SWITZERLAND — SMALLPOX

Mr. Ambassador — Appreciate invitation for myself & colleagues to discuss with you certain of the issues & problems now confronting us all — i.e. problem of terrorism.

Note: on my background

12 yrs. @ CDC — EIS

1966 to Geneva — (for 11 years) But seldom in Geneva — enough however to do liaison with a bunch of Medical degrees — helpful.

Dean Johns Hopkins

Science advisor to Pres. G HW Bush. — concerned re: bioweapons.

relatively ignored — med. / Pit / planners.

Colin Powell —

Adm. Stansfield Turner — words — Bush + nuclear — potential to push a country beyond the point of recovery.

4 yrs. ago — classic case. — which of the inf. dis. — potential

Smallpox and anthrax —

Priority for me

Week after Sept. 11 — asked by Secty Thompson to come to D.C.

Head a new office — Public Health Preparedness

Focus attention on Smallpox. — how to deal with this

Need to understand something of the disease itself

Smallpox

D.A. Henderson M.D., M.P.H.
March 20, 2003

Ali Maalin - 26 October 1977

Deaths During the 20th Century

Due directly or indirectly to armed conflict:

100,000,000

Due to smallpox

300,000,000+

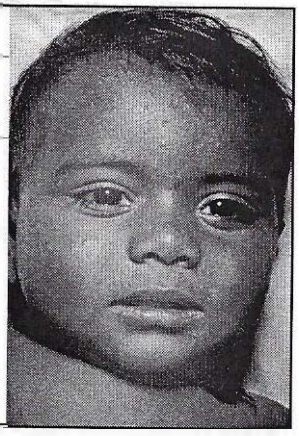
"On May 8, 1980, WHO announced that smallpox had been eradicated from the planet... Soon after the WHO announcement, smallpox was included in a list of viral and bacterial weapons targeted for improvement in the 1981-85 Five-Year Plan.... Where other governments saw a medical victory, the Kremlin perceived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

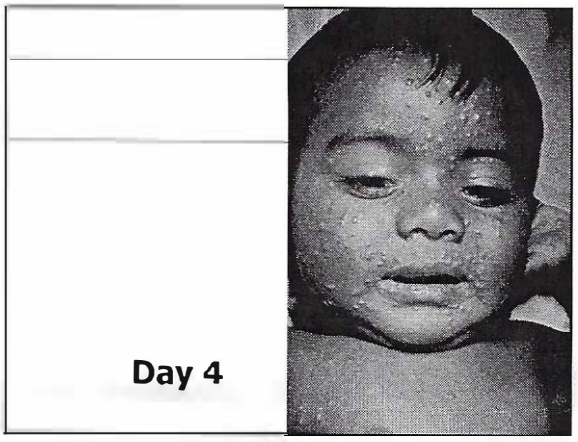
Alibek, 1998

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)**

Day 2





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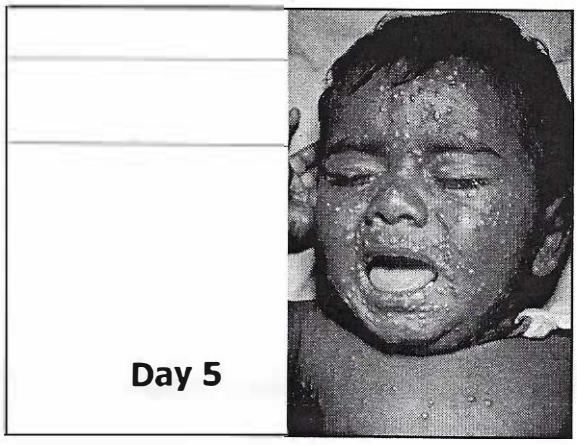

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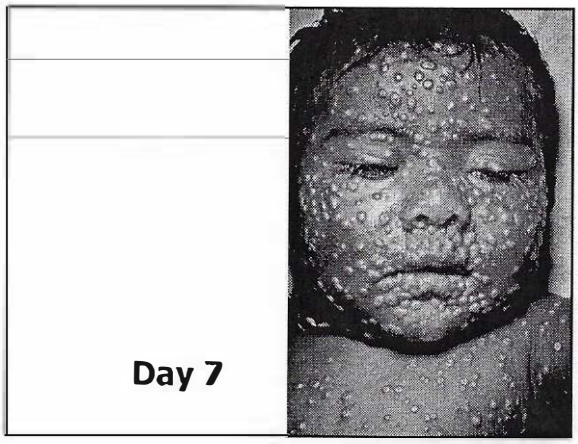

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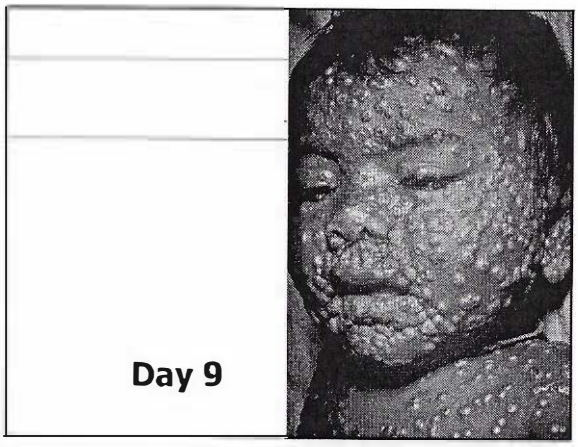

