6-28

Opportunity to address a distinguished group of leaders in the health care field
regret I can't be here longer need to be in D.C. for an emergency about which I will say
a word at the end.
DR HANFLING FREDRICKSON

Medical and Public Health Preparedness

Leadership Institute Roundtable

D.A. Henderson M.D., M.P.H.

March 28, 2003

focus - biological threats

Organisms of Greatest Concern

- **Smallpox**
- **Anthrax**
- Hemorrhagic fevers
- Plague
- Tularemia
- Botulinum toxin

Deaths During the 20th Century

Due directly or indirectly to armed conflict:

100,000,000

Due to smallpox

300,000,000+

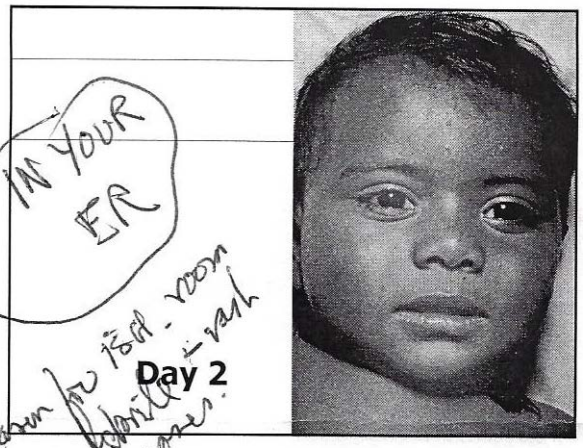
Ali Maalin - 26 October 1977

"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."

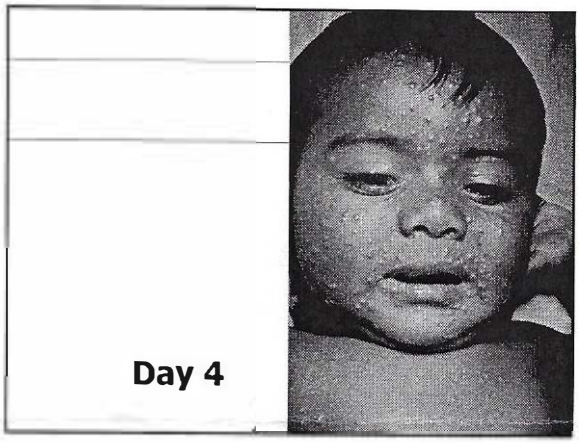
Alibek, 1998

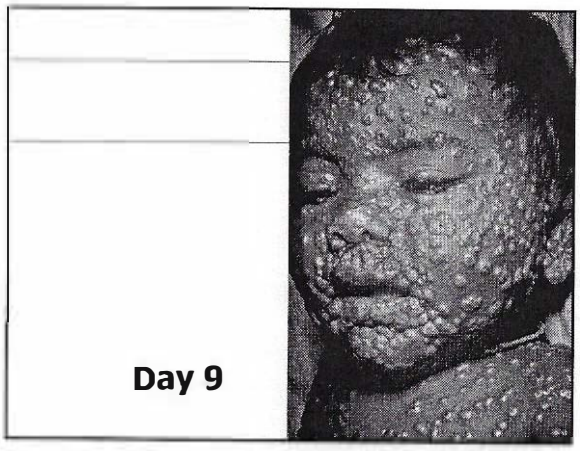
Facts About Smallpox

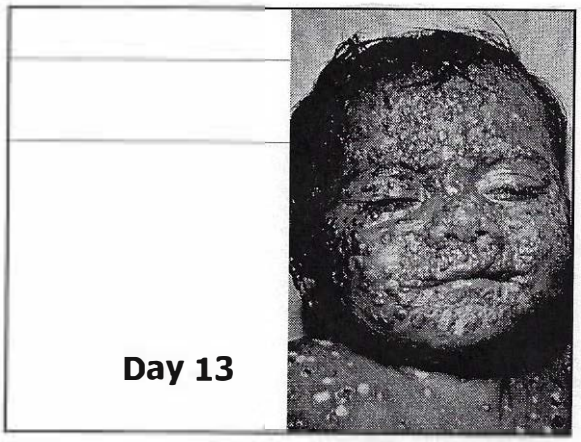
- **Time between infection and illness 12 days**
- **Fever, flu-like symptoms then rash**
- **Case fatality rate --30 %**
- **Not infectious until ill with fever and rash**
- **Transmission affected by temp and humidity**
  - **Summer: Low**
  - **Winter: High (3 to 4 fold higher)**

