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As you already will stay on Saturday, July 24 in Würzburg, my wife Margit and myself would like to invite you for a dinner at our home on **Saturday, July 24, 2004. 7.30 p.m.** Our address is:

Margit and Jörg HACKER
Edith-Stein-Straße 6
97070 Würzburg
Tel. 0931 / 70 95 89
Fax. 0931 / 70 79 66

Please take a taxi from your hotel to our house (15 minutes drive).

Travel expenses reimbursement

A special form for reimbursement will be handed out during the conference. After your return, please send this form including your original tickets to the indicated address. Your accommodation will be paid directly by us.

You will receive the given information also by E-mail. If there are any changes in your schedule, please inform us as soon as possible. I am looking forward meeting you in Würzburg this month.

With best regards

(J. Hacker)

Enclosures: Time table for railway, only attached by regular mail
(connection Würzburg – Frankfurt Airport)
Scientific Programme
City map of Würzburg

Smallpox from eradication to resurrection

D.A. Henderson MD, MPH

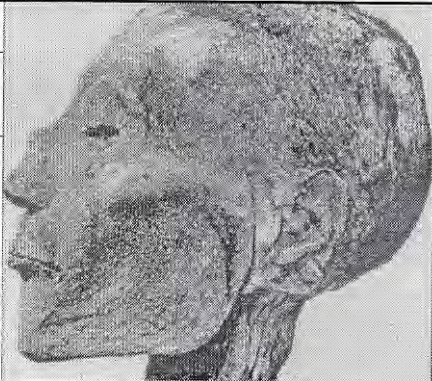
International Symposium
Microbes of High Pathogenic Potential

Wurzburg, Germany

27 July 2004



Ali Maalin - 26 October 1977



Ramses V

"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

Deaths in the 20th Century

Due directly or indirectly to armed conflict:

100,000,000

Due to smallpox

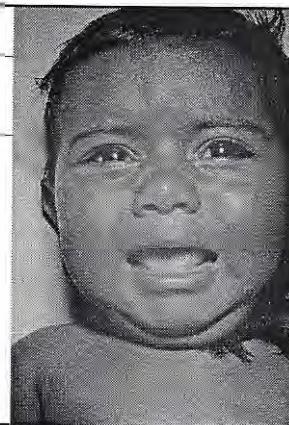
300,000,000+



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



Day 3

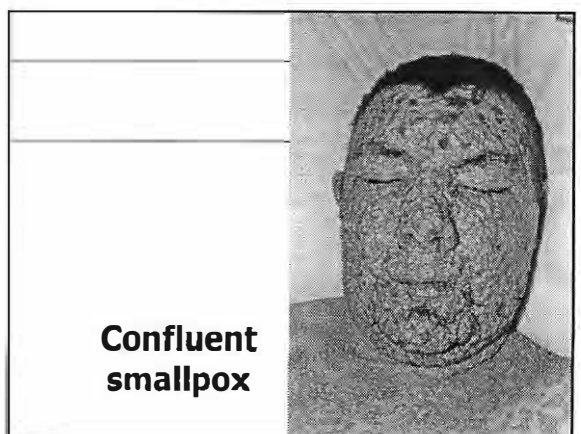
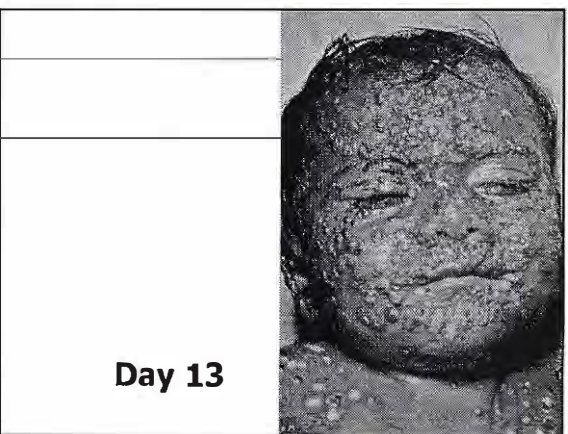
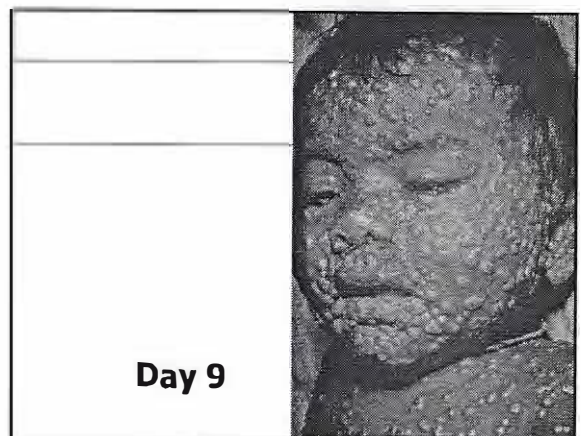
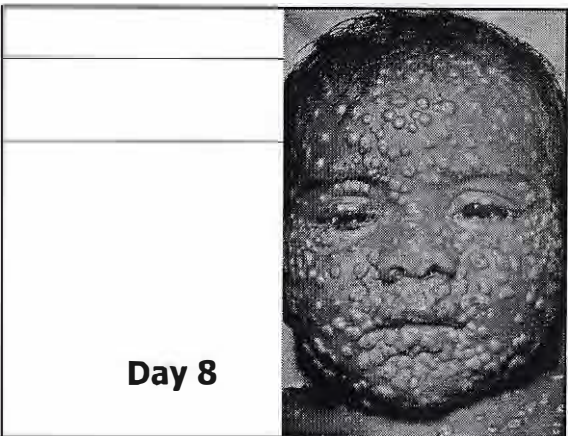
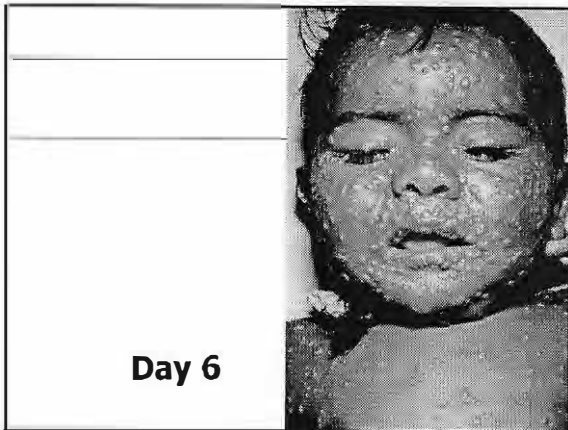


