

Variola

Patricia Bolívar MS., CLS, PHM

Description and Significance



- Smallpox was one of the most notorious infections of mankind.
- It was declared eradicated by the World Health Assembly in 1979, 2 years after the last natural case in Somalia in 1977.
- The remaining known samples of Variola virus are held under secure containment at the U.S. Centers for Disease Control and Prevention (CDC), Atlanta, Georgia and the Russian State Center for Virology and Biotechnology, Koltsovo, Russia.
- The entire population younger than 30 is fully susceptible to smallpox.

History

- Smallpox was an infectious disease unique to humans, caused by either of two virus variants, *Variola major* and *Variola minor*.¹
- The disease is also known by the Latin names *Variola* or *Variola vera*, which is a derivative of the Latin *varius*, meaning "spotted", or *varus*, meaning "pimple".
- The term "smallpox" was first used in Europe in the 15th century to distinguish variola from the "great pox" (syphilis)

History continuation...

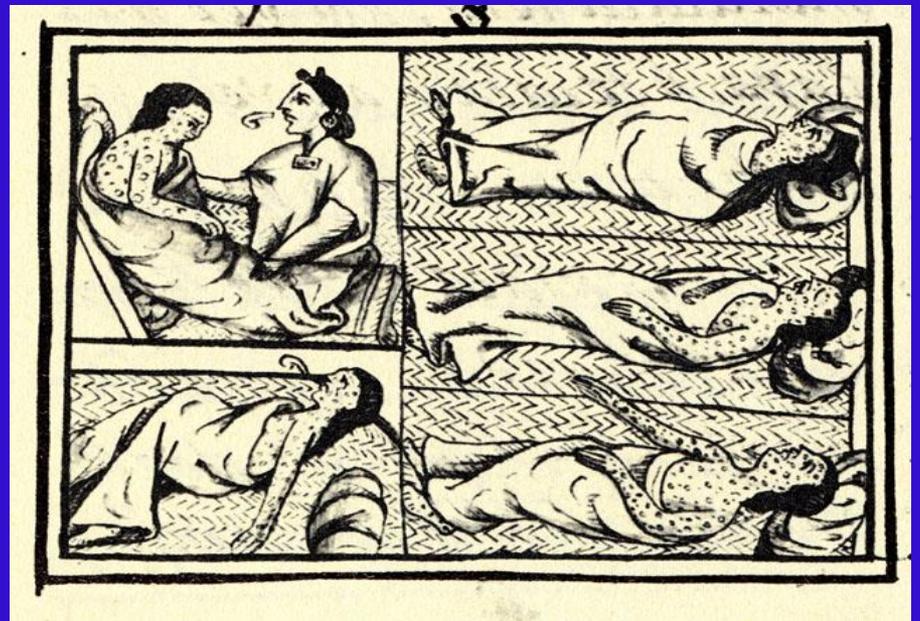
- Smallpox is believed to have emerged in human populations about 10,000 BC
- The earliest physical evidence of smallpox is probably the pustular rash on the mummified body of Pharaoh Ramses V of Egypt
- The disease killed an estimated 400,000 Europeans per year during the closing years of the 18th century (including five reigning monarchs) and was responsible for a third of all blindness.
- Of all those infected, 20–60%—and over 80% of infected children—died from the disease.^[9] Smallpox was responsible for an estimated 300–500 million deaths in the 20th Century



America's Variola



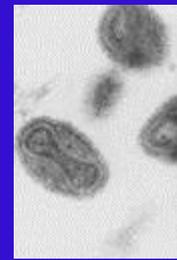
Drawing accompanying text in Book XII of the 16th-century *Florentine Codex* (compiled 1540–1585), showing Nahaus of conquest-era central Mexico suffering from smallpox.



Background

- The family *Poxviridae* comprises eight genera and a few unclassified species.
- Two species: *Variola virus* (genus *Orthopoxvirus*) and molluscum contagiosum virus (genus *Molluscipoxvirus*), only infect humans.
- Other orthopoxviruses that infect humans are monkeypox virus, vaccinia (the prototype orthopoxvirus and smallpox vaccine), and cowpox virus.
- Other poxviruses that infect humans belong to the genus *Parapoxvirus* (orf, milker's nodule, papulosa stomatitis, sealpox virus) and the genus *Yatapoxvirus* (Tanapox, Yaba monkey tumor virus).