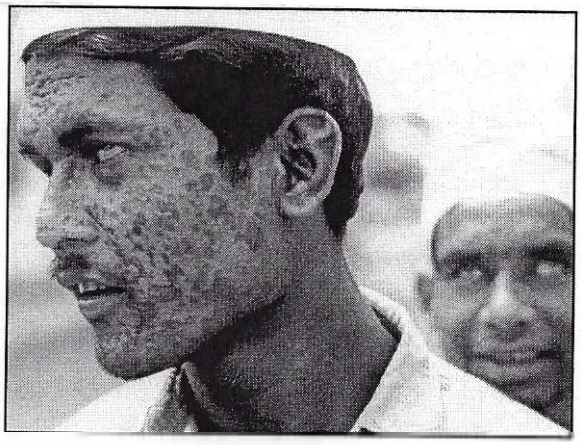


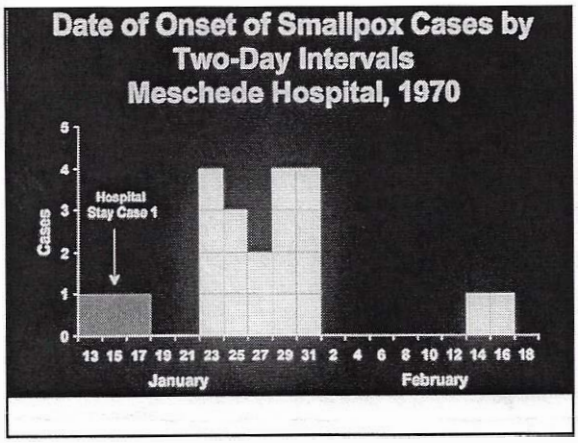
Reason for ISOL room for febrile cases.

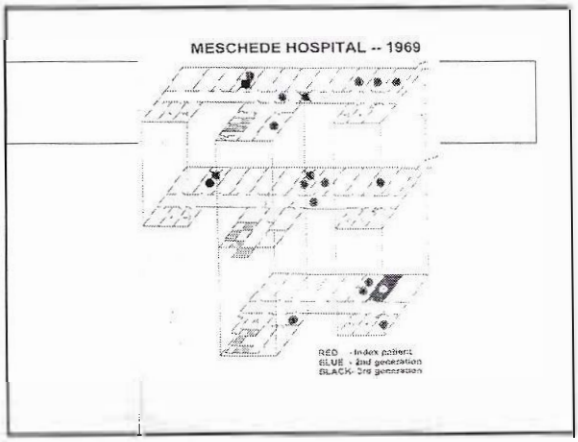












September 2001
The Smallpox Threat

- Vaccination stopped in 1972
  - Few < 32 years have been vaccinated -- 45% of the population
  - Americans vaccinated once pre- 1972 have minimal immunity- 35% of population
- Vaccine immediately available -- 90,000 doses

Wyeth DryVax — 15 million

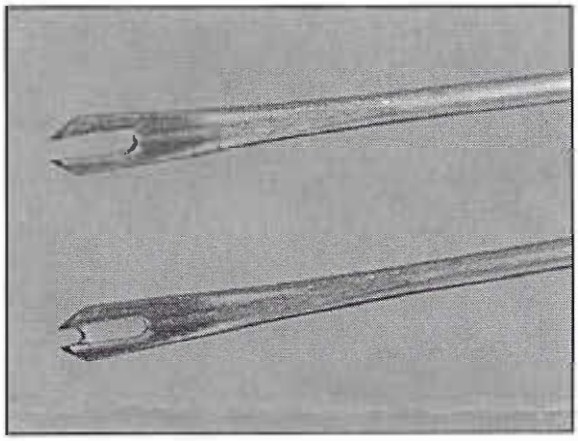
- NYCBH strain, calf skin, lyophilized
- Licensed
- Efficacy (take rate) in unvaccinated adults*
  - Undiluted 97% (103/106)
  - 1:5 99% (232/234)
  - 1:10 97% (335/340)

Aventis Pasteur — 85 million

- NYCBH, calf skin, wet frozen, glycerol
- Not licensed – IND status
- Emergency use only
- 100 dose vials: can be diluted 5:1

ACAM 2000 — 209 million

- Acambis/Baxter
- Seed virus -- Wyeth seed (NYCBH)
- Produced in Vero cells
- Lyophilized, 100 dose vials
- Licensure – early 2004



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

Lc16m8 – A Next Generation Vaccine?