Day 4

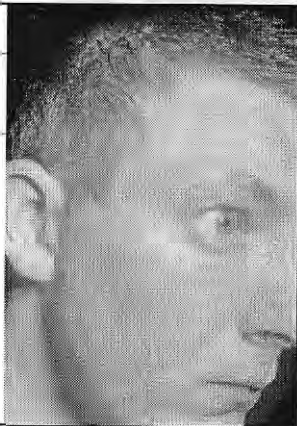


Day 5



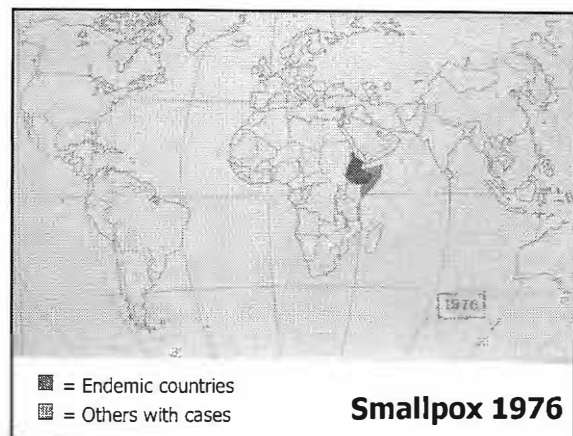
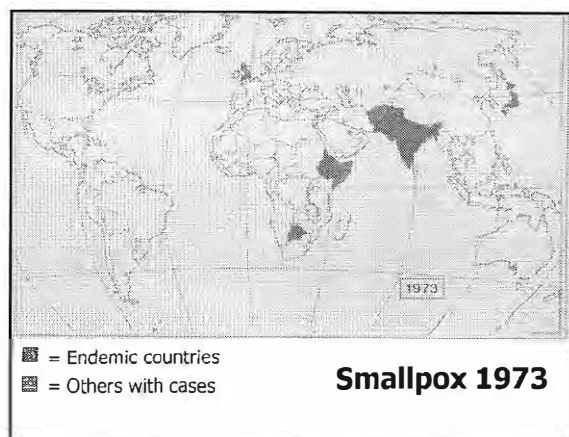
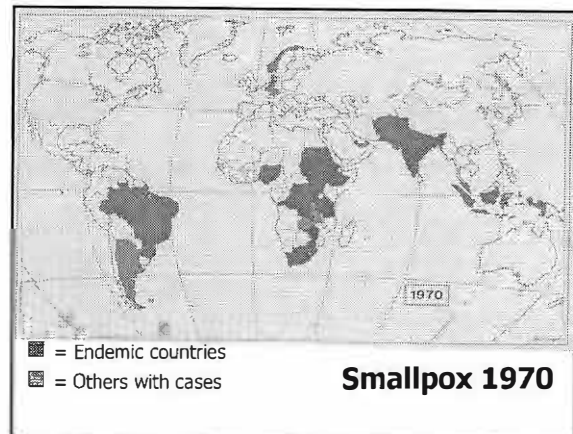
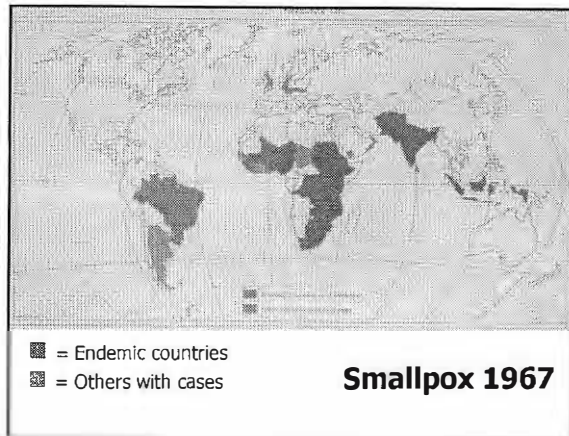


