

LAH: Actual date, Apr 20 2005

Smallpox from eradication to biodefense

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Principles of Biodefense

Georgetown Medical Center

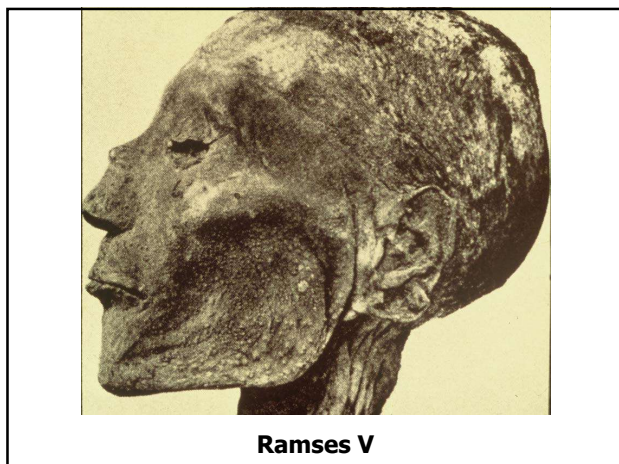
19 January 2005

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Ali Maalin - 26 October 1977

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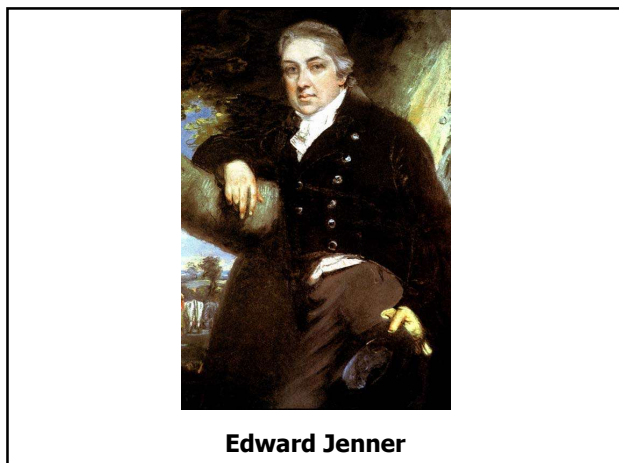
Ramses V

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"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

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Edward Jenner

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Deaths in the 20th Century

Due directly or indirectly to armed conflict:

100,000,000

Due to smallpox

300,000,000+

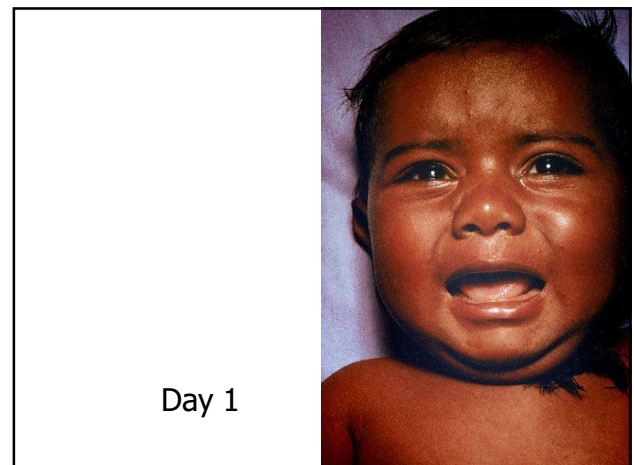
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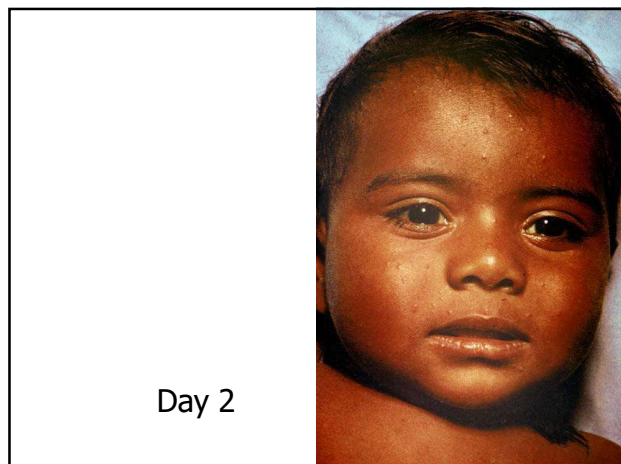
Smallpox -- characteristics

