

from those you specially target.

Dear -

Spz - ~~Ad~~ - most serious pestilence with the most victims in the world has ever known, 3500 yrs.

② Deities

③ 2016. 300x10<sup>6</sup>

Since 1961.

## Smallpox: Death of a Disease

What it taught us or did it?

D.A. Henderson, MD, MPH

Professor of Medicine

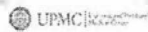
Center for Biosecurity, University of Pittsburgh

Biosecurity, Biotechnology, Global Security Symposium

Princeton University

27 March 2009

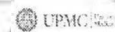
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## Outline

- Eradication -- the concept
- Targeting smallpox - 1950-66
- From 10 million to 0 - 1967-80
- The fate of the virus
- Global security

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## Global efforts to eradicate a disease

- Hookworm 1909-23 14 years
  - Rockefeller support
  - Treatment, sanitation
- Yellow fever 1915-32 17 years
  - Rockefeller Foundation
  - Stop *aegypti* mosquito breeding
- Yaws - 1948-66 18 years
  - World Health Organization
  - Penicillin treatment of patients
- Malaria - 1955-73 18 years
  - World Health Organization
  - DDT insecticide

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## Smallpox as a target

- 1950 -- Regional eradication in the Americas
  - PAHO approves a smallpox eradication program
- 1953 -- Director General proposes
  - "...a practical world program, of importance and value to every country...demonstrating the importance of WHO to every Member State"

*Rejected by Assembly as uneconomical and unfeasible*

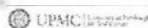
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## Smallpox, the disease

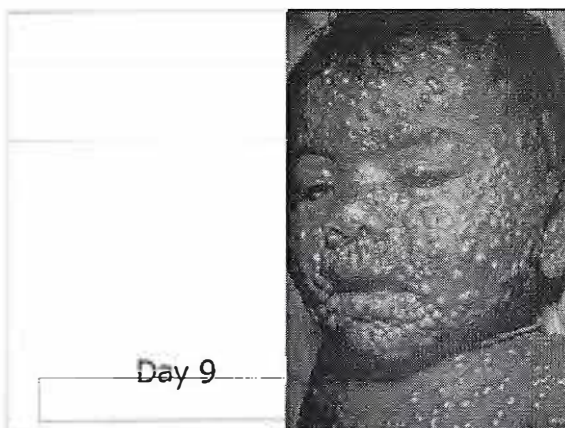
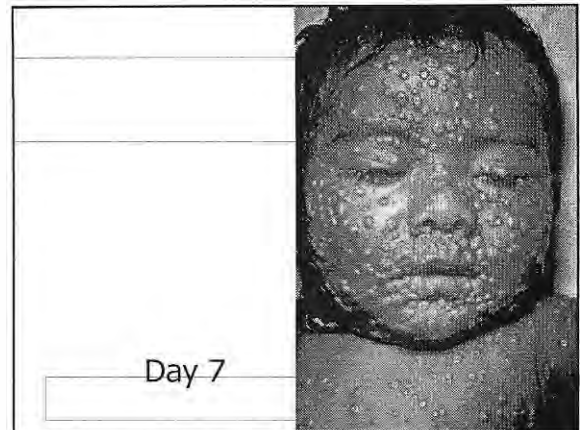
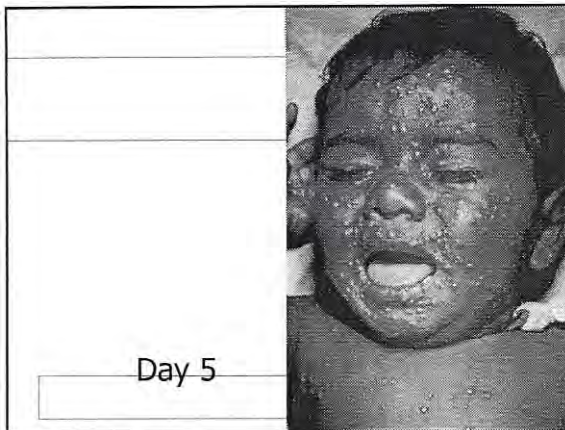
- Virus -- spread only during rash; face-to-face
- Man is the only host
  - Chain of infection extending back 3500+ years
  - Only disease with deities in Asia and Africa
- Death rate = 30%
  - But permanent immunity among survivors
- A highly stable vaccine protects with one dose

