

Date Dec 5 2002

Author DA Henderson

Title Keynote address

Event International emerging infectious diseases
and bioterrorism

Event Sponsor Univ of California Davis

Event location Davis CA

Notes Speech books indicate 2 speeches for this date and event, one on smallpox and a keynote address on the history of eradication. Although 2 text drafts and 2 very similar sets of slides were included, neither matched well with the subject matter indicated. Examined together, however, it is most likely that that the documents represent a single event. One text draft, clearly reworked from a previous speech, addresses smallpox, its eradication, and the current status of smallpox vaccine. The other, marked "keynote", describes DA's personal involvement & experience with bioterrorism and the government response. It has a good last line. This probably served as a conclusion to the full address. One set of slides is based on but goes beyond the other (marked "redo"), and corresponds well to the body of the text.

The title of the event is also unclear. DA used 2 different versions.. The only external reference found used the title above. Whether it was an international conference, or simply dealt with international aspects of the issue, is unknown.

We celebrate this year the 25th anniversary of occurrence of the last case of ~~smallpox~~ ^{smallpox} - Throat of greatest ~~throat~~ ^{throat}.

Spox, to persist, went to man in continuing chain of transmission - 0 transmission but
so last case in a continuing chain going back at least

K Ramses II - 3500 yrs. ago

Over the centuries, the most deadly disease known to man

300 million deaths

A priority disease for Russian bioweaponers

ALISEK QUOTE

To ~~understand~~ ^{appreciate} the impact of spox and the human measures employed to eradicate - a brief review

- 1) Smallpox in hx.
- 2) Clinical features
- 3) Eradication efforts
- 4) Issues surrounding vaccination.

Gods + Goddesses

MC. Anley - 30%+ deaths.

control of spox / growth of cities / Industrial Revolution occurred contemporaneously.

Jenner 1796 - one of greatest advances in medicine

FACE OF SMALLPOX - a mild case.

Incubation period 7-17 days - no transmission.

Prodrome - high fever - 1-2 days No transmission.

Risk - droplet spread primarily in household and hospital.

Ordinary spox. Indonesia

Before and after

Blindness

Diff. Dx - chickenpox - usually easy to distinguish.

- Monkeypox

Intervent in eradication - 300×10^6

STRATEGY

1967

INSERT
GB
Fibers
re: smallpox

27 1970

28 1973

29 30 31 India - the heroic effort. Parenthetical India 1 strain.

32 1976

33 Ali Maalin.

1980 Vaccines stopped
Vaccine prod. facilities were destroyed.

One episode of special note -

34 35 36 37 Mosquito

As of a year ago - we were greatly concerned.

15×10^6 doses of smallpox in U.S.

? 60-80 $\times 10^6$ doses worldwide

A Pop. susceptible

acc. prod.

B C

D E

Vaccine production - no producers.

Previous means of production.

Many few bifunctional needles.

important vs. vaccine admin.

F

Smallpox vaccines

G H I

J

VIG.

K L

New Vaccines

M

Vaccine options

N O

Adverse events.

P

Contact vaccination

Q

A balance of risks

R

Office is ~~not~~ orchestrating

S

Goals.

T

Watchwords

U

Focus areas.

V

website for vaccination ops.

Finally a word about outbreaks contain must.

X-1

Facts about contagion

X-2

" " spread

X-3

European experience

X-4

What to do.

NEW

WEBSITE - VACCINA

Approved opportunity to participate
But - emerging dis. inseparable.

DAVIS CALIF
15 DEC.

We celebrate this year the 85th anniversary of occurrence of the last case of smallpox.
Spox, to present, man to man in continuing chain of transmission - 0 minimal host
2. last case in a continuing chain going back at least
to Roman II - 3500 yrs. ago

Over the centuries, the most deadly disease known to man

300 million deaths

A priority decision for Russian bioweapons

ALISEK QUOTE

Among lack of knowledge - spox + vaccination

To appreciate the impact of spox and the home measures employed to eradicate - a brief recap.

