

Smallpox Physician and Clinician Seminar

January 6, 2003



North Dakota Department of Health

Smallpox Overview

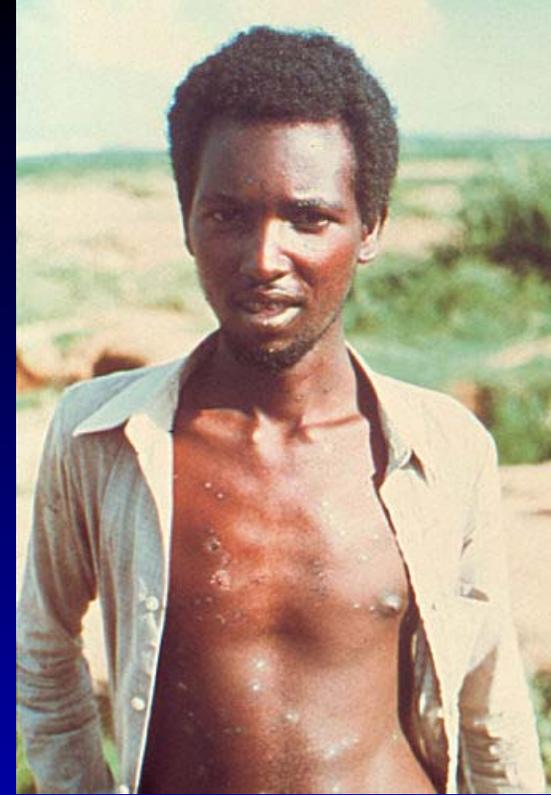
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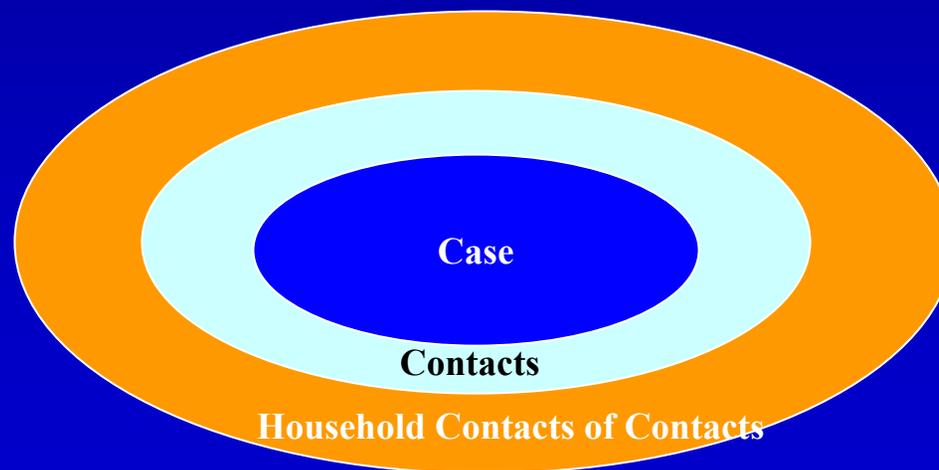
History

- 1977 – Last naturally acquired case in Somalia
- 1978 – Laboratory-related death at the University of Birmingham, England
- 1980 – Global eradication certified by the World Health Organization
- Method of eradication – Ring vaccination, not mass vaccination



Ring Vaccination Concept

- Isolation of confirmed and suspected cases
- Identification, vaccination and surveillance of significant contacts of proven cases
- Vaccination of household contacts of contacts



Smallpox – Basic Facts

- Cause – Variola Virus
- Can infect only humans
- Transmission – Close face to face (generally within 6 feet) via respiratory droplets of a person who has the disease

Smallpox - Disease

- Onset is 12 to 14 days after exposure
- Days 2 to 3 – High fever, bed-ridden, headache and backache
- Days 4 to 5 – Onset of the rash (small bump – blister – pustule – scab)
- Most infectious during the first week of the rash. No longer infectious once the scabs fall off (3 to 4 weeks)
- Death rate is about 30 percent

Smallpox



Smallpox Vaccination

- Live virus vaccine – Vaccinia (this is not the smallpox virus)
- Highly effective in preventing illness or severe disease if given within 3 to 4 days of definite exposure to smallpox

Smallpox Vaccination

- Routine vaccination discontinued in the US in 1972
- Generally discontinued in the world in 1982
- US military discontinued vaccination in 1990

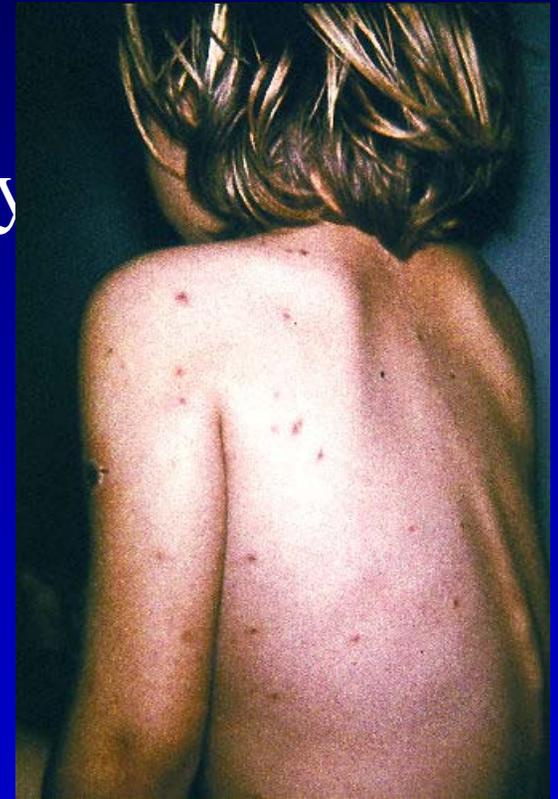
Smallpox Vaccination

- Skin reactions are an indicator that the vaccine was effective
 - 3 to 4 days – Redness and itching
 - 7 to 11 days – Vesicle (blister) develops into a pustule, redness increases
 - 14 to 21 days – Pustule dries, scab forms
 - 21 days – Scabs falls off, leaving a permanent scar
- Commonly see fever and tender, enlarged lymph nodes



