Myocarditis, Pericarditis, and Dilated Cardiomyopathy after Smallpox Vaccination among Civilians in the United States, January–October 2003


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Myocarditis was reported after smallpox vaccination in Europe and Australia, but no association had been reported with the US vaccine. We conducted surveillance to describe and determine the frequency of myocarditis and/or pericarditis (myo/pericarditis) among civilians vaccinated during the US smallpox vaccination program between January and October 2003. We developed surveillance case definitions for myocarditis, pericarditis, and dilated cardiomyopathy after smallpox vaccination. We identified 21 myo/pericarditis cases among 37,901 vaccinees (5.5 per 10,000); 18 (86%) were revaccinees, 14 (67%) were women, and the median age was 48 years (range, 25–70 years). The median time from vaccination to onset of symptoms was 11 days (range, 2–42 days). Myo/pericarditis severity was mild, with no fatalities, although 9 patients (43%) were hospitalized. Three additional vaccinees were found to have dilated cardiomyopathy, recognized within 3 months after vaccination. We describe an association between smallpox vaccination, using the US vaccinia strain, and myo/pericarditis among civilians.

Adverse reactions to smallpox vaccination (i.e., generalized and progressive vaccinia, eczema vaccinatum, fetal vaccinia, and postvaccinial encephalitis) are documented in association with smallpox vaccines worldwide. Cardiac complications, including myocarditis, pericarditis, and arrhythmias, also have been reported [1–16]. Most reports were from Europe and Australia, where vaccinia strains were thought to be more “reactogenic” than the New York City Board of Health (NYCBOH) strain used in the United States [17]. Before 2003, only 6 cases of cardiac complications after smallpox vaccination had been reported in the United States. Five are individual case reports [9, 10, 13, 14, 16]. The sixth case was detected in 1 of the 5 large US surveillance studies [18] that assessed rates of adverse events after smallpox vaccination in 1947 and in 1963 and 1968 [18–22]. All 6 persons previously reported to have cardiac complications after smallpox vaccination in the United States would have received vaccine derived from the NYCBOH strain.

Myocarditis and pericarditis are inflammatory processes involving the myocardium, pericardium, or both (myopericarditis). Myocarditis has a variable and unpredictable clinical presentation and course; confirmation of the diagnosis is often difficult [23]. Disease manifestations depend in part on the underlying etiology, which varies from infections, systemic diseases, drugs, and toxins. [24]. Clinical features range from abnormal electrocardiograms (ECG) of asymptomatic patients to fulminant congestive heart failure caused by dilated cardiomyopathy (DCM). Viruses probably cause most cases of infectious myocarditis in North America.
and Europe. Reports of myocarditis associated with vaccines other than vaccinia are rare [25–28].

In December 2002, the President of the United States recommended initiation of a national program for voluntary smallpox vaccination among civilians. On 24 January 2003, the Department of Health and Human Services (DHHS) authorized the voluntary smallpox vaccination of health care and public health workers who might be called on to care for persons exposed to smallpox or to serve as local smallpox-response team members [29]. To counter the possibility of the intentional release of variola virus against the US military, the Department of Defense (DoD) began its smallpox vaccination program in December 2002 [30]. Dryvax, a vaccine derived from the NYCBOH strain, was used for both programs.

The Centers for Disease Control and Prevention (CDC), the US Food and Drug Administration, and state health departments conducted surveillance for vaccine-associated adverse events among civilian smallpox vaccinees. The DoD conducted parallel surveillance among military vaccinees. In the first 2 months of the DHHS vaccination program, 7 cardiac-related adverse events (2 fatal) were detected among the 25,645 civilians who had received smallpox vaccine [31]. After these unexpected reports, the CDC established a Cardiac Team to identify and investigate cardiac adverse events. The Cardiac Team formed part of the Smallpox Vaccine Adverse Events Monitoring and Response Activity (SVAEMRA) at the CDC, which was established to assist clinicians and state health departments with vaccination adverse events and to conduct adverse events surveillance [32]. SVAEMRA, with expert opinion from smallpox experts, cardiologists, and immunologists and in collaboration with counterparts at the DoD, developed case definitions for the surveillance and classification of myocarditis, pericarditis, and DCM. The joint Smallpox Vaccine Safety Working Group (SVS WG) of the Advisory Committee on Immunization Practices (ACIP) and the Armed Forces Epidemiology Board reviewed and revised the surveillance case definitions, and these are presented in tables 1–3 [33].

