

Smallpox Preparedness and the Global Vaccine Reserve

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Tokyo
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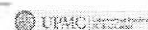
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Current assessment of threat

- Basis for threat is unchanged
 - A Soviet Union high priority program
 - Outdoor Soviet aerosol studies in 1971
 - Sergiev Posad – a secret production plant
 - VECTOR – smallpox research program
 - Financial stress in labs; departure of scientists
- No certain knowledge of other virus stocks
- Probable spread – by aerosol

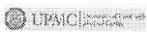
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Vaccines—prospective use in U.S.

- Aventis (WETVAX) – manu. 1958
 - 85 million doses
 - NYCBH strain, liquid, not licensed
 - 1:5 dilution produces satisfactory takes
 - For exceptional emergency use
- Wyeth (DRYVAX) – manu. 1975
 - 8 million doses
 - NYCBH strain, freeze-dried, licensed
 - For military and at-risk research personnel use until ACAM 2000 licensed

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Vaccines—prospective use in U.S.

- Acambis/Baxter (ACAM2000) – manu. 2004
 - 200 million doses
 - Cloned NYCBH strain
 - Assumed to provide equivalent protection against smallpox as DRYVAX
 - To replace DRYVAX for military and at-risk research worker use when licensed
 - *Other civilian use only if needed because of by actual or imminent smallpox release*

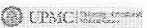
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Vaccines—prospective use

- MVA – Two possible manufacturers
 - ? Licensure in 2007
 - Preventive use – probably provides adequate protection but unable to be tested in man
 - Particularly for persons with actual or possible immune deficiencies and immediate families
 - Might be used for persons with other contraindications such as atopic dermatitis, etc.
 - *To be used only if needed because of actual or imminent smallpox release*

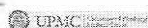
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Vaccines—prospective use in U.S.

- LC16m8 – Kaketsuken/VaxGen
 - Licensure -- ?
 - Preventive use – probably provides adequate protection but unable to be tested in man
 - For possible use for persons with contraindications other than immune deficiency disorders
 - May be suitable for others as well
 - *To be used only if needed because actual or imminent smallpox release*

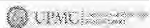
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Other supplies in stock

- Diluent vials containing 0.25 and 1.25 mls.
- Bifurcated needles >300 million
- Vaccinia immune globulin
 - For treatment of up to 30,000 patients
- Instructional material

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Strategic response –levels of risk

unofficial draft

- Level A – status today
 - No smallpox
 - Threat of release is small
- Level B -- moderate risk
 - Outbreak(s) in country outside of North America or
 - Smallpox virus in hands of terrorists and a medium probability that it would be released
- Level C – high risk
 - Outbreaks in U. S., Canada or Mexico

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Vaccine need for Level A and B risk

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- Level A
 - Military and orthopoxvirus researchers
 - Needed: limited supplies of DRYVAX and ACAM 2000 after licensure *No other vac. community*
- Level B
 - For high-risk groups (ER, ICU, some first responders and families)
 - ACAM 2000 – perhaps 2 to 10 million doses
 - Attenuated vaccine – perhaps 100,000 doses

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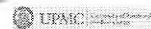


Vaccine use -- Level C risk

unofficial draft

- In infected area (e.g. city, state, region) – high risk group – contraindications ignored
 - ACAM 2000 (EUA)
 - All contacts of patients and families
 - All workers in smallpox hospitals, visitors and most patients
 - All first responders apt to be in contact with patients
- Elsewhere in infected area, all persons encouraged to be vaccinated
 - ACAM 2000 (EUA) except for those with contraindications
 - Attenuated vaccine
 - For use in those with contraindications

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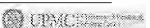


Vaccine use -- Level C risk

unofficial draft

- Elsewhere in country
 - Vaccine to be made available in clinics throughout the country for those without contraindications who desire to be vaccinated
 - Vaccination of medical and public health staff and families as well as those likely to transport patients. ACAM 2000 (EUA)
 - Attenuated vaccine for those with contraindications

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Special preparations

- Emergency national teams (CDC)
 - Epidemiological investigation
 - Assistance in setting up vaccination
- Laboratory network for PCR diagnosis
- Emergency rooms in hospitals to have isolation rooms for screening of patients
- Plan in each urban area for treating emergency patients – 500 per 1 million pop.

