ORIGINAL ARTICLE

Optimal Bandaging of Smallpox Vaccination Sites to Decrease the Potential for Secondary Vaccinia Transmission Without Impairing Lesion Healing

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OBJECTIVE. To assess the optimal method for covering smallpox vaccination sites to prevent transmission of vaccinia.

DESIGN. Randomized, nonblinded clinical trial.

SETTING. Tertiary care medical center.

PARTICIPANTS. Vaccinia-naive and vaccinia-experienced volunteers.

INTERVENTIONS. After vaccination, study participants were randomized to receive 1 of 3 types of bandage: gauze, occlusive with gauze lining, or foam. Vaccination sites were assessed every 3 to 5 days until the lesion healed. During each visit, specimens were obtained from the vaccination site, the bandage surface before removal, and the index finger contralateral to the vaccination site and were cultured for vaccinia. Time to lesion healing was assessed.

RESULTS. All 48 vaccinia-naive and 47 (87%) of 54 vaccinia-experienced participants developed a vesicle or pustule at the injection site 6-11 days after vaccination. Fourteen (14%) of 102 participants had bandage cultures positive for vaccinia. All but 1 of these vaccinia-positive cultures were of a bandage from participants randomized to the gauze bandage group, and all but 3 were of bandages from vaccinia-naive participants. No finger-specimen cultures were positive for vaccinia. One episode of neck autoinoculation occurred in a vaccinia-naive individual who had vaccinia recovered from his gauze bandage on multiple visits. The foam bandage was associated with more local adverse effects (skin irritation and induration). The time to healing did not differ among the bandage groups.

CONCLUSIONS. The potential for transmission of vaccinia from a vaccination site is greater if the site is covered by gauze than if it is covered by occlusive or foam bandages. Use of an occlusive bandage with a gauze lining is the best choice for coverage of smallpox vaccination sites because of a reduced potential for vaccinia transmission and a lower reactogenicity rate. Bandage choice did not affect vaccination lesion healing.

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With the reintroduction of smallpox vaccination in 2002 after threats of bioterrorism,[1] questions quickly arose regarding the risk of transmission of the live vaccinia virus from recently vaccinated persons to close contacts.[2] Because vaccinia virus actively replicates at the inoculation site, the Centers for Disease Control and Prevention recommended that the site remain covered with a bandage until the vaccination lesion scab had fallen off. Because of the potential for close contact with high-risk patients, healthcare workers were advised to cover the vaccination site with a gauze pad covered by a semipermeable occlusive bandage.[3] For persons other than healthcare workers, a simple gauze bandage was recommended. Although occlusive bandages have been thought to reduce the degree of viral shedding outside the bandage,[4] their potential to lead to maceration and delayed healing of the vaccination site has caused their use to be questioned.[5,6]

Studies that compared different bandages with respect to the risk of transmission of vaccinia and their impact on lesion healing are limited, and, to our knowledge, only one randomized study that examined different vaccination site bandages has been published to date.[7] However, this prior study only examined the degree of viral shedding outside the bandage for vaccinia-naive individuals and at only one time point after vaccination. The purpose of the present study was to directly compare 3 different types of vaccination site bandages over time among both vaccinia-naive and vaccinia-experienced volunteers with respect to recovery of vaccinia, reactogenicity, tolerability, and ease of use.

