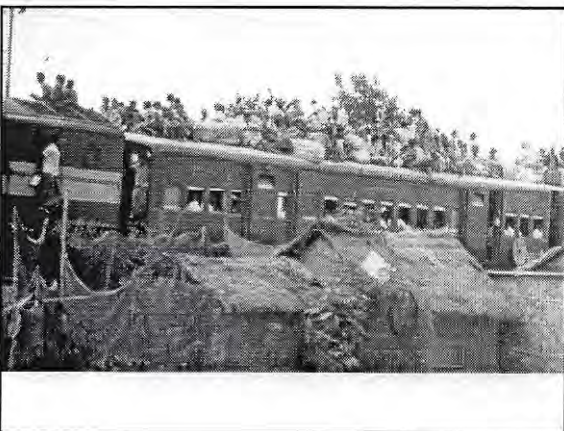
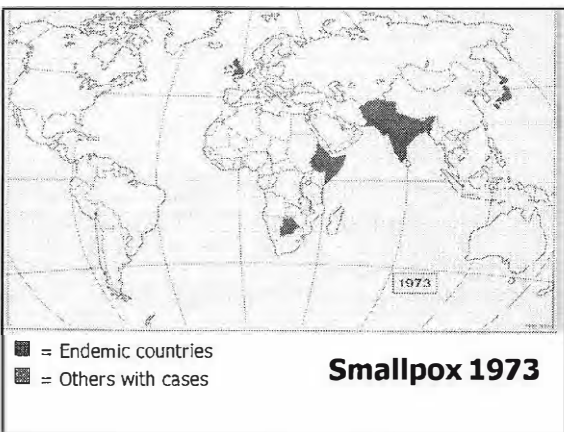
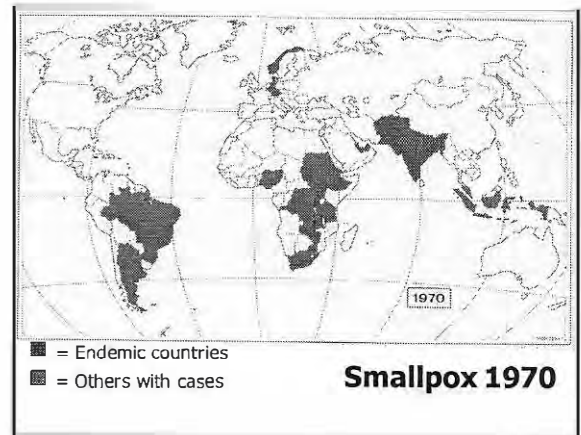
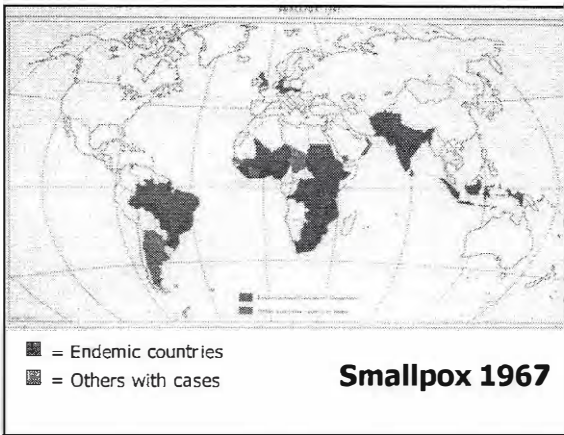


