



History and Epidemiology of Global Smallpox Eradication



Smallpox

Three Egyptian
Mummies
1570-1085 BC

Ramses the Vth
Died 1157 BC



Early Written Description of Smallpox India 400 AD

“Severe pain is felt in the large and small joints, with cough, shaking, listlessness and langour; the palate, lips, and tongue are dry with thirst and no appetite. The pustules are red, yellow, and white and they are accompanied by burning pain. The form soon ripens ...the body has a blue color and seems studded with rice. The pustules become black and flat, are depressed in the centre, with much pain.”



Smallpox and History

- In the Elephant war in Mecca 568 AD, smallpox decimated the Ethiopian soldiers
- Introduction of smallpox into the new world (Caribbean 1507, Mexico 1520, Peru 1524, and Brazil 1555) facilitated Spanish conquest
- Smallpox destroys Hottentots (1713)
- In 1738, smallpox killed half the Cherokee Indian population
- Smallpox disrupted colonial army in 1776



Smallpox Control Strategies

- Smallpox hospitals (Japan 982 AD).
- Variolation 10th Century.
- Quarantine 1650s.
- Home isolation of smallpox in Virginia 1667.
- Inoculation and isolation (Haygarth 1793).
- Jenner and widespread practice of vaccination throughout Europe and rest of the world.
- Mass vaccination.
- Surveillance containment.



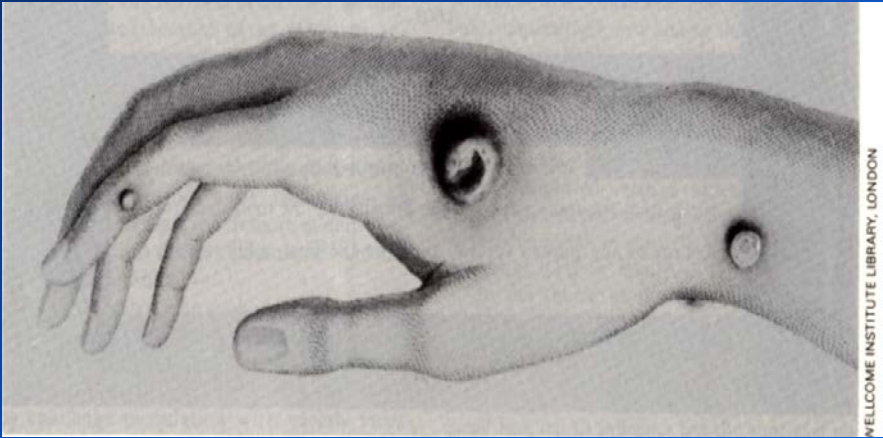
Variolation Inoculation with Smallpox Pus

- Observations:
 - Pocked marked persons never affected with smallpox
 - Persons inoculated with smallpox pustular fluid or dried scabs usually had milder disease
- Not ideal control strategy
 - Case fatality rate still 2%
 - Can transmit disease to others during illness



The 1st Smallpox Vaccination

Jenner 1796



Cowpox lesions on the hand of Sarah Nelmes (case XVI in Jenner's *Inquiry*), from which material was taken for the vaccination of James Phipps below in 1796



