Eczematous Skin Disease and Recall of Past Diagnoses: Implications for Smallpox Vaccination

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Background: Persons with atopic dermatitis or eczema, regardless of disease severity or activity, may develop eczema vaccinatum if they or their close contacts receive the smallpox vaccine. According to current recommendations, a preexposure vaccination program should identify these persons and exclude them from participating.

Objective: To determine the prevalence of diagnosed atopic dermatitis or eczema in a defined population and assess the sensitivity of screening questions to identify patients who have received these diagnoses.

Design: Population-based prevalence survey and telephone interview.

Setting: 14 ZIP code regions in Wisconsin.

Patients: Persons given a diagnosis of atopic dermatitis or eczema in 2000 and 2001 were identified from a population-based cohort. Persons with a history of atopic dermatitis diagnosed since 1979 were eligible for the telephone survey.

Measurements: Prevalence of diagnosed atopic dermatitis or eczema; proportions of respondents able to recall a past diagnosis of atopic dermatitis, eczema, or recurrent rash.

Results: The prevalence of atopic dermatitis or eczema diagnosis in 2000 or 2001 was 0.8%. At least 2.4% of the cohort would be ineligible for smallpox vaccination because of active skin disease in themselves or household members. Among 94 adult respondents with atopic dermatitis, 55 (59%) correctly self-reported skin disease. Seventy-nine (60%) of 133 household contacts of adults with atopic dermatitis correctly reported the presence of skin disease in a household member. Parental recall of skin disease in children with atopic dermatitis was 70% (123 of 177).

Conclusions: Identifying dermatologic contraindications to smallpox vaccination by relying only on a self-reported history of rash illnesses is likely to miss a substantial proportion of individuals who should not receive smallpox vaccine in a preexposure vaccination campaign.

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Context
People with a history of atopic dermatitis or eczema in themselves or their close contacts should not receive pre-exposure smallpox vaccination because of the risk for eczema vaccinatum.

Contribution
This population-based study suggests that about 40% of people would not correctly report that they or a close contact has these skin conditions even though medical records confirm that they do.

Implications
Relying on patient self-report about dermatologic contraindications to smallpox vaccination would miss a substantial proportion of people with true contraindications.

–The Editors

adults (24, 25), and most estimates have been based on self-reported data (18, 20, 22, 23, 26, 27). We sought to determine the prevalence of clinically diagnosed eczema and atopic dermatitis in a defined population and to estimate the proportion of this population with contraindications to smallpox vaccination. Self-reported medical conditions may be used to screen potential recipients of smallpox vaccine; thus, we attempted to determine how well adults could accurately recall past diagnoses of atopic dermatitis for themselves, their children, or other members of their household.

This study was reviewed and approved by the Marshfield Clinic Institutional Review Board. All survey respondents provided verbal informed consent before the telephone interview.

Methods
Marshfield Clinic is a multispecialty group practice providing comprehensive care at 40 regional locations in north-central Wisconsin. Physicians at Marshfield Clinic use the Marshfield Enhanced Charting and Coding Acquisition (MECCA) system to record diagnoses and procedures in a computerized medical record. MECCA stores diagnoses and other patient information using standardized, clinically relevant terms, often with more precision than International Classification of Diseases, 9th Revision (ICD-9) codes. MECCA terms are selected by physicians for each patient encounter and are then automatically mapped to traditional ICD-9 diagnosis codes.

Population
The central region of the Marshfield Epidemiologic Study Area (MESA) includes 14 ZIP codes within the primary service area of the Marshfield Clinic. MESA was established in 1991 as a resource to facilitate population-based health research by linking residency in a defined population with the extensive electronic medical data resources of Marshfield Clinic (28). Marshfield Clinic provides medical care for nearly the entire residential population in this ZIP code region. Previous validation surveys of the MESA population indicate that Marshfield Clinic data systems capture more than 95% of the people, 100% of deaths, 94% of hospital discharges, and 92% of outpatient visits (28). According to the U.S. Census, 53,753 people were living in the central region of MESA in 2000. Residents of MESA are mostly non-Hispanic white persons (97.4%). With the exception of residents of the city of Marshfield (population, 19,000), most MESA residents live in areas that meet the federal definition of “rural” (population < 2500).

