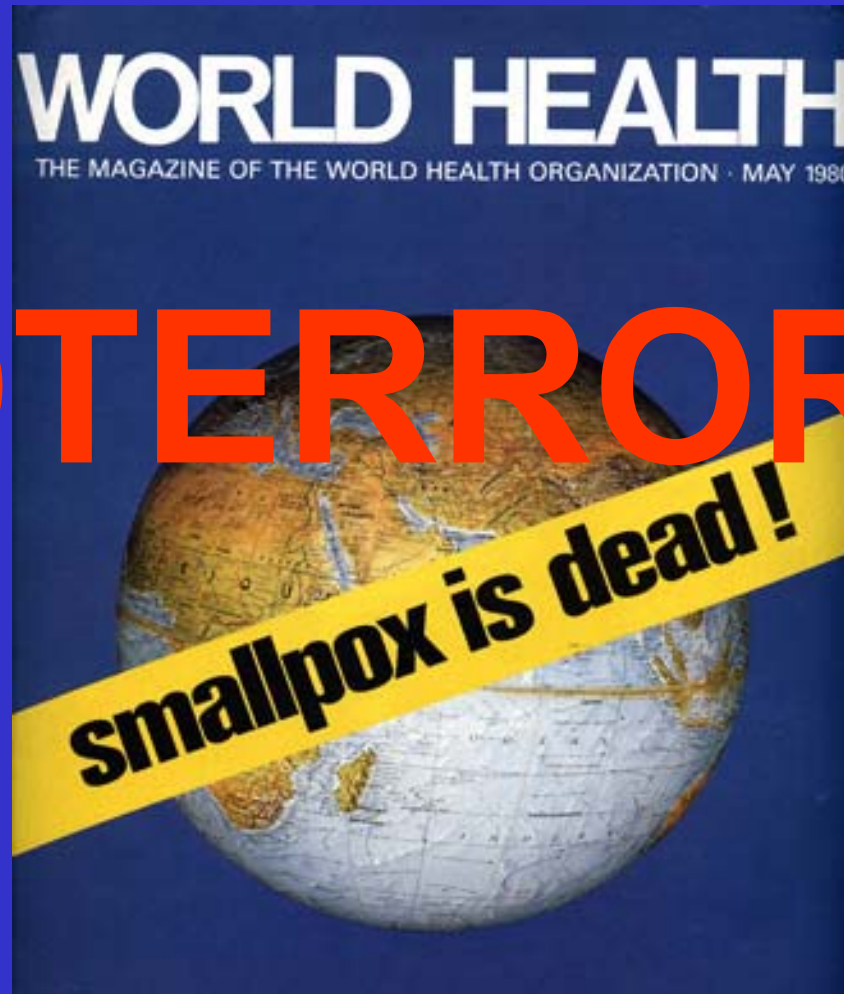


SMALLPOX: DIAGNOSIS AND EPIDEMIOLOGY



BIOTERRORISM

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Smallpox - March 25, 2002

Bioterrorism

Bioterrorism is the use or threatened use of biological agents against a person, group, or a larger population in order to create fear or illnesses for purpose of intimidation, gaining an advantage, interruption of normal activities, or for ideological objectives.

7 TYPES OF SMALLPOX

- No rash – *Variola sine eruptione*
- Modified
- Discrete
- Semi-confluent
- Confluent
- Flat
- Hemorrhagic – early and late

SMALLPOX

VARIOLA SINE ERUPTIONE

- **Fever 39° C**
- **Headache, backache**
- **Recovery in 48 hours**

- **Requires laboratory studies**
- **Virus isolation up to day 3**
- **Neutralizing Antibody**
- **No rash**
- **Not thought to be infectious**

SMALLPOX - DISCRETE

Areas of
normal skin
between
pustules,
even on
face



FIG. 53. Benign, mature 'pearls' deep-set in skin of forearm, seventh day.

SMALLPOX - SEMICONFLUENT

- Pustules confluent on face but discrete elsewhere



SMALLPOX - CONFLUENT

- **Confluent rash on face and forearms**



SMALLPOX - FLAT

- Pustules
confluent or
semiconfluent
– appear flat

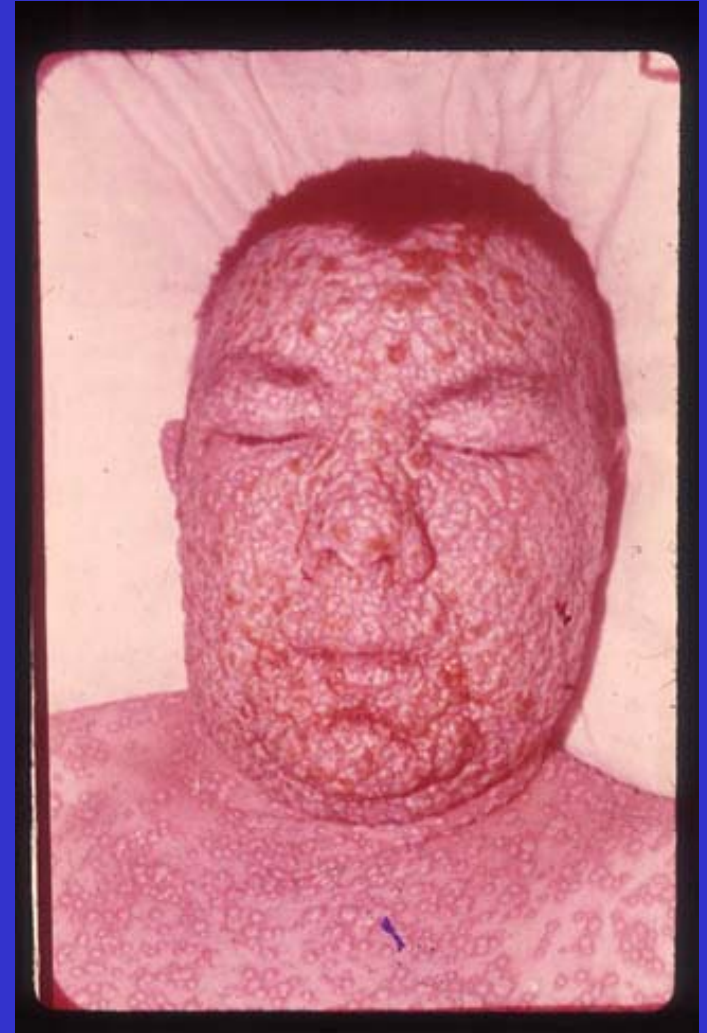




FIG. 32. Malignant. Flat soft vesicles, some with adherent roofs, simulating haemorrhage, ninth to tenth day.