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Smallpox Vaccine

Expected Adverse Events (U.S. Studies-1960s)

- Life-threatening complications (per million)
 - Post-vaccinal encephalitis (3)
 - Progressive vaccinia (1)
 - Eczema vaccinatum (12)
- Less serious
 - Generalized vaccinia
 - Accidental inoculation
 - Rash and fever
- If 100 million vaccinated, 100+ deaths might occur

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Smallpox Vaccination (DRYVAX)

Military experience*

- Total screened 757,000
- Total vaccinated 708,500 (94%)
 - Post-vaccinal encephalitis 1
 - Progressive vaccinia 0
 - Eczema vaccinatum 0
- Infection in contacts 49
- Doses of VIG used 3
 - As of 1 December 2004

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Smallpox Vaccination (DRYVAX)

Cardiac complications -- military

- Myopericarditis 84
 - Onset: 7 to 19 days
 - Fever, chest pain, ECG changes, cardiac enzymes increased
 - Follow-up of 64 -- normal, ECG, echocardiograms and treadmill tests
- Incidence¹⁻²
 - Previously Unvaccinated 16 per 100,000
 - Previously Vaccinated 2 per 100,000
 - Normal background rate 2 per 100,000

1. Arness, et al, Am J Epidemiology 160:642, 2004
2. Polard, et al, Vaccine 23:2076, 2005

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Contraindications

- No contraindications for persons at high risk in infected areas
- Contraindications for use -- NYCBIH strain
 - Immune deficiency disorders
 - Including AIDS patients; those receiving drugs for the treatment of cancer or for organ transplants; systemic steroid therapy
 - Eczema, atopic dermatitis, serious skin disorders
 - Pregnancy
 - Household contacts of those with contraindications

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Reasons for establishment of a Global Vaccine Reserve

- Threat of smallpox recurrence
 - Risk is small but not zero
 - Smallpox anywhere is a threat to all countries
 - 75% of population is now fully susceptible
 - Vaccine production stopped in 1978; only a few manufacturers in 2005
 - Few countries have any vaccine

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National Smallpox Vaccine Stockpiles

Nation	# doses (millions)	% population covered
United States	300	100
Germany	100	100
United Kingdom	80	100
France	60	100
Netherlands	20	100
Czech Republic	10	100
Israel	7	100
Denmark	6	100
Singapore	4	100
South Africa	30	70
Malaysia	15	65
Austria	3	40
Switzerland	3	40
Japan	31*	25*
Korea (Rep. of)	10	20
Canada	6	20
Greece	2	20

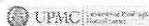
* Data are estimates and not official

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ational Smallpox Vaccine Stockpiles (part 2)

Nation	# doses (millions)	% population covered
Spain	6	15
Ireland	<1	15
Norway	<1	15
Italy	5	10
Belgium	1	10
Hungary	1	10
Sweden	1	10
Iran	2	5
Australia	<1	5
Poland	<1	5
India	6	1
Croatia	<1	1
Slovakia	<1	1
Turkey	<1	1
World Health Organization	2.5	NA
Total	approx. 720	10

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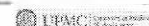


Smallpox Vaccine Production Capacity

Company	Country of Production	Production Capacity (million doses/year)	Production Capacity (million doses/month)
Acambis/Baxter	United States/Austria	100	8.3
Bavarian-Nordic	Denmark/Germany	150	12.5
RIVM	Netherlands	2-4	0.16-0.30
Kaketsuken	Japan	(10-20)*	(0.83-1.6)*
Total Production (Combined)		274	22.8
Combined Emergency Production (Estimated)		480	40

* Russian capacity unknown: ~ 25M doses/year??

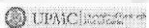
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Challenges in establishing reserve

- Vaccine licensure
 - Most vaccine is not licensed but approved by authorities for use in an emergency
- Agreement on minimum standards
 - Efficacy, stability, purity
- Agreement on acceptable strains
- Question of possible dilution in emergency
- Emergency dispersal of vaccine
- Bifurcated needles, immune globulin
- Limited WHO resources for storage, testing, etc
- Legal issues pertaining to liability

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WHO Committee – August, 2004 Decisions

- Global reserve should be established
 - 5 million doses in Geneva
 - 200 million doses committed by countries
- Member States should establish 2 reserve manufacturing sites, each able to produce at least 20 million doses
- Standing expert WHO committee should be appointed to deal with continuing issues of vaccine strains, procedures for vaccine release, etc
- WHA approval should be sought – now approved.

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