Variola virus



- Poxviridae are linear, double-stranded deoxyribonucleic acid (DNA) viruses that replicate in the cytoplasm
- Electron microscopy was one historical method of choice for laboratory diagnosis of smallpox and other poxviruses.
- In negatively- stained electron microscopic preparations all but the parapoxviruses, which are ovoid, resemble brick-shaped particles with rounded corners length ranges from 220-450 nm, and width and depth from 140-260 nm.



Monkey pox virus

- Is an infection that has caused human epidemics in West and Central Africa, most notably in the Democratic Republic of Congo
- Maintained in a reservoir of wild animals but can incidentally infect humans and cause epidemics.
- A febrile exanthematous disease, characterized by a vesiculopustular rash.
- Human disease can be quite severe and present similarly to smallpox or can be confused with chickenpox.
- Monkeypox appears to be poorly transmissible between people, with a secondary attack rates below 10%.
- Smallpox vaccination is thought to provide some degree of protection against infections with monkeypox virus.

Cow pox and Vaccinia

- Infect humans, localized and secondary transmission only occurs by direct contact.
- Cowpox virus a virus of rodents, gerbils and susliks (a large central Eurasian ground squirrel) that are indigenous to certain parts of Europe and adjoining Asian countries.
- Can be transmitted to humans from rodents via cows domestic cats, which may serve as intermediate hosts.
- Vaccinia is now mainly a laboratory virus; some strains are widely used to vaccinate humans against smallpox.
- Cowpox and Vaccinia viruses commonly produce only a localized lesion at the site of introduction into the skin that sometimes leads to a low-grade fever, but rarely results in serious complications.
-

Parapoxvirus

- The Parapoxvirus, orf virus, an occupational disease of sheep and goat handlers, also causes localized ulcerative lesions.
- Person-to-person transmission of Orf has not been reported.
- Other parapoxviruses can cause similar localized ulcerative lesions in human handlers of infected animals.

Molluscum contagiosum virus

- Characterized by firm, umbilicated papular skin lesions, and the illness has no observable systemic symptoms.
- The disease is transmitted by direct contact, can be sexually transmitted, but is classically a disease of children.
- The lesions take weeks to months to resolve.
- H&E staining reveals characteristic pathology: Henderson-Paterson inclusion cells.
- Individuals with AIDS tend to have large, disfiguring, unremitting molluscum infections after acquisition of the virus.

Variola

- Variola and monkeypox are primarily transmitted between persons by inhalation of large respiratory and salivary droplets.
- Infectious Variola virus is released from sloughing oropharyngeal lesions during the first week of the rash occurring 12-14 days after the initial infection (range 7-14 days).
- Crusted pustule scabs consist of virus contained within large fragments of thickened, dried material, accounting for the low transmissibility associated with scabs.

Variola Pathogenesis

- Following infection of the respiratory tract or skin, the virus remains localized for about three days.
- Primary viremia during which the virus moves to the regional lymph nodes. The virus replicates and is then found in macrophages of the lymphatics and eventually the blood stream.
- Secondary viremia occurs 10-14 days after infection, during which the virus invades the mucosal membranes of at least the oropharynx, and basal layer of the skin.