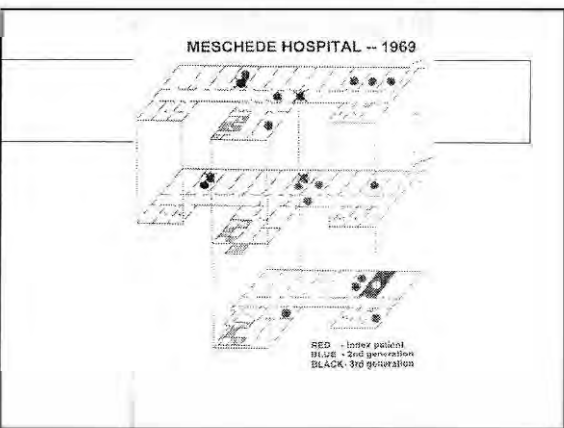
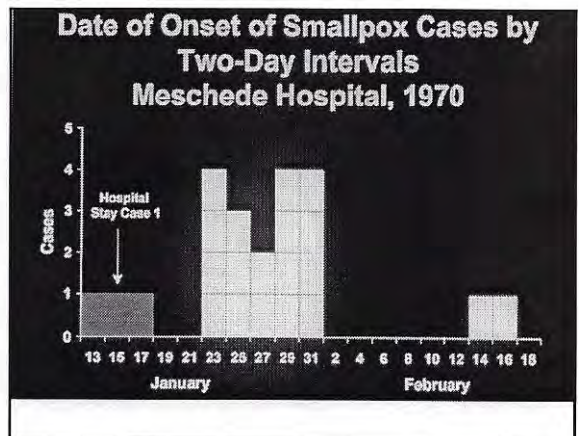
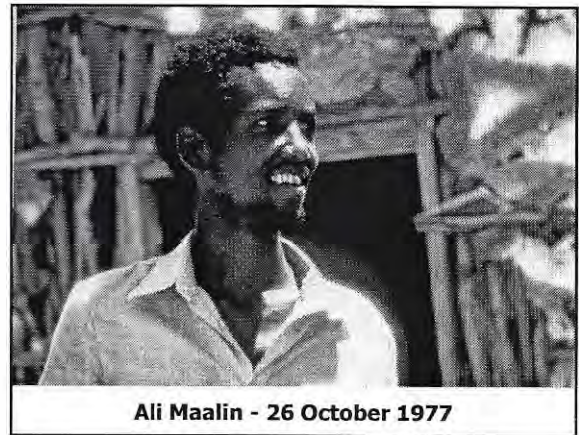
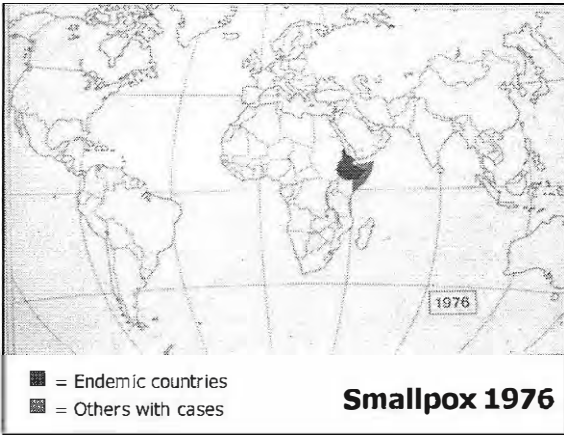




Characteristics of Smallpox Favoring Eradication

- Man -- the only host
- Virus spread -- only during rash
- Permanent immunity after recovery
- Spread of virus -- face-to-face contact
- Transmission stops in remote areas
- Vaccine -- long-lasting protection





“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 -- 2003

- Vaccination stopped in 1972
- Few under 32 years of age have been vaccinated -- 45% of population
- Americans successfully vaccinated only once before 1972 have limited immunity- about 35% of population

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

U.S. Smallpox Vaccines

	<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

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 and public response in 2003
- 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 Experience to date*

- Numbers are still small – 475,000

- Post-vaccinal encephalitis - 1
- Progressive vaccinia - 0
- Eczema vaccinatum - 0

- Generalized vaccinia - 39
- Infection in contacts - 21

*Note: data are provisional

Smallpox vaccine Cardiac complications

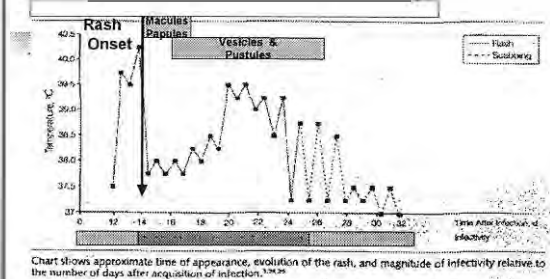
- Myopericarditis 32*
 - Onset 7 to 17 days
 - Fever, chest pain, EKG changes, enzymes increased
 - Recovery
- Ischemic events 10*
 - Angina, myocardial infarct
 - Difficult to distinguish from normal background
 - Almost certainly coincidental

*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

Clinical Course of Smallpox



JAMA, June 9, 1999; Vol 281, No. 22 2129

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
- Seasonal variation
 - Dec to May 24 importations average +45.6 cases
 - Jun to Nov 10 importations average + 0.5 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 twice daily temperatures
 - If the 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
- Communicate with public and professionals frequently and promptly (anticipate CNN)
- 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 7-10 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

- Are we now better prepared than on 9/11 ?
- Are we fully prepared ?
- How long must we sustain our efforts ?