Smallpox

- Orthopox Viruses (DNA):
  - Monkeypox, Gerbilpox, Camelpox, others
  - Cowpox
  - Vaccinia
  - Variola
- Diseases:
  - Variola Major: mortality >30%
  - Variola Minor: mortality ≤ 1%

- 1796 Edward Jenner demonstrated that cowpox protected against Smallpox.
- 1949 Last case Smallpox in US
- 1967 WHO begins global campaign to eradicate disease
- 1972 Routine smallpox vaccination ceased US (age 1)
- 1980 World Health Assembly recommend all countries cease smallpox vaccination. WHO recommends all labs destroy samples of virus or send to:
  - Institute of Virus Preparations, Moscow
  - CDC in Atlanta
- 1990: US unveils plans to sequence smallpox DNA, destroy remaining Russian and American stores of disease by 1993
- 1998: Clinton postpones destruction of last smallpox
- 2002: Three phase smallpox vaccination program proposed
  - Phase One: Smallpox response teams
  - Phase Two: HCPs
  - Phase Three: Public

- Disease most prominent in winter and early spring (possibly because virus survives poorly with increased temperature and humidity.)
- Incubation:
  - 12-14 days with range 7-17 days
- Transmission:
  - Person-person by droplets or aerosols, or direct contact with contaminated clothing/bedding, (within 6 feet most common)
  - Infectious with onset rash. Not during prodrome. Until last scab separated.
  - Risk to household contact and those with face to face contact
  - Less contagious than measles, influenza. More contagious than TB. 36-88% unvaccinated household contacts become infected.
- Symptoms:
  - Prodrome: high fever, malaise, prostration, headache, backache (non-specific) lasting 3-4 days
  - Maculopapular rash, starting on oral mucosa and pharynx
  - Over 1-2 days rash becomes papular then vesicular then pustular
    - Rash is everywhere in same stage.
    - Prominent on hands, soles, extremities, face
    - Fever decreases after rash appears (Biphasic fever curve)
  - Crusts over 8-9 days leaving pitted scarring.
  - Death usually in 2nd week from toxemia, circulating immune complexes and soluble Variola antigens
Smallpox

- Presentations:
  - Ordinary
    - Discrete
    - Semi-confluent
    - Confluent
  - Flat – 20% of cases. Severe.
  - Hemorrhagic – 18% of cases. Intense erythema and hemorrhages. Often misdiagnosed as meningococcemia or drug eruption. Very lethal.
  - Modified Smallpox: Milder symptoms. 25% of individuals with history of vaccination. (Unlikely in US now since vaccination stopped over 30 years ago). Lesions evolve more rapidly.
Smallpox

- **Diagnostic tests:**
  - Not a lot of modern data about lab tests
  - Specimens should be collected by someone who has been vaccinated and who wears gloves/mask
  - Send vesicle fluid to Public Health authorities in double sealed container. Laboratory examination requires high-containment facilities
    - EM examination – orthopox virus (brick shaped virions)
    - PCR techniques, DNA probes.
    - Definitive ID: cell culture or culture on chorioallantoic egg membrane and characterization of strain by use of various biologic assays (PCR, restriction fragment length polymorphisms)

- **Treatment:**
  - Supportive.
  - Experimental - cidofovir

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**Differentiating Smallpox - Chickenpox**

<table>
<thead>
<tr>
<th></th>
<th>Smallpox</th>
<th>Chickenpox</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Fever</strong></td>
<td>2 to 4 days before rash</td>
<td>At time of rash</td>
</tr>
<tr>
<td><strong>Rash</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Appearance</td>
<td>Pocks in same stage</td>
<td>Pocks in several stages</td>
</tr>
<tr>
<td>- Development</td>
<td>Slow</td>
<td>Rapid</td>
</tr>
<tr>
<td>- Distribution</td>
<td>More pocks on arms and legs</td>
<td>More pocks on body</td>
</tr>
<tr>
<td>- On palms and soles</td>
<td>Usually present</td>
<td>Usually absent</td>
</tr>
<tr>
<td><strong>Death</strong></td>
<td>Usually 1 in 10 die</td>
<td>Very uncommon</td>
</tr>
</tbody>
</table>
Smallpox Vaccination

- Vaccinia
  - >95% protection against disease
  - Duration of immunity never satisfactorily measured.
    - Antibody levels decrease after 5-10 years
    - Levels may persist 30 years following second/third vaccination
  - Two types – live virus: multiplies in superficial layers of skin.
    - Tissue culture cell vaccine (Baxter)
  - Vaccination effective if given within 4 days post-exposure
  - Must document “Take”

Contraindications to Smallpox Vaccine

- Immunodeficiency (HIV, organ transplant, malignancy, autoimmune diseases, immunosuppressing medications)
- Atopic dermatitis or eczema (or home contact with these conditions)
- Other skin conditions: burns, impetigo, psoriasis etc.
- Pregnancy now or possible within the next month (home contact with pregnant individual).
- History anaphylactic reaction to: polymixin B, streptomycin, tetracycline, neomycin, phenol.
- Moderate or severe acute illness
- Not recommended for persons less than age 18
- If actual exposure to Smallpox disease, the conditions/factors listed above are no longer contraindications
Normal reactions to Vaccinia vaccination