Pathogenesis

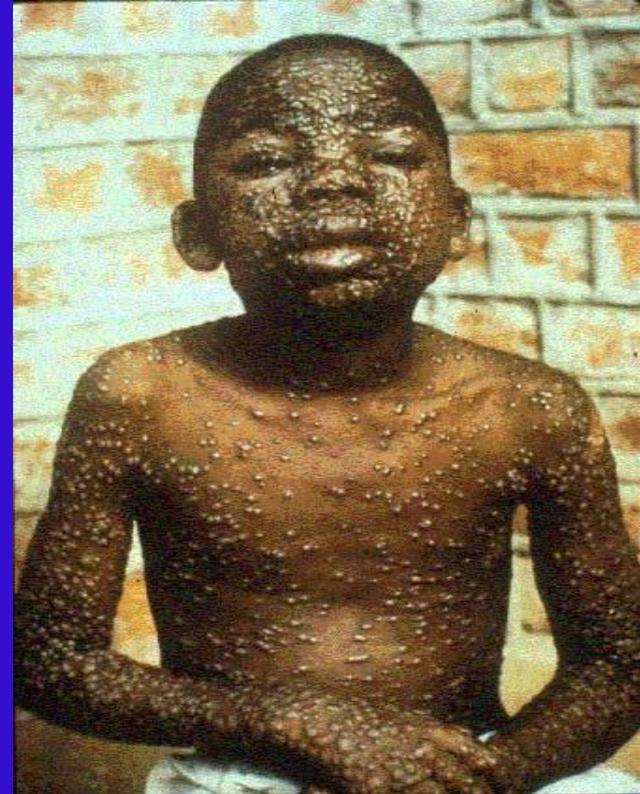
Secondary viremia correlates with the three phases of illness:

1. Prodromal (onset of secondary viremia) Fever, backache and other flu-like symptoms
2. Enanthem (vesicular eruption in the oropharynx)
3. Exanthem (vesicular eruption in skin).

Other features include small hemorrhages in the heart and liver, but generally vital organs are not damaged enough to cause death. Death is associated with a profound “toxemia” and results in respiratory and/or heart failure

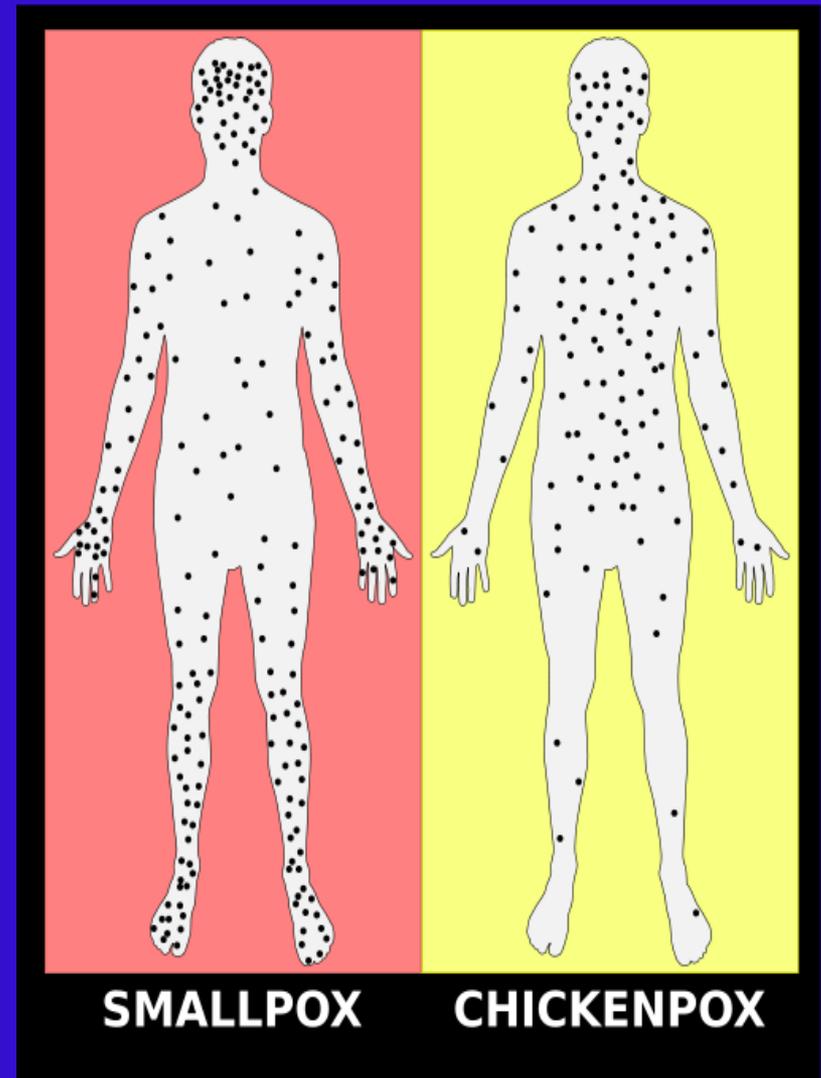
Clinical Presentation

- Smallpox has three classical clinical presentations:
 1. ordinary
 2. flat
 3. hemorrhagic.
- Ordinary smallpox is the most common form, and characteristic skin lesions appear as a discrete centrifugal rash



