BW THREAT REDUCTION
MEDICAL PROPHYLAXIS
IN THE CZECH REPUBLIC

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**Report Documentation Page**

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AIM OF THE PRESENTATION

• Medical response to BW threat
• Preexposure and postexposure medical prophylaxis
• Czech vaccination policy
Medical Response to BW Threat
BW threat

Who are 1st Responders?

- Primary Care Personnel
- Hospital Staff
- EMS Personnel
- Public Health Professionals
- Other Emergency Preparedness Personnel
- Laboratory Personnel
- Law Enforcement
MEDICAL RESPONSE

• Pre-exposure period
  - surveillance system (to monitor unusual illnesses or outbreaks of disease)
  - detection, identification of threat / use
  - chemoprophylaxis
  - immunization
  - education

Difference must be made between
- detection of biological agents in the environment (detection, monitoring)
- medical diagnostics (detection of B-agents, components of agents, or antibodies to B-agents in tissue samples – blood, body fluids)
MEDICAL RESPONSE

• Post – exposure period
  – incubation period
    • active and passive immunization
    • antimicrobial or supportive therapy
    • isolation precaution
      – observation, quarantine, ROM
  – disease onset period
    • diagnosis
    • treatment
    • direct patient care
Pre-exposure and Post-exposure Medical Prophylaxis

The main goal:
Minimize potential impact of BW
PRE-EXPOSURE MEDICAL PROPHYLAXIS

• **Immunoprophylaxis**
  – vaccines against a number of potential BW agents are available
  – many of these vaccines were developed for the protection of laboratory workers or individuals in endemic areas
  – vaccines which are effective under natural circumstances, may not provide a similar degree of protection to people exposed to BA attack
  – vaccines do not immediate protection

• **Chemoprophylaxis**
  – using appropriate drugs offers additional protection
  – must be available for all personnel in BW area
POST-EXPOSURE MEDICAL PROPHYLAXIS

- Chemoprophylaxis
  - anthrax (for 60 days)
    - Ciprofloxacin 500 mg PO 2x a day
    - Doxycycline 100 mg PO 2x a day
    - Amoxycilin 500 mg PO 2x a day
  - plaque (7 days)
    - Doxycycline 100 mg PO 2x a day
    - Ciprofloxacin 500 mg PO 2x a day
  - Tularemia (14 days) – Gentamicin, Ciprofloxacin
  - Cholera (7 days)
  - Brucellosis (3 weeks) – ?? Rifampicin, Doxycycline
  - VHF: Ebola, Lassa
    - antivirals Ribavirin
**POST-EXPOSURE MEDICAL PROPHYLAXIS**

- **Active and passive immunization**
  - Vaccines exist against
    - Anthrax
    - Smallpox
    - Plaque – a killed whole-cell vaccine (pneumonic form?)
    - Tularemia – as investigational new drug in US
    - Cholera – DUKORAL, oral live attenuated vaccine, 1 dose
    - Q Fever – Q-VAX, formalin killed *C. burnetii*, 1 dose, 5 Y protection
    - VEE – live attenuated vaccine (experimental TC – 83)
    - WEE, EEE – inactivated vaccines
    - Botulism – pentavalent toxoid of *C. botulinum* types A,B,C,D,E
  - Vaccines don`t exist against
    - Brucellosis, VHF (except Yellow fever), AHF – under development, Ricin, Saxitoxin
SMALLPOX VACCINATION

• Different vaccinia strains have been used for production of vaccine
  – New York City Board of Health (NYCBOH) for US vaccine
    • Dryvax; Aventis Pasteur vaccine
    • newly developed ACAM 1000 (human embryonic lung cell culture) and ACAM 2000 (African green monkey cells – vero cells)
  – live lyophilised Czech vaccine – VARIE + solution VARISOL
    • vaccinia strain used to infect heifer`s skin
    • old vaccine from the 1980`s
VACCINATION

- Intradermal innoculation with bifurcated needle (scarification)
- Vaccinia virus replicates in the dermis of the skin
  - “Major reaction”-
    - Pustular lesion or area of induration surrounding a central lesion (scab or ulcer) 6-8 days after primary vaccination
    - can be misdiagnosed as bacterial superinfection
  - Low grade fever, axillary lymphadenopathy
  - Scar constitutes permanent record of successful vaccination
FIGURE 4. Example of a major reaction (i.e., a take) in a first-time smallpox vaccinee at 6 (left), 10 (middle), and 15 (right) days postvaccination.

Source: Reproduced with permission of Stephen P. Heyse, M.D., National Institutes of Health.
Note: Vaccination reactions in vaccinia-naïve and previously vaccinated volunteers in a clinical study of diluted Dryvax® smallpox vaccine; volunteers were enrolled at the NIAID-supported Vaccine Treatment and Evaluation Unit at Saint Louis University in 2002.
VACCINIA CONTACT PRECAUTIONS

- Vaccinia present at lesion from papule (2-5 d) until scabbed (10-19 d p vaccination)
  - lesion covered by dry semipermeable dressing
    - transparent dressings predispose to local secondary inoculation
    - strict handwashing after dressing change
- Vaccinia can be transmitted from a vaccinee`s unhealed vaccination site
  - by close contact
  - can lead to the same adverse events as in the vaccinee
- Excluded from care of vaccinia lesions if pregnant, immunocompromised, or with chronic exfoliative dermatoses
• The frequencies were identified in studies of the 1960s.
• Unknown prevalence of risk factors among today`s population
• Precise predictions of adverse reaction rates are unavailable
• Range from mild and self-limited to severe and life-threatening
VACCINIA-COMPLICATIONS