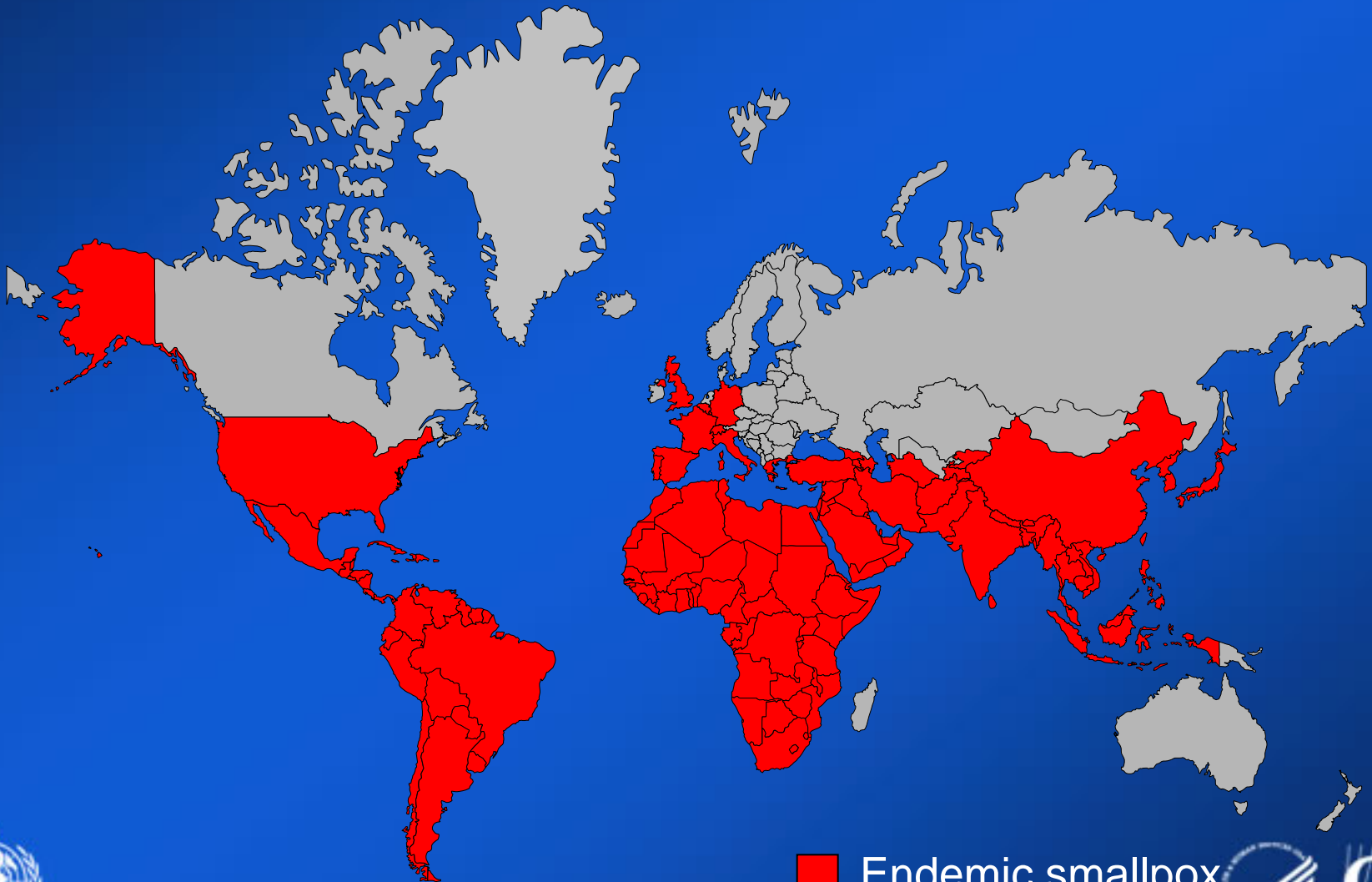
History of Smallpox Vaccination

1805	Growth of virus on the flank of a calf in Italy.
1864	Publicity about vaccine production at a medical congress.
After WWI	Most of Europe smallpox free.
After WWII	Transmission interrupted in Europe and North America.
1940's	Stable freeze-dried vaccine perfected by Collier.

* Henderson DA, Moss M, Smallpox and Vaccinia in Vaccines, 3rd edition, 1999



Smallpox Endemic Areas 1945



■ Endemic smallpox



History of Smallpox Eradication

1950	Pan American Sanitary Organization decides to undertake eradication hemisphere-wide.
1959	World Health Assembly adopts goal to eradicate smallpox.
1966	World Health Assembly decides to intensify eradication and provide more funds.

† Henderson DA, Moss B, Smallpox and Vaccinia in Vaccines, 3rd edition, 1999



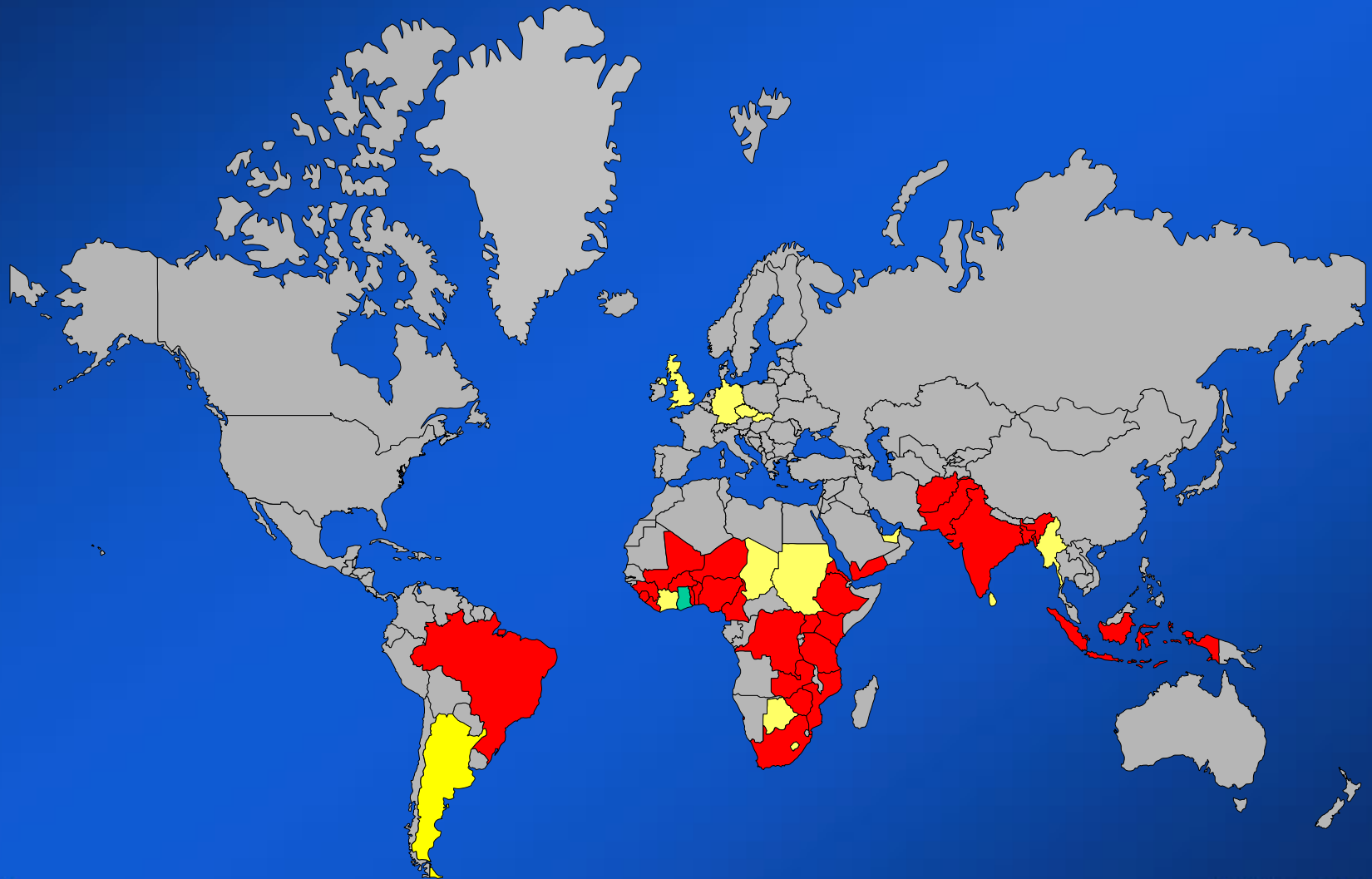
Principal Indicators of Eradicability

- Humans essential for the life cycle.
- Practical diagnostic tools.
- Effective intervention capable of interrupting transmission.