- Temperature-sensitive clone of Lister strain develop in Japan in the 1970s
- Trials to begin soon in U.S. and Japan
- Grown in primary rabbit kidney
- Tested in 50,000 Japanese children – less skin reaction and fewer systemic symptoms; apparently similar serological responses to Lister strain

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

Smallpox Vaccine Expected Adverse Events

- Life-threatening complications
  - Post-vaccination encephalitis
  - Progressive vaccinia (vaccinees and contacts)
  - Eczema vaccinatum (vaccinees and contacts)
- Less serious
  - Generalized vaccinia
  - Accidental inoculation (may result in blindness)
  - Rash and fever
- If 100 million are vaccinated, 100-400 deaths and 2500 serious, potentially fatal complications are expected

Contact Vaccinia Infection

Source of Vaccinia (1963-68 studies)

Age of infected patients	Siblings/ playmates	Parents/ close relatives	Son/ daughter/ grandchild	Other
0-4	75	11	0	5
5-19	21	2	0	1
20+	1	0	24*	3
Total	97**	13	24	9

*Primarily parents and grandparents
**81 siblings; 16 playmates

2. Adult to adult

Actual experience
DOD -2003

- Numbers vaccinated -- 325,000
  - Sick leave – Hosp. staff 3% (av. 1.5 days)
- Noteworthy events
  - **Contact spread –**
    Spouse – 4 Intimate contact –2
    Friend -- 3 Patient - 0
  - **Encephalitis** – 2 (recovered)
  - **Eczema vaccinatum** – 0
  - **Progressive vaccinia** -- 0

A Balance of Risks

- What is the likelihood that smallpox will be used as a weapon?
- What will the frequency of adverse reactions be and how will a risk-averse public deal with this?
- How effectively could we control an outbreak?

Clinical Course of Smallpox

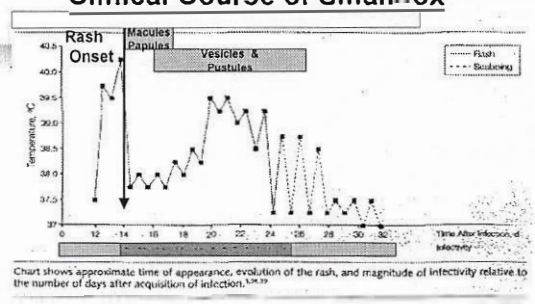


Chart shows approximate time of appearance, evolution of the rash, and magnitude of infectivity relative to the number of days after acquisition of infection.[34,35]

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

Spread of Infection

Spread of disease is comparatively slow

- **Household spread --Secondary attack rates**
  Measles76%
  Chickenpox 74%
  Smallpox 58%
- **Community spread –measles and chickenpox spread even 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

- **Vaccinate and isolate patient in designated hospital or ward (rooms under negative pressure)**
- **Identify and vaccinate all persons who had been in a room with the patient since he became febrile (primary contacts)**
- **Place primary contacts under surveillance with twice daily temperature**
  - **If a primary contact develops fever, isolate at home or special facility until diagnosed**
- **Vaccinate all household contacts of primary contacts (secondary contacts)**

Other Steps/Principles

- **Make vaccine available on request to those in the general geographic area**
- **Prompt, current, accurate communication to public**
- **Not generally desirable:**
  - **Compulsory vaccination**
  - **Quarantine of city or groups of people**
  - **Closure of airports, suspension of transport**

Preparatory steps

- Vaccine –
  - Stockpiled--available anywhere in 12 hours
- Each region within a state must have plan to make vaccine widely available within 7-10 days
- Each region within a state should be prepared to accommodate 500 infectious patients
- Every ER to have negative pressure rooms for examining patients with rash and fever

Support to States

- One program – flexible, accountable
  - FY02 -- $1,000,000,000+
  - FY03 -- $1,500,000,000+
- Hospitals
  - FY02 -- $125,000,000
  - FY03 -- $500,000,000

Corona Virus Respiratory Disease

- Cases as of 26 March

	Cases	Deaths
China	792	31
Hong Kong	316	10
Singapore	74	1
Viet Nam	58	4
Canada	19	3
U.S.	45 (?)	0
Eight other countries	____	____
	1328	49 (c. 3%)

Corona Virus – a new challenge

- Spread
  - Hospitals (high numbers)
  - Households (moderate)
  - Air travel (at least 3)
- Canada
  - All cases to designated hospital
  - Quarantine of family