Case Ascertainment
Case ascertainment for prevalence estimation focused on current MESA residents in whom atopic dermatitis or eczema had been diagnosed in 2000 or 2001. We selected patients given a diagnosis with one of five MECCA lexicon terms—atopic dermatitis; atopic eczema; dermatitis, atopic; eczema; or eczematous dermatitis—on two or more occasions separated by at least 60 days. We excluded patients with a diagnosis of nummular eczema, dyshidrotic eczema, or focal (hand/ear) eczema because these conditions have not been identified as risk factors for eczema vaccinatum.

Ascertainment of diagnoses was restricted to a 2-year period because MECCA was not universally used at Marshfield Clinic before 2000. However, ICD-9 diagnosis codes are available in Marshfield Clinic automated records dating back to 1979. The ICD-9 code for atopic dermatitis (691.8) is specific for that diagnosis, but the ICD-9 code for eczema (692.9, unspecified dermatitis) is nonspecific. The latter includes many other types of dermatitis (for example, contact dermatitis, photodermatitis, seborrheic dermatitis) and therefore could not be used to estimate the prevalence of eczema before the implementation of MECCA in 2000.

Medical Record Review
To assess the validity of the MECCA terms for atopic dermatitis and eczema, we manually abstracted medical records for a randomly selected sample of 100 patients given a diagnosis with the selected MECCA terms. Records were also reviewed for a random sample of 100 MESA residents in whom unspecified dermatitis (ICD-9 code, 692.9) was diagnosed from 2000 through 2001 during two or more medical encounters separated by at least 60 days, but who did not have a MECCA diagnosis code for eczema or atopic dermatitis. Although no specific diagnostic test is available for atopic dermatitis or eczema, several groups of researchers and clinicians have developed various criteria lists for the diagnosis of atopic dermatitis (17, 22, 29). Recurrent pruritic skin lesions, a personal or family history of atopy, and early onset of symptoms are criteria common to all of these classification schemes. Data on lesion struc-
tecture, symptoms, and history of asthma and allergy were abstracted from patient charts.

Prevalence of Atopic Dermatitis and Eczema

For this study, we defined prevalence as the proportion of MESA residents on 31 December 2001 who had a history of physician-diagnosed atopic dermatitis or eczema (on two or more visits ≥ 60 days apart) in 2000 and 2001. Population counts from the 2000 U.S. Census for the MESA ZIP codes were used as the denominators for all rate calculations. Age- and sex-specific prevalence estimates and 95% CIs were calculated (30).

Telephone Survey

We conducted a telephone survey to determine the proportion of individuals who could accurately recall a history of atopic dermatitis or eczema for themselves, their children, or another household member. We selected an additional group of patients with more remote diagnoses for this survey so that we could assess the relationship between recall of skin disease and time elapsed since the most recent diagnosis. Current MESA residents were eligible for this survey if they had a history of atopic dermatitis diagnosis (ICD-9 code, 691.8) on two or more occasions separated by at least 60 days since 1979.

Eligible patients with atopic dermatitis were divided into three groups. The first group comprised children younger than 18 years of age on 1 July 2002. The telephone survey was administered to a parent or guardian of these children. The second group was composed of adult patients with atopic dermatitis who were the sole adult listed on their Marshfield Clinic billing accounts. The third group consisted of adult household contacts of adult patients with atopic dermatitis. We initially identified household contacts through Marshfield Clinic billing account numbers, which usually represent family members living in the same household. Residential addresses were then manually reviewed to ensure that these individuals were true household contacts of the patient.

Potential respondents were invited to participate in a short survey about immune-related medical conditions. Questions about diagnosis of asthma, hay fever, rheumatoid arthritis, diabetes, and food allergies were included to blind participants to the specific purpose of the study. Respondents were asked about a history of atopic dermatitis, eczema (pronounced by the interviewer as both ek’zē-mah, or an “itchy rash that was coming and going for at least 6 months” (23).

Statistical Analysis

To assess the potential utility of different screening questions, we calculated the proportions of participants in each survey group who could accurately recall various combinations of the following: diagnosis of atopic dermatitis, diagnosis of eczema, or history of recurrent rash. Generalized additive models (31) and logistic regression were used to determine whether the time since last diagnosis of atopic dermatitis influenced recall. To select the appropriate representation of time since last diagnosis in logistic regression models, we examined graphical plots and accompanying statistical tests derived from generalized additive models, with time since last diagnosis entered as a nonparametric term. For each type of respondent (parent, patient, household contact), we fit a logistic regression model and generated predictions within the observed range of values for time since last diagnosis. Generalized additive models were fit by using S-PLUS software (Insightful Corp., Seattle, Washington), and logistic regression analyses were performed by using SAS software (SAS Institute, Inc., Cary, North Carolina).