* Dowdle WR, Hopkins DR, *The Eradication of Infectious Diseases*, John Wiley & Sons, Chichester 1998. pp47-59



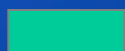
Smallpox Endemic Areas 1967



Endemic



Importations

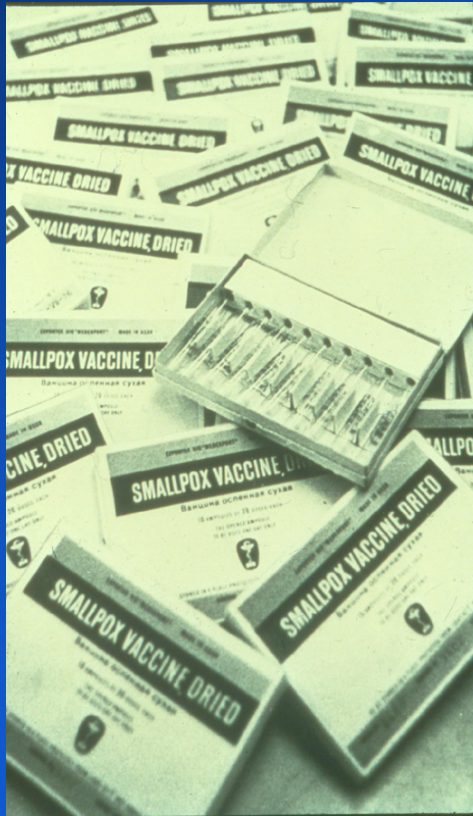


Transmission Interrupted



CDC

R & D Contributions



Freeze-Dried
Smallpox Vaccine



Bifurcated Needle
98%+ take



Smallpox Eradication Strategy

1. Mass vaccination campaigns in each country, using vaccine of ensured potency that would reach $\geq 80\%$ of population.
2. Development of a system to detect and contain cases and outbreaks.

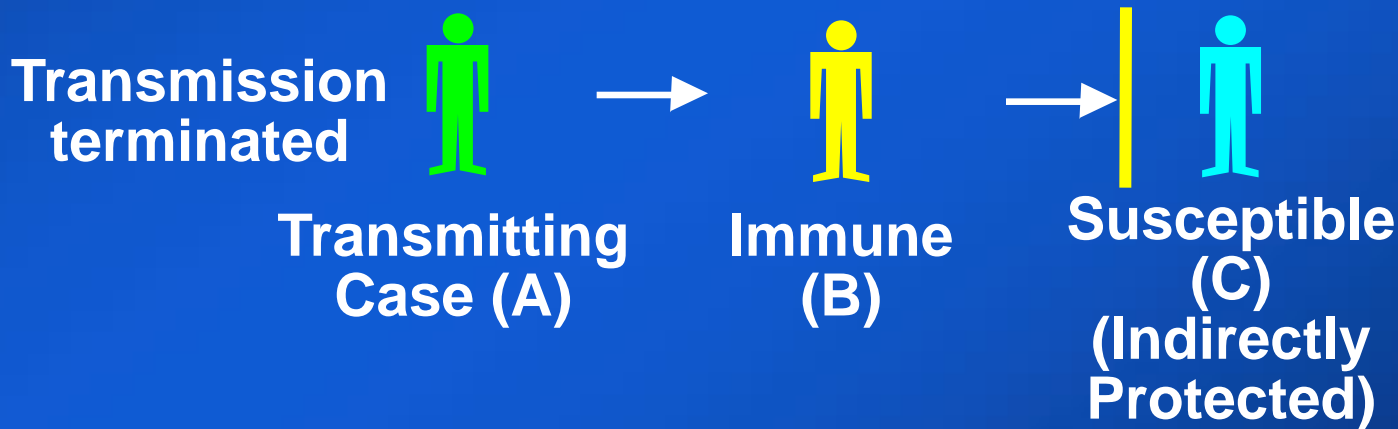
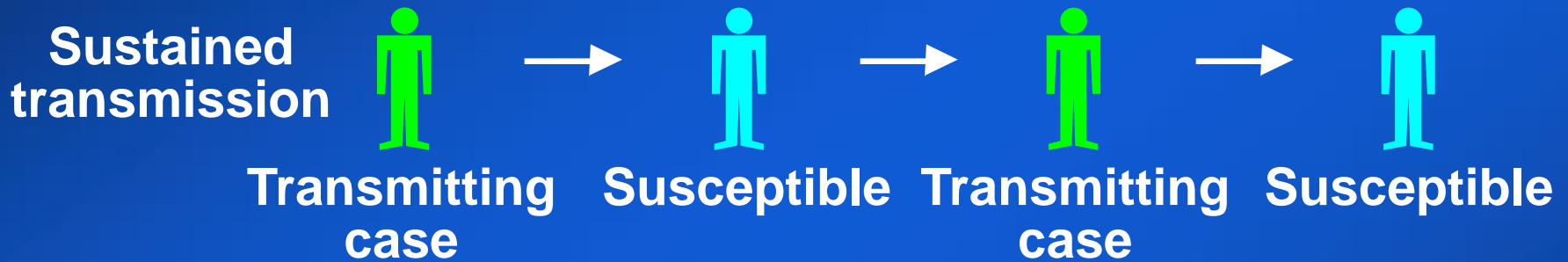
† Henderson DA, Moss B, Smallpox and Vaccinia in *Vaccines*, 3rd edition, 1999



Mass Vaccination



Herd Immunity



Herd Immunity Thresholds for Selected Vaccine-Preventable Diseases

Disease	R_0	Herd Immunity	Immunization Levels	
			1999 19-35 Months	1997-1998 Pre-School
Diphtheria	6-7	85%*	83%*	9%
Measles	12-18	83-94%	92%	96%
Mumps	4-7	75-86%	92%	97%
Polio	5-7	80-86%	90%	97%
Rubella	6-7	83-85%	92%	97%
Smallpox	5-7	80-85%	—	—

*4 doses

† Modified from *Epid Rev* 1993;15: 265-302, *Am J Prev Med* 2001; 20 (4S): 88-153, *MMWR* 2000; 49 (SS-9); 27-38



Assumptions About Smallpox Prior to Eradication Program

- Highly contagious
- Vaccine-induced immunity short-lived
- High vaccination coverage needed to meet herd-immunity threshold



What Was Learned about Smallpox Transmission During the Eradication Program

- Common transmission: Airborne by droplets
 - Close, face-to-face contact
 - Greater transmission with prolonged contact
- Rare transmission: Airborne over long distance
 - More frequently seen in hospital associated outbreaks where cough was present
- No carrier state
- Rare transmission: fomites
 - Bedclothes, linens, blankets.
- No evidence transmission by: food, water.