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

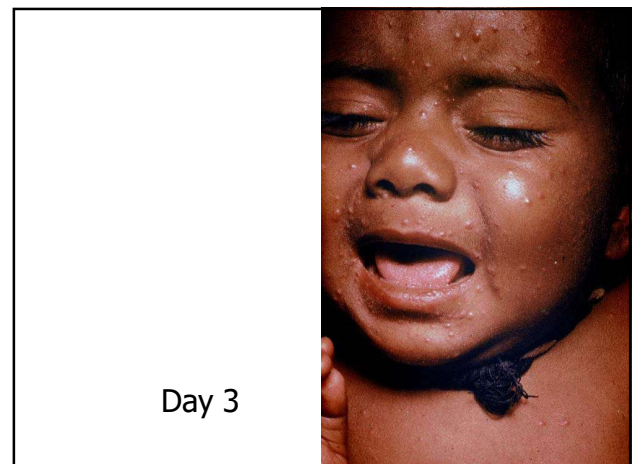
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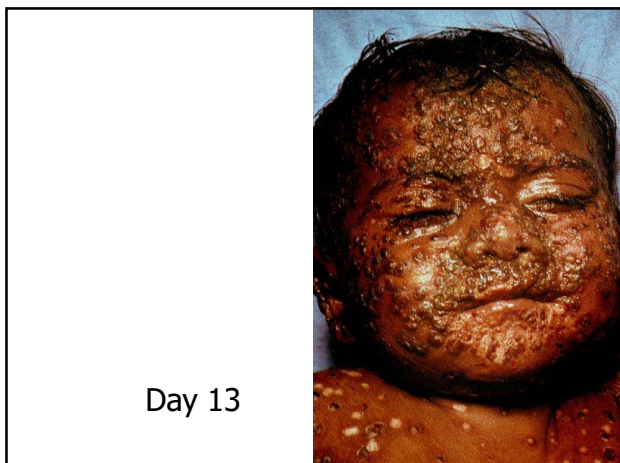
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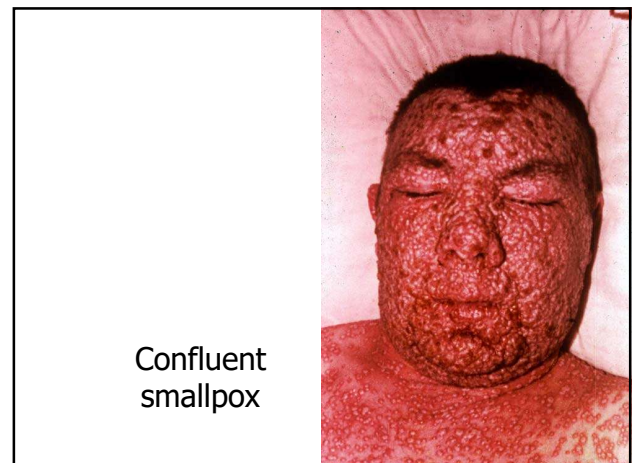
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Confluent
smallpox
(recovered)