The cardiac events led the CDC, following discussion with the SVS WG, to broadcast a health alert on 26 March 2003 that described the possible association of cardiac events with smallpox vaccination and listing provisional cardiac risk-factor exclusionary criteria for screening potential smallpox vaccinees. After an emergency meeting of the ACIP, cardiac risk factors and deferral recommendations were published in final form on 4 April 2003 [34].

In this report, we describe patients with suspected or probable myocarditis, myopericarditis, pericarditis, and DCM after smallpox vaccination during the civilian vaccination program in 2003 and an association between myocarditis and/or pericarditis (myo/pericarditis) and smallpox vaccination among civilians.

METHODS

Case definitions. We use the term “myo/pericarditis” to refer to cases with symptom onset within 6 weeks after smallpox vaccination that meet the case definitions for smallpox adverse event surveillance for myocarditis, pericarditis, or both (tables 1 and 2). We classified all cases of myo/pericarditis as “suspected,” “probable,” or “confirmed.”

The surveillance case definition of DCM as an adverse event after smallpox vaccination includes both structural and functional cardiac criteria (table 3). The onset of DCM is often insidious, so we did not establish a postvaccination cutoff for the onset of symptoms after smallpox vaccination for patients with DCM.

Case ascertainment. We used both active and passive surveillance systems to detect smallpox vaccination–associated adverse events among civilian vaccinees. Active surveillance included a 21–28-day follow-up of vaccinees and telephone surveys conducted among a sample of vaccinees at days 10 and 21 after vaccination. Passive surveillance involved health care workers, hospital and local health department personnel who cared for vaccinees, and adverse event coordinators (state health department staff involved in smallpox vaccination programs) who submitted adverse event reports to the Vaccine Adverse Event Reporting System (VAERS), a national passive surveillance system for suspected adverse events associated with US-licensed vaccines that is jointly administered by the CDC and the FDA [35]. Some adverse events were reported by telephone calls received by the CDC Clinician Information Line, a toll-free number staffed 24 h/day by trained nurses [32]. Events detected through active surveillance and calls to the Clinician Information Line were also reported to VAERS.

We searched the VAERS database for reports containing any of the following symptom codes: myocardial infarct, myocardial ischemia, angina pectoris, dyspnea, myocarditis, pericarditis, chest pain, hypertension, arrhythmia, atrial fibrillation, ventricular fibrillation, extrasystoles, ventricular tachycardia, palpitations, heart failure, and cardiomyopathy. We investigated all identified reports.

We collected pertinent clinical and diagnostic information for each identified patient with a potential cardiac event, using a standard questionnaire. We contacted and interviewed persons who provided the initial adverse event report, as well as the case patients. Data collected included demographic information, vaccination history and response, onset of cardiac symptoms after vaccination, presence and characteristics of symptoms, prior medical history, ischemic cardiac risk factors, medications, diagnostic workup, and outcome. We also ob-
# Table 1. Case definition of myocarditis, for surveillance of adverse events after smallpox vaccination in the United States, 2003.

<table>
<thead>
<tr>
<th>Level of diagnosis certainty</th>
<th>Signs and symptoms</th>
<th>Cardiac enzymes</th>
<th>Electrocardiogram findings (beyond normal variants) not previously documented</th>
<th>Imaging studies&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Histopathology</th>
</tr>
</thead>
<tbody>
<tr>
<td>Suspected</td>
<td>Dyspnea, palpitations, and chest pain of probable cardiac origin, in the absence of evidence of any other likely cause of symptoms</td>
<td>Not performed or normal</td>
<td>ST-segment or T-wave abnormalities; paroxysmal or sustained atrial or ventricular arrhythmias; atrial ventricular nodal conduction delays or intraventricular conduction defects; continuous ambulatory electrocardiographic monitoring that detects frequent atrial or ventricular ectopy</td>
<td>Evidence of diffuse or focal depressed left ventricular function of indeterminate age</td>
<td>Not performed or normal</td>
</tr>
<tr>
<td>Probable</td>
<td>Dyspnea, palpitations, and chest pain of probable cardiac origin, in the absence of evidence of any other likely cause of symptoms</td>
<td>Elevated troponin I or T or creatine kinase–myocardial band; a troponin is preferred</td>
<td>Not performed, normal, or abnormal</td>
<td>Evidence of focal or depressed left ventricular function that is documented to be of new onset or increased severity in absence of a previous study, findings of depressed left ventricular function are considered of new onset if, on follow-up studies, these findings improve or worsen; myocardial inflammation</td>
<td>Not performed or normal</td>
</tr>
<tr>
<td>Confirmed</td>
<td>Dyspnea, palpitations, and chest pain of probable cardiac origin, in the absence of evidence of any other likely cause of symptoms</td>
<td>Not performed, normal, or elevated</td>
<td>Not performed, normal, or abnormal</td>
<td>Not performed, normal, or abnormal</td>
<td>Evidence of myocardial inflammatory infiltrate with necrosis and myocyte damage</td>
</tr>
</tbody>
</table>