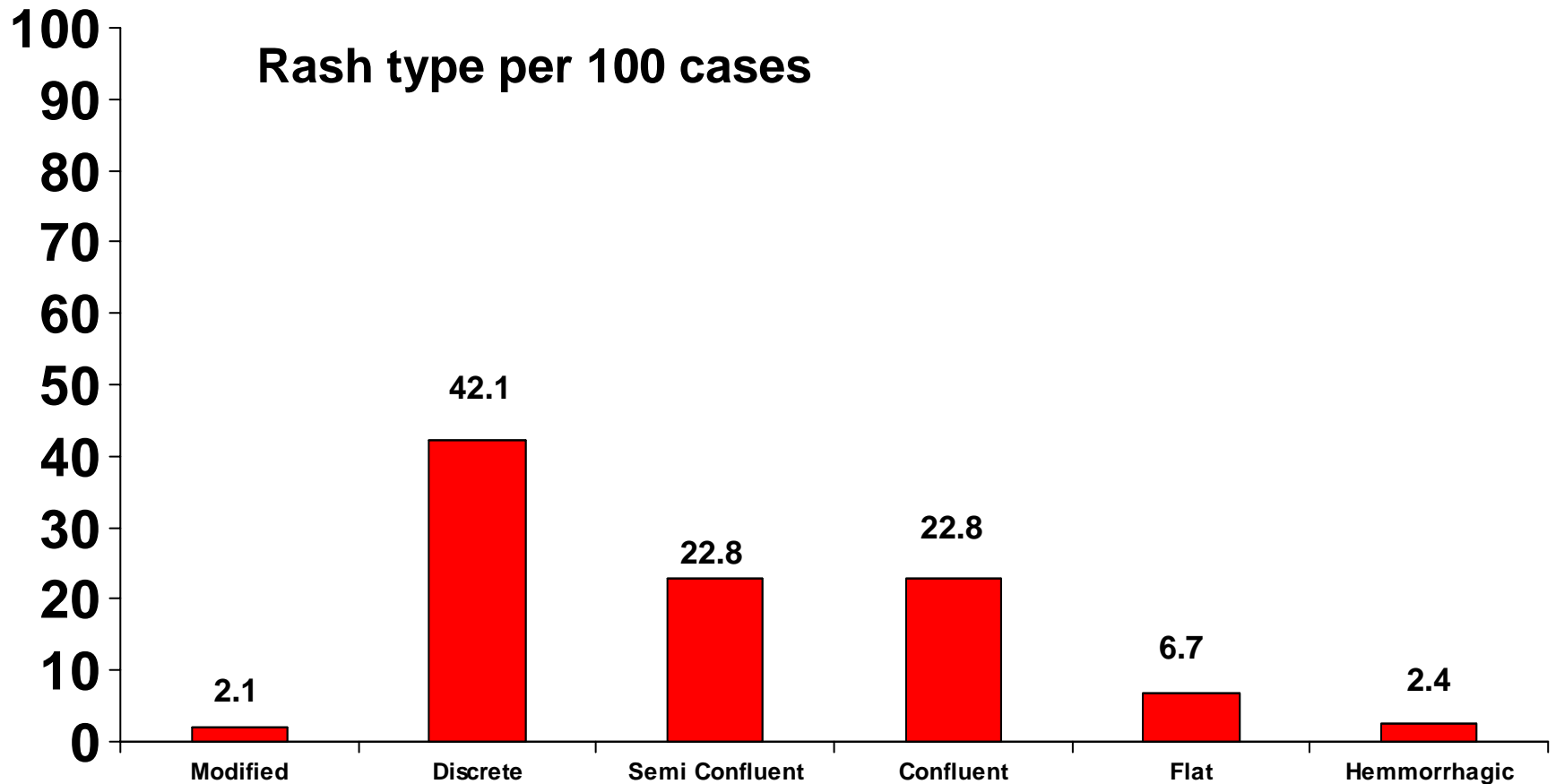
HEMORRHAGIC SMALLPOX

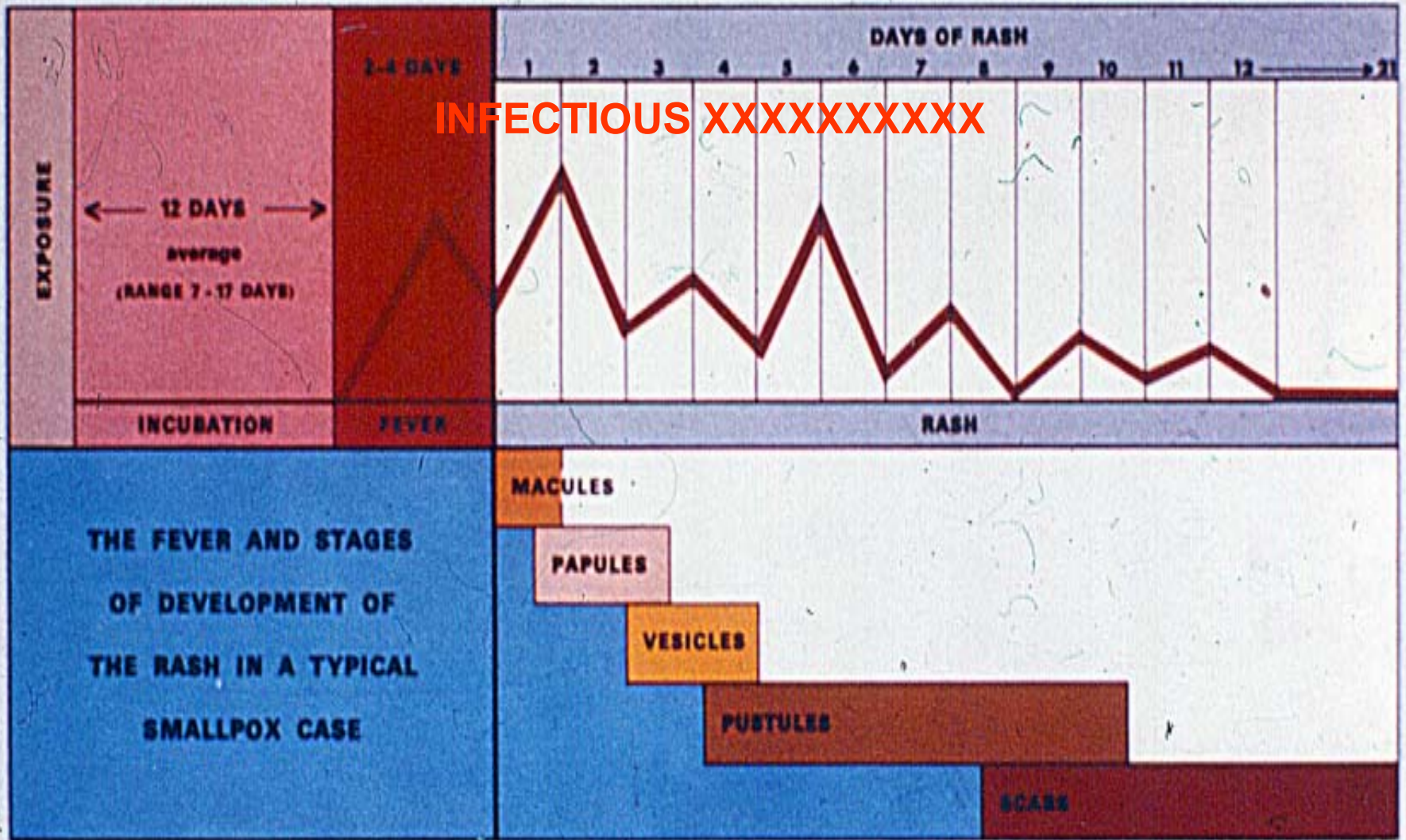
- Widespread hemorrhage into skin
- Two types (early and late) both 98% case fatality