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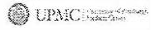
Day 3





### Global eradication approved

- World Health Assembly adopts 1959 USSR proposal for a global program
- 1959 -1966
  - Strategy: mass vaccination
  - Surveillance (improved case reporting): none
  - Budget of <\$100,000 per year
  - Six staff members
  - Program made little progress

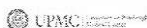
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## Meanwhile -- West Africa 1962-66

- NIH measles vaccine evaluation – 1962-64
  - Trial in Upper Volta > national vaccination > 9 countries
  - CDC asked to assume direction
- CDC proposal to USAID -- 1965
  - Smallpox eradication and measles control in 18 countries

*Rejected by USAID – Spring, 1965  
Accepted by White House – Fall, 1965*

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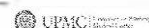


## WHO's "intensified" program

"Go or no go"--May 1966

- Assembly requires DG to submit a plan
  - Strategy
    - Large-scale vaccination
    - Surveillance and containment
    - Research
  - 10 year program --budget of \$ 2.4 million/year
- Objections by delegates
  - Not feasible
  - Demand for no further increases in WHO budget
- 58 votes needed for acceptance; 60 voted for

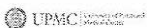
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## Program leadership

- Director General believes program will fail (malaria eradication collapsing)
- Demands an American serve as Director
  - The candidate declines:
    - Responsibilities for new CDC African program
    - Limited resources -- <\$50,000 each for 50 countries
      - Not enough even to buy the vaccine required
    - He receives a career option

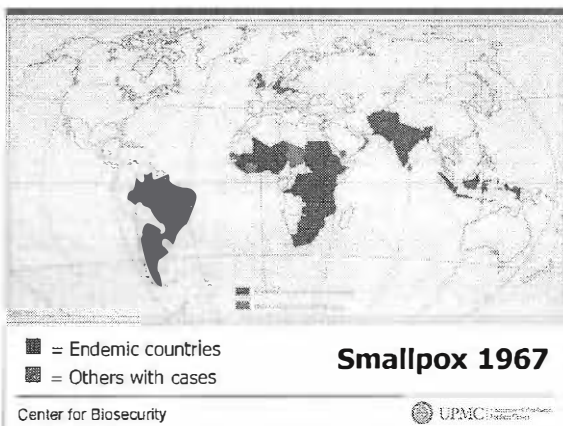
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## The Challenge

- Status of smallpox – 1967
  - >10,000,000 cases
    - 2,000,000 deaths
  - 43 countries reported cases
- Program staff
  - Headquarters – 4 medical, 2 admin, 3 secretaries
  - Regions – one each in 4 WHO Regions
  - International staff – never more than 150

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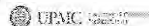
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## Vaccination Strategy

- Target – 80% of population
- Quality control of vaccine
  - 42 labs – independent international control by labs in Netherlands and Canada
- Develop national capacity
  - Production manual
  - On-site consultant assistance
  - Research on production methods

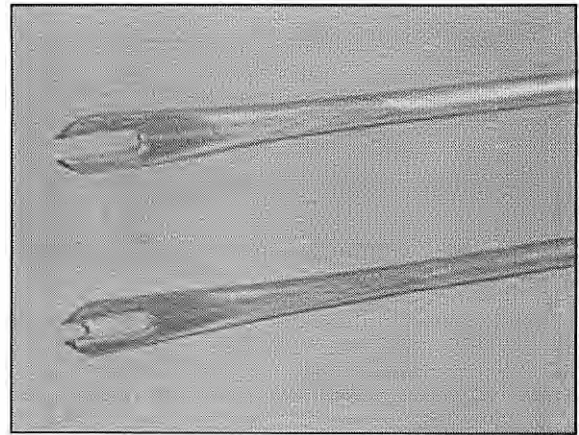
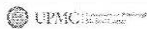
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## Vaccination pace and quality

- Research- faster, better methods
  - Jet Injector gun
  - Bifurcated needle—multiple puncture method
    - One-fourth as much vaccine required
    - Training time -- 15 minutes
    - Easily sterilized and reused
    - Cost -- \$5 per thousand
- Quality control of vaccination
  - Evaluation teams