- 1) Smallpox in hx.
- 2) Clinical features
- 3) Eradication efforts
- 4) Issues surrounding vaccination.

Gods + goddesses

MC. Anley - 30%+ deaths. - control of spox / growth of cities / industrial revolution occurred contemporaneously.

Jenner 1796 - one of greatest advances in medicine

FACE OF SMALLPOX - a mild case.

~~Smallpox spread by direct contact with infected person.~~

~~Also by high fever & skin lesions.~~

Risk - droplet spread proximity in household and hospital.

Ordering spox. Indonesian

Before and after

Blindness

Diff. Dx - chickenpox - usually easy to distinguish.

- Monkeypox

STRATEGY - SURVEILLANCE

1967

Conference in Bioterrorism and New and Emerging Infections

D.A. Henderson M.D., M.P.H.

Davis, California

December 5, 2002

1



Ali Maalin
26th October, 1977

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2



Ramses V

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3

Deaths During the 20th Century

Due directly or indirectly to armed
conflict:

100,000,000

Due to smallpox

300,000,000+

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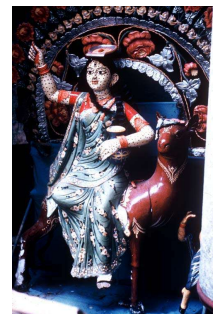
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"On May 8, 1980, WHO announced that smallpox had been eradicated from the planet... Soon after the WHO announcement, smallpox was included in a list of viral and bacterial weapons targeted for improvement in the 1981-85 Five-Year Plan.... Where other governments saw a medical victory, the Kremlin perceived a military opportunity...the Soviet military command issued an order to maintain an annual stockpile of 20 tons."

Alibek, 1998

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5



Sitala Mata
South Asia

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6



Sapona
West Africa

7



"That disease was the most terrible of all the ministers of death. The horror of the Plague...visited our shores only once or twice within living memory but the smallpox was always present, filling the churchyards with corpses...and making the eyes and cheeks of the betrothed maiden objects of horror to the lover."

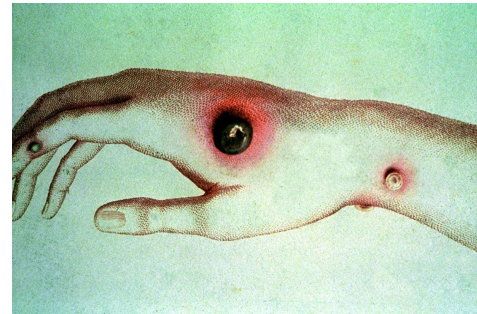
Macauley

8



Edward Jenner

9



Cowpox on the hand of Sarah Nelmes

10

Facts About Smallpox

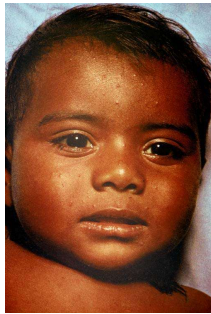
- Time between exposure and illness 12 to 14 days
- Fever, flu-like symptoms then rash
- Case fatality rate 30 percent
- Not infectious until ill with fever
- Most infectious once rash has developed
- Transmission rates affected by temperature and humidity
 - Summer: Low
 - Winter: High (3 to 4 fold higher)

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Day 1

12



Day 2

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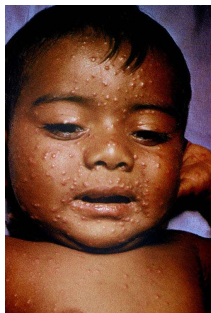
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Day 3

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Day 4

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15



Day 5

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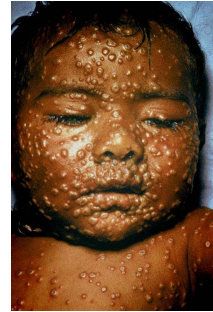
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Day 6