SMALLPOX Proportion by Rash Type Among Unvaccinated Persons

*Rao, Smallpox in Bombay, Kothari, Bombay, 1972 (6942 cases)





INCUBATION PERIOD

- Usual incubation period (interval between exposure/infection and first symptoms) is 10-14 days
- Can be as short as 7 days and as long as 19 days

PRE-ERUPTION PRODROME

- Sudden onset of high fever (38.5-40.5°C or 101.3 -104.9°F) and malaise
- Toxic during first two days
- Fever drops and patient feels better when rash appears

PRODROMAL SYMPTOMS

6942 CASES OF VARIOLA MAJOR

Rao, Smallpox in Bombay, Kothari, Bombay, 1972

SYMPTOM	PERCENT
Fever	100
Headache	90
Backache	90
Chills	60
Vomiting	50
Pharyngitis	15
Diarrhea	10
Delirium	15
Abdominal Pain	13
Convulsions	7

MACULES

- Minute red spots (first of tongue and palate)
- Lesions of the face and forehead (“herald spots”)
- Proximal part of extremities
- Distal parts extremities
- All in 1-2 days
- Difficult to see on dark skinned people





FIG. 116. Early maculo-papular rash on the scalp, *variola minor*.

PAPULES

- Day 2 of rash
- Pharyngeal lesions evolve quickly to papules, vesicles, and break down (virus present)
- Raised above the skin
- Fluid accumulating



VESICLES

- Day 4 and 5
- Accumulation of fluid
- Over next 24-48 hours, clear fluid becomes cloudy and begins to thicken



FIG. 44. Benign (in contrast) Type 6, discrete, early vesiculation, sixth day.



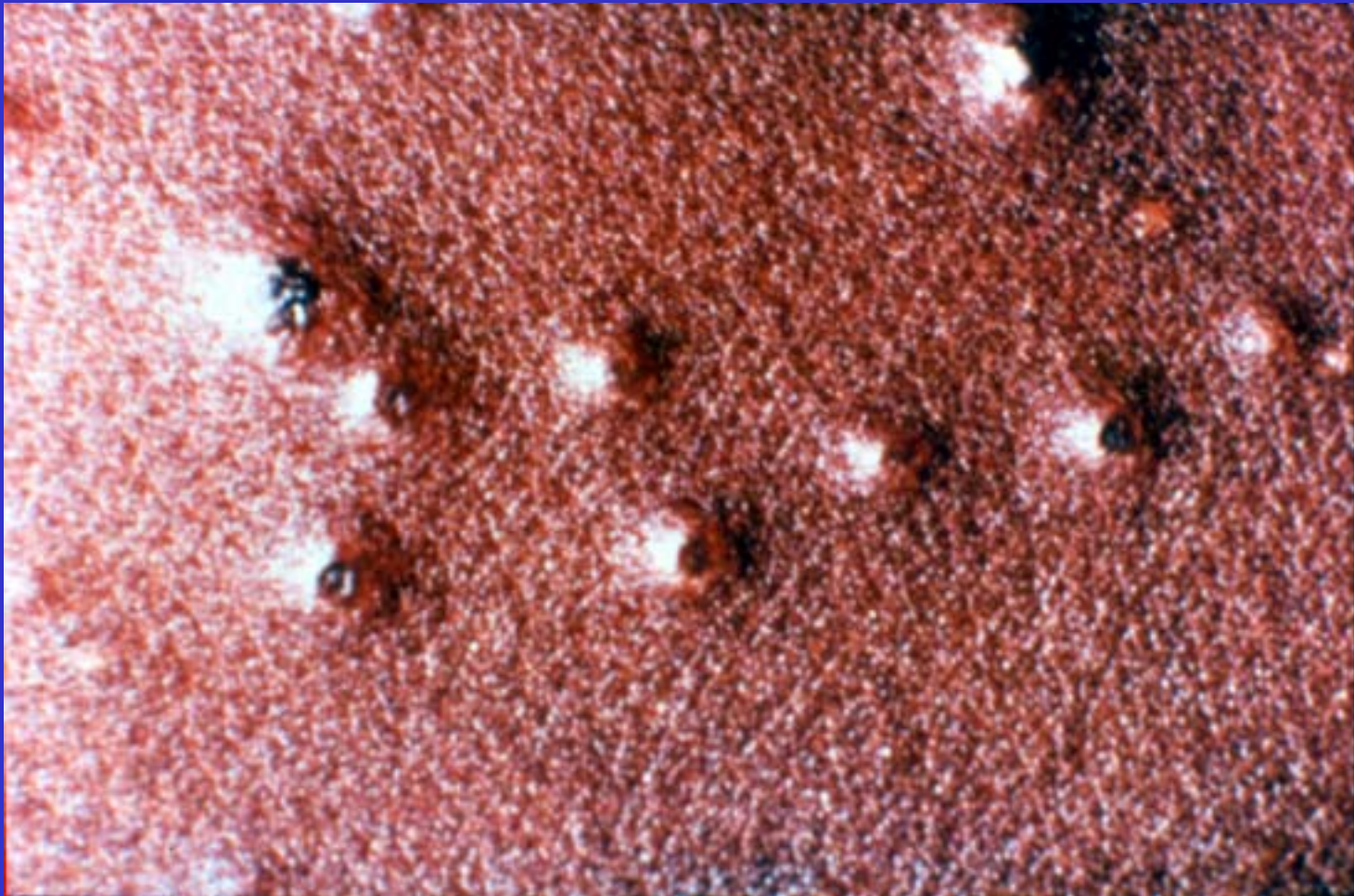
PUSTULES

- Vesicular fluid becomes pus
- Most lesions are pustules by day 7
- Reach maximum size by day 11
- As fluid absorbed, lesions become flatter
- Feel like hard peas in skin



UMBILICATED LESIONS

PUSTULES TURNING INTO SCABS



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SCABS ON FEET



SCABS BEGIN TO FALL OFF

- Scabs form as pustular fluid is absorbed
- Because scabs contain viable virus, patients are infectious until all scabs separate
- In calloused areas (palms and soles) scabs are deeply embedded and may take 2-3 weeks to fall



COMPLICATIONS

- **Bacterial infection of the skin, e.g., boils, impetigo (2-5% in dirty environment); blood stream infection (septicemia)**
- **Corneal ulceration and blindness: corneal opacity (4.4%), corneal ulcer (1%)**
- **Bones and joints**
- **Bronchitis and pneumonia probably due to secondary infection**
- **Encephalitis: 1 in 1000 cases**

SEQUELAE

- **Pock Marks**
 - Scarring
 - “Not-marriageable”
 - Epidemiologic importance – scar survey
- **Blindness (Hughes et al, Bangladesh)**
 - Corneal Opacities 2.1%
 - Blindness 0.9%
- **Limb Deformities**



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MORTALITY RISK FACTORS

- **Type of Virus (Major vs. Minor)**
- **Case Type**
- **Age**
- **Vaccination Status**
- **Environmental sanitation (soap and water)**
- **Treatment (antibiotics)**
- **Antivirals ?????**

