

Smallpox Vaccine Studies in the US and the Myopericarditis Issue

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1

Smallpox Vaccine Studies - US

- **Dryvax** (NYCBH strain)-- produced 1975
 - Military – 708,000 vaccinated
 - Civilian -- 40, 000 vaccinated
- **ACAM2000** (NYCBH strain) – produced 2004
 - Phase 1,2,3 trials (a few thousand)
- **MVA**
 - Phase 1,2 trials (<500 vaccinated)
- **LC16m8**

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2

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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3

Smallpox Vaccination (DRYVAX) Cardiac complications -- military

- Myopericarditis 84
 - Onset: 7 to 19 days
 - Fever, chest pain, myalgias, headache, ECG changes (ST segment elevation), cardiac enzymes increased (troponin)
 - Follow-up of 64 – Normal ECG, echocardiograms, cardiac enzymes, treadmill tests
- Incidence^{1,2,3}
 - 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

3.Eckart, et al, J.Amer Coll Cardiology 44:201,2004.

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4

An explanation for the discovery of Myopericarditis at this time

- Myocarditis and pericarditis infections are not uncommon with viral infections
- Not detected in US during 1960s vaccination program despite the same vaccine being used. Very probable that cases did occur
- In military program, ECGs and cardiac enzyme tests were frequently used for those reporting minor chest discomfort

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5

Monitoring for Myopericarditis

- FDA has stringent requirements for conduct of smallpox vaccine trials
- Cardiac safety monitoring important
- Safety of subjects assured by
 - Careful screening
 - Close monitoring during trial
 - Specific follow-up of suspected cardiac events

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6

LC16m8 US Trial - Screening

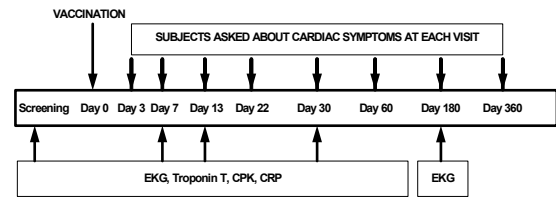
- Exclusion Criteria for Trial Subjects
 - Known cardiac disease
 - 3 or more Cardiac Risk Factors:
 - High blood pressure
 - Diabetes mellitus
 - Smoking
 - Hypercholesterolemia
 - Heart disease at age 50 or earlier in a first degree relative
 - Obesity (BMI>30)

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7

US Trial Cardiac Monitoring



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8

Potential Events Follow-Up

- Any abnormal ECG, enzymes or cardiac symptoms require investigation
- Repeat ECG, enzymes, chest x-ray, echocardiogram etc as appropriate
- Any further abnormality requires cardiologist's evaluation

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9