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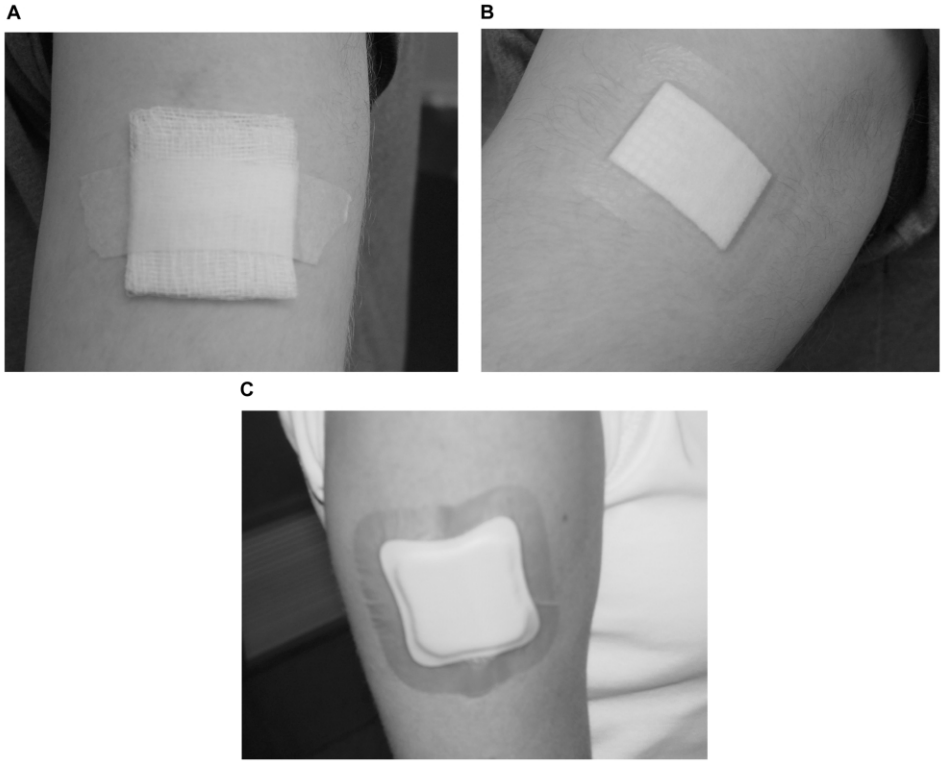

FIGURE 1. Bandages used to cover smallpox vaccination sites. *A,* Gauze bandage (Curity Gauze Sponges Sterile, Kendall Healthcare) attached with a single strip of adhesive tape. *B,* Occlusive semipermeable bandage (OpSite, Smith and Nephew). *C,* Foam hydrocellular bandage (Allevyn Adhesive, Smith and Nephew).

METHODS

Study Design

This study took place at Vanderbilt University Medical Center, a tertiary care medical center. Healthy adults aged 18 to 49 years were eligible for enrollment in this randomized, open-label trial. Approval was granted for this study by the Vanderbilt University institutional review board, and human experimentation guidelines of the US Department of Health and Human Services and Vanderbilt University were followed. Eligible volunteers were classified on the basis of prior smallpox vaccination history into 1 of 2 exposure groups: vaccinia-naive, if the volunteer was 18-33 years of age with no prior history of smallpox vaccination and no vaccination scar, and vaccinia-experienced, if the volunteer was 34-49 years of age with a prior vaccination scar or a record of prior smallpox vaccination. Volunteers were excluded if they had any of the conditions noted in the Appendix. All volunteers underwent a comprehensive screening process, as described elsewhere.[8]

To eliminate volunteers with potential risk factors for ischemic cardiac events, we excluded persons with a history of myocardial infarction or ischemic heart disease, angina, congestive heart failure, cardiomyopathy, cerebrovascular event, or other heart conditions who were under the care of a physician. Persons with an immediate family member who had a history of ischemic heart disease before the age of 50 years or who were estimated to have a 10% or greater risk of myocardial infarction or coronary death within the next 10 years were also excluded.[9] All volunteers underwent electrocardiography (ECG) analysis at baseline to ascertain whether there had been prior ischemic heart disease.

Vaccine Specifics and Vaccination Methods

Eligible volunteers were vaccinated with a 1 : 5 dilution of smallpox vaccine (Sanofi Pasteur).[8] The vaccine was diluted with sterile water and administered to the deltoid area via scarification by 15 punctures with a bifurcated needle.[10]

Vaccination Site Bandages and Site Care

After vaccination, each volunteer was randomized to receive 1 of 3 types of vaccination site bandage: a 5 × 5-cm gauze bandage (Curity Gauze Sponges Sterile, Kendall Healthcare) attached with a single strip of adhesive tape, a 6.5 × 5-cm semipermeable occlusive bandage with a gauze lining (OpSite Post-Op, Smith and Nephew), or a 7.5 × 7.5-cm foam hydrocellular bandage (Allevyn Adhesive, Smith and Nephew) (Figure 1). Randomization was stratified by prior smallpox vaccination history. Bandage changes were performed by the study staff using the assigned bandage until the vaccination

site scab had fallen off. Volunteers were trained about bandage removal and application in the event an unscheduled bandage change was needed. Sterile gloves and bandages were provided, and attention to hand hygiene after bandage contact was stressed.