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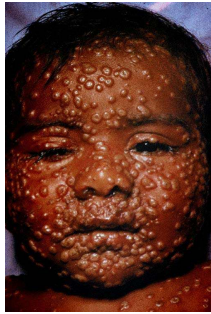
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Day 7

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18



Day 8

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19



Day 9

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20



Day 13

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21



Day 20

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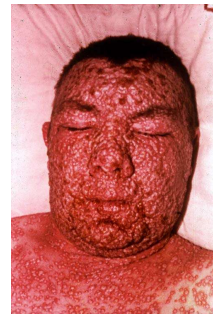
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Ordinary smallpox

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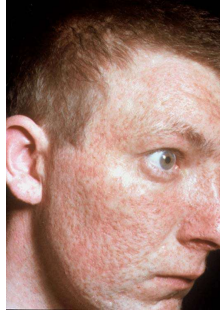
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Confluent smallpox - acute

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Confluent smallpox – after recovery

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A blind patient, recovered from smallpox

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Chickenpox

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Monkeypox

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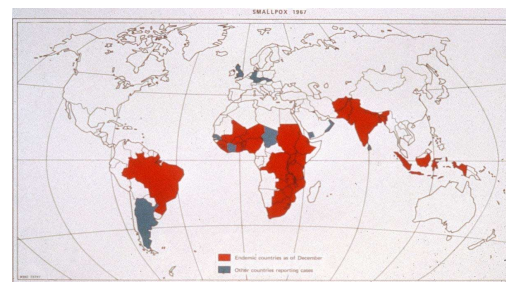
Characteristics of Smallpox Favoring Eradication

- Man was the only host
- Virus transmitted only during period of rash
- Permanent immunity after recovery
- Spread of virus during face-to-face contact
- Transmission stopped spontaneously in remote areas
- Vaccine provided long-lasting protection

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Smallpox, 1967

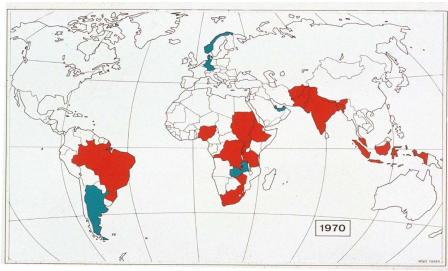


- = Endemic countries as of December
- = Other countries reporting cases

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Smallpox, 1970

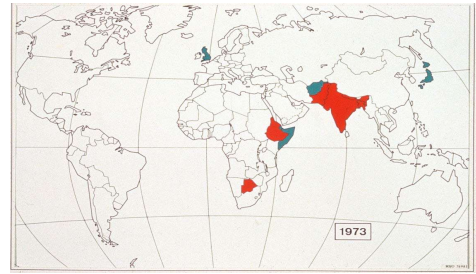


■ = Endemic countries as of December
■ = Other countries reporting cases

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Smallpox, 1973



■ = Endemic countries as of December
■ = Other countries reporting cases

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India - 1974

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33



India - 1974

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34



India - 1974

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Smallpox, 1976



■ = Endemic countries as of December
■ = Other countries reporting cases

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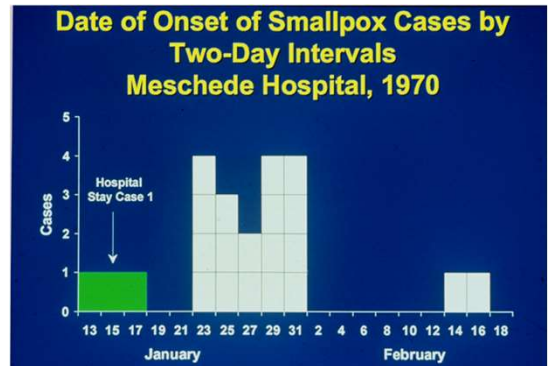
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Meschede, Germany
January 1970

