

Be careful where you work in a laboratory
new policy
Sept 97 - chamberlain - A.B. no interest
OSTP -

How is policy formulated - see by 2
? 2 if it is
time

SMALLPOX ERADICATION - THE STRATEGY

Objective : zero cases of smallpox

Improve immune status to deter spread

+ Vaccinate 80% of population - i don't feel stable / easy to apply.

Quality assurance - vaccine potency/stability

- coverage
- vaccine efficacy

Surveillance - Containment

- + All health units to report weekly
- + Team to investigate/contain outbreaks
- + On-going analysis of surveillance data

Research program

- + Alternative methods for vaccination
- + How to improve vaccine quality
- + Epidemiology of smallpox
- + Operational approaches
- + Natural reservoir of smallpox

A reluctant CDC finally launched
a badly coordinated, poorly directed
program -
Even one year ago - as I addressed the club
There was little support for funds going into any
part of that program - and then school as AAP
and then came 9/11 followed by anthrax
Preparedness - 200 million
Office of P-H - Preparedness - you
still better off.

When prog. began - already demonstrated feasible in a no. of countries
Note: importance of vaccine.

Pay for vaccine
Everyone who thought

45 PDP

Be careful you undertake a new policy - you
might realize more than you can handle.
95-98 budget overruns
Sept 97 - 1st epidemic
for \$1.25 x 100
no support from PHS -
By May 98 - 2nd epidemic
for \$1.25 x 100
no support from PHS -
Sept 98 - 3rd epidemic
for \$1.25 x 100
no support from PHS -

Status of Smallpox Vaccines – 1967

WHO standards for vaccine established – 1959

Vaccine production in many different laboratories

- **Most labs did own QA**
- **National QA was uncommon even in industrialized countries**
- **International QA – voluntary and seldom**

Findings during first years of program

- **About 5-10% met potency standards**
- **<5% met stability standards**
- **Bacterial contaminants up to 1000/ml approved**
- **Vials varied in size from 0.25 ml to 5.0 ml**
- **Many different strains of vaccinia in use**
- **No seed lot system for production**

What was done to change the system

*Research. - production
tissue cultures*

Manufacture of Smallpox Vaccine

**Growth on flank of calf (cow), sheep, water buffalo
under very clean conditions**

Material scraped off after 7 days and centrifuged

**Small amounts of phenol (anti-bacterial) added
Peptone (5%) added for stabilization**

Vaccine put in vials and freeze-dried

Tests:

Potency -- $>10^8$ p.f.u. per ml.

Stability -- $>10^8$ pf.u./ml after 28 days @37°C.

Bacteria -- < 500 per ml.

Pathogenic bacteria -- no tetanus spores

Seed lot system after 1962

**Before 1962 -- Sequential passage with occasional
passages to rabbit testicle to human to calf**

OLD SMALLPOX VACCINE

Live vaccine – grown on calves

Two major strains

- **NY Board of Health -- Americas**
- **Lister – most of rest of world**

Protection – 95% + for 5 years, one dose

Reserve stocks

- **U.S. – 6 to 7 million doses**
- **World – perhaps 50 to 75 million**

Manufacturing capacity – nil

Complications of vaccination

Policy and Planning

An Adventure in Bureaucracy

1996 (April)

A joint research committee of DHHS and DOD

Recommends special committee to work out details for producing and procuring 100 million doses of smallpox vaccine

— why Russia

CDC tasked with responsibility

CDC response

Issue:

Can we afford to be without protection vs. a disease
so ~~important~~ potentially devastating as ~~sp.~~
Russia!

Policy and Planning II

An Adventure in Bureaucracy

1997

Nothing whatsoever was done

Policy and Planning III

An Adventure in Bureaucracy

1998

February -- Proposal to HHS Secty to develop a blueprint

DOD issues contract for 300,000 doses of vaccine

Company: Dyneport

Cost: \$30,000,000

Deliver: 2005 (later revised to 2006)

Level of capability: ?

*note
cost & who
for purchase*

HHS ordered to coordinate efforts with DOD to avoid waste

Summer -- Dyneport proposes to develop questions to be answered in developing a blueprint -- cost: \$250,000

Expected cost of developing blueprint -- "much more"

Suggested that Japanese strain LC16m8 be evaluated

Policy and Planning IV

An Adventure in Bureaucracy

1999

February -- White House states that procurement of vaccine is a top priority

March -- Conference call chaired by Office of Secretary

**Series of actions decided- responsibilities assigned
Monthly report calls to be initiated
Team assigned to investigate LC16m8**

March -- Administration reverses decision to destroy smallpox virus on grounds of need to develop an antiviral drug and a new vaccine

June -- CDC issues solicitation to determine interest of possible producers

August -- Conference in Atlanta to decide series of actions to be taken; responsibilities assigned

Decision: Use only proven strain (NYCBH)

September -- DOD embarks on field trials using a strain that has not been tested in the field

December -- contract for vaccine supposed to be issued

Policy and Planning

An Adventure in Bureaucracy

2000

Summer-- DoD issues contract for purchase of smallpox vaccine (NYBH -National Drug strain) that a joint government group (including DoD) decided was unsatisfactory as never having been subjected to field challenge. Vaccine to be produced on MRC-6 cells: FDA prefers chick embryo fibroblast.

Delivery date 2005 → 2006

September -- HHS/CDC issues contract for

purchase of 40 million doses of smallpox vaccine

Strain will be NYBH-Wyeth (adequately field tested) grown on chick embryo fibroblast. *(MRC-5 cells)*

to be delivered early 2005

~~2005 - 2006~~

and stand by capacity

Policy and Planning

An Adventure in Bureacracy

2001

September-October--

Decision -- ONE DOSE OF VACCINE FOR EVERY CITIZEN

- 1) Dilution of vaccine 1:5 -- the needle adventure
- 2) Procurement of additional 150 million doses to be delivered by end 2002 -- How?
- 3) An unexpected ?bonanza?

Elsewhere in the world

- + Global reserves
- + PAHO
- + Other countries

An insurance Policy

How do we use the vaccine? Many, many requests.

- 1) Keep in storage
- 2) Vaccinate those at high risk (optimal)
- 3) + anyone who wishes it.
- 4) Advocate/recommend those at high risk and population.

Problems:

- 1) Vaccine packaging.
- 2) Cost.
- 3) Expiration contracts

Who is to decide?

CRITERIA FOR GRADING BW AGENTS

Anatoliy Vorobyov (1954)

- 1. Human susceptibility to microbe**
- 2. Infective dose by aerosol route**
- 3. Contagiousness**
- 4. Possible routes of infection
(oral, parenteral, aerosol)**
- 5. Stability in aerosol and/or environment**
- 6. Case-fatality rate**
- 7. Ease of production**
- 8. Possibility of rapid diagnosis**
- 9. Availability of prophylaxis**
- 10. Availability of treatment**

RATING OF POSSIBLE BW AGENTS

• Smallpox	26
• Plague	23
• Anthrax	21
• Botulism	21
VEE	20
• Tularemia	20
Q fever	20
• Marburg	18
Influenza	17
Melioidosis	17
Typhus	15