May 8, 1980 - WHA - old enemy. / Not to be. Once again concerned and for past 5 years.

PUBLIC LECTURE

# The Death and Resurrection of a Virus

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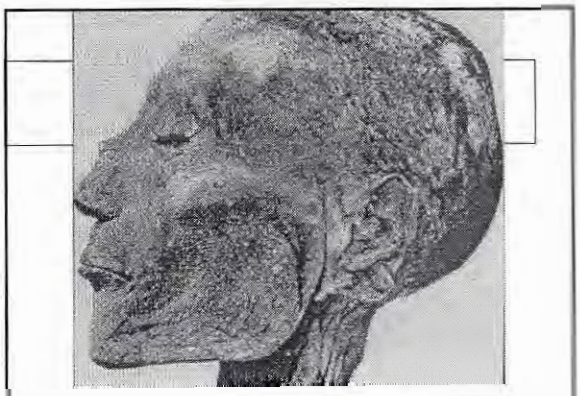
Biomedical Research Council
Distinguished Visitor Lecture

27 June 2005

## Lecture Elements

- History – The most serious of all pestilential diseases
- Clinical aspects
- Eradication – why and how
- Recurrent concerns about smallpox
  - Policies
  - The future

Ali Maalin - 26 October 1977



Ramses V

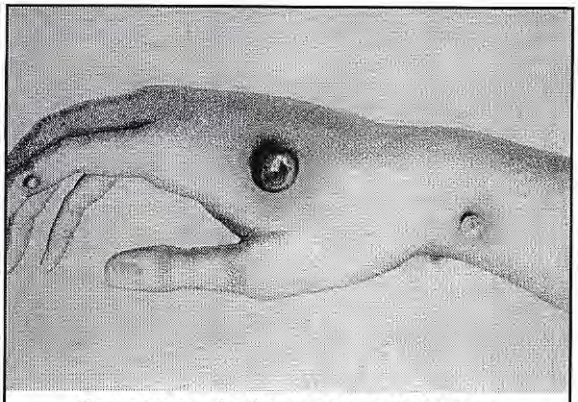
**Sitala Mata**

**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**

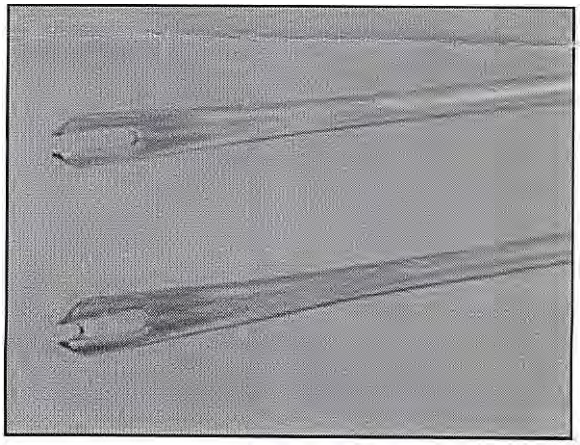
**Edward Jenner**



**Cowpox on the hand of Sarah Nelmes**

## Smallpox vaccine

- 1796 – 1870/90 Arm-to-arm
- 1870 – Growth on calves, sheep
- 1920 – Dried vaccines
- 1950s – Freeze dried vaccine
- 2002 – Tissue culture vaccine



## Deaths in the 20th Century

Due directly or indirectly to armed conflict:

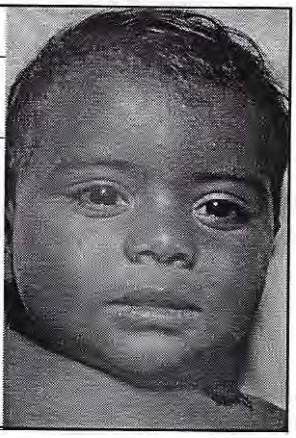
**100,000,000**

Due to smallpox

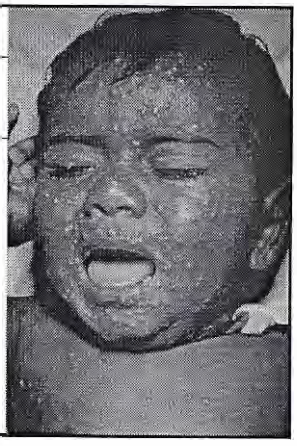
**300,000,000+**

## Smallpox -- characteristics

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

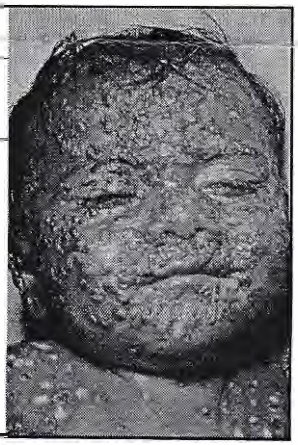


Day 2



Day 5

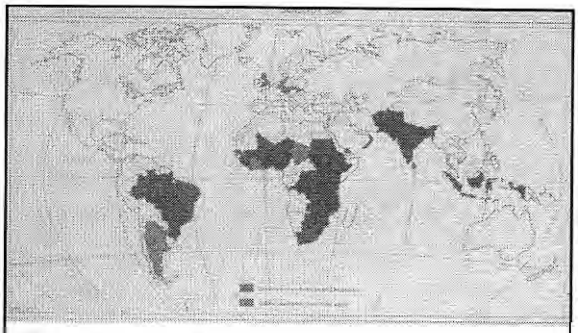
Day 8



Day 13

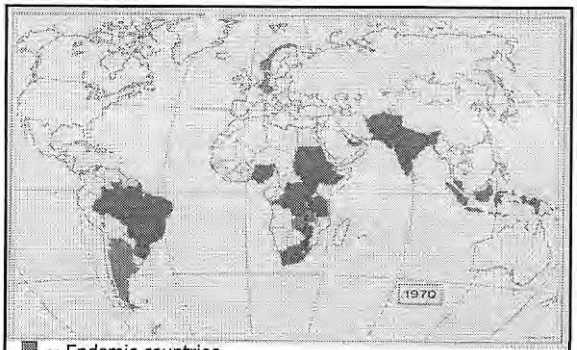
## Characteristics of Smallpox Favoring Eradication

- 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



= Endemic countries
= Others with cases

**Smallpox 1967**




= Endemic countries
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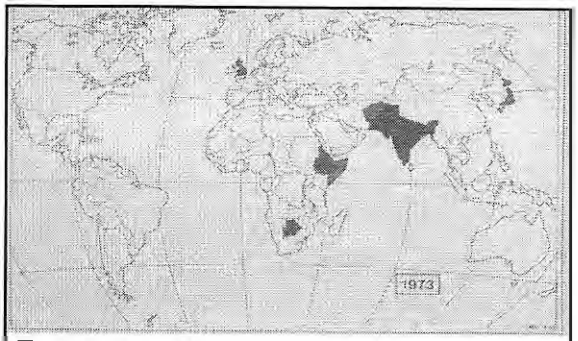
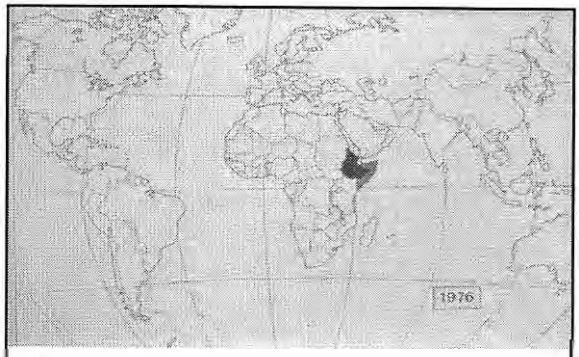
**Smallpox 1970**