Role of the Funding Source

Funding was provided through a contract with the Centers for Disease Control and Prevention (CDC). All data collection and analysis were performed at the Marshfield Clinic Research Foundation. Authors from the CDC were involved with the design and conduct of the study and the decision to submit the manuscript for publication.

RESULTS

Case Ascertainment

According to the MECCA files, 419 MESA residents had two or more diagnoses of eczema or atopic dermatitis separated by at least 60 days from 2000 through 2001. Two hundred seventy-seven (66.1%) of these 419 patients received at least one of their diagnoses from a dermatologist. Patients also commonly received their diagnosis from pediatricians (34.8% of patients), family practitioners (17.4%), internists (16.9%), and allergists (8.6%). According to Marshfield Clinic billing accounts, there were 881 household contacts for these patients, and the average household size was 3.02 persons (range, 1 to 10).

Medical Record Review

Written confirmation of eczema, eczematous dermatitis, or atopic dermatitis diagnoses was found in 97 of the 100 charts reviewed for patients with MECCA diagnostic codes for eczema or atopic dermatitis. Sixty-three percent of this sample also had documentation of pruritus, erythema, and scaling skin lesions in their charts, and 90% had at least two of these three criteria documented. A family history of asthma or atopy was recorded for 33% of these patients, and a personal history of asthma or atopy was noted for 37%.

We reviewed medical records for an additional 100 patients who had at least two ICD-9 diagnoses of unspecified dermatitis but did not have a MECCA diagnosis code for eczema or atopic dermatitis. Four patients had written diagnoses of either eczema or atopic dermatitis in their medical records.

Prevalence of Atopic Dermatitis and Eczema

The prevalence of active atopic dermatitis and eczema was similar for males and females and was highest among children younger than 5 years of age (Table 1). The overall
prevalence of these conditions among MESA residents was 0.8%. Given an average household size of 3, preexposure smallpox vaccination would be contraindicated in at least 1 in 42 (2.4%) MESA residents who either have a recent history of atopic dermatitis or eczema or are household contacts of such persons.

Telephone Survey
Six hundred thirty-three MESA residents were eligible for the telephone survey (Figure 1). We reviewed medical records for 44 of these individuals as part of the validation described earlier, and all had a documented diagnosis of atopic dermatitis or eczema. Participation rates for the telephone survey ranged from 85% to 90% among persons successfully contacted. We could not contact 145 persons (23%) during the survey period. Contact rates were lower among the adults selected for the adult patient interview (57%) than among those selected for the parent–guardian interview (86%) or the household contact interview (84%). In the adult patient interview group, the persons contacted were older and more likely to be female than the persons who could not be contacted, but the length of time since last diagnosis of atopic dermatitis did not differ between those contacted and those who could not be contacted (data not shown).

The accuracy of recall in all survey groups was lowest for the question about a history of atopic dermatitis diagnosis and highest for the question on eczema diagnosis (Table 2). The greatest sensitivity was provided by a positive response to questions about a history of any one of the following: atopic dermatitis diagnosis, eczema diagnosis, or history of an “itchy rash that was coming and going for at least 6 months.” However, the combination of these three questions did not identify 30% to 40% of individuals with two or more diagnoses of atopic dermatitis.

Time since the last diagnosis of atopic dermatitis influenced the ability of survey participants to accurately recall past diagnoses of atopic dermatitis or eczema or previous rashes (Figure 2). Similar patterns in predicted recall were observed for parents and patients in relation to time since last diagnosis. A sharp decline followed by a gradual decline was evident in these groups. Among household contacts, predicted recall declined modestly and gradually.