Clinical Presentation

- After the prodromal symptoms the eruptive phase begins with the appearance of rash lesions, first on the buccal and pharyngeal mucosa, then on the face, forearms, and hands.
- The distribution of the rash is centrifugal; profuse on the face, more abundant on the forearms than the upper arms, and on the lower legs than the thighs



Bioterrorism

- The subtleties of smallpox, monkeypox, and chickenpox differential diagnosis will not be critical to the public health response to an established and documented smallpox epidemic, but will be important for accurate identification of initial suspect cases, and possibly to determine a bioterrorism event.



Bioterrorism

Smallpox is a high-priority (category A) agent for bioterrorism, defined as follows:

- Easily disseminated or transmitted from person to person
- High mortality rate and potential for significant public health effect
- Probable instigator of panic and social disruption
- Special actions required for public health preparedness

Diagnosis

Orthopoxvirus infections are readily diagnosed:

- Electron microscopy
- PCR methods
- Microscopic evaluation of H&E stained biopsy specimens
- Cytoplasmic inclusion bodies: A type and B type. B type inclusion bodies (Guarneri bodies) are the sites of viral replication and are produced by all species of poxvirus.



Variolation

- The earliest procedure used to prevent smallpox was inoculation (also known as variolation).
- Inoculation was possibly practiced in India as early as 1000 BC
- Powdered smallpox scabs applied through the nose or by scratching material into the skin.
- ¹Accounts of inoculation against smallpox in China can be found as early as the late 10th century, and the procedure was widely practiced by the 16th century, during the Ming dynasty

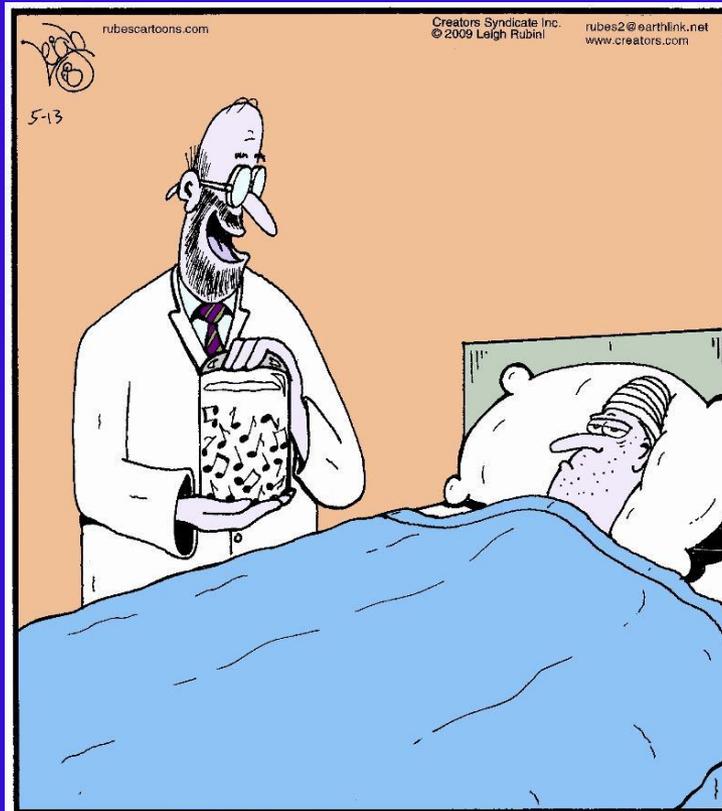


Vaccination

- Edward Jenner demonstrated in 1796 that an individual could be protected against disease
- Presently, smallpox (Vaccinia) vaccine and Vaccinia Human Immunoglobulin (VIG), which is used to treat severe post-vaccination adverse effects, are available in the USA



Questions?



"Good news, Mr. Burgess. We've successfully removed the tune that was stuck in your head."

References

- Center of Disease Control (CDC),
“Introduction: Variola virus”, Laboratory
Response Network(LRN).