Smallpox Vaccine: Adverse Event Rates, 1968

(number per million vaccinees)

	NATIONAL SURVEY		TEN-STATE SURVEY	
	All primary (i.e., first-time) vaccinees	**Vaccinees ≥ 1 yr old**	**All primary (i.e., first-time) vaccinees**	**Vaccinees ≥ 1 yr old**
Serious, but not life-threatening reactions:				
Inadvertent Inoculation	25.4	27.1	529.2	532.0
Generalized Vaccinia	23.4	17.7	241.5	222.8
Erythema Multiforme	Not Available	Not Available	164.6	131.3
Total number of serious, but not life-threatening reactions:	**48.8**		**935.3***	
Life-threatening reactions:				
Postvaccinal Encephalitis	2.9	2.4	12.3	8.6
Progressive Vaccinia (Vaccinia Necrosum)	0.9	1.0	1.5	1.7
Eczema Vaccinatum	10.4	10.6	38.5	41.5
Total number of life-threatening reactions:	**14.2***		**52.3***	
Deaths:	**1.1***	0.6	1.5	None Reported

***Note: Adverse event statistics cited in document are marked with an asterisk and highlighted.

The table above presents smallpox vaccine adverse event rates from two studies done in 1968 (see references below). The two studies were carried out using different methodologies. In the national survey, information was gathered from seven nationwide sources, with most of the information on adverse reactions coming from the American Red Cross Vaccinia Immune Globulin (VIG) distribution system. Reactions that did not require use of VIG (that is, less severe reactions) are less likely to be reported through this system. In the ten-state survey on the other hand, doctors were directly surveyed to report all adverse reactions, even those considered less severe. For this reason, the ten-state survey data may present a better estimate of the number of people having adverse reactions to the vaccine.

Adverse event rates in the United States today may be higher because there may be more people at risk from 1) immune suppression from cancer, cancer therapy, organ transplantation and other illnesses, such as HIV/AIDS, and 2) eczema or atopic dermatitis. The outcome associated with adverse events may be less severe than previously reported because of advances in medical care. Rates may be lower for persons previously vaccinated.

IN DEPTH:

The National Survey

In this study, patients with suspected complications of smallpox vaccination in 1968 were detected through seven nationwide sources, including the American Red Cross Vaccinia Immune Globulin (VIG) distribution system, state and territorial epidemiologists, pharmaceutical companies producing smallpox vaccine and products used to treat adverse reactions, and the CDC's disease surveillance systems.

The authors identified 572 persons in the U.S. who had confirmed vaccination complications in 1968. Patients receiving VIG from the American Red Cross during 1968 represented the majority (82.5%) of the cases in this study. 68% of the patients were primary vaccinees, 7% were revaccinees, 20% acquired vaccinia through contact with a vaccinee (e.g., a playmate or sibling), and 5% had unknown histories of vaccination. The total number of persons who received smallpox vaccinations in 1968 was determined using CDC's United States Immunization Survey. The estimated total number of vaccinations given during that year was 14,168,000 (including an estimated 5,594,000 primary vaccinations). The incidence rates for adverse events per 1 million vaccinated persons are presented in the table above.

The Ten-State Survey

In this study, practicing physicians in ten states (AL, AK, IA, KY, ME, MD, RI, SC, WA, WV) were surveyed to obtain information about whether they had seen any patients with smallpox vaccination complications in 1968, the types of complications seen, and the age, sex, date of vaccination, vaccination history, and date of onset of complications of each patient. Clinical descriptions of patients were also elicited, and were supplemented by chart reviews of hospitalized patients. The average physician response rate for 8 out of the 10 states was 83.9%. Two of the states had response rates of 49% and 44%.

968 patients who experienced vaccination complications were detected. 84% of the patients were primary vaccinees, 11% were revaccinees, and 5% were contacts of vaccinees; only 6.6% of the patients had received VIG. The total number of persons who received smallpox vaccinations in each of the ten states in 1968 was determined using CDC's National Immunization Survey. The estimated total number of vaccinations given in the participating states during that year was 1,648,000 (including an estimated 650,000 primary vaccinations). The incidence rates for adverse events per 1 million vaccinated persons are presented in the table above.

Differences in Adverse Event Rates

The adverse event rates per million vaccinations are considerably higher in the ten-state study, particularly those for the less severe complications (generalized vaccinia and accidental autoinoculation). The authors of the studies assert that previous research demonstrates that direct survey techniques, such as those used in the ten-state survey, uncover at least 10 times as many cases of generalized vaccinia, accidental inoculation and mild eczema vaccinatum as the VIG distribution system detects. The VIG distribution system also fails to detect many patients with vaccinial encephalitis, because the condition is not treatable with VIG. Most of the life-threatening complications occurring in the ten states, on the other hand, were detected by the national surveillance program.

The authors of the studies state that the national survey statistics should be considered *minimal estimates* of the risks of smallpox vaccination. The authors assert, on the other hand, that a small number of patients included in the ten-state survey may have been vaccinated prior to or after 1968. Those rates, therefore, may *overestimate slightly* the true incidence of complications. Thus, when describing rates of the more severe smallpox vaccine adverse events in 1968 (vaccinial encephalitis, vaccinia necrosum, and eczema vaccinatum), it appears to be preferable to use the range presented by the two studies. The ten-state survey data may present a better estimate of less severe adverse event rates from 1968 (generalized vaccinia and accidental autoinoculation).

1. Lane JM, Ruben FL, Neff JM, Millar JD. Complications of smallpox vaccinations, 1968: national surveillance in the United States. New Engl J Med 1969;281:1201-1208.
2. Lane JM, Ruben FL, Neff JM, Millar JD. Complications of smallpox vaccination, 1968: results of ten statewide surveys. J Infect Dis 1970;122:303-309.

For more information, visit www.cdc.gov/smallpox, or call the CDC public response hotline at (888) 246-2675 (English), (888) 246-2857 (Español), or (866) 874-2646 (TTY)
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