

Pleasure -

25 yrs ago - May 1980 - eradication - vaccination stopped &

and so did vaccine manufacturing.

With smallpox again a threat. - ~~need for possible~~ vaccination - surprising how little known

So - appropriately a word about the first and oldest vaccine

No one <60 has
received vaccination

Preventive Tools for Terrorist Attacks: Smallpox

Canadian Conference on Counter-
Terrorism and Public Health

D.A. Henderson M.D., M.P.H.
30 October 2003

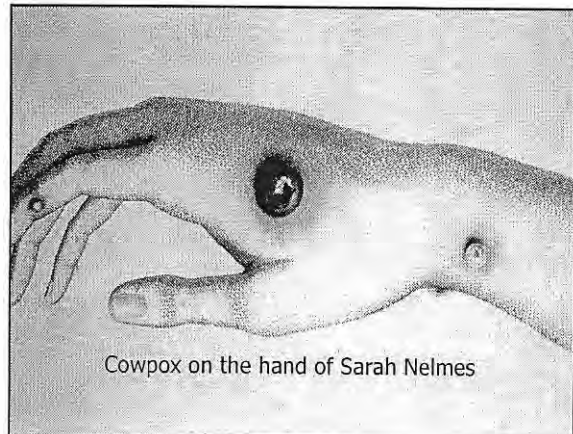
Tools for disease prevention or spread

- Smallpox vaccine – first generation
 - Traditional calf-lymph
 - Tissue culture
- Smallpox vaccine – second generation
 - MVA (Modified Vaccinia Ankara)
 - Lc16m8 – replicating strain
- Antiviral agents
 - None available or on the horizon
- Vaccinia Immune Globulin

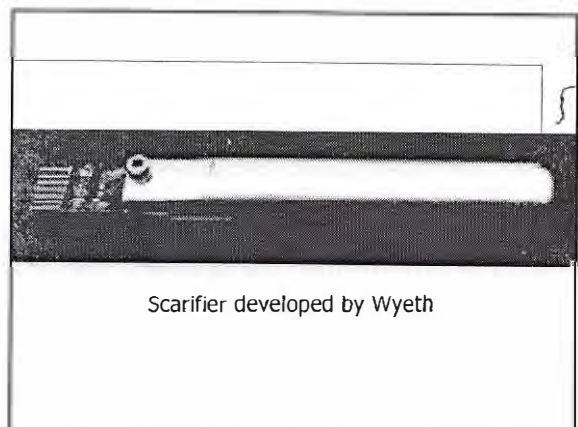
Edward Jenner



Cowpox on the hand of Sarah Nelmes



Scarifier developed by Wyeth

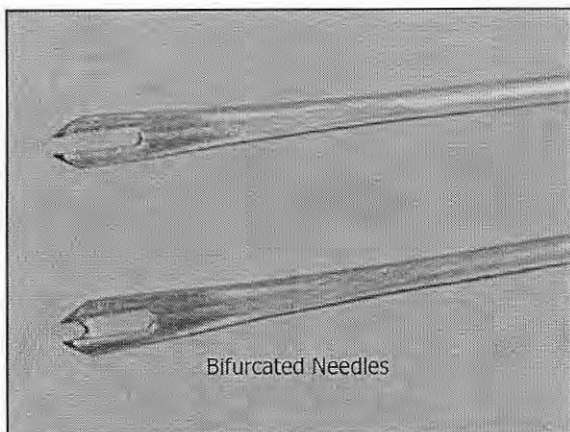


Vaccines produced – to the present

- Calf-lymph, freeze-dried vaccine
 - NYCBOH (N.Y. City Board of Health strain)
 - Americas (including Connaught Laboratories)
 - Lister strain
 - Europe, Africa, some Asia
 - Other strains
 - Patwadanger -India, Temple of Heaven-China
- Embryonated egg vaccine
 - Brazil, Sweden

Calf-lymph vaccine characteristics

- Freeze-dried in 0.25 ml. Vials (100 doses)
- Very heat stable before reconstituting
- Could be diluted 10 fold+ for primaries: and at least 5 fold+ for revaccinees
- Attenuation efforts: generally not successful
- Efficacy: 95%+ with proper technique



Vaccine availability

September 2001

- Vaccine manufacturers
 - None
- Vaccine in storage
 - U. S. 15 million doses
 - World ? 80 million doses
- Ready for emergency shipment – U.S.
 - 90,000 doses
 - Limited quantities -- bifurcated needles, VIG

U.S. Smallpox Vaccines

No. of doses

- | | |
|-----------------------------------|--------------------|
| ■ Wyeth DryVax (licensed) | 15 million |
| ■ Calf lymph 1978-9 | |
| ■ Aventis Pasteur | 85 million |
| ■ Calf lymph 1958 | |
| ■ Acambis/Baxter ACAM 2000 | 209 million |
| ■ Tissue cell | |

Vaccines can be diluted 1:5 in emergency

MVA – Next Generation Vaccine?

- NIH is contracting for development and initial manufacture of Modified Vaccinia Ankara (MVA)
- Non-replicating strain
- Probably two doses
- Much more costly
- Phase I trials have begun

(7100+ doses as smallpox vac)

0.25 .0025
.5

Lc16m8 – Next Generation Vaccine?

- Japanese attenuated replicating strain
- Grown in primary rabbit kidney cell culture
- Developed in the 1970s – a temperature-sensitive clone of the Lister strain
- Tested in 50,000 Japanese children – less skin reaction and fewer systemic symptoms
- Animal trials begin soon in U.S. and Japan

Smallpox Vaccine: Expected Adverse Events

- Life-threatening complications (per million)
 - Post-vaccination encephalitis (3)
 - Progressive vaccinia (1)
 - Eczema vaccinatum (12)
- Less serious
 - Generalized vaccinia
 - Accidental inoculation (may result in blindness)
 - Rash and fever
- If 100 million vaccinated, 100-400 deaths and 2500 serious, potentially fatal complications are expected

Vaccination Adverse Events



Accidental Inoculation



Progressive Vaccinia



Eczema
Vaccinatum



Intravenous Vaccinia Immune Globulin

- Used for treatment of
- Progressive vaccinia
 - Eczema vaccinatum
 - Severe cases of accidental inoculation
 - Produced from plasma from revaccinated donors
 - Estimated need – 30 treatment doses per million persons vaccinated

CANADIAN
WINNIPEG
or
CALGARY

Options for pre-event Vaccination

- Vaccinate no one
- Vaccinate those at highest risk:
 - Healthcare workers
 - First responders
 - Essential personnel
- Vaccinate anyone desiring vaccination
 - Recommend vaccination
 - Recommend against vaccination
- Make vaccination compulsory

A Balance of Risks

- Likelihood that smallpox will be used as a weapon
- Frequency of adverse reactions ?
- Rapidity with which an epidemic could be contained?

Vaccination experience -- 2003

- Vaccinated through 1 October
 - Military 479,925
 - Civilian 38,489
- **Serous Adverse Events**
 - Progressive vaccinia 0
 - Eczema vaccinatum 0
 - Post-vaccinal encephalitis 2
 - Nosocomial contact transmission 0
- VIG Treatments 2

Vaccination Experience -- 2003 Unexpected findings

- Myopericarditis
 - Military -- 56 probable cases
 - Civilian -- 6 cases
- Dilated cardiomyopathy
 - 2 cases in military; 2 among civilians

Final thoughts

- For some countries (e.g. U.S. and Canada), smallpox now poses a far less catastrophic threat than 12 months ago but that threat is not zero.
- Global concerns dictate now the need for global strategies and policies