Follow-up Assessments

Volunteers were seen every 3-5 days for scheduled bandage changes and assessment of vaccine responses and adverse events. The development of a vesicle or pustule at the injection site 6 to 11 days after vaccination indicated that the vaccination was successful.[8,10] At each follow-up visit, study staff inspected and measured the vaccination site vesicle or pustule and the surrounding erythema and induration. Volunteers were questioned at each follow-up visit about the presence of any adverse events and were instructed to note in a diary daily oral temperatures and the presence and severity of various local and systemic symptoms for at least 2 weeks after vaccination until symptom resolution.

Volunteers were actively screened at each visit for the development of chest pain, dyspnea, or peripheral edema, and all positive responses were evaluated by symptom assessment, physical examination, cardiac enzyme measurement, and ECG analysis, if indicated. Follow-up visits occurred until the vaccination lesion was deemed healed by the study staff. Additional clinic visits at 1 month and at 2 months and a telephone interview at 6 months were conducted to evaluate volunteers for any delayed adverse events. An on-site independent safety monitor promptly reviewed all adverse events.

Culture Methods

Samples for viral culture were obtained from each volunteer every 3-5 days at each scheduled visit. Cotton-tipped swabs wer used to collect specimens from the palmar surface of the index finger on the hand contralateral to the dressing site (the finger sample), from the outer surface of the outer bandage before it was removed (the bandage sample), and from the vaccination site lesion (the lesion sample) at each visit until the lesion was well healed.[4] The finger and bandage samples were collected using saline-moistened swabs that were run back and forth 5 times against the target area (ie, the finger pad or outer bandage surface). To collect the lesion sample, a dry swab was rolled against the vaccination site in one back-and-forth motion, to avoid disruption of the healing process. Study staff changed gloves between the removal of the old bandage and the placement of the new bandage. Specimens were tested for the presence of vaccinia cytopathic effect and plaque formation using the methods described elsewhere.[4,11]

Clinical Data Collection

Demographic information was obtained at the time the volunteer enrolled in the study. At each follow-up visit, data on the number of bandage changes performed by the volunteer since the previous visit and data on concurrent illnesses were collected. Volunteers also completed a questionnaire on local reactions to the bandage and bandage tolerability.

Statistical Analysis

Statistical comparisons were made among the bandage groups, stratified by prevaccination status (naive vs experienced). Categorical variables were compared using Fisher's exact test, whereas continuous variables were compared using the *t* test for normally distributed data and the Wilcoxon rank sum test for nonparametric data. Clinical characteristics were compared among bandage groups using the Kruskal-Wallis test for nonparametric data and analysis of variance for parametric data. Tolerability assessments for each bandage were compared using the Cochran-Mantel-Haenszel test, with adjustment for prior vaccination status. Volunteers without a vaccination site vesicle or pustule were not included in analyses of lesion size, reactogenicity, viral shedding, and lesion healing.

RESULTS

Baseline Characteristics

A total of 102 volunteers were vaccinated (48 vaccinia-naive and 54 vaccinia-experienced). The mean age ($\pm$SD) of the vaccinia-naive cohort was 24.2 $\pm$ 3.9 years, whereas that of the experienced cohort was 42.7 $\pm$ 4.8 years. Four volunteers (3 vaccinia-naive and 1 vaccinia-experienced) did not complete all follow-up visits, but all volunteers were seen in the clinic for at least 14 days after vaccination, and all but 1 volunteer had a healed vaccination lesion before early study termination. Vaccinia-naive volunteers required a mean ($\pm$SD) of 14.7 $\pm$ 5.6 bandage changes (scheduled and unscheduled), whereas vaccinia-experienced volunteers required 6.9 $\pm$ 4.0 changes ($P < .001$). No statistically significant difference was found in the mean number of bandage changes among the bandage groups within each cohort (vaccinia-naive or vaccinia-experienced) (Table 1).