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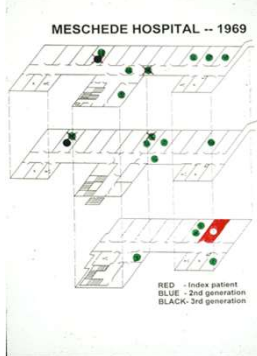
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Meschede Hospital Layout



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Susceptibility of US Population to Smallpox

Isolation of patients and vaccination – the only tools available to stop an epidemic

- Vaccination stopped in 1972
- No persons under 32 years old have been vaccinated, and make up 45% of the population
- Persons vaccinated once before 1972 with minimal immunity make up 35% of the population

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Vaccine collection from
cows seeded with vaccinia

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Scarifier developed by Wyeth

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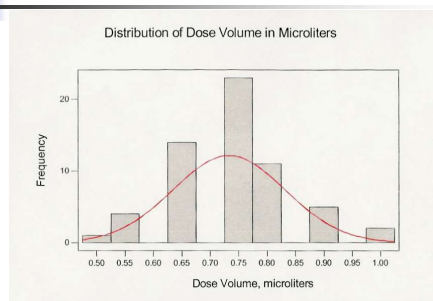


Bifurcated Needles

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Bifurcated Needle Dose Volume



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U.S. Smallpox Vaccines

	No. of doses
■ Wyeth DryVax	15 (75) million
■ Manufactured 1978-9	
■ Aventis Pasteur	85 million
■ Manufactured ca. 1958	
■ Acambis ACAM1000	54 million
■ MRC-5 cell production	
■ Acambis/Baxter ACAM 2000	155 million
■ Vero cell production	

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Wyeth DryVax

- NYCBH strain, calf skin, lyophilized
- Currently used for laboratory personnel
- Efficacy (take rate) in unvaccinated adults*
 - Undiluted 97% (103/106)
 - 1:5 99% (232/234)
 - 1:10 97% (335/340)
- Stability after rehydration 30 days at 2-8°C

*NEJM 346: 1265-1274, 2002

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Aventis Pasteur

- NYCBH, calf skin, wet frozen, glycerol
- Emergency use only -- IND status
- 100 dose vials: can be diluted 5:1

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ACAM 1000/ACAM 2000

- Acambis and Acambis/Baxter
- Seed virus -- Wyeth seed (NYCBH)
- Produced in Vero cells
- Lyophilized, 100 dose vials
- Licensure -- end 2003

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Intravenous Vaccine Immune Globulin

CDC contract with Cangene, Aug. 2002

- 30,000 treatment units
- Plasma from paid revaccinated donors
- Delivery began in Oct. 2002

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MVA – A Next Generation Vaccine?

- NIH is contracting for development and initial manufacturing of modified vaccinia Ankara (MVA)
- Initial phase I trials begin this year
- Request for Proposal issued – contracts to be awarded January 2003
- Purchase contract -- up to 30M doses

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Lc16m8 – A Next Generation Vaccine?

- Japanese attenuated strain Lc16m8 soon to undergo trials in U.S. and Japan
- Developed in the 1970s – a temperature-sensitive clone of the Lister strain
- Grown in primary rabbit kidney
- Tested in 50,000 Japanese children – less skin reaction and fewer systemic symptoms; apparently similar serological responses to Lister strain

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Options for Vaccination Before an Event

- Vaccinate no one
- Vaccinate those at highest risk, candidates:
 - Healthcare workers
 - First responders
 - Essential personnel
 - Truck drivers
- Vaccinate anyone desiring to be vaccinated
 - Recommend vaccination
 - Recommend against vaccination
- Make vaccination compulsory

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Smallpox Vaccine Expected Adverse Events

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

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Vaccination Adverse Events



Accidental Inoculation



Progressive Vaccinia



Eczema Vaccinatum



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Contact Vaccinia Infection Source of Vaccinia

Age of infected patients	Siblings/ playmates	Parents/ close relatives	Son/ daughter/ grandchild	Other
0-4	75	11	0	5
5-19	21	2	0	1
20+	1	0	24*	3
Total	97**	13	24	9

*Primarily parents and grandparents

**81 siblings; 16 playmates

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A Balance of Risks

- What is the likelihood that smallpox will be used as a weapon?
- What will the frequency of adverse reactions be and how will the public deal with this?