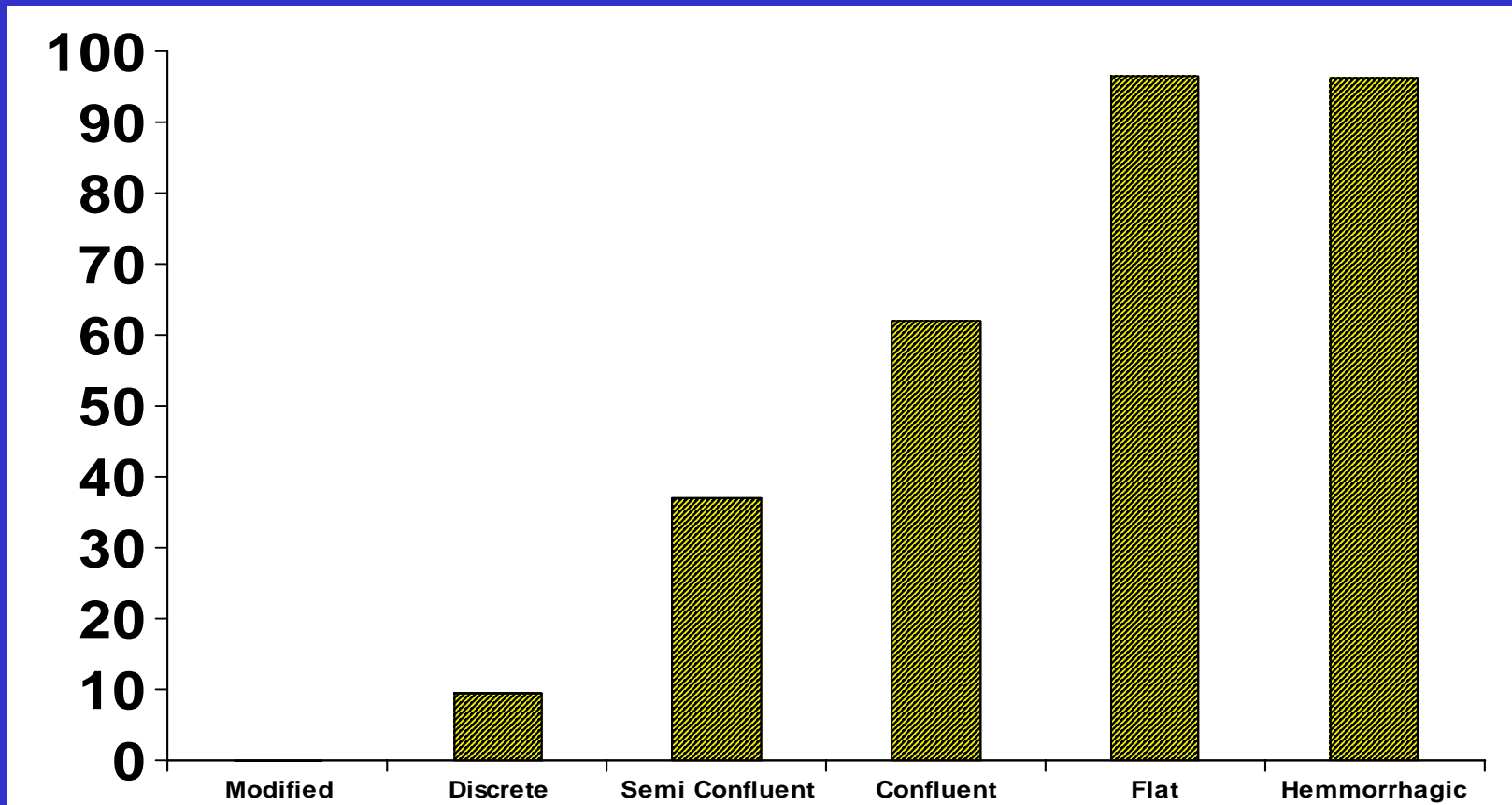
VARIOLA (MINOR & MAJOR) RASH TYPES & CASE FATALITY

STRAIN	MILD	MODERATE	SEVERE	CASE FATALITY
Variola Minor	Most	Some	Few	1 %
Variola Major	30%	60%	10%	5-30%

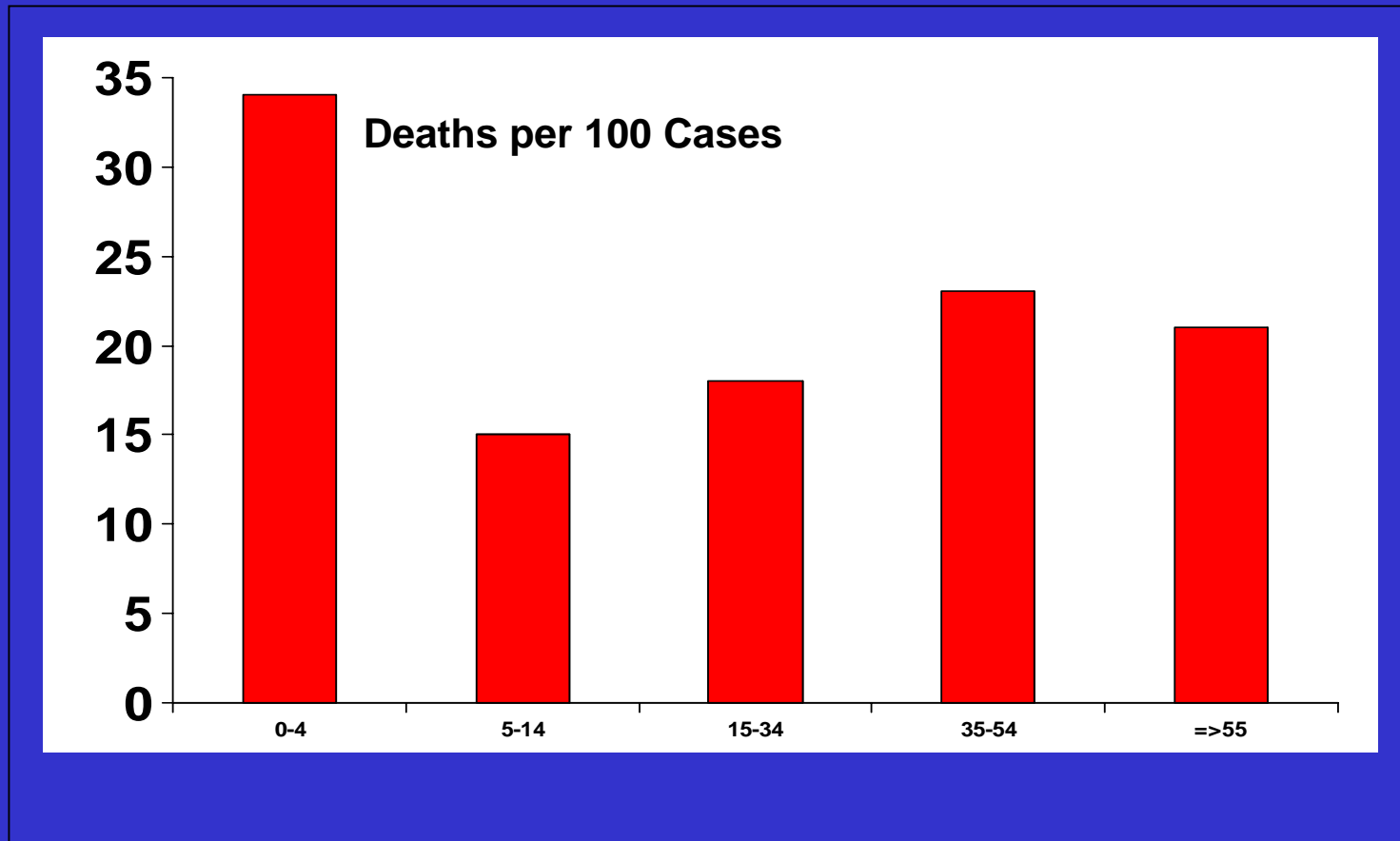
SMALLPOX CASE FATALITY RATES* BY CASE TYPE