Vaccination – Adverse Reactions

- Death – 1 / million
- Accidental infection of other body part (i.e. eye) – 1 / 2000
- Generalized vaccinia – 1 / 5000
- Eczema vaccinatum – 1 / 26,000



Vaccination – Adverse Reactions

- Post vaccination encephalitis –
1 / 300,000
- Progressive vaccinia – 0.83 / million

Pre-Event Vaccination Plan

- Enough vaccine in the US to vaccinate every person in the US
- Pre-event vaccination program will require strict screening for contraindications

Vaccine Contraindications

- Pregnancy or planning pregnancy within 4 weeks
- Compromised immune system
- Eczema, atopic dermatitis, history of eczema or atopic dermatitis or other active chronic skin conditions
- Allergy to vaccine components (ie polymixin B, streptomycin, tetracycline, neomycin)
- Household contacts with chronic skin conditions, pregnancy, or immune compromise

Vaccine Contraindications

- After a known exposure there are no contraindications for vaccination

Smallpox Vaccination of HealthCare Workers

Smallpox vaccination of HCW

Impact on patients: transmission of vaccinia

Risk of vaccinia transmission from primary vaccinees to contacts (Neff et al, JAMA, 2002):

- Eczema vaccinatum among contacts: 17–20 per million vaccinees
- Accidental infection among contacts: 45 per million vaccinees
- Other manifestations of vaccinia among contacts (vaccinia necrosum, generalized vaccinia, encephalitis): none reported

Smallpox vaccination of HCW

Impact on patients: transmission of vaccinia

Risk of transmission: re-vaccinees vs. primary vaccinees (Lane et al, JID 1970, Neff et al, JAMA, 2002)

- Any manifestations of vaccinia among contacts
 - None reported for contacts of re-vaccinees
 - 65 per million for contacts of primary vaccinees
- Auto-inoculation (marker of risk of transmission to contacts??)
 - 42 per million re-vaccinees
 - 529 per million primary vaccinees
- Viral shedding (Cooney et al, Lancet, 1991)
 - Viral titer at vaccination site ~5X greater for primary vaccinees
 - Duration of viral shedding ~3X greater for primary vaccinees

Smallpox vaccination of HCW

Impact on patients: transmission of vaccinia

Risk of vaccinia transmission within healthcare settings (Neff et al, JAMA, 2002 and Fries et al, J Ped, 1947)

- “Denominator-based data”
 - N.Y.C., 1947 (3.3 million primary vaccinations): 28 cases of vaccinia among close contacts; only 3 of 28 acquired from a nurse in a healthcare setting
 - U.S., nat'l & state data, 1968 (5.6 million primary vaccinations): 127 cases of vaccinia among close contacts; only 1 of 127 acquired from a nurse in a healthcare setting
 - Completeness of case-finding unknown
 - No data available regarding degree of exposure, i.e., the numbers of recently vaccinated HCWs

Vaccinia Transmission

(Courtesy Kent Sepkowitz, submitted for publication)

- 12 previous reports (85 cases) of nosocomial transmission
 - Source case usually with eczema vaccinatum
 - Underlying skin disorder in secondary cases
 - 16% mortality
 - Spread to nearby wards: ? HCW vs airborne
 - Brief (hours) of exposure appear adequate

Smallpox vaccination of HCW

Impact on patients: transmission of vaccinia

Risk of vaccinia transmission within healthcare settings:

- **Mode of spread not always clear**
 - **Glasgow, 1935: attack rate 100% (n=11) on ward and ~36% (n=10 or 12) on adjacent ward with shared HCWs**
 - **Marseilles, 1952: 4 cases among cribbed infants**
 - **California, 1975: case and source in different areas but passed through same hall**
 - **Source in all three episodes eczematous and presumably covered with high concentrations of vaccinia virus**

Smallpox vaccination of HCW

Impact on patients: transmission of vaccinia

Can we extrapolate low historic risks of vaccinia transmission in health care settings to current circumstances?