What Was Learned about Smallpox Transmission During the Eradication Program

- Vaccine can provide protection for several years but full protection decreases over time
- Vaccination soon after exposure can still provide some degree of protection
- Transmission did not occur before onset of symptoms
- Surveillance and targeted vaccination could significantly decrease transmission during outbreaks



Factors Influencing Smallpox Spread

- Temperature/Humidity – Lower temperature/humidity, higher viability
- Intensity and duration of contact
- Length of contagious period
- Coughing/sneezing



Exposure Factors for Smallpox West Pakistan, 1968-1970

Exposure Factor	Contacts (N)	Cases (N)	AR (%)
Residence status			
Same house	258	45	17.4
Same compound	206	45	22.3
Pattern of exposure			
Constant	302	81	26.8
Daily	160	10	6.3
Duration of Exposure			
≥ 7 days	449	91	20.3
<7 days	15	0	0

Heiner et al Amer J Epidemiol 1971; 91:316-326



Secondary Attack Rate for Smallpox Among Unvaccinated Household Contacts

2° Attack Rate(%)	# Studies
36.9 - 47	5
73.3 – 88.4	3
Average	58.4%
Average for vaccinated	3.8% (1.2-26.2)

† Adapted from Fenner F et al. Smallpox and its Eradication, pp200





Examples of Slow Smallpox Transmission Within a Single Compound

Source	Contacts in addition to index case	Contacts without history of vaccination	Interval between onset of symptoms in index case and onset of symptoms in last compound case
Nigeria (Abakaliki)	21	4	31 days
Nigeria (Abakaliki)	32	14	47 days
Nigeria (Abakaliki)	14	5	51 days
United Rep. of Cameroon (N'Game)	?	4	Approx. 53 days
Nigeria (Adepe-Ipiga)	30	27	Approx. 60 days
Nigeria (Gerere)	24	15	Approx. 80 days