Vaccination Success

After vaccination, 100% (exact 95% confidence interval, 94%–100%) of vaccinia-naive volunteers and 87% (exact 95% confidence interval, 75%–95%) of vaccinia-experienced volunteers developed a vaccination site vesicle or pustule ($P = .01$). No significant differences were found in the rates of vesicle or pustule development among the bandage groups within each cohort (Table 1).

Culture Results

A total of 673 lesion specimens, 623 bandage specimens, and 643 finger specimens were obtained for culture. Vaccinia was recovered from a total of 17 (2.7%) of the bandage specimens; it was recovered from 11 vaccinia-naive volunteers (23%) and from 3 vaccinia-experienced volunteers (6%) (Figure 2). All but vaccinia-positive bandage specimens except 1 were from

TABLE 1. Comparison of Smallpox Vaccination Site Parameters for Vaccinia-Naive and Vaccinia-Experienced Volunteers After Smallpox Vaccination, According to the Type of Bandage Tested

Variable	Vaccinia-naive volunteers (n = 48)				Vaccinia-experienced volunteers (n = 54)[a]			
	Gauze bandage	Occlusive bandage	Foam bandage	P[b]	Gauze bandage	Occlusive bandage	Foam bandage	P[b]
Vaccination success, no. (%) of volunteers	16/16 (100)	16/16 (100)	16/16 (100)	NS	15/18 (83)	16/18 (89)	16/18 (89)	NS
Maximum vaccination lesion size, median (range), mm	17 (8-23)	19 (12-25)	17 (12-21)	NS	13 (6-21)	15 (8-30)	16 (8-31)	NS
Maximum diameter of surrounding erythema, median (range), mm	82 (9-200)	82 (0-200)	84 (30-195)	NS	32 (13-60)	23 (0-45)	55 (0-160)	NS
Maximum diameter of surrounding induration, median (range), mm	54 (0-130)	80 (0-210)	65 (0-150)	NS	40 (0-100)	19 (0-45)	51 (0-140)	.09 (gauze vs occl); .55 (gauze vs foam); .04 (occl vs foam)
Peak lesion titer, mean ± SD, PFU/mL	3.9 ± 1.1	5.6 ± 0.8	5.7 ± 0.7	<.001 (gauze vs occl); <.001 (gauze vs occl); .60 (occl vs foam)	2.3 ± 1.7	2.4 ± 1.9	4.8 ± 1.5	.80 (gauze vs occl); <.01 (gauze vs foam); <.01 (occl vs foam)
Time to peak lesion titer, median (range), d	11 (7-16)	15 (12-16)	13 (7-17)	<.001 (gauze vs occl); .12 (gauze vs foam); .40 (occl vs foam)	8 (3-14)	9 (2-14)	10 (4-21)	NS
Mean time until lesion healed, d	29.9	30.0	32.5	NS	18.4	20.5	22.0	NS
Mean no. of bandage changes (scheduled and unscheduled)	12.8	15.1	16.1	NS	7.4	5.8	7.5	NS
No. (%) of volunteers with a vaccinia-positive bandage specimen at any time after vaccination	10/16 (62)	0/16 (0)	1/16 (6)	<.001 (gauze vs occl or foam)	3/18 (17)	0/18 (0)	0/18 (0)	NS
No. (%) of bandage specimens positive for vaccinia	13/112 (12)	0/117 (0)	1/124 (2)	<.001 (gauze vs occl or foam)	3/82 (4)	0/92 (0)	0/96 (0)	.03 (gauze vs occl or foam)

NOTE. Occl, occlusive bandage; PFU, plaque-forming units.

[a] Data regarding lesion size, erythema, induration, lesion titer, and lesion healing are from vaccinia-experienced volunteers with evidence of a vaccination site a vesicle or pustule (n = 47).

[b] Values are for comparisons between bandage types within each volunteer cohort.