Historically –

- **HCW mostly re-vaccinees (who rarely transmit)**
- **Most patients vaccinated thus partially protected**
- **Many fewer pts. with risk factors (dermatologic, immunologic)**
- **Much less placement & manipulation of invasive lines, catheters, & tubes on wards**
- **HCW interacted with fewer, often less-sick pts for longer periods**
- **Only ~30 large hospitals vaccinated HCW, often via campaigns**
 - **HCW often reassigned or vaccinated before holiday**
- **Less attention to infection control**

Smallpox vaccination of HCW

Impact on patients: transmission of vaccinia

Lab data relating to risk of vaccinia transmission

- 1. Vaccinia may persist in environment 3-4 days (Johnson et al, Western J Med 1975)**
- 2. Nasopharyngeal (NP) carriage of vaccinia (Gurvich et al, J Hyg Epidemiol Microbiol Immunol, 1974):**
 - 80 vaccinated children studied (9 - 84 months of age)**
 - European strain vaccine (less attenuated?)**
 - 16/146 (11%) NP specimens positive, most at low titer**
 - Specimens isolated from 4 of 43 healthy children but 3 of 3 children with adverse vaccinia reactions**

Smallpox vaccination of HCW

Impact on patients: transmission of vaccinia

Lab data relating to risk of vaccinia transmission

3. Virologic and immunologic studies of smallpox vaccinees (Koplan et al, Am J Trop Med Hyg, 1975)

- 62 vaccinees enrolled, almost all re-vaccinees
- Virus at vaccination site by day 2 in 54/60 (90%)
- Duration of viral isolation 0-18 days (mean = 7.8 days)
- Sharp decrease in viral shedding as scab separated (at 7-10 days), but viral isolation “after scabs fell off” in 5/42 (12%)
- Variable viral isolation from separated scab, it’s surface, &/or underlying skin among subgroup of 4 vaccinees
- No viral isolation from throat & urine at days 2, 4, 7, 10 among a subgroup of 8 vaccinees

Smallpox vaccination of HCW

Impact on patients: transmission of vaccinia

Lab data relating to risk of vaccinia transmission

4. Phase 1 trial of recombinant vaccinia vaccine expressing HIV envelope glycoprotein (Cooney et al, Lancet 1991):
 - Control group of 15 re-vaccinees and 2 primary vaccinees received vaccinia vaccine at 1 of 3 doses
 - 11/15 re-vaccinees and 2/2 primary vaccinees shed virus
 - ✓ Re-vaccinees: mean of 5.5 days
 - ✓ Primary vaccinees: mean of 16.7 days
 - ✓ Low-titer virus isolated from outer surface of semipermeable dressing [OpSite]
 - ✓ No virus with 2 layers OpSite + gauze under dressing

Smallpox vaccination of HCW

Impact on patients: transmission of vaccinia

Lab data relating to risk of vaccinia transmission

5. Phase 1 trial of recombinant vaccinia vaccine expressing HIV envelope glycoprotein (HIVAC-1e) (Graham et al, JID 1992):
 - Controls: 12 naïve subjects received vaccinia at 1 of 2 doses
 - Last day of shedding: median 19 days (range: 9-21 days)
 - Vaccinia isolated from dressing surface (control & HIVAC-1e)
 - ✓ 1 layer OpSite, no underlying gauze: 12/66 (18%) cultures
 - ✓ 2 layers OpSite, underlying gauze: 3/103 (3%) cultures
 - Note: affect of dressings on irritation or pruritis (thus touching or itching of site), on resolution of lesion, and on duration of viral shedding not reported

Smallpox vaccination of HCW

Impact on HCW: local reactions and vaccine take

Impact of dressings on local reactions:

- Occlusive dressings lead to maceration and delay resolution
 - Routinely observed by smallpox experts
 - Noted in study settings
 - Recombinant vaccinia studies using semipermeable OpSite
 - Reaction mitigated by underlying OpSite with gauze
 - Not consistently seen
 - Plastic film sprayed on site well tolerated (Rylander, 1968)

Smallpox vaccination of HCW: Impact on HCW: local reactions and vaccine take

Impact of dressings on local reactions: USAMRIID tissue culture-based SP vaccine trial (Coster, unpublished)

- 58 healthy adult vaccinees, band-aid dressings used
- 24/58 developed debilitating local reactions (erythema, pruritis)
- 11/24: no relief with changes in dressings or adhesive (rotating dressings, gauze, changes in tape, Kerlix)
- Attempted protocol deviation: “dressing holiday,” leaving site uncovered, with immediate and impressive resolution

Smallpox vaccination of HCW: Impact on HCW: local reactions and vaccine take

Impact of site preparation on local reactions:

- Issue has not been studied in controlled trials
- Historically, bacterial infections of vaccine site not described
- Current recs don't specify antisepsis for SP (or other vaccines)
- Skin antisepsis not required for diabetics prior to insulin shots
- Acetone defattens and irritate skin without necessarily reducing bacterial counts or risk of line infections (Maki, 1987)
- Theoretical concerns with skin preparation:
 - Skin irritation due to antisepsis might predispose to local vaccine adverse reactions
 - Alcohol & other agents could inactivate vaccinia, reduce take

Smallpox vaccination of HCW

Impact on HCW: local reactions and vaccine take

Impact of site preparation on local reactions:

- In the multicenter NIH study of SP vaccine, 1 site used no prep, 2 sites used acetone, and 1 site used 10% acetone/70% alcohol
 - Latter site had 15 no takes whereas other 3 sites had none
 - However, other minor discrepancies distinguished the 4 sites
- In an ongoing NIH study of SP vaccine, small numbers of subjects responded fully to vaccine after skin preparation with either acetone or 10% acetone/70% alcohol

Smallpox vaccination of HCW

Impact of skin site on vaccinia spread & local reactions:

- Volar forearm, ankle, and other skin sites used for vaccination
- No data on efficacy, reactogenicity or transmission by skin site
- Considerations in selecting skin site would include accessibility, ability to scratch, ease of dressing changes, occlusion of site, and ability to read a take

Smallpox vaccination of HCW

Historic and current vaccination practices

Historic practices in the U.S. for vaccination of HCW:

- Prior to mid-1960's: HCW should be vaccinated every 3-4 years
- Mid/late 1960's: ~30 hospitals conducted vaccination of HCW, often prior to holidays or reassigning HCW to lower-risk units
- Most HCW kept their vaccination sites uncovered though most probably did wear garments over the site
 - Some sewed a gauze into their garments to protect the site
- Vaccine site typically not prepped or prepped with water; some used acetone - alcohol was avoided as it caused frequent no takes
- In 1940s, a hemisphere-shaped device with holes was taped to site to provide protection, prevent scratching, allow air exchange

Smallpox vaccination of HCW

Historic and current vaccination practices

Current ACIP recommendations for vaccinees: HCW

- Avoid contact with patients with risk factors until scab falls
- If such contact unavoidable, keep site well covered & use meticulous hand hygiene
 - “In this setting, a more occlusive dressing might be required”
 - Accumulation of exudates can be decreased by first covering site with dry gauze then applying the dressing over the gauze
 - Dressing should be changed at least once a day

Smallpox vaccination of HCW

Historic and current vaccination practices

- Non – HCW – loose covering
- CDC – responders – loose covering
- DoD – uncovered or loose covering
- Israel – gauze covering or shirt sleeve
- NIH trial – Drivax – folded gauze + 2 semipermeable membranes

Smallpox vaccination of HCW: working group

Dressings

- While participating in direct patient care
 - Recommendations unchanged but more directive
 - Semi-permeable dressing over absorbent material (gauze)
 - Products combining absorbent base with overlying semi-permeable layer can be used
 - Emphasis on meticulous hand hygiene after contact with site
 - Hospitals to include site-care component to SP vaccine programs
 - Designated staff to evaluate vaccinees and vaccination site, change dressing, and reinforce excellent hand hygiene
- While not involved in patient care and not among high risk persons
 - Recommendations unchanged
 - Site uncovered or covered with porous bandage (e.g., gauze)
 - Change any dressings frequently to prevent maceration

Smallpox vaccination of HCW: working group

Site preparation

- Recommendations unchanged
 - Skin preparation for vaccination generally unnecessary
 - If site visibly contaminated clean with soap and water

Site selection

- No strong basis to consider use a new site

Summary Important Points

- Smallpox vaccination site sheds live vaccinia virus that can be dangerous to some individuals
- With proper care of the vaccination site, the risk of transmission to patients from a healthcare worker is very low, particularly in the previously immunized

Summary Important Points

- Historically most nosocomial transmission occurred from HCW's with eczema vaccinatum
- Primary vaccinees shed 5X more virus than those previously vaccinated
- Viral shedding generally occurs until the scab falls off (ie 21 days)
- Virus can live on environmental surfaces for a few days and is found in the scab
- Virus is inactivated by antiseptic cleaners (ie alcohol)

Summary Important Points

- At risk – chemotherapy, leukemia, lymphoma, organ transplants, HIV infected, infants, skin diseases (ie burns, dermatitis)
- Dry gauze + semi-permeable membrane decreases viral dispersion by at least 97%

Patient Care Points

- Avoid caring for patients at increased risk until the scab separates – Not practical
- Can provide patient care without risk by practicing good vaccine site care
- With high risk patients – use additional semi-permeable membrane, prefer the previously immunized
- Use good hand hygiene – soap and water
- Avoid touching the vaccine site

Patient Care Points

- Reasons to exclude HCW from patient duties
 - Systemic symptoms – fever etc.
 - Vaccine complication – eczema vaccinatum
 - Difficulty covering the entire lesion
 - Inadequate attention to hygiene

Vaccine Site Care

- Cover with gauze + semi-permeable membrane – should cover all lesions
- Change dressing every 3 days with no excessive discharge
- Change dressing whenever significant discharge is noted on the gauze
- Clothing should cover the dressing site (ie long sleeve shirts etc)

Vaccine Site Care

- Before each shift – vaccination site should be examined by a designated person trained in vaccine site care
- Day 7 evaluate for adequate take
- Severe itching / maceration – consider recommending dressing holiday when off duty
- Can bathe / shower – cover with semi-permeable or waterproof membrane. Do not submerge the site

Vaccine Site Care

- Home care –
 - Good hand hygiene
 - Avoid touching the site
 - Can participate in usual activities (except contact sports)
 - Site covered – dry gauze and clothing
 - Dressing changes by the vaccinee
 - Scab placed in sealed bag and placed in garbage
 - Launder clothing separately

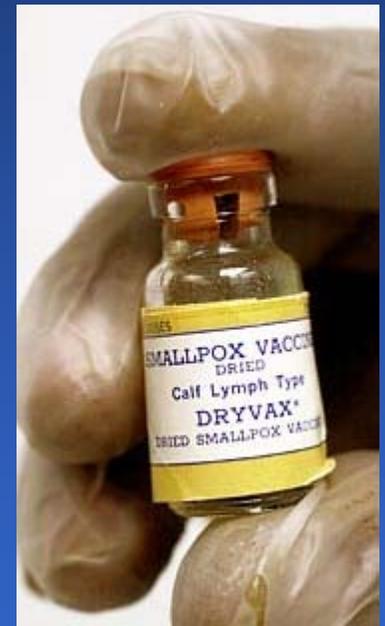
Smallpox

The Defense of North Dakota

James Hargreaves, D.O.