Table 1. Prevalence of Atopic Dermatitis or Eczema in the Marshfield Epidemiologic Study Area on 31 December 2001, Based on Diagnoses in 2000 and 2001*

<table>
<thead>
<tr>
<th>Age</th>
<th>Males</th>
<th></th>
<th>Females</th>
<th></th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Cases</td>
<td>Prevalence</td>
<td>Cases</td>
<td>Prevalence</td>
<td>Cases</td>
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<tr>
<td>y</td>
<td>n</td>
<td>%</td>
<td>n</td>
<td>%</td>
<td>n</td>
</tr>
<tr>
<td>0–4</td>
<td>54</td>
<td>3.0</td>
<td>45</td>
<td>2.7</td>
<td>99</td>
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<tr>
<td>5–9</td>
<td>30</td>
<td>1.6</td>
<td>27</td>
<td>1.5</td>
<td>57</td>
</tr>
<tr>
<td>10–19</td>
<td>16</td>
<td>0.4</td>
<td>33</td>
<td>0.8</td>
<td>49</td>
</tr>
<tr>
<td>20–39</td>
<td>23</td>
<td>0.3</td>
<td>40</td>
<td>0.6</td>
<td>63</td>
</tr>
<tr>
<td>40–59</td>
<td>27</td>
<td>0.4</td>
<td>67</td>
<td>0.9</td>
<td>94</td>
</tr>
<tr>
<td>≥60</td>
<td>26</td>
<td>0.6</td>
<td>31</td>
<td>0.6</td>
<td>57</td>
</tr>
<tr>
<td>Overall prevalence (95% CI)</td>
<td>0.7% (0.6%–0.8%)</td>
<td>0.9% (0.8%–1.0%)</td>
<td>0.8% (0.7%–0.9%)</td>
<td></td>
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</tbody>
</table>

* Atopic dermatitis and eczema cases identified with Marshfield Enhanced Charting and Coding Acquisition diagnostic terms in electronic medical records (see text for full description of methods).
DISCUSSION

Our findings suggest that 30% to 40% of individuals at risk for developing eczema vaccinatum after smallpox vaccination might not be identified by using a screening tool based on self-reported data only. An even greater proportion of persons with a remote history of eczematous skin disease may be missed because of declining recall over time. The question on eczema diagnosis emerged as the most sensitive single screening question in all survey groups, but a combination of questions about atopic dermatitis diagnosis, eczema diagnosis, and history of rash portion of persons with a remote history of eczematous skin disease may be missed because of declining recall over time. The question on eczema diagnosis emerged as the most sensitive single screening question in all survey groups, but a combination of questions about atopic dermatitis diagnosis, eczema diagnosis, and history of rash appeared to provide the best recall.

We did not evaluate the specificity of the questions in a sample of persons without a history of diagnosed atopic dermatitis to determine how many people might be incorrectly excluded from vaccination. However, in a preexposure setting, smallpox vaccine screening procedures should emphasize sensitivity over specificity because a false-positive screen (that is, no vaccination) currently poses no elevated risk for smallpox acquisition. Vaccination recommendations and screening procedures may change rapidly if a single case of smallpox is identified anywhere in the world.

Our study has several limitations that must be considered when the results are being interpreted. We assessed patient recall under the guise of a telephone survey about immune-related medical conditions, and patient recall of past eczematous skin disease may be better in the context of impending smallpox vaccination. In addition, our population is mainly rural and white, and the survey results may not be generalizable to more ethnically diverse or urban populations. Finally, although the overall survey participation rate was high, we could not contact 30% of adults younger than 30 years of age. In the group of adult patients we contacted, recall was generally lower among adults younger than 30 years of age than among older adults. If we had been able to contact more of the young adults in our sample, our recall rates may have been even lower than those we reported.

In our study sample, the prevalence of eczematous skin disease appears to be lower than some other published figures. Data from other epidemiologic studies suggest that the prevalence of eczema in children ranges from 0.3% to 20% (18, 20, 22–24, 27). The American Academy of Dermatology estimates that the prevalence of eczema or atopic dermatitis is approximately 10% in U.S. infants and 3% in the general population (19). Many of these estimates are based on self-reported data in which eczema is defined as an “itchy rash that was coming and going for at least 6 months” (23). Such self-reported information without confirmation of a physician diagnosis increases the potential for misclassification and overestimation of prevalence rates (20). In this study, we used specific MECCA diagnosis codes to identify cases from electronic medical encounter data, and we validated a sample of these diagnoses by abstracting medical records. Cases of nummular eczema, dyshidrotic eczema, and localized eczema were also excluded from our prevalence calculations to provide a more specific estimate of the number of patients who would be at greatest risk for developing eczema vaccinatum after smallpox vaccination.