Lymphadenopathy 25-50%
Myalgia, headache, chills, nausea, fatigue 0.3-37%
Fever > 37.7 degrees 2-16%
Adverse Reactions to Smallpox Vaccination (Vaccinia)

- Autoimmune injury
- Accidental Implantation (including cornea)
- Bacterial infection
- Generalized vaccinia
- Post-vaccinial encephalitis

Accidental Implantation

- The vaccination site contains high titers of vaccinia virus
- Any disrupted skin can lead to implantation, but the severity of accidental implantation parallels the degree of skin involvement
- Covering the lesion and screening of vaccinees minimizes the risk.
- HCWs may continue to work and care for immunosuppressed patients.
Accidental Implantation

• Treatment:
  – One or few lesions: none
  – Multiple or confluent lesions over large portions of the body: Vaccinia Immune globulin (VIG) 0.6 mg/kg IM
  – (Vaccinia Immune Globulin is contraindicated for vaccinia keratitis)

Generalized Vaccinia

• The result of systemic spread of virus from vaccination site.
• It is a totally benign complication of primary vaccination
• Rare

Generalized Vaccinia

• Usually no treatment required. If extensive lesions, use antiglobulin.
Progressive Vaccinia

- Implies T cell deficiency:
  - Of 900,000 HIV infected in US – 300,000 don’t know it, Cancer patients, Organ transplant patients
- The most severe complication of vaccination
- Life threatening
- Also called:
  - vaccinia necrosum
  - vaccinia gangrenosa
  - disseminated vaccinia

Eczema Vaccinatum

- Individuals with eczema (atopic dermatitis) are at special risk from implantation of vaccinia into the diseased skin, sometimes with a fatal outcome. Condition results from implantation and subsequent spread.
- Atopic dermatitis implies both a skin abnormality (disrupted skin) and an immunologic difference (underlying T-cell immunologic defect)
- If smallpox is not an immediate risk, vaccination should not be performed in these patients and they should not be in contact with vaccinees.
Eczema vaccinatum

- Requires urgent treatment with VIG
- IM-VIG at 0.6-1.0 ml/kg body weight. If extensive, 5-10 ml/kg IM-VIG may be given, divided into multiple doses and given over several days.
- With early recognition and appropriate use of vaccinia immune globulin (VIG) mortality can be reduced to zero.
- If VIG treatment is delayed viremia ensues with spread of infection.
**Congenital Vaccinia**

- Rare
- Usually due to third trimester vaccination.

**Smallpox Vaccine Adverse Effects – first dose**

- Postvaccinial encephalitis: 1 / 115,000 – 415,000
- Progressive vaccinia: 1 / 590,000 – 1,000,000
- Eczema vaccinatum: 1 / 94,000 – 220,000
- Generalized vaccinia: 1 / 4,500 – 57,000
- Inadvertent inoculation: 1 / 1,900 – 37,000

**Response to Smallpox Exposure**

- Isolate
- Vaccinate all household contacts and those with face-to-face exposure (no contraindications – Smallpox worse than any Vaccinia complication)
- Vaccinate within 3 days – may prevent disease. Within 4 days may significantly ameliorate subsequent illness.
- Contacts take temperature daily – Isolate if temp > 38 during 17 days post exposure
- Hospital: Negative pressure isolation, Autoclave/incinerate laundry
- Preferred: Manage out of hospital

**Hospital transmission**

- 1950-1971: 49 imported outbreaks in Europe
  - 50% cases in medical setting
  - Most transmission – contact within 6 feet.
- Decontamination:
  - If released as an aerosol, May persist for as long as 24 hours under favorable conditions.
  - Vaccinia in scabs is more durable – may survive for a few weeks (3-12) but is less transmissible.

**Bioterrorism**

- French-Indian Wars 1754-1767: British soldiers distributed blankets that had been used by smallpox patients to Indians. Epidemics ensued killing >50% of many affected tribes.
- Why:
  - High case fatality rate
  - Person – person spread
  - Lack of population immunity
  - Lack of treatment
- Europe 1960s-1970s: Imported Smallpox in Dec-April months resulted in high transmission, 10-20 second generation cases from single patient with widespread concern/panic.
- 1980: Soviet Union began program to mass produce smallpox as bioweapon (aerosol release) and adapt for use in bombs, missiles (Ken Alibek former deputy director of Soviet civilian bioweapons program)
<table>
<thead>
<tr>
<th>Control Strategy and Cause of Death</th>
<th>Low Impact</th>
<th>High Impact</th>
<th>Low Impact</th>
<th>High Impact</th>
</tr>
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<tbody>
<tr>
<td>1. Contact isolation and vaccination alone</td>
<td>0</td>
<td>3</td>
<td>288</td>
<td>295</td>
</tr>
<tr>
<td>2. Isolation only</td>
<td>0</td>
<td>3</td>
<td>288</td>
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<td>3. Post-outbreak vaccination of healthcare workers</td>
<td>0</td>
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<td>295</td>
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<td>295</td>
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<tr>
<td>5. Prior vaccination of healthcare workers</td>
<td>25</td>
<td>28</td>
<td>271</td>
<td>278</td>
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<td>6. Prior vaccination of healthcare workers and post-outbreak vaccination of public</td>
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* Contact isolation and vaccination are part of all control strategies.

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