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Letters to the Editor

Cautious Interpretation of Data Regarding Myopericarditis Associated With Smallpox Vaccination

We congratulate Cassimatis et al. (1) for their excellent review of myopericarditis associated with smallpox vaccination. We suggest a different interpretation of the data regarding some important issues.

First, the true incidence of myopericarditis secondary to smallpox vaccination with Dryvax (NYBOH strain) vaccine remains unknown and it is likely higher than the quoted rates of one case per 9,360 (1), 10,000 (2), or 12,819 (3) vaccinations, which represent the recognition of overt, symptomatic myopericarditis in a highly selected, very fit military population. We suspect myopericarditis is underdiagnosed in this population because of the wide spectrum of presenting clinical symptoms and signs that confound accurate diagnosis, the potential for minimal or no-symptom cases that could lead to missed cases, and the characteristics of young, volunteer, military personnel who could conceivably overlook or minimize symptoms that do not limit their service duties. A higher rate of myopericarditis is supported by the 2% to 3% incidence of electrocardiographic changes after smallpox vaccination in Swedish military personnel in the 1960s (4,5). Importantly, a higher incidence of myopericarditis would likely be recognized if mass smallpox vaccination were applied to the general population with higher prevalence rates of cardiovascular and immunologic disease, in an attempt to protect citizens against smallpox bioterrorism.

Second, the long-term sequelae of myopericarditis due to smallpox vaccination remain unknown. Subclinical or overt abnormalities due to vaccinia viremia or its immunologic responses, such as direct viral toxicity or immune-mediated myocyte necrosis, persistent myocardial inflammatory infiltrates, or development of myocardial fibrosis, may manifest years later, with ventricular dysfunction, conduction system abnormalities, or sudden death. Although almost all recently vaccinated patients with myopericarditis recovered clinically, the possibility of residual low-grade myocardial inflammation and fibrosis cannot be excluded or prevented.

Third, endomyocardial biopsy probably is of greater than "limited utility" after smallpox vaccination. We advocate endomyocardial biopsy for all patients with suspected new-onset ventricular dysfunction (ejection fraction ≤45%) and symptoms of heart failure after smallpox vaccination. The rationale for this approach is the documentation of possible steroid responsive eosinophilic myocarditis, which occurred in one recent patient after smallpox vaccination, and the need to exclude uncontrolled vaccinia virus replication within the myocardial that may be responsive to immune globulin. Endomyocardial biopsy under echocardiographic guidance is a relatively safe procedure in experienced hands and may provide a definitive actionable diagnosis in high-risk patients (6).

It is a profound tragedy that vaccination against an eradicated disease whose elimination marked the single greatest human success against a communicable disease is now required for U.S. soldiers because of the threat of biowarfare. Current smallpox vaccine appears to carry significant risks of serious adverse events. The true incidence and long-term sequalae of current smallpox vaccine remain unknown.

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doi:10.1016/j.jacc.2004.10.006

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REPLY

We appreciate the comments on our review (1) of myopericarditis associated with smallpox vaccination. The recently published rates of myopericarditis may indeed be underestimates, for they are based on reporting of clinical encounters with symptomatic patients from an occupational cohort, as we noted previously (2). To better assess the true incidence rate, we will soon enroll volunteers in a prospective trial of smallpox vaccinees with baseline and follow-up electrocardiography, laboratory markers, and questionnaires.

We described the need to follow patients diagnosed with postvaccinial myopericarditis to establish whether long-term sequelae exist (1), and we recently have published the results of such follow-up (3). On the basis of these data, long-term sequelae are