**Rao, Smallpox in Bombay, Kothari, Bombay, 1972, 6942 cases

Deaths per 100 Cases



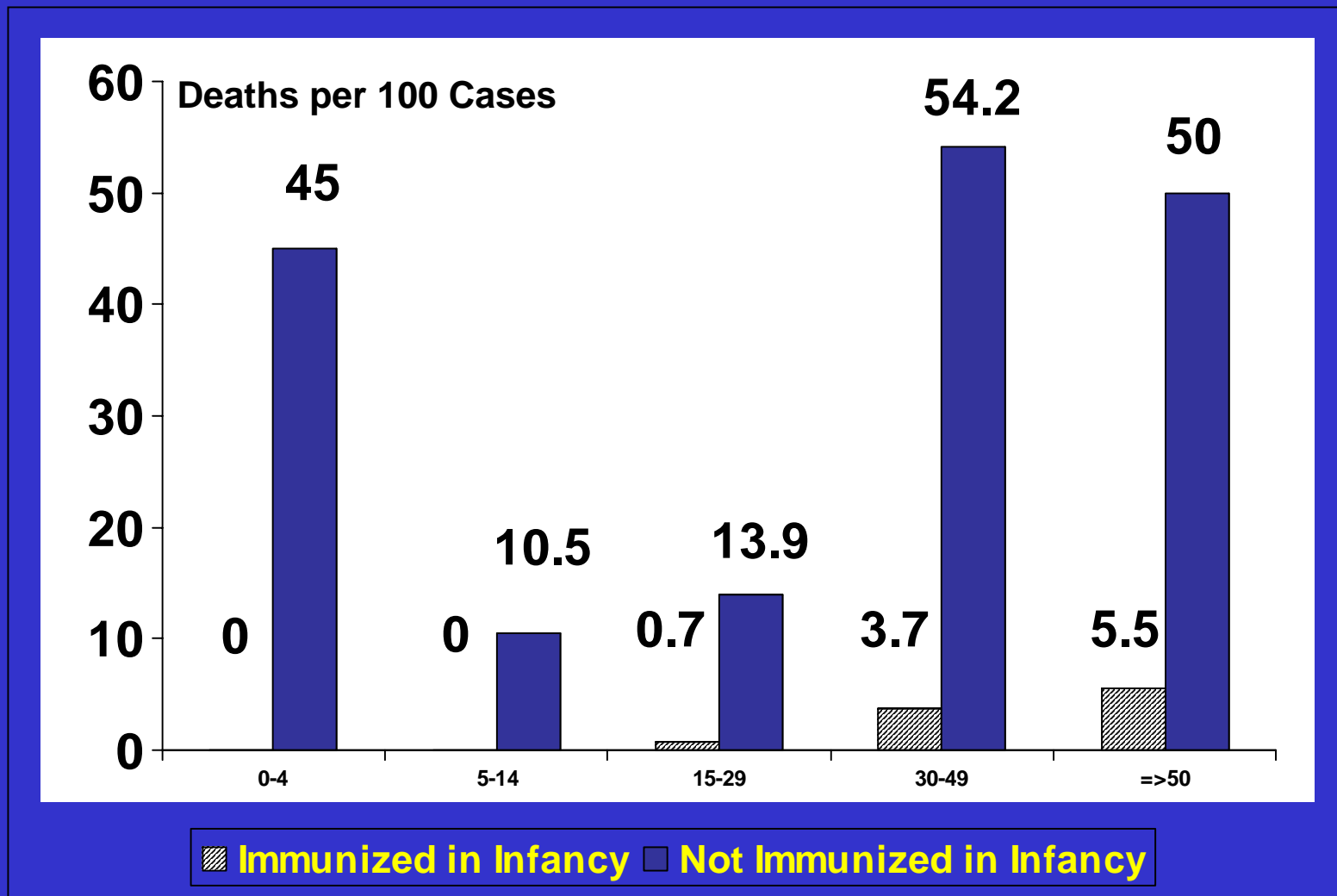
AGE-SPECIFIC CASE FATALITY UNVACCINATED



Koplan, Azizullah, Foster. Trop Geog Med 1978, 30:355-358

SMALLPOX CASE FATALITY*

INFANT IMMUNIZATION AND AGE OF INFECTION



EPIDEMIOLOGY OF SMALLPOX

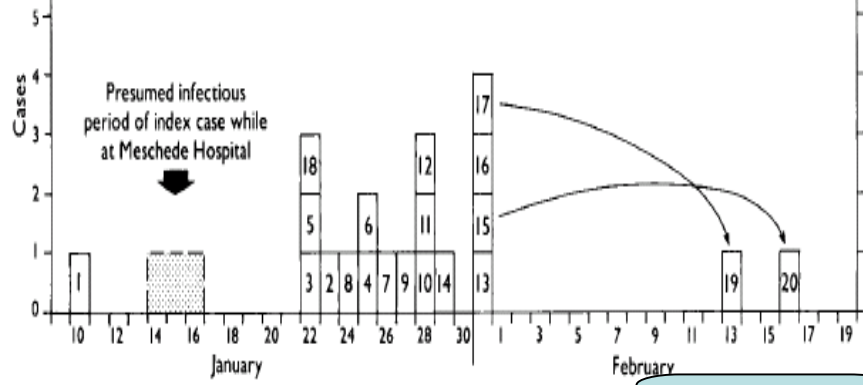
- **Smallpox has limited infectivity (compared to measles)**
- **Transmission primarily by droplets**
- **Transmission primarily among close contacts (within 6 feet)**
- **Occasional cases where lesions occur in nasopharynx, cough aerosolizes small particles**

Herd Immunity Thresholds for Selected Vaccine-Preventable Diseases†

Disease	R ₀	Herd Immunity	Immunization Levels	
			1999 19-35 months	1997-98 pre-school
Diphtheria	6-7	85%*	83%*	97%
Measles	12-18	83-94%	92%	96%
Mumps	4-7	75-86%	92%	97%
Pertussis	12-17	92-94%	83%*	97%
Polio	5-7	80-86%	90%	97%
Rubella	6-7	83-85%	92%	97%
Smallpox	5-7	80-85%	—	—