Infectious Diseases

Altru Health System



The Vaccine

- Recommendation
- Contraindication/Precautions
- Local Reaction
- Serious Reaction
- Grand Forks Process



Prevention



- Smallpox Vaccine
- Government Plan
 - Phase 1 500,000 Healthcare Workers and the Military
 - Phase 2 10 million Healthcare Workers, Public Safety, and Emergency Responders, etc.
 - Phase 3 280 million (General Population)

Dryvax Vaccinia Vaccine

- Available in US since 1970's
- Lyophilized
- Still potent - 15.4 million doses
- Diluted 1:5 without loss of potency - so now 77 million doses



Clinical Response to Undiluted and Diluted Smallpox Vaccine

NEJM 2002; 346 : 1265 - 74

- $n = 680$
 - Adults
 - Immune naïve
 - 1/3 undiluted; 1/3 1:5; & 1/3 1:10

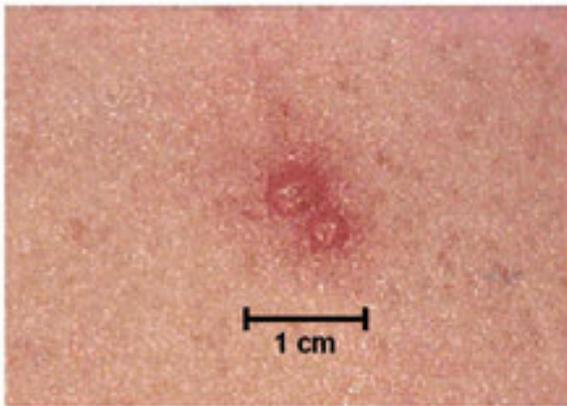
Clinical Response to Undiluted and Diluted Smallpox Vaccine

Days after Vaccination

	7-9	10-12	13-14
Pustule Size (mm)	9.6	11.9	12.4
Erythema	17.6	51.4	17.0
Induration (mm)	12.0	48.1	11.8
Local Satellite Lesions	16/659 (2.4%)	5/76 (6.6)	38/656 (5.8%)

Primary Site Reaction Smallpox Vaccine

Primary Vaccination Site Reaction



Day 4



Day 7



Day 14



Day 21

Clinical Response to Undiluted and Diluted Smallpox Vaccine

Regional Lymphadenopathy

None	455/655 (69.5%)	37 / 80 (46.2%)	530/653 (81.2)
Mild	173/655 (26.4)	39 / 80 (48.8)	119 / 653 (18.2)
Moderate	27 / 655 (4.1%)	4 / 80 (5.0%)	4 / 653 (0.6%)
Severe	0 / 655	0 / 80	0 / 653

Signs and Symptoms After Vaccinia Vaccine n=665

Variable	Days 0 – 6	Days 7-9	Days 10-12	Days 13-14	Days 15 +
Oral Temperature					
>37.7°C	15 (2.3)	59 (8.9)	35 (5.3)	4 (0.6)	2 (1.0)
>38.3°C	6 (0.9)	20 (3.0)	19 (2.9)	2 (0.3)	0
>38.8°C	2 (0.3)	5 (0.8)	2 (0.3)	0	0
Headache					
None	371 (55.8)	395 (59.4)	412 (62.0)	559 (84.1)	173 (84.4)
Mild	194 (29.2)	178 (26.8)	161 (24.2)	76 (11.4)	21 (10.2)
Moderate	86 (12.9)	78 (11.7)	75 (11.3)	25 (3.8)	8 (3.9)
Severe	14 (2.1)	14 (2.1)	17 (2.6)	5 (0.8)	0

Signs and Symptoms After Vaccinia Vaccine n=665

Variable	Days 0-6	Days 7-9	Days 10-12	Days 13-14	Days 15 +
Muscle aches	400 (60.2)	330 (49.6)	381 (57.3)	603 (90.7)	191 (93.2)
None	204 (30.7)	198 (29.8)	176 (26.5)	52 (7.8)	10 (4.9)
Mild	55 (8.3)	120 (18.0)	94 (14.1)	7 (1.1)	1 (0.5)
Moderate	6 (0.9)	17 (2.6)	14 (2.1)	3 (0.5)	0
Severe					
Chills					
None	575 (86.5)	547 (82.3)	562 (84.5)	653 (98.2)	199 (97.1)
Mild	68 (10.2)	75 (11.3)	59 (8.9)	8 (1.2)	2 (1.0)
Moderate	16 (2.4)	31 (4.7)	34 (5.1)	2 (0.3)	0
Severe	6 (0.9)	12 (1.8)	10 (1.5)	2 (0.3)	0

Signs and Symptoms After Vaccinia Vaccine n=665

Variable	Days 0-6	Days 7-9	Days 10-12	Days 13-14	Days 15+
Nausea					
None	560 (84.2)	572 (86.0)	586 (88.1)	640 (96.2)	195 (95.1)
Mild	77 (11.6)	67 (10.1)	52 (7.8)	17 (2.6)	4 (2.0)
Moderate	20 (3.0)	19 (2.9)	21 (3.2)	6 (0.9)	2 (1.0)
Severe	8 (1.2)	7 (1.1)	6 (0.9)	2 (0.3)	1 (0.5)
Fatigue					
None	314 (47.2)	348 (52.3)	380 (57.1)	549 (82.6)	166 (88.8)
Mild	246 (37.0)	186 (28.0)	184 (27.7)	88 (13.2)	32 (15.6)
Moderate	89 (13.4)	114 (17.1)	84 (12.6)	21 (3.2)	6 (2.9)
Severe	16 (2.4)	17 (2.6)	17 (2.6)	7 (1.1)	0