**Confluent
smallpox
(recovered)**



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

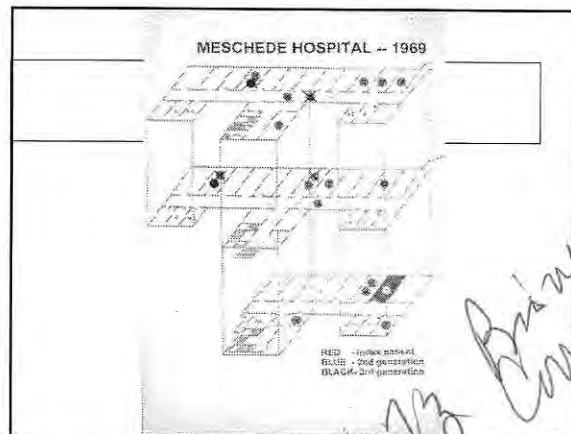
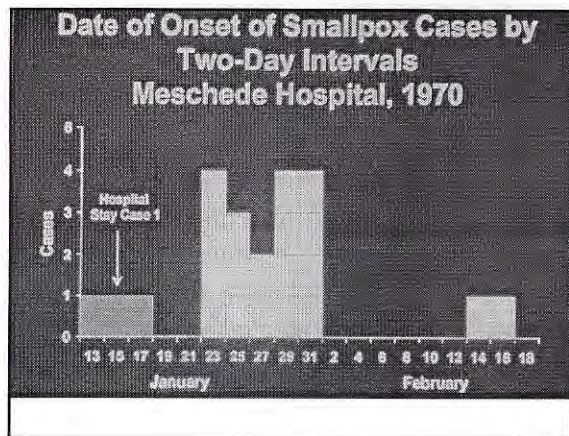




Ali Maalin - 26 October 1977



Meschede, Germany - January 1970



** Note the first bio weapons program - Smallpox is #1 (1999)*

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

- "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

*Smallpox is #1
How are they?*

*Sept 15
Positives*

Susceptibility of population to smallpox -- 2004

- 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

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

Producing ~ 200,000 doses

A Balance of Risks

- OK* ■ Probability that smallpox will be used as a weapon
- ↓* ■ Frequency of adverse reactions
- ↑* ■ Likely effectiveness of outbreak control

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

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)

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

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

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 assume the lead

Present vaccine - 95-98% protective. but complications
 ? other vaccines that produce fewer complications. - MVA / LC16 m8.
MVA - non-replicating; partially protective monkeypox/monkeys.
 appears to cause no complications but only given to 500 people.
 Now - in late phase II trials.
LC16 m8 - replicating, protective - monkeypox/monkeys.
 no complications yet - 50 000 people.
 Now moving toward phase 3 trials
Big question - will either protect vs. smallpox
 - cost MVA \$10 - \$20 x 2 doses
 70 x 10⁶ people & contradictions (incl. family)
 \$1.2 - \$2.4 bill in
 - cost LC16 m8 - ~ \$2 / dose but problem of replicating