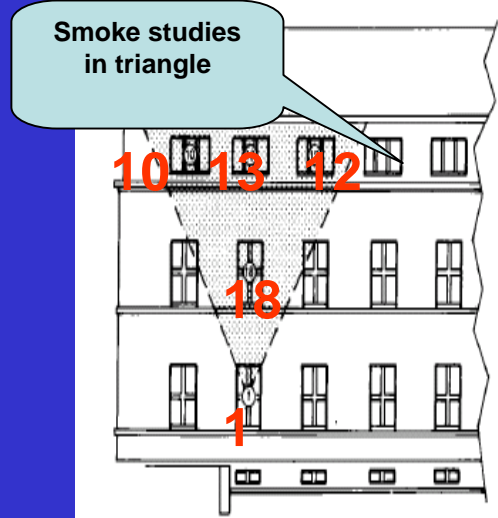
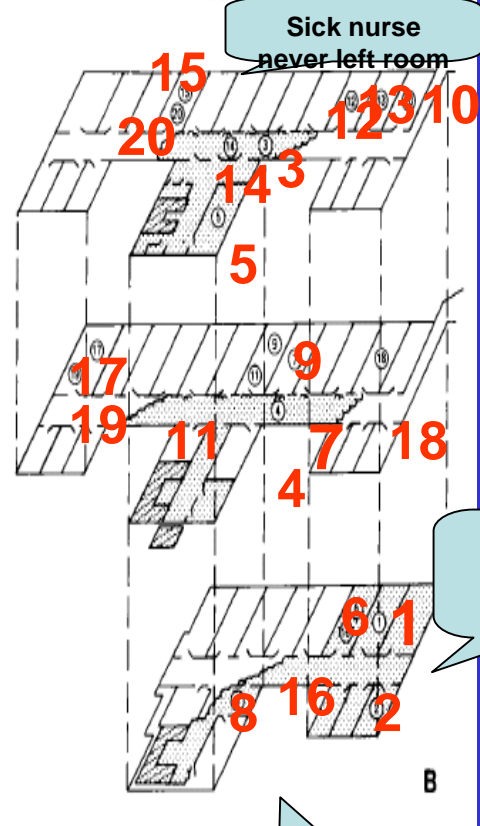
*4 doses

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



Airborne transmission of smallpox Meschede, Germany 1972

- ⊙ Case number
- ▨ Stairs
- ▤ Smoke pattern



Index case five days in room

Visitor 15 minutes in hospital

Smallpox - March 25, 1972

	SMALLPOX	CHICKENPOX
FEVER	2 to 4 days before rash	At time of rash
RASH		
Appearance	Pocks in same stage	Pocks in several stages
Development	Slow	Rapid
Distribution	More pocks on arms and legs	More pocks on body
On Palms and Soles	Usually present	Usually absent
DEATH	Usually 1 in 10 die	Very uncommon

DIFFERENTIAL DIAGNOSIS

CONDITION	VARIOLA MAJOR, United Kingdom 97 Cases	VARIOLA MINOR, SOMALIA 29 Cases
Chickenpox	41	20
Syphilis	3	4
Erythema Multiforme	7	
Allergic Dermatitis	7	1
Drug Rash	6	1
Vaccinia	5	1
Septicemia	4	
Herpes	2	
Measles	2	

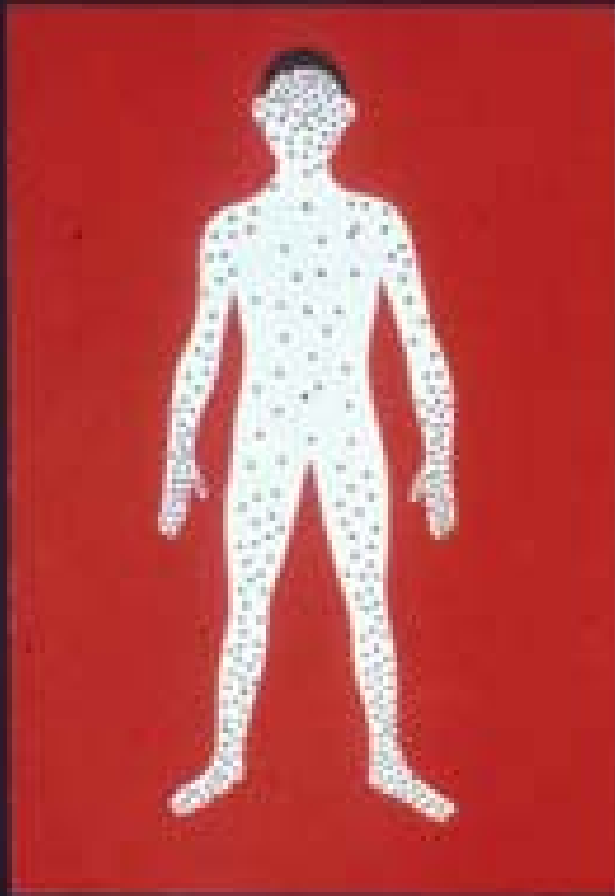
EVOLUTION OF SMALLPOX RASH

- A major diagnostic characteristic of smallpox is that lesions in a given area are similar in appearance and feel
- Lesions appear first on the head and evolve distally:
 - Pharynx, Palate
 - Face
 - Proximal Extremities
 - Hands and Feet

SMALLPOX



Smallpox - March 25, 2002



SMALLPOX



CHICKENPOX

CHICKENPOX



SMALLPOX ERADICATION STRATEGIES

STRATEGY	METHOD	MEASURE
Traditional	Isolation of Cases	
Outbreak Response	Quarantine & Vaccination	Number of Cases
Vaccination	Routine Vaccination	Number of vaccinations
Campaign Vaccination	Campaigns & Survey	Vaccination coverage
Surveillance Containment	Active Search Containment	Number of infected villages





**William Foege
MD, MPH**

- 1. In the fall of 1966 with little vaccine available, a smallpox outbreak in Ogoja, Nigeria was stopped by vaccinating infected villages**
- 2. Bill drew a series of spot maps of infected villages. Maps showed entry from north and spreading to the south. He asked me, if I stop the first will I stop the others?**
- 3. An outbreak occurred in Abakaliki with 95% coverage. Smallpox found its way into a faith community that refused vaccination**
- 4. Bill noted that smallpox transmission was high in the dry season, and low in rainy season (What if we focus surveillance on the period of low transmission?)**