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Public Health Emergency Preparedness

- The Office of Public Health Emergency Preparedness in the Office of the Secretary, Department of Health and Human Services
- A one-department approach

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Overall HHS Goal

Ensure nation is prepared for:

- Bioterrorism
- Other infectious disease outbreaks
- Other public health threats and emergencies

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One Program: Three Watchwords

SPEED in making funds available for use

FLEXIBILITY in how funds are used

ACCOUNTABILITY for results obtained

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Focus Areas

- A – Preparedness planning and readiness assessment
- B – Surveillance and epidemiology capacity
- C – Laboratory capacity – biological
- D – Supplemental funding not available
- E – Health Alert Network/communication and information technology
- F – (NEW) Communicating health risks and health information dissemination
- G – (NEW) Education and training

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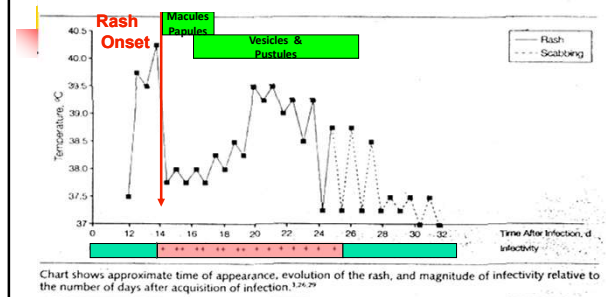
Adverse Reactions Website

www.bt.cdc.gov/training/smallpoxvaccine/reactions

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Clinical Course of Smallpox



JAMA, June 9, 1999; Vol 281, No. 22 2129

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Epidemiology of Smallpox Spread and Virulence

Spread of disease is comparatively slow

- Secondary household attack rates (approx.)

Measles	76%
Chickenpox	74%
Smallpox	58%

- Note slower community spread of smallpox than either measles or chickenpox, both of which can be transmitted before symptoms appear

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Epidemiology of Smallpox Transmission Patterns in Europe: 1958-1973

- Outbreaks: 34
- Cases: 573
 - Due to transmission in hospital: 277 (48%)
 - Due to transmission in home: 143 (25%)
- Hemorrhagic and malignant cases – a threat to hospitals
 - Bradford, UK (1961) Hemorrhagic smallpox 10 cases
 - Germany (1970) Malignant smallpox 16 cases
 - Yugoslavia (1972) Hemorrhagic smallpox 38 cases
- Seasonal variation
 - Dec to May 24 importations average=45.6 additional cases
 - Jun to Nov 10 importations average=0.5 additional cases

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Surveillance and Containment Steps in Containment

- Vaccinate and isolate patient in designated hospital or ward
- Identify and vaccinate all persons who had been in a room with the patient since he became febrile (primary contacts)
- Place primary contacts under surveillance with temperature taken twice daily
 - If a primary contact develops fever, isolate at home or special facility until diagnosis is known
- Vaccinate all household contacts of primary contacts (secondary contacts)

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January 11 - \$3 billion (desert + monsoon)
Decisions - One department. Accountability. How to deliver.
Funds to go on doc. to states \$1 billion
Speed Priority Accountability
\$200 immediately + \$800 million of plans.
Goal: Bot.

Inf. dis.
Emergency response.
President's budget - next year \$4.5 billion.
Nixon in my career - so much resources.
Prior: Long term investment.
Bot. and Now and Emerging Infections.
+ Need for ~~the~~ expanding research base.
If we are a profession - med & pub health - can expect continued support.
Conversation on Air Force 1

Best drive is expected to be in the field of p.h. and infectious diseases.