<sup>a</sup> Imaging studies include echocardiograms and radionuclide ventriculography using cardiac MRI with gadolinium or gallium-67.
<table>
<thead>
<tr>
<th>Level of diagnosis certainty for acute pericarditis</th>
<th>Signs and symptoms</th>
<th>Electrocardiogram findings not previously documented</th>
<th>Echocardiogram</th>
<th>Histopathology</th>
</tr>
</thead>
<tbody>
<tr>
<td>Suspected</td>
<td>Typical chest pain (i.e., pain made worse by lying down and relieved by sitting up and/or leaning forward) in the absence of evidence of any other likely cause</td>
<td>Not performed, normal, or with pre-existing or new abnormalities not described below</td>
<td>Not performed, normal, or abnormalities not described below</td>
<td>Not performed or normal</td>
</tr>
<tr>
<td>Probable</td>
<td>Typical chest pain (i.e., pain made worse by lying down and relieved by sitting up and/or leaning forward) in the absence of evidence of any other likely cause; pleuritic or other chest pain not characteristic of any other disease; or pericardial rub</td>
<td>Diffuse ST-segment elevations or PR depressions without reciprocal ST depressions</td>
<td>Presence of an abnormal collection of pericardial fluid (e.g., anterior and posterior effusion or a large posterior effusion alone)</td>
<td>Not performed or normal</td>
</tr>
<tr>
<td>Confirmed</td>
<td>Typical chest pain (i.e., pain made worse by lying down and relieved by sitting up and/or leaning forward) in the absence of evidence of any other likely cause; pleuritic or other chest pain not characteristic of any other disease; or pericardial rub</td>
<td>Not performed, normal, or abnormal</td>
<td>Not performed, normal, or abnormal</td>
<td>Evidence of pericardial inflammation</td>
</tr>
</tbody>
</table>
Cardiac muscle dysfunction characterized by ventricular dilatation (e.g., left ventricular end-diastolic dimension >55 mm) and impaired contraction of one or both ventricles (e.g., left ventricular ejection fraction <0.45)

No evidence of DCM or congestive heart failure before vaccination, either by history (e.g., dyspnea on exertion or fatigue) or by cardiac evaluation, including chest radiography or echocardiography if available

No other cardiac or noncardiac disease can likely account for the symptoms or abnormalities present; if another cardiac disease coexists, it is not sufficient to cause the degree of myocardial dysfunction present (e.g., ischemic or valvular heart disease or long-standing hypertension)

Criteria that must be met in a person who received the smallpox vaccine

RESULTS

Vaccination program and adverse event reporting. During 24 January through 31 October 2003, 37,901 health care and public health workers were vaccinated with licensed NYCBOH strain vaccine (Dryvax; Wyeth). The median age of the vaccinees was 48 years (range, 18–82 years), 64% were women, 54% of those for whom race information was available were white, and 75% were revaccinees. Revaccinees had at least 1 previous smallpox vaccination, usually ≥30 years previously.

By 31 October 2003, 824 total VAERS reports of adverse events among these smallpox vaccinees were submitted; 210 (25%) included ≥1 key word indicating a possible cardiac complication, and 21 (10%) met the myo/pericarditis case definitions. Two vaccinees (1%) fulfilled criteria for DCM. An additional DCM case was reported after October 2003, and it is included in the descriptive analysis because vaccination and symptom onset occurred between January and October 2003.

Although 90% (185) of reports of possible cardiac events were received after the 26 March health alert, 78% of case patients (161) had been vaccinated before that date, and almost half (96; 48%) experienced symptom onset before 26 March. The health alert and subsequent articles in Morbidity and Mortality Weekly Report that describe cardiac events among smallpox vaccinees may have stimulated reporting of events, rather than eliciting the events themselves.