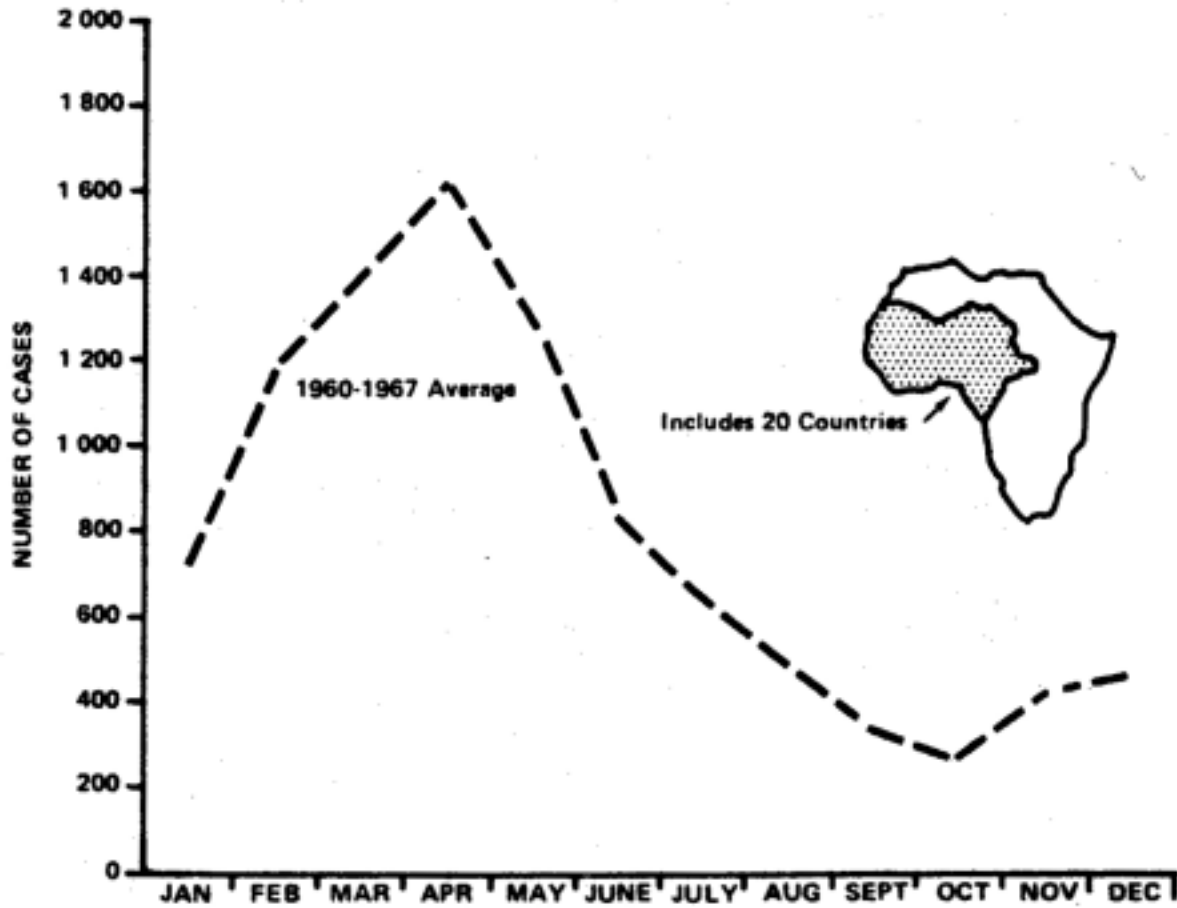
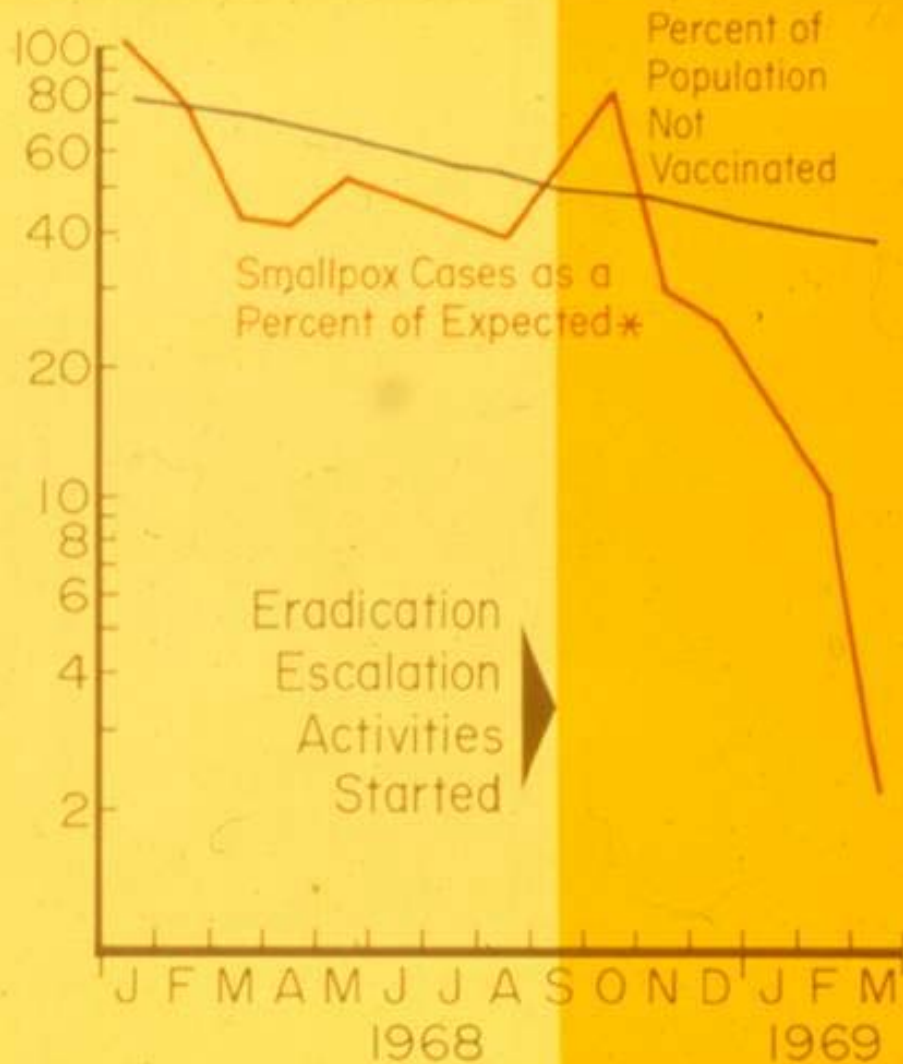


Fig. 3. Average number of reported smallpox cases in West and Central Africa by month, 1960-67. Source: World Health Organization.

Bull WHO 1975; 52: 209-222

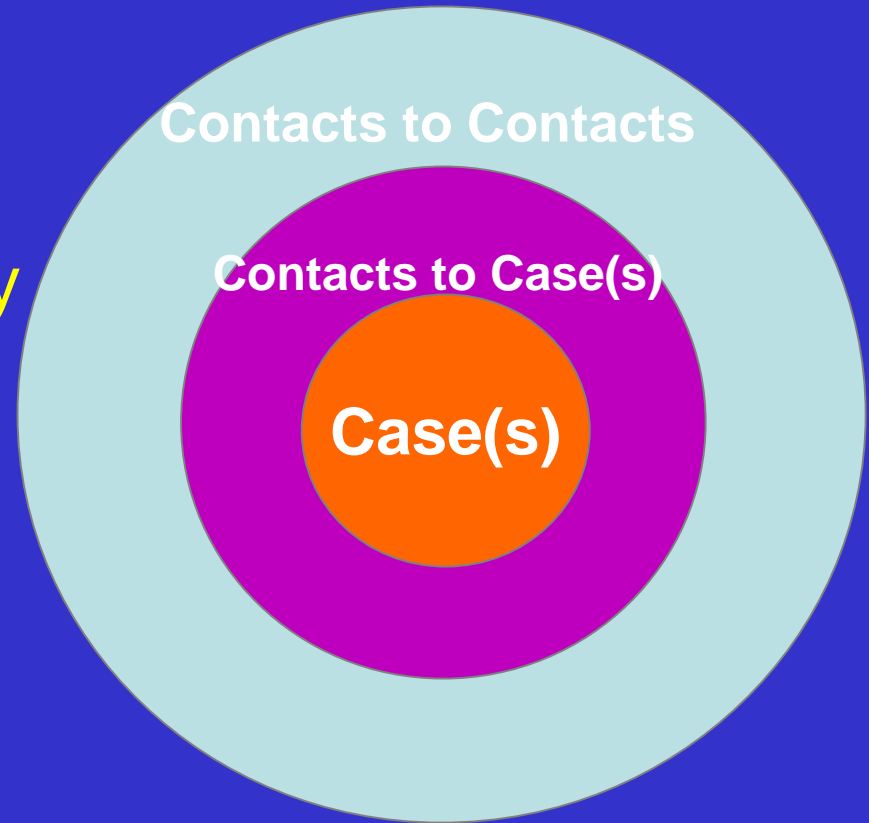
Percent of Population not Vaccinated in the Smallpox Eradication Program Area Compared with the Ratio (%) of Reported Smallpox Cases to the Expected Smallpox Cases*



* Expected-1960-1967 Monthly Average.