Bull WHO 1975; 52: 209-222

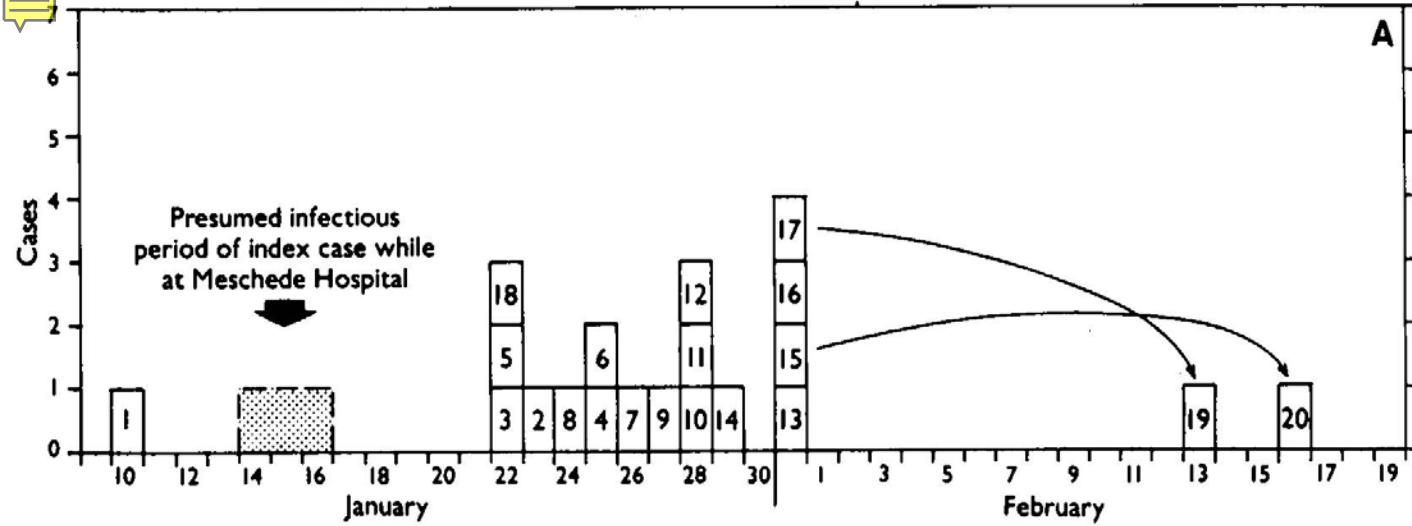




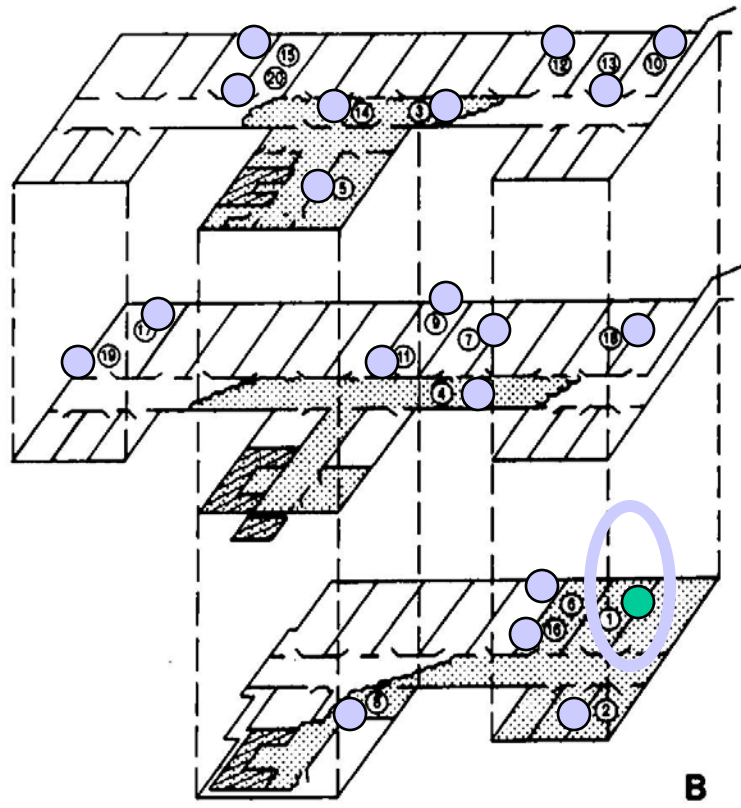
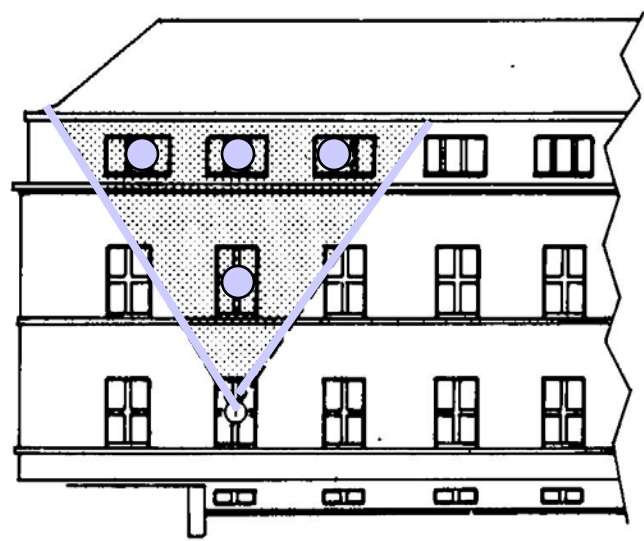
Examples of Slow Smallpox Transmission Within a Single Compound

Source	Susceptibles Exposed	Smallpox case	Cases per 100 Susceptibles Exposed
Nigeria (abakaliki)	27	12	44.4
United Rep. of Cameroon (N'Game)	10	4	40.0
Nigeria (Gerere)	45	12	26.2





- ⊙ Case number
- ▨ Stairs
- ▨ Smoke pattern



Airborne Spread of Smallpox in the Meschede Hospital

Fenner. 1988. Fig. 4.9

Recovery of Variola Virus from the Vicinity of Smallpox Patients

Recovery of variola virus from the vicinity of patients with variola major ^a

Source of Sample	Number of patients	Number of Specimens	Positive	
			Number	%
Impinger, near mouth	29	47	5	11
Settling-plate, near mouth	13	30	12	40
Circumoral swab	32	58	42	72
Pillow Swab	40	67	41	61
Impinger, near bedclothes	9	15	5	33
Settling-plates, near bedclothes	13	20	11	55
Bedclothes Swab	11	16	15	94
Back Swab	35	66	25	38
Urine	16	34	17	50

^a Based on on Downie et al. (1965a).



Secondary Attack Rates by Pre-exposure Vaccination Status West Pakistan, Sheikhpura District

Never vaccinated	26/27	96%
Vaccinated within prior 10 years	5/115	4%
Vaccinated >10 years previously	8/65	12%

†Adapted from Mack et al, Summarized in Fenner et al. Smallpox and its eradication, pg 688



Duration of Protection

Age Group	Vaccination in Infancy	Case-Fatality Rate
0-4	Yes	0%
	No	45%
5-14	Yes	0%
	No	10.5%
15-29	Yes	0.7%
	No	13.9%
30-49	Yes	3.7%
	No	54.2%
≥50	Yes	5.5%
	No	50.0%

†From Outbreak in Liverpool, England, 1902-1903 In Fenner F et al. Smallpox and its Eradication, pp53



Case-Fatality Rate of Smallpox After Importations into Western Countries 1950-1971

Successfully Vaccinated	Case-Fatality Rate
Never	52%
Only after the exposure	29%
0-10 years before exposure	1.4%
11-20 years before exposure	7%
> 20 years before exposure	11%

†In Fenner F et al. Smallpox and its Eradication, pp53



Effects of Post Exposure Vaccination

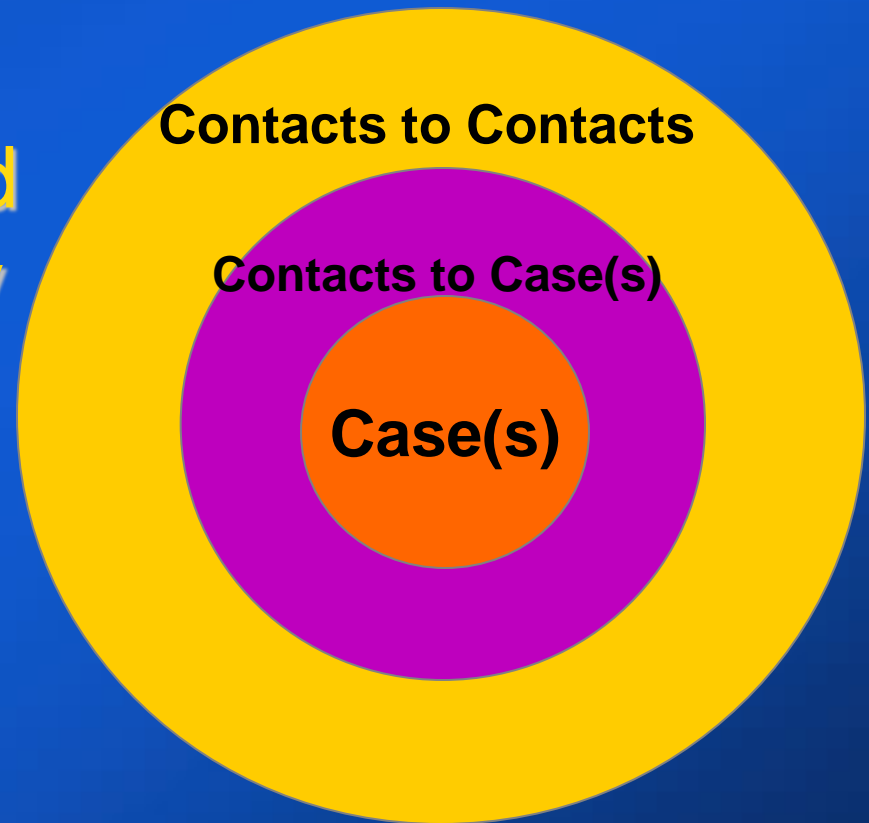
		2° Attack Rate
(Rao 1968)	Primary vaccination post exposure	29.5%
	Never vaccinated	47.6%
(Mack 1972)	1° vaccination ≤ 10 days post exposure	75.0
	Never vaccinated	96.3
(Helmer 1971)	Vaccinated or revaccinated ≤ 7 days	1.9
	Never Vaccinated	21.8