Myo/pericarditis cases. The 21 vaccinees who met the case definition for myo/pericarditis included 14 women (67%); the median age was 48 years (range, 25–70 years). Eighteen (86%) were revaccinees. These demographic characteristics did not differ from those for the rest of the civilian vaccinees. Case patients did not cluster geographically. Figure 1 displays the intervals between vaccination and onset of symptoms. The median time from vaccination to onset of symptoms was 11 days (range, 2–42 days). Three patients with myo/pericarditis (14%) met the exclusionary criteria (≥3 cardiac risk factors); 2 (10%) had 2 risk factors, and 16 (76%) reported 1 or no risk factor for cardiac disease.

Table 4 presents the clinical characteristics of the 21 myo/pericarditis case patients. Twelve met criteria for either myocarditis or myopericarditis, and 9 met criteria for pericarditis only and are presented separately. Only 9 had serum cardiac enzymes tested. In 8 cases, both creatine phosphokinase–myocardial band fraction (CK-MB) and troponin (T and I) levels were determined at the time of symptom onset. No tested cardiac enzymes were elevated. All myopericarditis cases had electrocardiograms performed at the time of presentation; all but 1 pericarditis case and 1 myocarditis case had echocardiograms performed at least once.

Of the 12 case patients with myocarditis or myopericarditis (table 4), 9 presented with chest pain, and 4 had atrial and/or ventricular arrhythmias documented on ECG, including Holter monitoring for 3. Holter monitor findings for these 3 vaccinees demonstrated frequent premature ventricular beats in 2 (21% and 16% of total beats) and frequent ventricular ectopy, including couplets and bigeminy, and frequent premature atrial
Table 4. Clinical findings for 21 civilian case patients with suspected or probable myocarditis, myopericarditis, or pericarditis after smallpox vaccination, United States, 24 January through 31 October 2003.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Myocarditis or myopericarditis (n = 12)&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Pericarditis (n = 9)&lt;sup&gt;b&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Signs and symptoms, no. of cases</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chest pain or pressure</td>
<td>9</td>
<td>9</td>
</tr>
<tr>
<td>Shortness of breath or dyspnea on exertion</td>
<td>7</td>
<td>3</td>
</tr>
<tr>
<td>Fever or sweats</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Palpitations</td>
<td>6</td>
<td>1</td>
</tr>
<tr>
<td><strong>Objective findings</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Electrocardiogram abnormalities</td>
<td>5 had T-wave abnormalities, 4 had new onset of pathologic arrhythmias (atrial and/or ventricular), 1 had nonspecific ST-segment changes, and 3 had IVCD (1 had new left bundle branch block, 1 had new right bundle branch block and left anterior fascicular block, and 1 had nonspecific IVCD)</td>
<td>2 had ST-segment elevation, 2 had sinus tachycardia, 1 had first-degree AV block, and 1 had low voltage</td>
</tr>
<tr>
<td>Echocardiogram abnormalities</td>
<td>2 with pericardial effusions and hypokinesis that resolved on follow-up studies; other findings not associated with myo/pericarditis (e.g., left ventricular hypertrophy and mitral valve prolapse) were found in 3 case patients</td>
<td>1 had an effusion</td>
</tr>
<tr>
<td>Cardiac enzymes</td>
<td>None of the 9 whose cardiac enzymes (CK-MB and troponins) were drawn had elevated levels</td>
<td>None of the 5 whose cardiac enzymes (CK-MB and troponins) were drawn had elevated levels</td>
</tr>
</tbody>
</table>

**NOTE.** CK-MB, creatine kinase–myocardial band; IVCD, intraventricular conduction defect.

<sup>a</sup> 10 suspected and 2 probable.

<sup>b</sup> 6 suspected and 3 probable.
depolarization with aberrant conduction in the other. ECG abnormalities included T-wave or ST-segment abnormalities in 7 of the 12, intraventricular conduction defect in 3, and bradycardia (30 beats/min) in 1. Among the 12 case patients with myocarditis or myopericarditis, 2 met criteria for the probable classification on the basis of echocardiogram findings. The other 10 met criteria only for suspected classification on the basis of ECG findings. The echocardiograms from the 2 probable cases demonstrated diminished ejection fraction (42%); apical hypokinesis and a small pericardial effusion was found in one, and inferior hypokinesis and a small circumferential effusion with normal ejection fraction (55%–60%) was found in the other. Both demonstrated resolution of these abnormalities on repeat echocardiography performed 2 and 4 months, respectively, after the initial studies.

