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14. ABSTRACT: In response to threats of bioterrorism, US military personnel began receiving smallpox vaccinations in 2003. Although some adverse health effects associated with smallpox vaccination are well described, much less has been documented about reproductive health outcomes. Smallpox vaccine, as a live-virus product, has caused fetal vaccinia in rare cases when given in pregnancy. The potential for the product to cause pregnancy loss, birth defects, or other birth problems has not been as well documented, especially in the recent era. The objective of this study is to describe the incidence and prevalence of adverse reproductive health outcomes among military members who received smallpox vaccine. Methods are based on evaluating electronic birth records accessed directly from the Standard Inpatient Data Record (SIDR), Standard Ambulatory Data Record (SADR), Health Care Service Record (HCSR); and immunization data obtained from the Defense Eligibility and Enrollment System (DEERS). All data are accessed through formal agreements established by the DoD Birth and Infant Health Registry. Using these data, adverse reproductive health outcomes are assessed, including birth defects, pregnancy loss, and infertility among military families exposed to smallpox vaccine. Analyses are ongoing.					
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INTRODUCTION

The US Department of Defense (DoD) established the Smallpox Vaccination Program for selected military personnel on 13 December 2002.(1) Although there is an adequate body of scientific literature on the adverse health effects associated with smallpox vaccination, much less is described about reproductive health. The US military, charged with maintaining the health of all service members and their families, and with a growing population of women members,(2) has recently developed a strong surveillance system for birth defects.(3,4) This system has been applied in a judicious way to evaluate alleged associations between anthrax vaccination and birth defects, and has developed strong methodology and data validation protocols.(5,6) We are leveraging the system to address the challenging questions surrounding the potential for smallpox vaccine to be associated with adverse reproductive health outcomes.

BODY

Although smallpox vaccination has been recommended in the US military since 2002, long-term health effects of such vaccinations have not been completely described. Of particular concern to young adults in the military population are potential reproductive health effects.

We will describe potential adverse reproductive health outcomes associated with smallpox vaccination in the US military. Primary outcomes include those associated with inadvertent vaccination of women during pregnancy. Other outcomes will be assessed among both women and men vaccinated before pregnancy or attempted conception.

The National Smallpox Vaccine in Pregnancy Registry was established to gather detailed information on all women who were inadvertently vaccinated during pregnancy. Assessment of reproductive health outcomes among men and women vaccinated before pregnancy or attempted conception is being performed through epidemiologic analyses of vaccination and healthcare databases

More than 350 women who inadvertently received smallpox vaccine during pregnancy have been followed through the National Smallpox Vaccine in Pregnancy Registry. No increases in rates of pregnancy losses, preterm births, or congenital malformations have been observed. No cases of fetal vaccinia have been diagnosed to date. Follow-up is ongoing. Among more than 13,000 service members who received smallpox vaccination before having children since 2002, analyses of other reproductive health outcomes are pending.

Preliminary analyses are reassuring that smallpox vaccine has not resulted in adverse reproductive health outcomes when inadvertently administered to pregnant women. These results have been shared with the US Advisory Committee on Immunization Practices and may guide recommendations for use of smallpox vaccine in national emergencies. Results of analyses of other reproductive health outcomes, among both men and women, are pending, but should also be considered important in guiding vaccination policy and risk communication efforts.

KEY RESEARCH ACCOMPLISHMENTS

Publications

- Napolitano PG, Ryan MAK, Grabenstein JD. Pregnancy discovered after smallpox vaccination: is vaccinia immune globulin appropriate? *Am J Obstet Gynecol.* 2004;191(6):1863-1867.
- Ryan MAK, Grabenstein JD, Broder K. Women with smallpox vaccine exposure during pregnancy reported to the National Smallpox Vaccine in Pregnancy Registry - United States, 2003. *MMWR* 2003;52(17):386-8. Reprinted in *Infectious Diseases in Children* 2003;16(6):16.

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2005

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2004

- Ryan MAK, Seward J, Rudy C, Chow S, Stiegman V, Strickler J, Conlin A, Kenyan K, Mulinare J. The National Smallpox Vaccine in Pregnancy Registry. 1st Conference of the CDC National Center on Birth Defects and Developmental Disabilities, 25-31 July 2004, Atlanta, GA.
- Ryan MAK. The National Smallpox Vaccine in Pregnancy Registry. Advisory Committee on Immunization Practices, 24 June 2004, Atlanta, GA.
- Ryan MAK, Aran R, Campbell KM, Chow S, Strickler J, Conlin A, Seward J, Kenyan K, Chaves S, Hutchins S, Mulinare J, Napolitano P, Pierce B, Kovac C, Engler R, Williams J, Grabenstein J. The National Smallpox Vaccine in Pregnancy Registry. San Diego Epidemiology Exchange, 7 May 2004, La Jolla, CA.
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2003

- Napolitano P, Aran R, Ryan MAK, Alexander B, Campbell KM, Grabenstein J, Pierce B, Engler R, Seward J, Mulinare J. The National Smallpox Vaccine in Pregnancy Registry. Annual Conference of the American College of Obstetricians and Gynecologists, 19-22 Oct 2003, San Antonio, TX.
- Aran R, Ryan MAK, Alexander B, Campbell KM, Grabenstein J, Napolitano P, Pierce B, Engler R, Williams J, Seward J, Cano M, Broder K, Mulinare J. The National Smallpox Vaccine in Pregnancy Registry. 43rd Annual Teratology Society Meeting, 21-26 Jun 2003, Philadelphia, PA.

REPORTABLE OUTCOMES

Pending. Research is ongoing.

CONCLUSION

Pending. Research is ongoing.

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4. Ryan MAK, Pershyn-Kisor MA, Honner WK, Smith TC, Reed RJ, Gray GC. The Department of Defense Birth Defects Registry: overview of a new surveillance system. *Teratology* 2001; 64(S1):S26-9
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6. Centers for Disease Control and Prevention. Notice to Readers: Status of U.S. Department of Defense Preliminary Evaluation of the Association of Anthrax Vaccination and Congenital Anomalies. *MMWR* 2002;51(06);127

APPENDICES

N/A

SUPPORTING DATA

N/A