† Adapted from Fenner F et al. Smallpox and its Eradication, pp 591

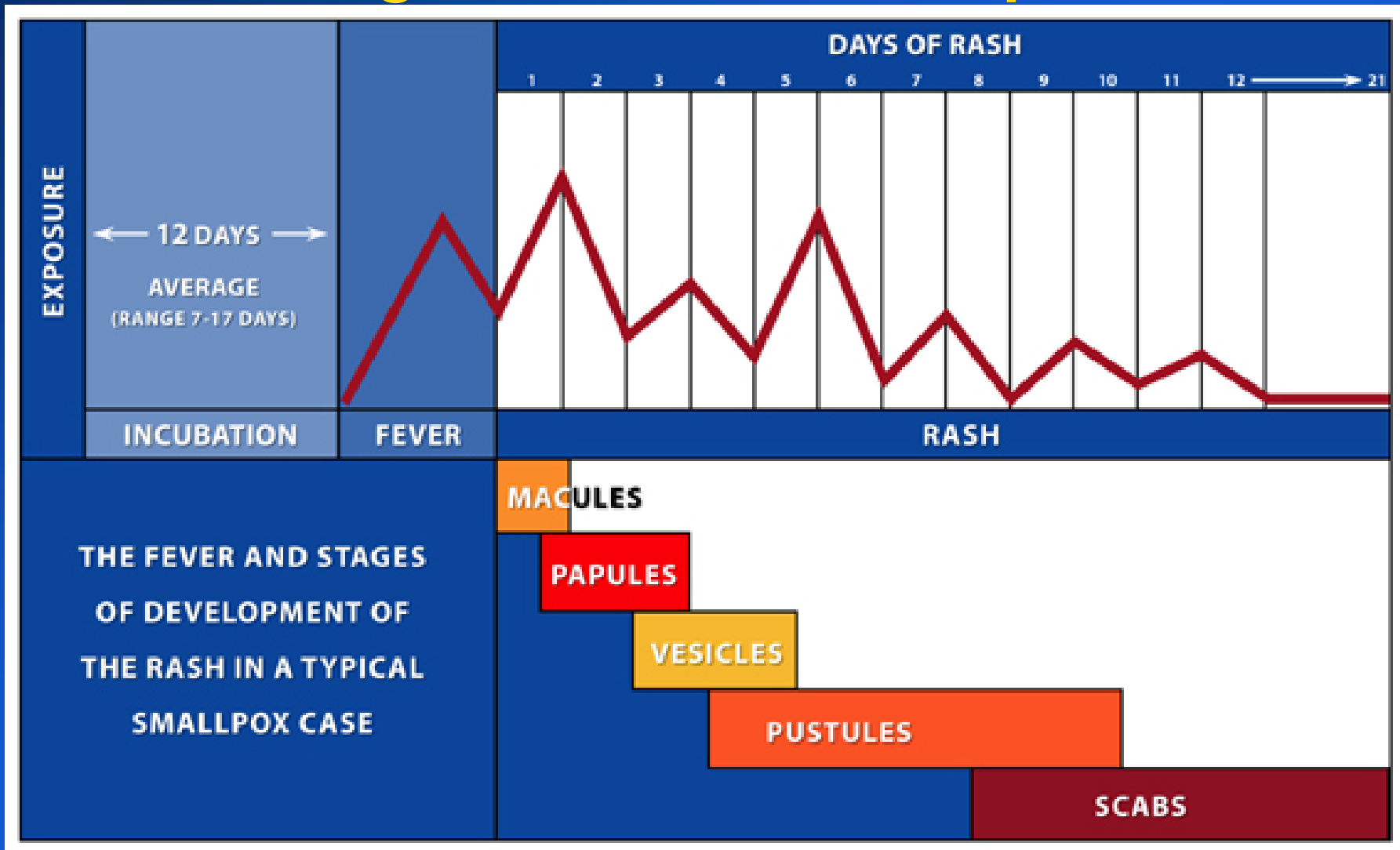


Surveillance and Containment Strategy

- Search for cases
- Containment of spread by vaccinating primary contacts and their contacts
- Most efficient strategy