Illness was mild in all cases, with no fatal outcomes. However, 9 case patients were hospitalized for evaluation and treatment, with a median hospital stay of 2 days (range, 1–4 days). An additional 4 received treatment in emergency departments. No cardiac biopsies were obtained.

The 9 vaccinees who met the case definition for pericarditis (table 4) included 6 classified as suspected and 3 as probable. All but 1 presented with positional chest pain typical of pericarditis. Four had ECG abnormalities: 2 with ST-segment elevations consistent with pericarditis, 1 with a borderline first-degree AV block, and 1 with diffuse low voltage. Two other patients had persistent tachycardia.

Patients with DCM. Three additional vaccinees met the criteria for DCM (table 3): 2 women and 1 man, 53–56 years of age. All were revaccinees who had similar clinical manifestations recognized within 3 months after vaccination, including insidious onset of fatigue and dyspnea. Two of the 3 had new left bundle branch blocks on ECG and new systolic murmurs. The other case patient had new-onset atrial fibrillation noted on ECG at the initial examination. All 3 had moderate-to-severe left ventricular dysfunction noted on echocardiogram and/or ventriculogram (ejection fractions, 23%–35%). None had evidence of coronary artery disease by either catheterization or adenosine stress test. One had 4 of the 5 cardiac risk factors, including hypertension; the other 2 had hypertension as a single cardiac risk factor. Two of the 3 were obese, and 1 consumed alcohol regularly (a bottle of vodka per week). None had symptoms suggestive of DCM before vaccination.

Myocarditis and pericarditis rates during the 2003 pre-event vaccination program among civilians. We identified 21 patients with myocarditis or pericarditis after 37,901 vaccinations, for an incidence of 5.5 per 10,000 civilian vaccinees during our study period. If only cases classified as probable myo/pericarditis are considered, the incidence of myo/pericarditis in our study population was 1.3 per 10,000 vaccinees (5 of 37,901).

**DISCUSSION**

Myo/pericarditis is a complex clinical entity with variable clinical manifestations and mostly unknown pathogenic mechanisms in humans [23, 24]. Its etiology, incidence, diagnosis, and management remain controversial. However, this article and reports from the US military [36–40] support a causal relationship between smallpox vaccination with the NYCBOH strain and myo/pericarditis. The clinical presentation and severity of civilian myo/pericarditis cases differ from the military experience. Several factors may have influenced these differences.

Inference of a causal relationship between smallpox vaccine and myo/pericarditis is complicated because accurate background rates of myocarditis and pericarditis in the general US civilian population are not known. Few studies assessing overall myocarditis incidence and “vaccinia myocarditis” among military personnel have been published. Karjalainen and Heikkila [41] reported the background incidence of myocarditis of any etiology among Finnish military conscripts to be 0.17 per 1000 person-years (95% CI, 0.14–0.21), or 1.3 cases per 10,000 persons. Halsell et al. [37] found the background incidence of myo/pericarditis among US military personnel for any 30-day period to be 0.21 cases per 10,000 persons (95% CI, 0.19–0.23). The incidence of “vaccinia myocarditis” among Finnish military vaccinees was found by Karjalainen et al. [12] to be 1 per 10,000 persons. The US military during the 2002–2003 smallpox vaccination program experienced rates ranging from 0.8 to 1.6 per 10,000 persons at >30 days after vaccination [37, 39, 40]. Accurate background DCM rates are not known. One review by Dec and Fuster [42] estimates annual incidence in the range 0.5–0.8 per 10,000 population for all ages. Karjalainen and Heikkila [41] reported the incidence of DCM among Finnish military conscripts to be 0.02 per 1000 person-years (95% CI, 0.006–0.03).

Prospective studies performed by the Finns and Swedes among military conscripts [43, 44] reported new ECG abnormalities among asymptomatic conscripts shortly after receipt of smallpox vaccination, suggesting vaccinia-related subclinical myocarditis. These studies established the plausibility of an association between one (unnamed) strain of vaccinia and myocarditis but did not address the pathophysiology of myocarditis. Other reports of cardiac complications after smallpox vaccination suggest that myocardial inflammation, with a predominance of mononuclear cells in autopsy histopathology [2, 9, 38], is caused by immunologic reactions [3, 4, 5, 14, 38, 40, 45]. Others suggest direct viral involvement [12, 13, 46]. One study recovered virus from the heart of a child who died of myocarditis, although cross-contamination at the time of autopsy may have occurred [11].