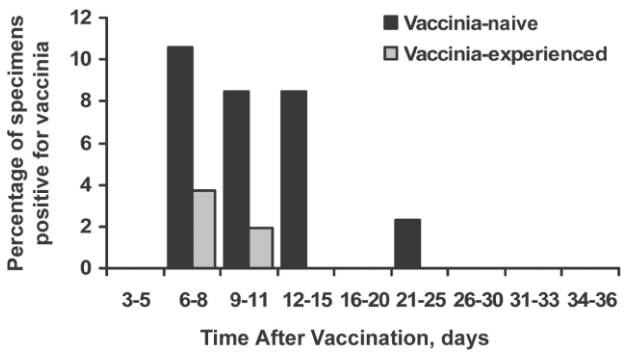

FIGURE 2. Time line of retrieval of bandage culture specimens positive for vaccinia in relation to the day of smallpox vaccination, according to prior smallpox vaccination status of the volunteer.

sites covered by gauze (16 [8.2%] of 194 gauze bandage specimens were culture-positive; $P < .001$ compared with other bandages). Vaccinia was recovered from the outer bandage surface after vaccination from 10 (62%) of 16 vaccinia-naive volunteers and 3 (17%) of 18 vaccinia-experienced volunteers randomized to the gauze bandage group ($P = .007$). Three vaccinia-naive volunteers randomized to the gauze bandage group had vaccinia-positive bandage specimens on 2 consecutive visits. The other vaccinia-positive bandage specimen was collected from a vaccinia-naive volunteer with a site covered with a foam bandage. Vaccinia was never recovered from the outer surface of the occlusive bandages. None of the finger samples were positive for vaccinia.

Peak titers of vaccinia recovered from the vaccination lesion were significantly higher in vaccinia-naive volunteers (5.1 ± 1.2 $\log_{10}$ plaque-forming units per mL) than in vaccinia-experienced volunteers who developed vaccination site vesicles or pustules (3.2 ± 2.0 $\log_{10}$ plaque-forming units per mL; $P < .001$). Among vaccinia-naive persons, peak lesion titers were significantly lower in those with gauze bandages than in those with sites covered by either occlusive or foam bandages (Table 1). However, among vaccinia-experienced volunteers who developed clinical vaccination site vesicles or pustules, peak titers were significantly higher in those with foam bandages than in those with either occlusive or gauze bandages.

Reactogenicity

Local induration or erythema of the vaccination site occurred in 47 vaccinia-naive volunteers (98%) and 46 vaccinia-experienced volunteers (85%) ($P = .02$). When stratified by exposure cohort, no significant differences were noted in the maximum vaccination lesion size or maximum erythema size among the bandage groups (Table 1). Among vaccinia-experienced volunteers who developed vaccination site vesicles or pustules, however, the maximum induration size was significantly smaller in the occlusive bandage group than in the foam bandage group. Maximum induration size did not differ among the bandage groups among vaccinia-naive volunteers. The time to maximum erythema size, time to maximum induration size, and time to lesion healing did not differ significantly among the bandage groups in either cohort. No statistically significant differences in the proportion of volunteers who reported local or systemic symptoms were detected among the bandage groups in either the vaccinia-naive or vaccinia-experienced cohorts.

Tolerability Assessments

Compared with the other bandage groups, significantly more vaccinia-naive volunteers who received the foam bandage reported that their bandage had fallen off before lesion healing (69%; $P = .02$). Vaccinia-experienced volunteers with the foam bandage reported a higher frequency of skin irritation (61%; $P = .03$). Volunteers in the gauze bandage group more frequently reported loosening of the bandage than did those in the occlusive bandage group ($P = .03$). No significant differences were found among the bandage groups with respect to volunteer reports of vaccination site drainage, leakage of drainage onto clothing, loosening of the bandage during showering or sleeping, or the need to scratch the dressing.

Satellite Lesions and Autoinoculation

Suspected satellite lesions were noted in 13 volunteers (9 vaccinia-naive and 4 vaccinia-experienced), but the incidence of satellite lesions did not differ significantly among the bandage groups in each cohort. Six days after vaccination, culture-confirmed vaccinia autoinoculation was detected on the neck of a vaccinia-naive volunteer randomized to receive the gauze bandage (Figure 3). Vaccinia was also recovered from the bandage of this volunteer on days 7 and 11 after vaccination.