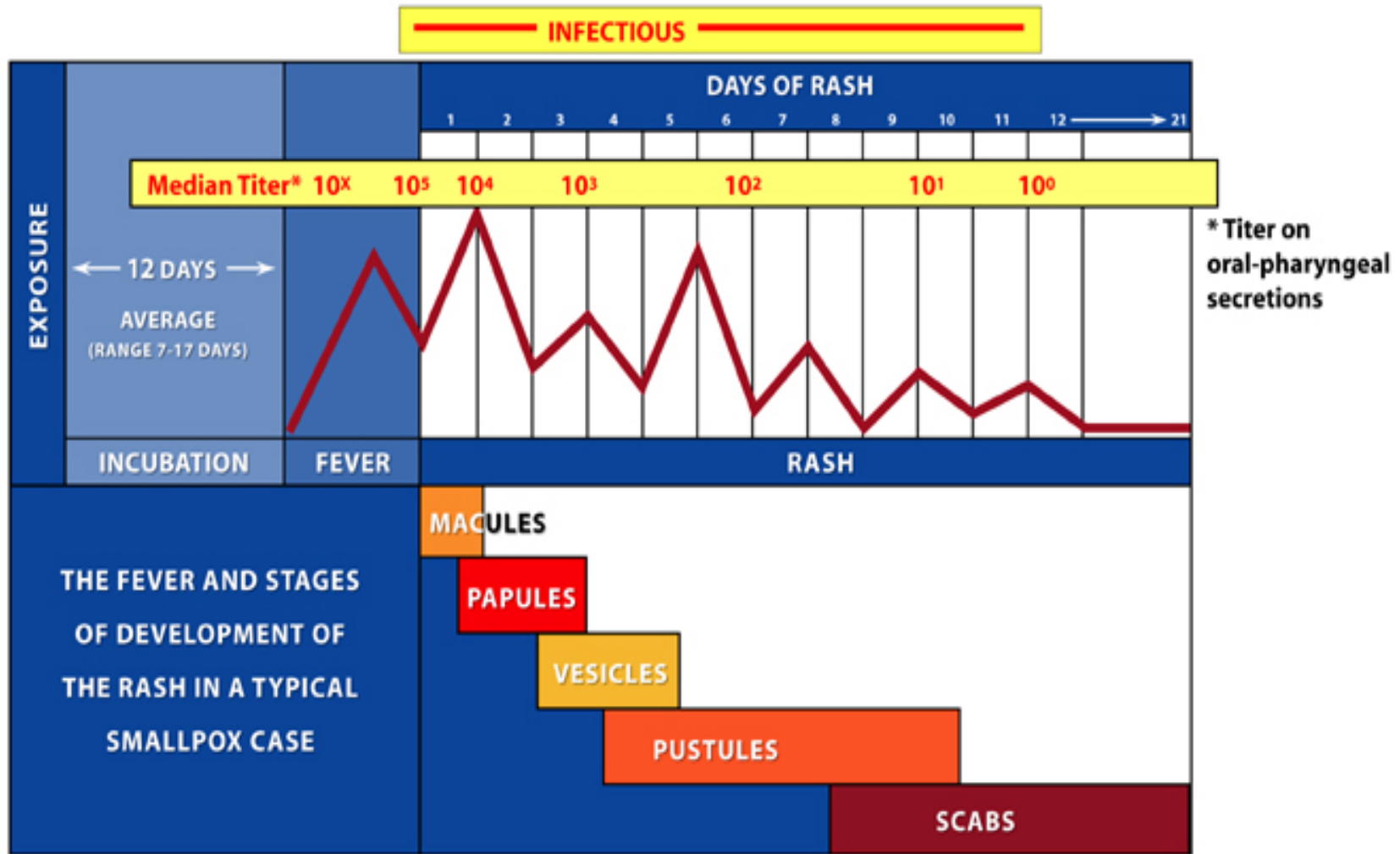
Progression of Smallpox



Source: Foege, Lane, and Millar, Am J. Epi, 1969



Progression of Smallpox



THE FEVER AND STAGES OF DEVELOPMENT OF THE RASH IN A TYPICAL SMALLPOX CASE



Source: Foege, Lane, and Millar, Am J. Epi, 1969



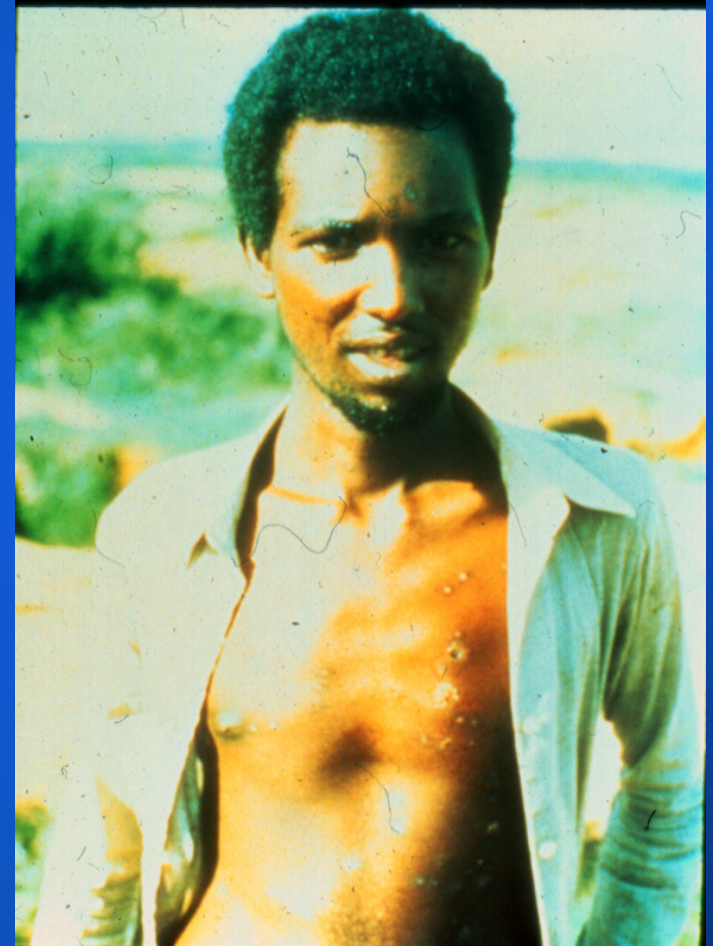
Last Village with Variola Major Kuralia, Bhola