Signs and Symptoms After Vaccinia Vaccine n=665

Variable	Days 0-6	Days 7-9	Days 10-12	Days 13-14	Days 15+
Rash at sites other than vaccination site					
None	643 (96.7)	628 (94.4)	598 (89.9)	631 (94.9)	182 (88.8)
Mild	17 (2.6)	31 (4.7)	51 (7.7)	31 (4.7)	16 (7.8)
Moderate	5 (0.8)	5 (0.8)	12 (1.8)	3 (0.5)	1 (0.5)
Severe	0	1 (0.2)	4 (0.6)	0	2 (1.0)
Pain at vaccination site					
None	301 (45.3)	156 (23.5)	155 (23.3)	488 (73.4)	157 (76.6)
Mild	311 (46.8)	284 (42.7)	307 (46.2)	163 (24.5)	44 (21.5)
Moderate	51 (7.7)	212 (31.9)	181 (27.2)	14 (2.1)	2 (1.0)
Severe	2 (0.3)	13 (2.0)	22 (3.3)	0	0

TABLE 3. RATES OF COMPLICATIONS FROM VACCINIA, ACCORDING TO VACCINATION STATUS AND AGE.*

COMPLICATION	PRIMARY VACCINATION (N=650,000)				REVACCINATION (N=998,000)			
	0-4 YR	5-19 YR	≥20 YR	A.L.L. AGES	1-4 YR†	5-19 YR	≥20 YR	A.L.L. AGES
	no. of events/1 million vaccinations							
Accidental infection	564	371	606	529	198	48	25	42
Generalized vaccinia	263	140	212	242	0	10	9	9
Erythema multiforme	209	87	30	165	73	2	9	10
Eczema vaccinatum	39	35	30	39	0	2	5	3
Postvaccinal encephalitis	15	9	0	12	0	0	5	2
Progressive vaccinia	3	0	0	2	0	0	7	3
Other	222	214	636	266	18	24	55	39

*Data are from a 1968 survey of 10 states.†† No deaths occurred.

†No children under the age of one year were revaccinated.

Normal Variants of Vaccine Reaction

- Local Edema at Vaccination Site
- Lymphangitis
- Regional Lymphadenopathy (nonfluctuant)
- Satellite Lesions



Local Reactions

- Allergic Reactions to Bandage and Tape Adhesives
- Large Primary Vaccination Reactions (“robust primary takes” – RPT)
- Secondary Bacterial Infection



Allergic reaction

Robust Primary Takes (RPT)

- Normal Variant
- >3 inches of Erythema with Induration, Pain, Warmth
- Occur in 5%-15%
- Peak at Day 8-10
- Resemble Bacterial Infection



Secondary Bacterial Infection

- More Common Among Children than Adults
- Usually Staphylococcus Aureus or Group A beta Hemolytic Streptococci
- Anaerobic and Mixed Infections may occur
- Evaluate with Gram Stain and Culture
- Antibiotic Therapy based on Culture



Rashes Following Smallpox Vaccine

- Flat, Erythematous, Macular, or Urticarial Lesions
- Usually do not Become Vesicular
- Do not appear to involve Viral Multiplication or Systemic Dissemination
- Occur Approximately 10 days after Vaccination
- Resolve Spontaneously within 2 to 4 Days

Generalized Vesicular Rash, Day 11



12/18/02

Generalized, Flat Erythematous Rash, Leg, Day 13



12/18/02

Localized Vesicular Rash on Hands



Localized Papular Rash, Elbow, Day 18



12/18/02

Erythema Induration from Pustule to Elbow



12/18/02

Erythema Multiforme

- May present as Macules, Papules, urticaria, or bulls-eye Lesions
- Usually Appear within 10 days
- Do not Progress
- Do not Contain Vaccinia Virus
- Occasional Stevens-Johnson Syndrome
- VIG not Indicated



Major Complications of Smallpox Vaccination

- Definitive studies of complications of smallpox vaccination by Lane et al, published in 1969 -1970
- Led to the recommendation to cease routine smallpox vaccination in the United States

Inadvertent Inoculation

- Transfer of Vaccinia virus from vaccination site to another site on the body, or to a close contact
- Most Frequent Complication
- Face, Eyelid, Nose, Mouth, Genitalia, Rectum
- Lesions Contain Vaccinia Virus



Inadvertent Inoculation

- Uncomplicated lesions require no therapy, self-limited, resolve in ~3 weeks
- VIG may speed recovery if extensive or painful genital involvement
- Hand washing after contact with vaccination site or contaminated material most effective prevention

Ocular Vaccinia

- May present as blepharitis, conjunctivitis, keratitis, iritis, or combination
- Treatment may include topical ophthalmic antiviral agents and VIG



Generalized Vaccinia

- Vesicles or pustules appearing on normal skin distant from the vaccination site
- Often accompanied by fever, headache, and myalgias
- Usually occur 6-9 days after vaccination



Generalized Vaccinia

- Differential Diagnosis
 - Erythema multiforme
 - Eczema vaccinatum
 - Inadvertent inoculation at multiple sites
 - Early progressive vaccinia
 - Disseminated herpes
 - Severe varicella
- Generally Self-limited, usually no Tx
- VIG considered for recurrent disease or severe disease
- Lesions contain Vaccinia

Eczema Vaccinatum

- Generalized spread in patient with Eczema or true Atopic Dermatitis, or a history of Eczema or Atopic Dermatitis
- Severity Independent of the activity
- Severe cases among contacts