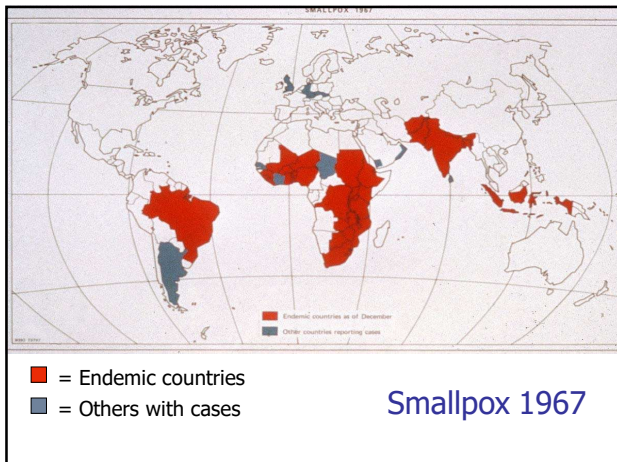


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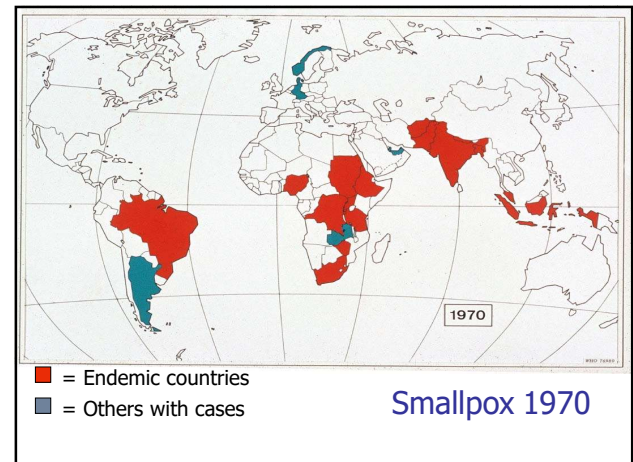
Characteristics of Smallpox Favoring Eradication

- Man -- the only host
- Virus spread -- only after symptoms develop
face-to face contact
- Permanent immunity after recovery
- Transmission stops spontaneously in remote areas
- Vaccine -- heat-stable, easy to administer
One dose provides long-lasting protection

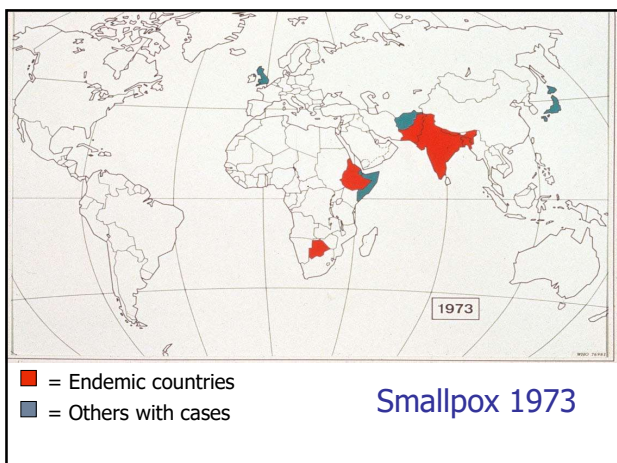
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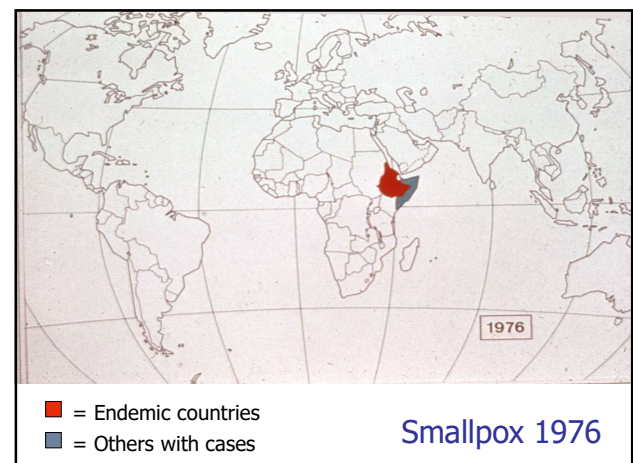
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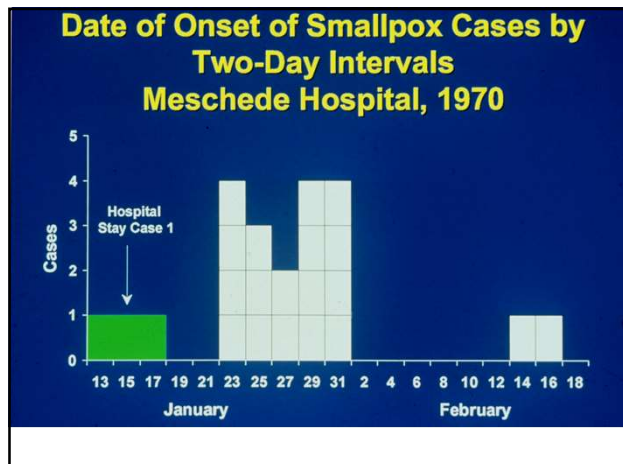
Ali Maalin - 26 October 1977