Last Cases of Smallpox**



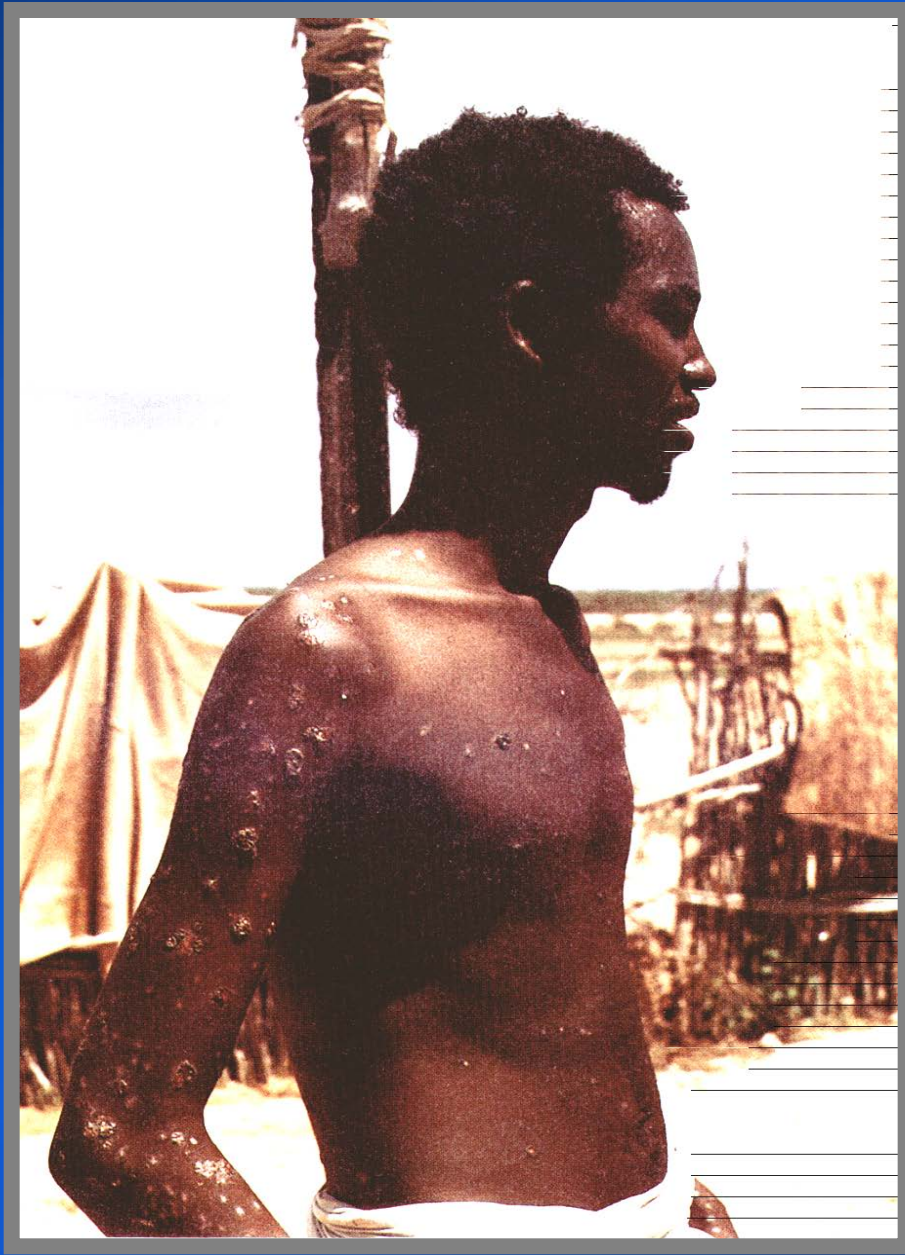
Rahima Banu – 16 October 1975
Variola Major-Bangladesh



Ali Maow Maalin – 26 October 1977
Variola Minor-Somalia

** Two laboratory acquired cases occurred in UK in 1978



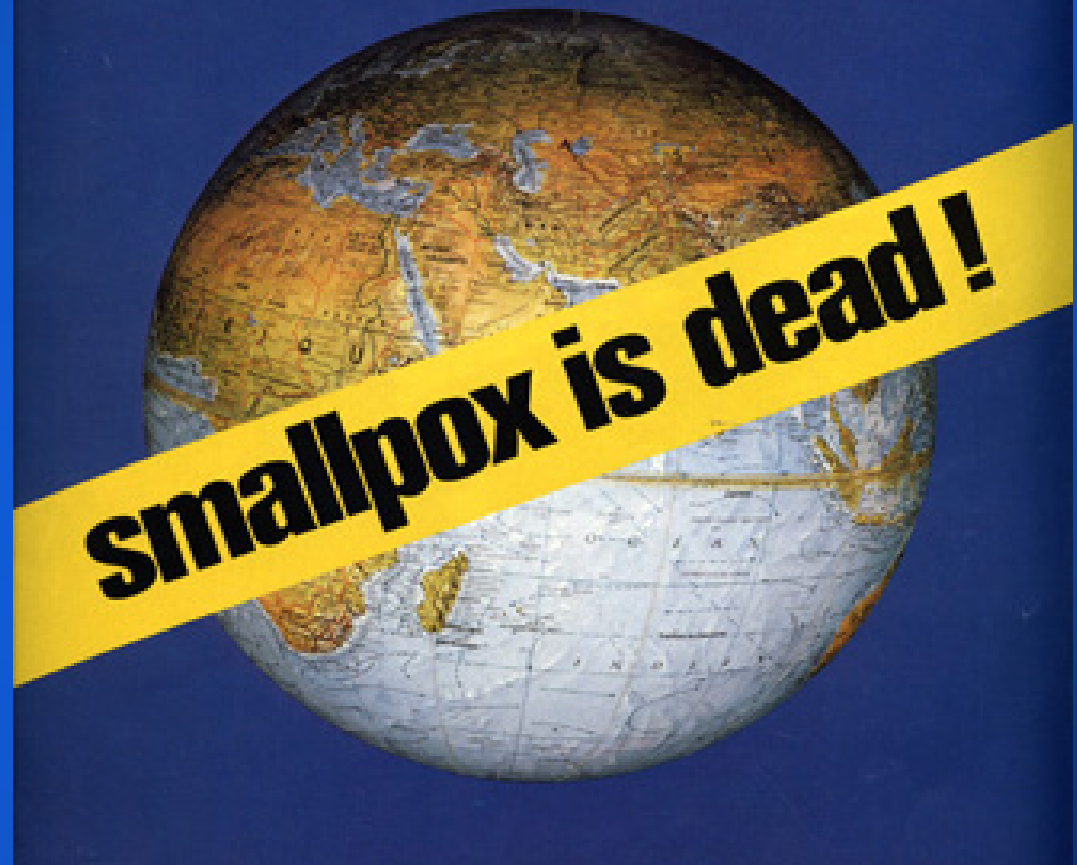




1980

WORLD HEALTH

THE MAGAZINE OF THE WORLD HEALTH ORGANIZATION · MAY 1980



Why Worry About Smallpox?

- Allegations that Soviet BW program produced smallpox virus for use in bombs and ICBMs
- Concerns that smallpox virus could be obtained and used by others as terrorist weapon



JAMA 1999; 281: 2127-2137



The Faces of Smallpox