Eczema Vaccinatum

- Skin lesions may be papular, vesicular, or pustular
- May occur anywhere on the body
- Predilection for areas of previous atopic dermatitis
- Patients often severely ill



Sibling contact

- **Eczema Vaccinatum in contact to recently vaccinated child.**
- **Recovered without sequelae or permanent ocular damage.**



Eczema Vaccinatum

- Management
 - Hemodynamic support
 - Meticulous skin care
 - Early treatment with VIG
 - Treatment of secondary bacterial or fungal infections as needed
- **Lesions contain vaccinia virus**



Progressive Vaccinia

- Primary Vaccination does not heal
- Progresses to ulcerative lesion, often with central necrosis
- Little or no Inflammation at the site and generally little pain
- Virus continues to spread locally and through viremia
- immunodeficiency



Progressive Vaccinia (vaccinia necrosum) in Patient with Chronic Granulocytic Leukemia



Progressive Vaccinia

- Requires Aggressive Therapy with VIG
- Antiviral Therapy?
- Surgical Debridement?
- Lesions contain Vaccinia Virus

12/18/02



Post-Vaccinial Encephalitis

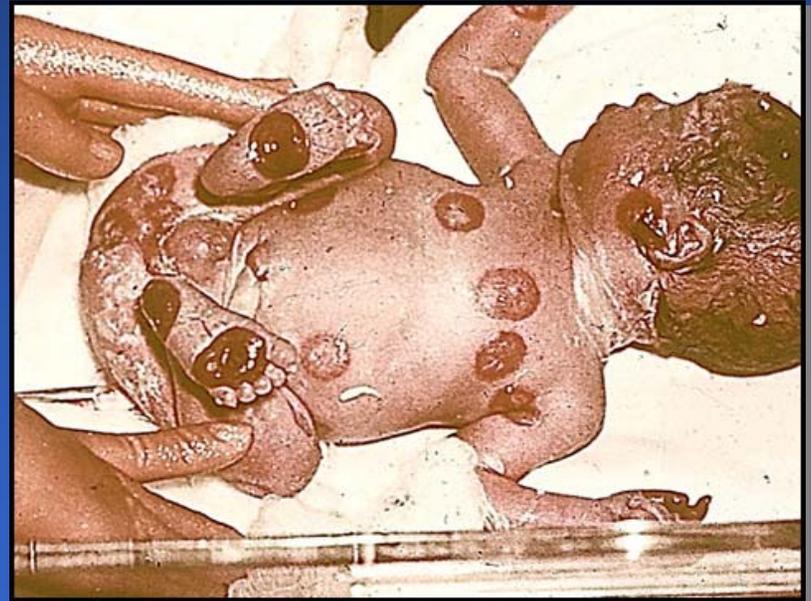
- Usually affects primary vaccinees
- Variety of CNS signs (e.g., ataxia, confusion, paralysis, seizures, or coma)
- 15%-25% die, 25% develop neurological sequelae
- Occurred 3-12 cases per million primary vaccinations

Post-Vaccinial Encephalitis

- Diagnosis of exclusion
- Pathophysiology not well understood
- CSF may have increased opening pressure, lymphocytosis, elevated protein
- Treatment is supportive
- VIG not effective
- Anticonvulsive therapy and intensive care may be required

Fetal Vaccinia

- Rare complication (<50 cases reported)
- usu second or third trimester
- Fetal infection - spontaneous abortion
Death usually occurs before birth or in perinatal period
- No known congenital malformations
- No known reliable intrauterine diagnostic test



Vaccinia Immune Globulin

- Immunoglobulin fraction of plasma from persons vaccinated with vaccinia vaccine
- Effective for treatment of eczema vaccinatum, progressive vaccinia, severe generalized vaccinia, and ocular vaccinia
- Not effective in post-vaccinial encephalitis

Cidofovir

- Nucleotide analogue of cytosine
- Broad spectrum of activity against herpesviruses
- Activity against orthopoxviruses in cell-based and animal models
- Currently approved for treatment of CMV retinitis in persons with AIDS
- Available for treatment of vaccinia under IND

Cidofovir Indications

- Second line treatment of complications of smallpox vaccination
- Use if patient fails to respond to VIG treatment
- Consult with CDC before use under IND
- Manufacturer recommends use with probenecid

Cidofovir Adverse Events

- Renal toxicity
- Neutropenia
- Proteinuria
- Anterior uveitis/iritis
- Metabolic acidosis
- Possible carcinogenicity and teratogenicity
- Probenicid adverse events

Smallpox Healthcare Response Teams Requirements

- Voluntary Willingness to be Vaccinated
- Preference for Revaccines to Decrease Incidence, Severity of Systemic Effects
- Administrative Leave **NOT** Routinely Required

Vaccinated Healthcare Workers for Smallpox

- Hand Hygiene, (include alcohol-based)
 - After contact with vaccination site or materials that have been in contact with site
 - Before and after patient contact
- Keep site covered with gauze overlaid by semi-permeable dressing until scab separated, approximately 21 days
- Cover dressing with clothing in healthcare setting

Vaccinated Healthcare Workers for Smallpox

- When Showering
 - Cover site with plastic wrap
 - Dry site last, keep towels separate, wash used towels with hot water ($\geq 71^{\circ}\text{C}$, 160°F) and soap
- Change dressing when exudate begins to accumulate (every 3-5 days)
- Discard contaminated dressing materials as regulated medical waste in hospital