Most of our knowledge of the pathogenesis of infectious myocarditis comes from mouse models. Virus is rarely isolated
from the myocardium; immune-mediated rather than direct viral injury is believed to be the predominant pathogenic mechanism in most cases of myocarditis in humans [47]. None of our cases had myocardial biopsies or fatal outcomes; histopathologic data are not available. Myocardial tissue from 4 military vaccinees with myocarditis during the 2002–2003 vaccination program was available for histopathologic examination. Direct viral invasion of the myocardium was not evident [40]. Viremia after vaccination with NYCBOH strain vaccinia is either nonexistent or at least very rare [48].

The clinical manifestations of our 21 case patients with myo/pericarditis were mild. This differs from the experience of the military patients, who had more-severe cardiac involvement with elevated cardiac enzymes, impressive clinical findings, and abnormal ECGs and echocardiograms [34–37]. Military and civilian vaccinees are not comparable in the 2003 program. There are marked differences in age, sex, and circumstances of intense physical exercise or stress between the 2 populations, which may have influenced the incidence and clinical manifestations of myo/pericarditis. Most civilian vaccine recipients (75%) and case patients with myo/pericarditis (86%) were re-vaccinees. In contrast, Arness et al. [39] found a 7.46 unadjusted risk among primary vaccinees in the US military and suggest that their findings support a causal relationship between smallpox vaccination and myo/pericarditis only among primary vaccinees. Differences in the incidence found among the different services (Army, Air Force, Navy/ Marine Corps, and Coast Guard/Merchant Marine) may reflect variability between the services in case ascertainment and detection. Case ascertainment differed between civilians and the military as well and might explain some differences. Despite the differences in populations and case ascertainment, the incidence of probable myo/pericarditis associated with smallpox vaccination in the civilian population (1.3 per 10,000) is similar to that in the military.

Follow-up echocardiograms and ECGs and the ability to return to previous activities did not identify residual cardiac damage or progression to DCM among military patients with myo/pericarditis [40]. All 12 civilian case patients with myo/pericarditis returned to their previous activities; no evidence of residual cardiac damage was documented at follow-up. One vaccinee had resolution of symptoms of probable pericarditis but documented recurrent pericarditis 9 months after initial symptom onset [49]. No civilian myo/pericarditis case progressed to DCM.

DCM has not been previously reported in association with smallpox vaccination. Given the now-documented association between smallpox vaccine and myo/pericarditis [37–40], it is biologically plausible that the 3 case patients who we identified may have been the result of the progression of vaccinia-induced myocarditis to DCM. However, none had symptoms or evidence of acute myocarditis after vaccination before the recognition of DCM. None of the 3 underwent endomyocardial biopsy; the diagnostic yield of this procedure with regard to DCM is limited, and it is not routinely recommended [41]. Because baseline DCM rates for the general population are uncertain and the number of cases is small, the epidemiologic significance of the 3 DCM cases detected among civilian smallpox vaccinees remains uncertain [50].

The large surveillance studies that assessed the rates of adverse events after smallpox vaccination campaigns conducted in the United States in 1968 and earlier did not include queries about cardiac conditions [18–22]. Myo/pericarditis had not been viewed as associated with the NYCBOH vaccinia strain. If the threat of intentional smallpox release continues, future US smallpox vaccination programs should include education material, appropriate clinical follow-up, and adequate surveillance to detect myo/pericarditis, as well as the other known adverse events. Surveillance should also allow for long-term follow-up, to assess the persistence of cardiac-related symptoms and the development of DCM. Unlike the military experience, in which first-time vaccinees had quantitatively greater risks, we did not detect obvious risk factors that might identify persons at increased risk of developing myo/pericarditis. Future postvaccination safety surveillance will be important to better characterize vaccinia-associated myo/pericarditis and DCM.

### SMALLPOX VACCINE ADVERSE EVENT MONITORING AND RESPONSE ACTIVITY

Members of the Smallpox Vaccine Adverse Event Monitoring and Response Activity who participated in the activity were: Charles Vitel, Eric Mast, Thomas Torok, Monica E. Parise, La Mar Hasbrouck, Madeline Y. Sutton, Sara Critchley, Bruce Tierney, James Sejvar, Rosaline Dhara, Herschel Lawson, Patricia Galloway, Anne Moore, Andrew Kroger, Michael Deming, Christine Robin Curtis, Nidhi Jain, Mona Marin, Francisco Averhoff, Kristina Ernst, Kirsten Ernst, Kathleen Fullerton, Daniel Fishbein, and Meredith Reynolds.

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