- **Normal host**
  - Inadvertent inoculation (skin, eye)
  - Generalized vaccinia
  - E. multiforme, urticarial eruptions
  - Postvaccinal encephalopathy, encephalomyelitis

- **Pregnancy**
  - Fetal vaccinia

- **Eczema/exfoliative dermatoses/burns**
  - Eczema vaccinatum

- **Immunocompromised**
  - Vaccinia necrosum
### Complication Rates: Vaccinia (Cases per million vaccines) *

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<tr>
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<td>Generalized vacc</td>
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<tr>
<td>E. vaccinatum</td>
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<tr>
<td>V. necrosum</td>
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<tr>
<td>Encephalitis</td>
<td>2</td>
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<tr>
<td>Other**</td>
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* Adapted from Lane et al., *J Infect Dis* 1970;122:303-309

** Incl. bacterial superinfections and lesions uncomfortable enough to result in physician contact. Unusual complications incl. fetal vaccinia, melanoma at vaccine scar, and monoarticular arthritis.
FIGURE 20. Generalized vaccinia with a substantial erythematous base in an infant; note the vaccination site at the left axilla and the apparently well child.

Source: Reproduced with permission of J. Michael Lane, M.D.
FIGURE 24. (Top left) A woman aged 22 years with eczema vaccinia acquired from a close contact. She became critically ill, with nearly total involvement of her body, and required thiosemicarbazones, as well as substantial doses of vaccinia immune globulin; (right) side view; (bottom left) residual scarring after resolution of systemic illness.

Source: Reproduced with permission of J. Michael Lane, M.D.
FIGURE 33. Fetal vaccinia in a premature infant, 28 week's gestation. Mother received vaccination at 23 week's gestation. The infant died at age 8 days, and vaccinia was isolated from the placenta

Source: Reproduced with permission of J. Michael Lane, M.D.
VACCINE CONTRAINDICATIONS

- Immunosupression
  - autoimmune condition, cancer, radiation treatment, immunosuppressive medications
- HIV infection
- History or evidence of eczema
  - possibly other exfoliative or extensive skin lesions-psoriasis, burns
- Pregnancy
- Household/close contacts with above
  - There were no contraindications to vaccinating contacts during era of endemic smallpox
Vaccinia Immune Globulin (VIG)

- Sterile solution of the Ig fraction of plasma with antibodies to vaccinia virus from vaccinated persons
- Must be available to give vaccinia safely, efficacy in the treatment of adverse reactions
- Dose: 0.6 ml/kg IM (can be given at multiple sites/divided doses over 24 -36 hrs)
- VIG administration is not without risk
- VIG is not recommended for prophylaxis of persons with Smallpox vacc. contraindications
- In Development:
  - IV product
  - Humanized monoclonal antibodies vs epitopes conserved between variola and vaccinia
SMALLPOX: MANAGEMENT OF CONTACTS

- Immediate vaccination (or boosting) of all potential contacts incl. HCWs
  - Clinical “take” within three years confers immunity
  - Most effective if given < 24 hrs post exposure
  - Given within 1 week of exposure can prevent or attenuate disease

- Pregnancy, dermatoses
  - Vaccine + VIG Vaccinia immune globulin (VIG) 0.6 ml/kg IM
    - VIG given using multiple doses/sites/24-36 hrs

- Immunocompromised
  - VIG
• Chemoprophylaxis no longer available

• Methisazone (Marboran, Burroughs Wellcome)
  – Decreased morbidity and mortality when given to susceptible contacts
  – Limiting side effects: GI intolerance
  – No longer manufactured-not available

• Cidofovir
  – Active in vitro vs variola
  – Active in vivo: postexposure prophylaxis, monkeypox model (rhesus macaques)
Czech Vaccination Policy
CZECH VACCINATION POLICY

• Civilian and military stockpile of Smallpox vaccines
• Only military stockpile of Anthrax vaccines
• Smallpox vaccination - when and who?
  – only in case of infection apparation as postexposure vaccination
  – for civilian and military people
• Anthrax vaccination – when and who?
  – before unit deployment in risk areas (abroad mission)
  – only military personal
ANTHRAX VACCINATION IN THE CZECH ARMY

- Anthrax Vaccine
  - produced by MRA/CAMR, Porton Down, Salisbury, UK
  - anthrax antigen + potassium – aluminium sulphate, thiomersal, sodium chlorid, aqua
- Volume: 0.5 ml
- Administration: i.m.
- Booster: 0.5 ml every year
CZECH VACCINE SCHEDULE

- Four shots over 7.5 months, plus annual boosters
US Vaccine Schedule

- Six shots over 18 months, plus annual boosters
- Do not compress the schedule
- Adjust schedule for individual delays
ADVERSE REACTIONS

• Approx. 353 vaccinees; 4 refused vaccination
• No clinical trial, only approximated data
  – local reactions – the most common reactions – pain, redness
  – systematic reactions – headache, myalgia, arthralgia, fatigue, fever up to 38°C
• 25 vaccinees found medical advice
  – 8 vaccinees had operating incapacity
• Persisting for 3-4 days
• Anaphylaxis reaction was not reported
SUMMARY

- **Medical prophylaxis** can minimize impact of BW threats.
- **Vaccination** is the only practical means of providing continuous protection against BW threats prior to, as well as during, hostile actions.
- Initiation of **chemoprophylaxis** during the incubation period is always helpful however the earlier the ATB is given the greater is the change of preventing disease.
- The **combined use** of medical countermeasures, physical protection, warning, detection and hazard management provides the basis of defence.
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