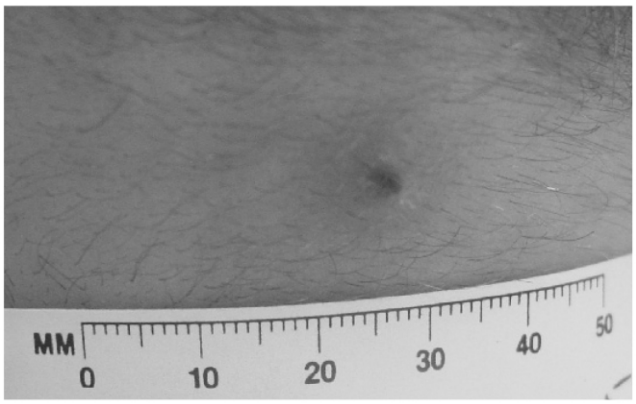

FIGURE 3. Culture-positive autoinoculation lesion that developed 6 days after vaccination on the neck of a previously vaccinia-naive volunteer. The patient's vaccination site had been covered with a gauze bandage. (A color version of this image appears in the electronic edition of the journal.)

Adverse Reactions

Rashes away from the vaccination site were noted in 5 volunteers. Most rashes were localized and self-limited; however, one volunteer developed erythema multiforme 10 days after vaccination that resolved in 5 weeks, and another volunteer noted the development of an erythematous papular rash on her hands 56 days after vaccination. The lesions coalesced and then resolved without scarring. Three volunteers (2 vaccinia-naive and 1 vaccinia-experienced) reported chest pain or tightness, and 5 volunteers (4 vaccinia-naive and 1 vaccinia-experienced) reported shortness of breath within 2 weeks after vaccination. These episodes were self-limited and were not associated with any abnormality on physical examination. Because of the low index of suspicion after detailed examination of these volunteers, further cardiac evaluation was deemed necessary for only 4 of them. ECG findings were normal and unchanged from baseline in all 4 study participants. One vaccinia-naive volunteer noted pleuritic chest pain suggestive of pericarditis; however, the findings of physical examination, ECG analysis, and serum cardiac enzyme measurement were unremarkable. All symptoms resolved without residual sequelae and had not recurred by 6 months after vaccination.

One vaccinia-experienced volunteer developed right facial-nerve palsy 16 days after vaccination and was treated with acyclovir and prednisone. Another vaccinia-naive volunteer noted single dermatomal herpes zoster infection 36 days after vaccination. Finally, an vaccinia-experienced volunteer was noted on routine ophthalmologic examination to have asymptomatic anterior uveitis 17 days after vaccination. Vaccinia was not detected in cultures of specimens from the involved eye. All these episodes resolved completely without residual sequelae.

DISCUSSION

Because all current smallpox vaccines are live virus vaccines and successful vaccination results in local viral replication, secondary transmission of vaccinia is a concern.[2,3] Patients who receive vaccines can shed vaccinia until scab separation, and contact transmission of vaccinia can result in localized and disseminated infections, particularly in immunosuppressed persons. To prevent transmission of vaccinia, the Centers for Disease Control and Prevention recommends covering smallpox vaccination sites with a gauze bandage.[3] Because of their potential exposure to immunocompromised patients, vaccinated healthcare workers are advised to cover the gauze bandage with a second occlusive bandage.[6]

Few investigations have specifically examined retrieval of vaccinia from the surface of vaccination site bandages (Table 2).[4,7,11-13] Before recent vaccination campaigns, studies conducted with recombinant human immunodeficiency virus vaccines in the late 1980s provided the best data on the infectivity of vaccination lesions and the protection provided by standard site dressings. In one such trial in which the vaccination site was covered with gauze and an occlusive bandage, vaccinia was not recovered from the outer bandage surfaces, and no household or sexual contacts developed clinical or serologic evidence of vaccinia exposure.[13] Graham et al.,[11] who used a semipermeable occlusive dressing over the inoculation site, recovered vaccinia from 18.2% of cultures from the dressing surface. The addition of a second occlusive dressing and a sterile gauze pad reduced the rate of positive culture results to 3%. We recently described an even lower rate of recovery from vaccinia-naive volunteers whose vaccination sites were covered by 2 occlusive bandages with an underlying gauze pad; vaccinia was recovered from only 0.65% of bandage specimens.[4]