The proportion of MESA residents with active atopic dermatitis or eczema is probably greater than 0.8%. The reported rates only include individuals who sought medical attention at Marshfield Clinic for their skin symptoms in 2000 and 2001, and they do not reflect undiagnosed cases of atopic dermatitis or eczema in MESA or cases diagnosed before the study period. The rates also do not include persons with a history of atopic dermatitis or eczema who moved into the MESA region but never received a diagnosis from a Marshfield Clinic physician. Although most residents of MESA receive nearly all of their health care from Marshfield Clinic, previous validation studies suggest that Marshfield Clinic data systems do not capture 8% of outpatient visits each year (28).

In our prevalence analysis, we identified persons at risk for complications from smallpox vaccination because of recently active eczematous skin disease only; however, preexposure vaccination is also contraindicated in persons with a remote history of these skin conditions (5). We could not identify all persons with remote diagnoses because the ICD-9 code for eczema is nonspecific; thus, the total proportion of MESA residents in whom preexposure vaccination would be contraindicated is probably much larger than our minimum estimate of 2.4%. For example, in 2000–2001, the proportion of patients receiving a diagnosis with ICD-9 codes 691.8 (atopic dermatitis) or 692.9 (unspecified dermatitis) who had eczema or atopic

<table>
<thead>
<tr>
<th>Reported History</th>
<th>Parent–Guardian Interview (n = 177)</th>
<th>Adult Patient Interview (n = 94)</th>
<th>Adult Household Contact Interview (n = 133)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atopic dermatitis diagnosis, n (%)</td>
<td>36 (20)</td>
<td>26 (28)</td>
<td>16 (12)</td>
</tr>
<tr>
<td>Eczema diagnosis, n (%)</td>
<td>106 (60)</td>
<td>47 (50)</td>
<td>61 (46)*</td>
</tr>
<tr>
<td>Itchy, recurrent rash lasting ≥6 mo, n (%)</td>
<td>66 (37)</td>
<td>36 (38)</td>
<td>35 (26)</td>
</tr>
<tr>
<td>Atopic dermatitis or eczema, n (%)</td>
<td>114 (64)</td>
<td>51 (54)</td>
<td>66 (50)</td>
</tr>
<tr>
<td>Atopic dermatitis, eczema, or recurrent rash (95% CI), %</td>
<td>70 (63–76)</td>
<td>59 (49–69)</td>
<td>60 (52–68)</td>
</tr>
</tbody>
</table>

* One participant declined to answer this question.

Table 2. Recall of Dermatologic Diagnoses and Symptoms by Parents or Guardians of Children with Atopic Dermatitis, Adult Patients with Atopic Dermatitis, and Adult Household Contacts of Adult Patients with Atopic Dermatitis
may have received a diagnosis of either atopic dermatitis or eczema since 1979. If that assumption is valid, it is possible to estimate the total number of persons who would be ineligible for smallpox vaccine because of eczematous skin disease in themselves or a household member. On the basis of an average household size of 3 in the MESA population, preexposure smallpox vaccination would be contraindicated in approximately 14% of residents.

The heightened concern about intentional release of smallpox has generated a new debate on the risks and benefits of voluntary preexposure vaccination as opposed to the current policy of ring vaccination after an exposure (1–3, 9). While the threat and scope of a potential smallpox attack are unknown, rare but serious risks, including death, are associated with smallpox vaccination. Thus, a preexposure vaccination campaign must accurately identify individuals and their close personal contacts who are at risk for developing vaccine-related complications. Individuals with a history of atopic dermatitis or eczema are at risk for eczema vaccinatum. As the number of individuals vaccinated in the present campaign increases, historical data suggest that cases of eczema vaccinatum will occur. However, as of 10 April 2003, more than 31 000 civilian health care workers have been vaccinated (32), and no cases of eczema vaccinatum have been reported to the CDC (Strikas R. Personal communication). In addition, over 250 000 Department of Defense operational forces and health care workers have received a primary smallpox vaccination, and no cases of eczema vaccinatum have been reported as of 10 April 2003 (6, 33). To minimize the risk for eczema vaccinatum, an effective prevaccination screening procedure is needed to identify persons with active or inactive eczematous skin disease.

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