Vaccinated Healthcare Workers for Smallpox

- Daily monitoring at local institution prior to beginning work assignment
 - Site inspection by vaccinated staff member
 - Dressing change when indicated
 - Assessment of fitness for duty
 - Triage adverse reactions with potential need for treatment
 - Reporting of experience to active surveillance system
 - Educational reminders re: hand hygiene
 - “Take” evaluation

Vaccination Issues: “Take” Evaluation

- If “take” successful:
 - Update vaccination card
 - Review site care and adverse reactions information with vaccinee
- If “take” is not successful, vaccinee will be referred for re-vaccination
- If second vaccination unsuccessful, medical referral will be necessary

Smallpox Vaccine Components

- Dryvax
 - Polymyxin B
 - Streptomycin
 - Tetracycline
 - Neomycin
 - Phenol
- New vaccines do not contain antibiotics



Smallpox Vaccine

Contraindications and Precautions (Nonemergency Situations)

- Serious allergic reaction to a prior dose of vaccine or vaccine component
- Immunosuppression in the recipient or household contact

Causes of Immunosuppression Diseases

- Leukemia
- Lymphoma
- Generalized Malignancy
- Solid Organ or Stem Cell Transplantation
- Humoral or Cellular Immunity Disorders
- HIV Infection

Causes of Immunosuppression Therapies

- Alkylating agents
- Antimetabolites
- Radiation
- High Dose Corticosteroid Therapy
 - ≥ 2 mg/kg/day, **OR**
 - ≥ 20 mg/day for ≥ 14 days

Screening for HIV Infection

- Mandatory HIV testing not recommended, but:
 - Recommended for persons who have history of risk factor and do not know status
 - Should be readily available for anyone concerned who wishes testing

Smallpox Vaccine

Contraindications and Precautions (Nonemergency Situations)

- Serious allergic reaction to a prior dose of vaccine or vaccine component
- Immunosuppression in the recipient or household contact
- Pregnancy or pregnant household contact

Screening for Pregnancy

- In pre-event setting, should **NOT** be given to:
 - Pregnant women
 - Women trying to become pregnant
- Educate women of child-bearing age about fetal vaccinia
- Advise avoidance of pregnancy for 4 weeks following vaccination
- If concerned, administer home test for pregnancy
- Establish pregnancy registry for women inadvertently vaccinated

Smallpox Vaccine

Contraindications and Precautions (Nonemergency Situations)

- Serious allergic reaction to a prior dose of vaccine or vaccine component
- Immunosuppression in the recipient or household contact
- Pregnancy or pregnant household contact
- Breastfeeding

Smallpox Vaccine

Contraindications and Precautions (Nonemergency Situations)

- Eczema or atopic dermatitis (current or past history) in the recipient or household contact
- Acute, chronic, or exfoliative skin conditions (until improved or resolved)

Smallpox Vaccine

Contraindications and Precautions (Nonemergency Situations)

- Eczema or atopic dermatitis (current or past history) in the recipient or household contact
- Acute, chronic, or exfoliative skin conditions (until improved or resolved)
- Children <12 months of age
 - Household contacts?
 - I would recommend < 5 years

Smallpox Vaccine

Contraindications and Precautions

(Nonemergency Situations)

- Eczema or atopic dermatitis (current or past history) in the recipient or household contact
- Acute, chronic, or exfoliative skin conditions (until improved or resolved)
- Children <12 months of age
- Moderate or severe acute illness

Conclusion

Conclusion

- Recommendation
- Contraindication/Precautions
- Local Reaction
- Serious Reaction

.....Questions?

12/18/02





Conclusion



- Public Perceptions of Smallpox
- Threat
- Epidemiology
- Clinical Features of Variola Major versus Minor
- Differential Diagnosis
- Prevention: Response Phase 1, 2, 3

Questions?

During this Live program

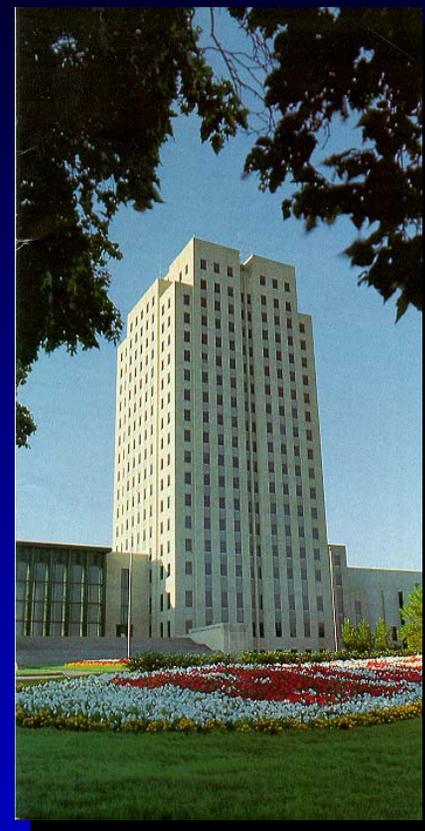
Call 701-328-2614

or

Send E-mail

Following the Live Program

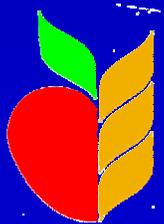
Call 701-328-2270 or Send E-mail to
twiedric@state.nd.us



North Dakota Department of Health

Smallpox Physician and Clinician Seminar

January 6, 2003



North Dakota Department of Health