Studies that directly compare vaccination site bandages are scarce. In a cohort of 41 recently vaccinated healthcare workers (vaccinia naive and vaccinia experienced), increased use of semipermeable dressings was significantly associated with an increased time to scab separation.[14] However, no association was found between increasing use of the semipermeable bandage and the maximum erythema size, the time to maximum erythema size, or time to first pustule appearance.

In another nonrandomized study from the same investigators, cultures of bandage specimens obtained at the time when the amount of lesion exudate was at maximum were obtained from 93 recently vaccinated healthcare workers of unclear vaccination history.[12] Culture (with confirmatory polymerase chain reaction [PCR] testing) detected vaccinia in 10 (7%) of 135 specimens from vaccination sites covered with a semipermeable dressing, compared with 15 (23%) of 64 specimens from sites covered by a nonocclusive gauze dressing. As in the current study, autoinoculation of vaccinia occurred in 1 person whose vaccination site was covered with a gauze bandage. In this study, however, healthcare workers self-selected the covering bandage, which could differ from one visit to the next.

Finally, results from the first randomized trial directly comparing vaccination site bandages were recently reported.[7] One week (range, 6-8 days) after vaccination, 63 vaccinia-naive volunteers were randomized to receive 1 of 3 types of bandages: a self-adhesive bandage, a gauze bandage, or gauze covered by a semipermeable bandage. After 8 hours of routine daily activity, specimens from the outer bandage and the vaccination lesion were obtained for vaccinia culture and PCR testing. Although the volunteers with gauze and a semipermeable dressing reported significantly less discomfort and had a lower percentage of specimens positive for vaccinia by PCR, the results did not significantly differ from those for the other types of bandage.[7]

The present study, in contrast, provides a more detailed comparison of different types of smallpox vaccination site bandages. This study followed up more individuals, stratified study participants by prior vaccination status, and obtained specimens throughout lesion development and healing. In this randomized trial of 3 smallpox vaccination site bandages, use of a simple gauze bandage was associated with a signif-

TABLE 2. Summary of Studies That Examined Rates of Vaccinia Isolation From the Surface of Smallpox Vaccination Site Bandages

Reference	Sample size	Study population	Type(s) of bandage used	Timing of specimen collection	Proportion (%) of specimens positive for vaccinia	
					Bandage specimens, by culture	Other specimens, culture or other test
Cooney et al.[13]	35	Healthy volunteers randomized to receive either recombinant HIV vaccinia or standard vaccinia vaccine	Gauze and transparent semipermeable dressing	Every 3-4 days until lesion healed	0/190 (0)	…
Graham et al.[11]	36	Healthy volunteers randomized to receive either recombinant HIV vaccinia or standard vaccinia vaccine	Transparent semipermeable dressing only, or 2 transparent dressings and gauze	Every 3-4 days until lesion healed, then day 28	Semipermeable: 12/66 (18); transparent: 3/103 (3)	…
Talbot et al.[4]	148	Healthy vaccinia-naive volunteers after vaccination with standard vaccine	Two transparent occlusive dressings and inner layer of gauze	Every 3-4 days until lesion healed, then on day 28	6/918 (0.65)	Specimens from the hands of the vaccinated person: 2/926 (0.22)
Hepburn et al.[12]	93	Hospital employees after vaccination with standard vaccine	Semipermeable dressing with gauze if had direct patient contact, or nonocclusive gauze if no direct patient contact	2-3 times per week, including during the time when the amount of lesion exudate was at maximum (usually days 6-10 after vaccination)	Semipermeable: 10/135 (7.4); nonocclusive: 15/64 (23)	…
Waibel et al.[7]	63	Vaccinia-naive soldiers after vaccinia vaccination	Randomized to receive either self-adhesive or gauze bandage or semipermeable dressing	Once between days 6 and 8 after vaccination obtained, after 8 hours of daily activity	Self-adhesive: 1/4 (25); gauze: 1/4 (25); semipermeable: 0/2 (0)	Vaccinia PCR on specimens: self-adhesive: 4/19 (21); gauze: 4/19 (21); semipermeable: 2/20 (10)[a]
Present study	102	Vaccinia-naive ($n = 48$) and vaccinia-experienced ($n = 54$) persons after vaccinia vaccination	Randomized to receive either gauze, semipermeable occlusive, or foam bandage	Every 3-5 days until lesion healed, then once during days 26-30	Gauze: 16/194 (8.2)[b]; semipermeable: 0/209 (0); foam: 1/220 (0.5)	…