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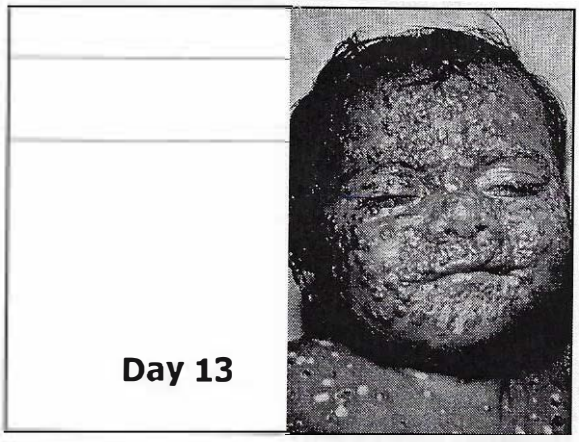

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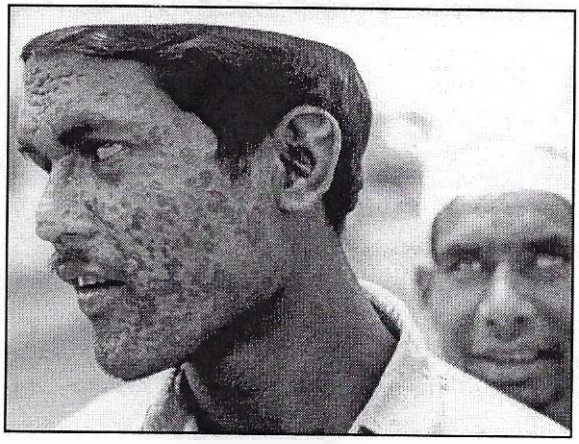
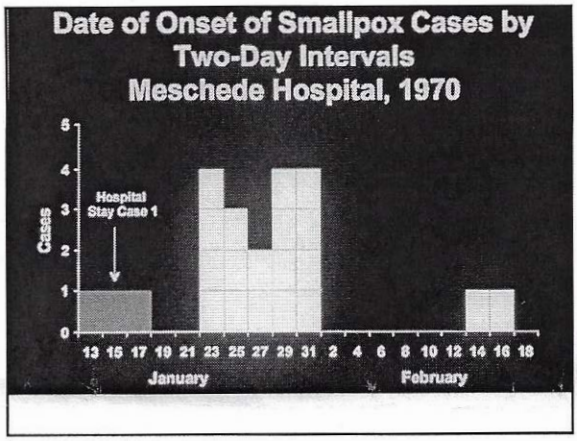
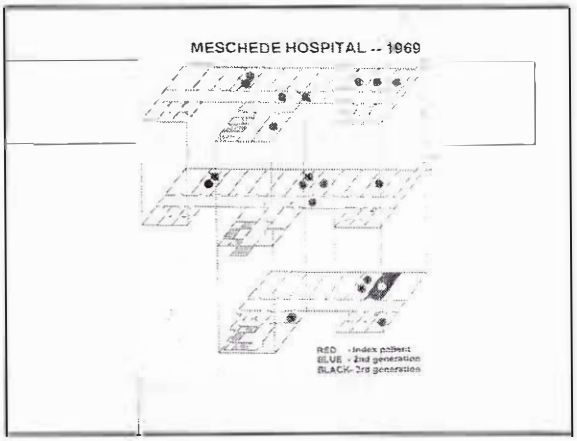


ERADICATION PROGRAM – STRATEGY – 1966–1977 (note Swiss Senum Restriction)

ONE EPISODE –





Go 000 doses.

Susceptibility of US Population to Smallpox -- 2003

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

1978

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)
- Stability after rehydration 30 days at 2-8°C

*NEJM 346: 1265-1274, 2002

1958

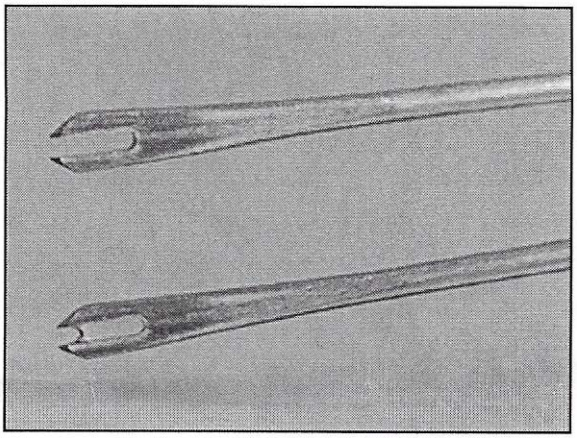
Aventis Pasteur 85 million

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

need 100 million

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

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

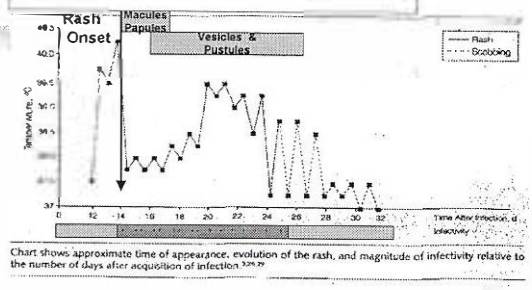


Chart shows approximate time of appearance, evolution of the rash, and magnitude of infectivity relative to the number of days after acquisition of infection.[329,29]

Spread of Infection

Spread of disease is comparatively slow

- **Household spread --Secondary attack rates**
  - Measles 76%
  - 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**
- **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 in progress

- Vaccine –
  - Stockpiled--available anywhere in 12 hours
- Each region now planning to make vaccination available to its population in 7-10 days and to accommodate 500 infectious patients
- Every ER to have negative pressure rooms for examining patients with rash and fever
- Educational material for community and health care providers in local hands