Search and Containment Strategy

- Principal global eradication strategy was search for cases and containment of spread by locating and vaccinating contacts
- Search and containment continues to be the most efficient strategy

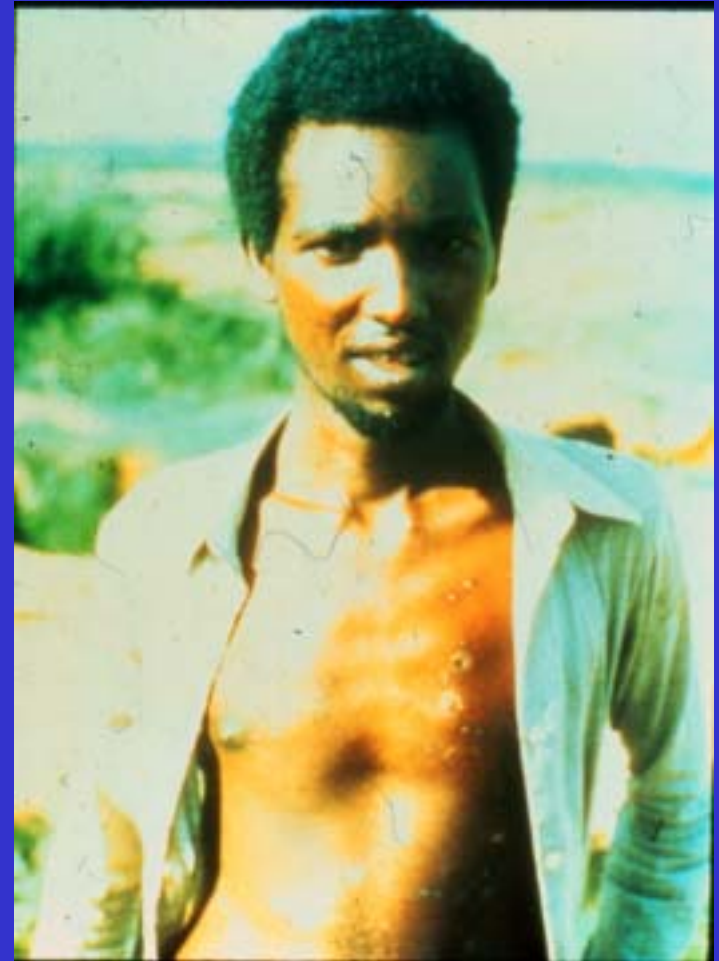


LAST CASES OF SMALLPOX**



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**

DANGEROUS ASSUMPTION

~~BIOTERRORISM
SMALLPOX WILL
BEHAVE AS
ENDEMIC
SMALLPOX~~

BIOTERRORISM

REINTRODUCTION SP INTO WORLD

- **UNITED STATES**
 - Preparedness
 - Infrastructure
 - Vaccine Supply
 - Plan
 - Media
- **WORLD**
 - Limited Vaccine
 - Limited Capacity
 - 100 million cases, 20 million deaths

FACES OF SMALLPOX



HOSPITAL RISKS

- **Delayed recognition in crowded emergency rooms**
- **Transmission to staff, other patients and visitors**
- **Aerosol spread**
- **Fomite contamination, e.g., laundry**
- **Atypical presentation delaying diagnosis**

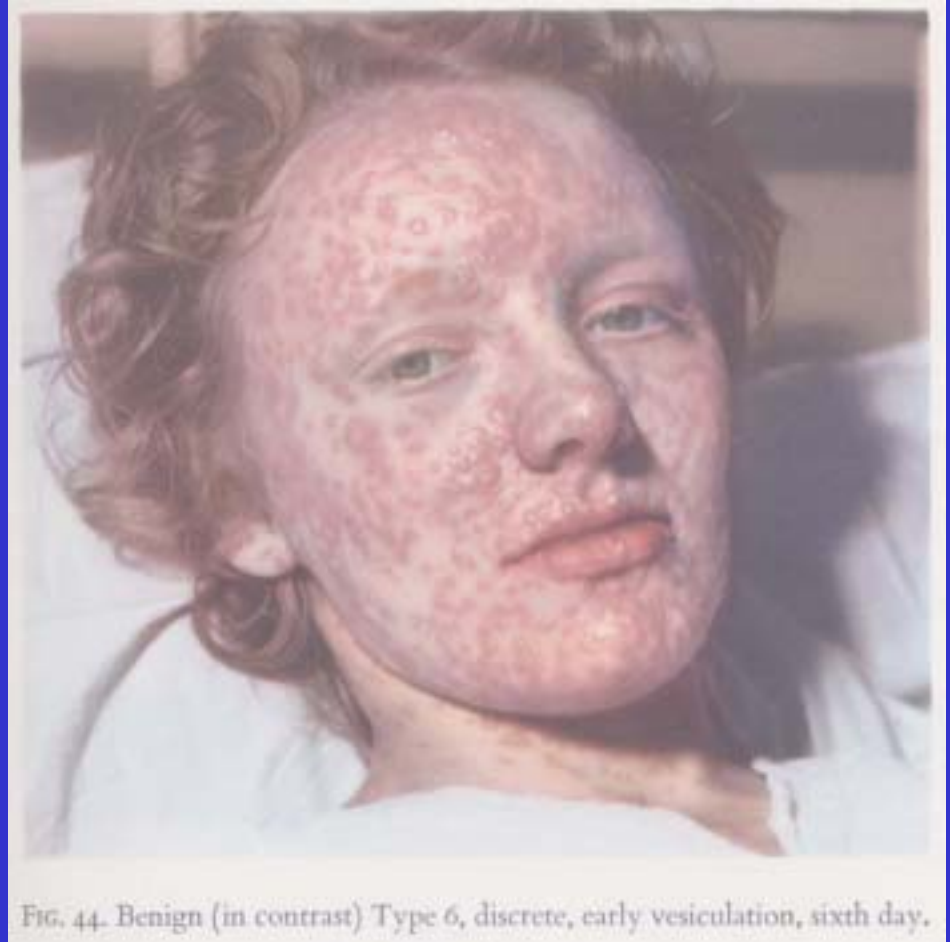
PEDIATRIC EMERGENCY

- 18 months
- 4 day history of high fever (>103)
- 1 day history of rash



ADULT EMERGENCY

- 30 year old women
- 4 day history of fever
- Contact with chicken pox
- Developed rash on face



ADULT EMERGENCY

- 40 year old female
- History of high fever
- Bleeding into skin
- Unconscious