NOTE. HIV, human immunodeficiency virus; PCR, polymerase chain reaction.

[a] $P = .57$ for comparison with other bandage groups.

[b] $P < .001$ for comparisons with other bandage groups.

icantly higher rate of retrieval of vaccinia from the bandage surface, suggesting a higher risk for secondary spread. This association occurred even though peak vaccinia titers from the vaccination lesion were lowest in volunteers with the gauze bandage. In addition, the only documented case of vaccinia transmission (neck autoinoculation) occurred in an individual whose vaccination site was covered by gauze. Use of the foam bandage was associated with more local adverse effects (skin irritation and induration) and was more likely to fall off prematurely, whereas use of the occlusive bandage with a gauze lining was associated with a lower rate of vaccination site induration and a lower frequency of bandage loosening. The rate of development of vaccination site vesicles or pustules, the time to lesion healing, and rates of local or systemic reactions did not differ between the 3 bandage groups. These data suggest that an occlusive bandage with gauze lining is the optimal smallpox vaccination site bandage. Importantly, this study did not find an increased incidence of skin maceration, site irritation, or delay in healing with the occlusive bandage.

There are some potential limitations to this study. Specifically, a systematic evaluation for secondary transmission other than autoinoculation was not performed, thus potentially limiting any conclusions regarding the actual risk of vaccinia transmission. Study participants and staff could not be blinded to bandage assignment, which may have led to some unintentional biases. Finally, PCR testing was not performed on the lesion specimens; doing so may have led to a higher rate of detection of vaccinia.

Transmission of vaccinia from smallpox vaccination sites, although unusual, can lead to significant morbidity if spread occurs in high-risk persons. The use of a bandage to cover the site during active viral replication is prudent. From the results of the current study, it appears that the occlusive bandage with a gauze lining coupled with vaccine education and strict adherence to infection control practices is the optimal strategy to reduce the potential for secondary vaccinia transmission in individuals receiving the smallpox vaccine.

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APPENDIX

EXCLUSION CRITERIA FOR VACCINIA VACCINATION

The exclusion criteria that applied to both the vaccinia-naive cohort and the vaccinia-experienced cohort were the following:

History of autoimmune disease
Use of immunosuppressive medications
History of human immunodeficiency virus infection
History of solid organ or bone marrow transplantation
History of malignancy
History of or current illegal injection drug use
Eczema (active or quiescent)
Current exfoliative skin disorders
Prior vaccination with any vaccinia-vectored or other pox-vectored experimental vaccine
Presence of medical or psychiatric conditions or occupational responsibilities which precluded subject compliance with the protocol
Acute febrile illness (temperature of 38.0°C or higher) on the day of vaccination
Allergies to components of the vaccine
Pregnant or lactating women
Cardiac risk factors (see Methods)
Household or sexual contacts with any of the following conditions: history of or concurrent eczema, a history of exfoliative skin disorders, history of the immunosuppressive conditions noted above, ongoing pregnancy, children younger than 12 months

The exclusion criterion that applied to the vaccinia-naive cohort only was presence of a typical vaccinia scar or history of smallpox vaccination.

The exclusion criterion that applied to the vaccinia-experienced cohort only was lack of confirmation of prior smallpox vaccination.

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