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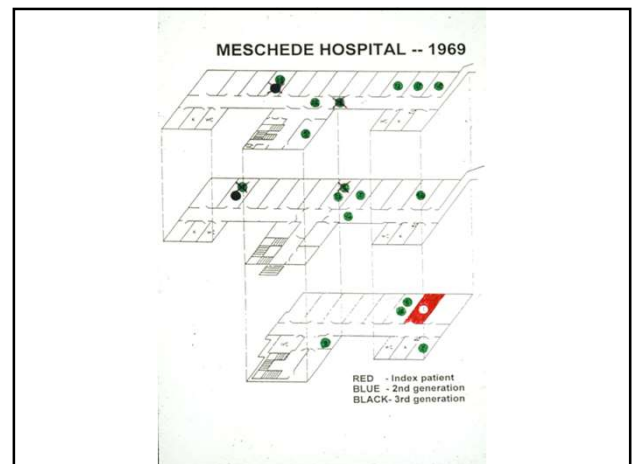


Meschede, Germany - January 1970

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 "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.... **Soviet military command issued an order to maintain an annual stockpile of 20 tons.**"

Ken Alibek, 1998

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 ■ "In December 1990, testing of the new large-scale reactor formulation (630 Liters) was completed. The weapon was ready to be accepted in armament."

Ken Alibek, 2003

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Susceptibility of population to smallpox -- 2005

- Vaccination stopped by 1980
- No persons under 25 years have been vaccinated
- Persons vaccinated only once pre-1980 have little or no immunity
- General population-- probably 75% are fully susceptible to smallpox

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Vaccine availability -- 2001

- Vaccine manufacturers
 - U.S. None
 - World None
- Vaccine in storage
 - U.S. 15 million doses
 - WHO 2 million doses
 - World ? 80 million doses

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A Balance of Risks

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

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Locations of smallpox virus -- 2004

- Known stocks of smallpox virus
 - Centers for Disease Control, Atlanta
 - Russian State Research Center of Virology, Novosibirsk
- Russian centers for smallpox virus production
 - Sergiyev Posad, Kirov, ?other
- Other countries
 - ?Retained stocks from 1970s
 - ?Virus and/or expertise from former Soviet labs

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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)

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Smallpox Vaccination Military experience*

- Total screened 757,000
- Total vaccinated 708,500 (94%)
 - Post-vaccinal encephalitis 1
 - Progressive vaccinia 0
 - Eczema vaccinatum 0
- Infection in contacts 49
- Doses of VIG used 3
 - As of 1 December 2004

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Smallpox vaccination

Cardiac complications -- military

- Myopericarditis 84
 - Onset: 7 to 17 days
 - Fever, chest pain, EKG changes, enzymes increased
 - Recovery
- Ischemic events 24
 - Expected (age adjusted) 40

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Outbreak control

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

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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

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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 case spread
 - Bradford, UK (1961) - Hemorrhagic 10 cases
 - Germany (1970) - Malignant 16 cases
 - Yugoslavia (1972) - Hemorrhagic 38 cases

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Surveillance and Containment

Steps in Containment

- Isolate patient
- Vaccinate all persons who had been in a room with the patient since he became febrile
 - Daily surveillance with temperatures: isolate if fever develops
 - Vaccinate their household contacts
- Make vaccine available on request to those in the area

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The future

- The threat will never go away
- With adequate supplies of vaccine and an ability to act quickly, a smallpox release can be readily managed
- International cooperation, especially communication and action, are vital

WHO must be given and must assume the lead

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Criteria for an antiviral drug

- As a preventive agent
 - Must have advantages not already offered by MVA or NYCBH vaccines
 - Protection by vaccines is ~100% even when given several days after infection
 - Only possible use – for administration during an epidemic but before infection for individuals with CD4 T cells below 300.
 - How many candidate patients?
 - Renal clearance studies before administration?

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Criteria for an antiviral drug

- As a therapeutic agent
 - Must be effective against disease after onset of symptoms
 - No anti-orthopoxvirus agent now on the horizon
 - For a new drug, cost is a factor
 - \$800 million development cost for new drug
 - Current cost/dose of one antiviral is >\$800
 - For one million doses – net cost is \$1.6 billion
 - Costs for replacement doses at expiry

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