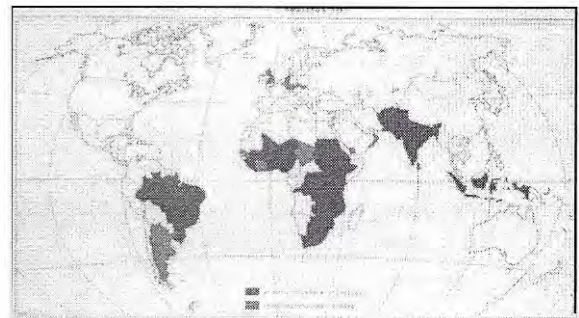
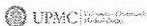
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## Surveillance-containment strategy

- Surveillance-containment
  - Surveillance -- weekly report from every health unit
  - Teams -- investigate and contain outbreaks
  - Epidemiological research on smallpox
    - The text books prove to be wrong
      - "Smallpox spreads like a prairie fire"
      - "Revaccination is needed every 3 to 5 years"
      - "Decontamination is critical"

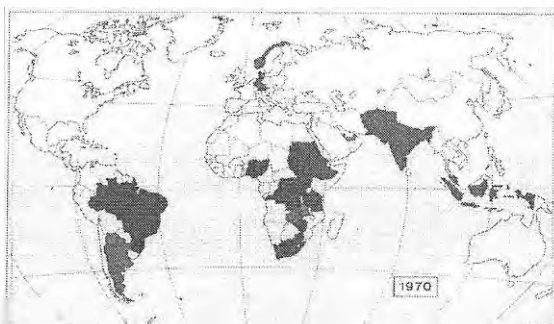
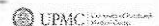
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- = Endemic countries
- = Others with cases

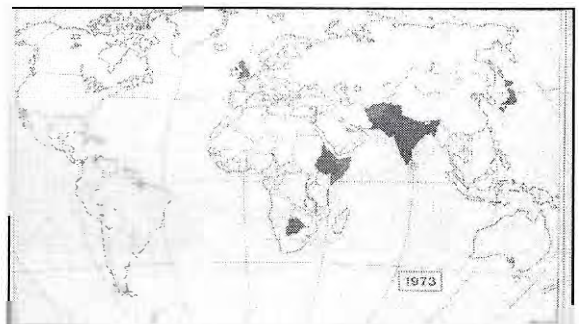
**Smallpox 1967**

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- = Endemic countries
- = Others with cases

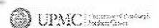
**Smallpox 1970**



- = Endemic countries
- = Others with cases

**Smallpox 1973**

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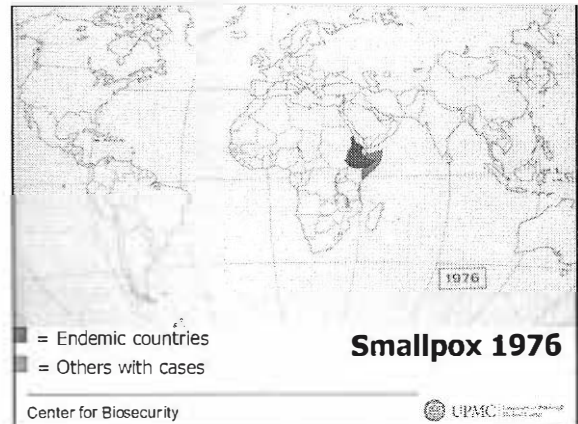
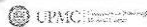


## India -- the pivotal challenge

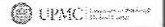
1973-75

- India -- the "home of smallpox"?
  - Population -- 550,000,000
  - Surveillance-containment strategy--not working
  - June 1973 -- search every village, eventually every house
    - 130,000 health staff in 10 days
    - Results of first search -- October
  - Spring 1974 -- the darkest days
    - Gas crisis followed by strikes of airlines, railway, health staff
    - India explodes a nuclear device
  - Containment methods tightened
  - Indian Independence Day -- 15 August 1975

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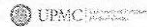


## The last strongholds

Ethiopia and Somalia

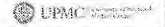
- Ethiopia
  - Country -- twice the size of Texas
    - Largely highland --over 5000 feet
    - Health facilities serve 5% of the 30 million people
    - Travel largely by donkey and on foot
  - Emperor is assassinated; Marxist take-over
    - No foreign staff outside of Addis except smallpox
  - Problem of resistance to vaccination
- Somalia -- the final chapter

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Ali Maalin - 26 October, 1977

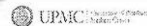
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## The Threat of Biological Weapons