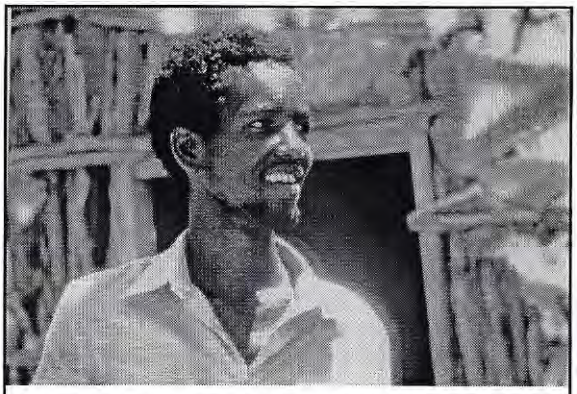

= Endemic countries
= Others with cases

**Smallpox 1973**

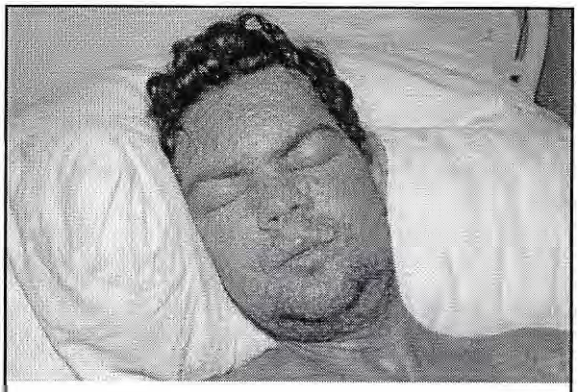



= Endemic countries
= Others with cases

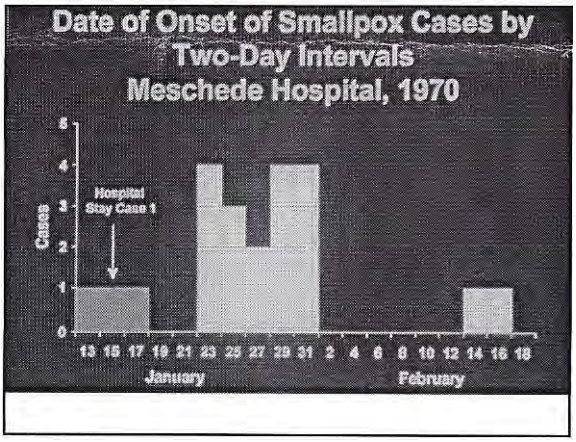
**Smallpox 1976**

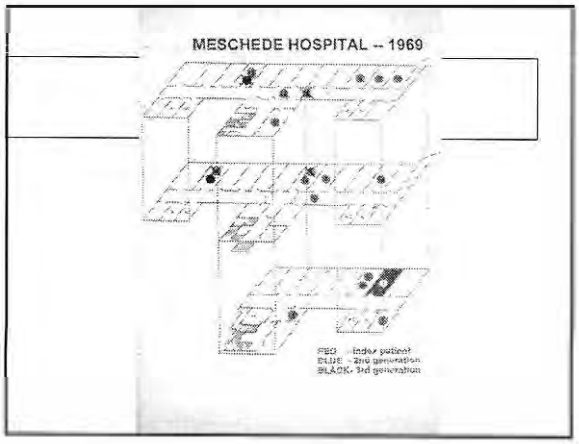


**Ali Maalin - 26 October 1977**



**Meschede, Germany - January 1970**



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

Alibek, 1998

## Susceptibility of the population to Smallpox -- 2005

- Vaccination stopped in 1980
- Persons under 25 years have not been vaccinated
- Persons vaccinated only once pre-1980 have little or no immunity
- Population-- >75% are fully susceptible

## Epidemic Response Capability September 18, 2001

- Vaccine manufacturers -- none
- Vaccine in storage
  - U.S. 15 million doses
    - 90,000 doses actually available
  - World ? 80 million doses

## Response capability -- 2005

- Perhaps 10-15 countries with sufficient vaccine for own emergency needs
- Global supply – about 400 million doses
- Trained and vaccinated teams prepared to move rapidly
- Diagnostic laboratories now expanding
- A WHO Global smallpox stockpile now in planning stage

## Should vaccination be restarted?

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

## Smallpox Vaccine
Expected Adverse Events (U.S.Studies)

- 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

a newly reported cardiac complication

- Myopericarditis 1:8,000
  - Almost all primary vaccinees
  - Onset 7 to 20 days
  - Fever, chest pain, EKG changes, enzymes increased
  - Recovery

## Effectiveness of outbreak control

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

## Epidemiology of Smallpox

Transmission Patterns in Europe: 1958-1973

- Outbreaks: 34
- Cases: 573
  - Transmission in hospital: 277 (48%)
  - Transmission in home: 143 (25%)
- Hemorrhagic cases – a threat to hospitals
  - Bradford, UK (1961) 10 cases
  - Germany (1970) 16 cases
  - Yugoslavia (1972) 38 cases

## Outbreak Control

- Isolate patient
- Vaccinate contacts since patient's fever began and household contacts
- Daily temperatures for contacts
- Make vaccine available on request in area but no compulsory vaccination
- No quarantine of city or groups; no airport closure

## The future

- How long must we remain on alert?