- Biological Weapons Convention--1972
    - Cessation of research on offensive weapons
    - Destruction of existing stocks
  - Attitude until late 1990s
    - Bioweapons are morally repugnant
      - Academic world-- deliberate refusal to have anything to do with them
    - Only possible sources are sophisticated laboratories
    - A moral barrier against their use
- Besides: "If used by someone, we would nuke them" R.Nixon

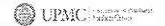
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## Clouds on the Horizon

- 1992 Bioweaponer Alibek defects from USSR
  - USSR program 50 laboratories; 60,000 staff
  - Preferred agents: smallpox, anthrax, plague
  - Smallpox virus production capacity -- 20+tons per year
  - Laboratory research staff disperse -- late 1990s
- 1995 Other centers with capability and intent
  - Aum Shinrikyo -- anthrax, sarin gas
  - Iraq's earlier program becomes known
    - Anthrax -- drones, shells

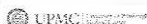
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## A new reality– September 11, 2001

- September 16 meeting with Secretary
  - A possible second attack  
Intelligence suggest smallpox or anthrax
  - Status of country
    - None <30 years have ever been vaccinated
    - Waning immunity among older adults
    - 75% of population susceptible
  - Vaccine availability
    - 15 million doses in storage; 90,000 doses usable
    - No vaccine manufacturer in the world
    - Earliest date for producing a new vaccine —5+ years
  - Emergency program – 200 million doses in 18 months

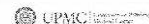
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## International realities - January 2005

- Atlantic Storm →a summit conference scenario including US, Canada, 9 European countries
  - Participants: Madeleine Albright as President and former ministers including Bernard Kouchner and Gro Bruntland
  - Cases appear in Turkey, then Frankfurt, Warsaw, and US
- Issues
  - Turkey has no vaccine and the few countries with vaccine insist that they cannot release any
  - Some want to close and seal borders
  - No mechanisms for rapid, collective decisions
  - WHO is small and has few resources

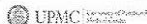
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## The Fate of the virus

- After the last case in 1977
  - Pressure from developing countries to destroy virus
  - Laboratory infection in England -- 1978
  - Labs with virus reduced from 75 to 2 (CDC, USSR)
- Meeting of first expert group on lab safety
  - Safety cabinets, glove boxes, air and waste control
- WHO international Committee
  - Survey of virologists – 55 of 60 favor virus destruction
  - Five national and international microbiological societies recommend destruction
  - HHS Secretary Sullivan (1990) informs World Health Assembly that US will destroy the virus and USSR is in agreement

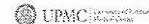
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## Implications of destroying the virus

- Some genetic information lost but...
  - High homogeneity between smallpox, cowpox, and camelpox
  - Human pathogenesis of monkeypox is almost identical to smallpox
  - Cloned virus fragment libraries available
  - More than 25 strains sequenced
- The gain
  - Possible escape from a laboratory is negated
  - Possession could be "a crime against humanity"

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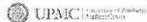


## David Baltimore's views

*Science January 7, 1994*

- *I find it hard to believe that we need to, or even will, continue research of a virus whose release from containment would be such a disaster while its present threat is nil...Much of the value of research can be gained from studying related viruses...Eradication of the virus as well as its disease will better serve the long term interests of humanity.*

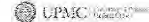
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## Unprecedented requirements

- World Health Assembly reluctantly agreed to continued research by US and Russia but:
  - Overall approval must be for finite periods and be reviewed at regular intervals by the Assembly
  - All protocols must have the approval of an independent international research committee
  - Laboratories must be inspected for security status every two years by independent scientists

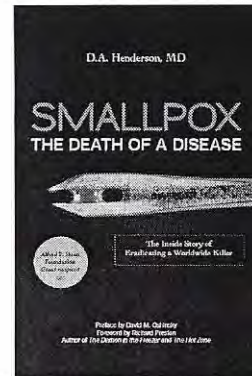
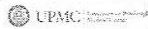
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## Status today

- U.S. and Russia oppose the imposed restrictions as well as virus destruction until a totally safe vaccine and two anti-viral drugs are developed
- Scheduled now--a formal report for the World Health Assembly in 2010; final vote on destruction in 2011
- Meanwhile, the U.S. has commissioned a special study by the IOM  
*What implications does this have for cooperative international efforts to obtain greater biosecurity?*

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