

INFORMATION PAPER

DASG-HCA
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SUBJECT: Pregnancy Discovered After Smallpox Vaccination

1. Purpose. This paper provides information to help women who discover they are pregnant shortly after receiving smallpox vaccination. This paper describes what is known and not known about the value of taking a medication called vaccinia immune globulin intravenous or VIG-IV. Experts disagree about whether taking VIG-IV could help a woman who discovers she is pregnant within a few days after receiving smallpox vaccine. This paper is intended to help women decide what steps are right for them in this unusual situation.

2. Facts.

a. Vaccination & Pregnancy. In the 20th century, smallpox vaccine was given to billions of women around the world. During smallpox outbreaks, health officials intentionally gave pregnant women smallpox vaccine to protect them from lethal smallpox infections.¹ During the New York City smallpox outbreak of 1947, an estimated 173,000 pregnant women were given smallpox vaccine. Today, because smallpox does not occur naturally, pregnant women are exempted from smallpox vaccination.

b. What is Fetal Vaccinia? Most women given smallpox vaccine during pregnancy deliver healthy babies. In very rare cases, the vaccinia virus used in the smallpox vaccine can infect an unborn baby (the fetus). When this happens, a condition called fetal vaccinia occurs.² This usually causes stillbirth or infant death shortly after delivery.³ Stillbirth is the birth of a dead fetus after the 28th week of pregnancy. There is no evidence that smallpox vaccine causes spontaneous abortion (miscarriage). There is no evidence that the smallpox vaccine used in the United States has caused birth defects in the past.⁴ Fetal vaccinia probably occurs if vaccinia virus moves from the mother's bloodstream, across the placenta, to the fetus. If it happens, vaccinia virus gets into a mother's bloodstream usually 7 to 10 days after smallpox vaccination.

c. What is the Risk? In the 20th century, only three cases of fetal vaccinia were reported in the U.S., and only 47 cases around the world. Other cases probably occurred, but were not reported. Because it is so rare, scientists do not know precisely how this condition happens. They do know that during the New York City smallpox outbreak of 1947, no cases of fetal vaccinia were reported, even though about 173,000 pregnant women were vaccinated. CDC estimates that 1 case of fetal vaccinia might occur for every 10,000 to 100,000 pregnant women getting the smallpox vaccine for the first time. Most women given smallpox vaccine during pregnancy would deliver healthy babies.

d. Can a Woman Lower The Risk? One theory is that giving a medication called vaccinia immune globulin intravenous (or VIG-IV) within a few days after vaccination

might reduce the amount of vaccinia virus in the mother's bloodstream and prevent the virus from reaching the unborn baby. This is a theory, not a proven fact. VIG-IV has been given to prevent fetal vaccinia in the past,⁵ but not enough women have been treated to know whether it works or not. Two published studies did not show any value of giving VIG,^{5,11} but these studies were small.

3. What Are a Woman's Choices?

a. We want you to know the facts so you can help guide the care we provide. Fetal vaccinia is possible in women given smallpox vaccine during pregnancy. But the chance of that happening is very small. The CDC says that smallpox vaccination during pregnancy should not ordinarily be a reason to terminate pregnancy.⁶

b. The following sections describe some of the reasons you might want to receive VIG-IV and some of the reasons you might want to decline VIG-IV. Some of these reasons may be more important than others. This is a personal decision based on your personal situation and should be discussed with your doctor.

c. Reasons to Use VIG-IV.

(1) Neutralization. VIG-IV might stop (neutralize) the vaccinia virus and prevent it from getting in the mother's blood, and then into the fetus, where it might cause harm. Nobody knows if this theory is true or not.

(2) Theory. The theory of VIG-IV neutralizing the vaccinia virus is based on commonly accepted scientific principles.

(3) Timing. There might be more value in using VIG-IV if you just received the first (primary) smallpox vaccination in your life. There might be more value if less than 7 to 10 days have passed since you received smallpox vaccine.⁷

(4) Safety. VIG-IV is in a category of medications called antibodies or immune globulins. Antibodies are naturally present in the human body. Millions of pregnant women have been successfully treated for other conditions with antibody injections during their pregnancy without harming the fetus.^{8,9}

(5) Personal Situation. There may be personal reasons for you. For example if you have gone to great effort to become pregnant (such as with in vitro fertilization), you may want to receive VIG-IV.

d. Reasons Not to Use VIG-IV.

(1) Investigational. VIG-IV has not yet gotten a license from the FDA (Food & Drug Administration). This means that not enough scientific evidence is available to know whether VIG-IV is safe and effective in a way to prevent fetal vaccinia. As a result,

VIG-IV is considered “investigational,” and will only be given to you with your consent, after you read more about it.

(2) Timing. The theoretical value of VIG-IV preventing fetal vaccinia decreases as more time passes since your smallpox vaccination. Beyond 10 or 14 days after smallpox vaccination, VIG-IV would be expected to not work. This is because the vaccinia virus would already have gotten into the mother’s bloodstream if it were going to do so.

(3) “Mild” Vaccine. The type of smallpox vaccine used in the United States is considered “milder” than the smallpox vaccine that was used in other parts of the world.¹⁰ By milder, we mean that the US-licensed smallpox vaccine appears to cause fewer serious adverse reactions than other kinds of smallpox vaccine. This difference may account for the low number of fetal vaccinia cases seen in the US, compared to other developed countries.

(4) Side Effects. All medications cause side effects. VIG-IV is given in a solution into the vein (intravenous). With VIG-IV, the most common side effects expected would be mild and temporary symptoms. These might include back pain, headache, muscle pain, itching, malaise, fever, palpitations, and rashes. In rare cases, maybe 1 in 100,000 people, you could have a serious allergic reaction to VIG-IV. These reactions are usually treatable, but there is a small chance the allergic reaction could kill you or your fetus.

(5) The Unknown. There is a small chance that giving VIG-IV could cause problems for the mother or fetus we don’t know about. One way this could happen is if the fetus is already infected when VIG-IV is given. Again, we don’t know for sure.¹¹

e. Natural Course of Pregnancy. We will do everything we can to help you deliver a healthy baby. In the United States, if six women recognize they are early in their pregnancy, one will have a miscarriage due to natural causes. And some babies (2% to 5%) will naturally be born with birth defects.¹² Unfortunately, you too have this risk, regardless whether you received smallpox vaccine or not.

4. How Can I Get Help? The doctors and nurses taking care of you will help explain your situation in more detail and answer your personal questions. Various technical resources are available to help them and you.¹³ You might also want to talk with your family, your friends, or a chaplain or other advisor of your choice.

Notes:

¹ Fenner F, Henderson DA, Arita I, Jezek Z, Ladnyi ID. *Smallpox and Its Eradication*. Geneva: World Health Organization, 1988.
<http://www.who.int/emc/diseases/smallpox/Smallpoxeradication.html>.

² Lane JM, Millar JD, Neff JM. Smallpox and smallpox vaccination policy. *Annu Rev Med* 1971;22:251-72.
CDC. Smallpox vaccine: recommendations of the Public Health Service Immunization Practices Advisory Committee. *MMWR* 1978;27:156--8, 163-4.
CDC. Adverse reactions to smallpox vaccination---1978. *MMWR* 1979;28:265-7.

³ Levine MM, Edsall G, Bruce-Chwatt LJ. Live-virus vaccines in pregnancy: Risks and recommendations. *Lancet* 1974;2:34-8.

⁴ Comparing 1501 children born to women in Iran vaccinated against smallpox during pregnancy and 1976 unvaccinated women, the incidence of club foot was 4.6 per 1000 live births among vaccinated women and 2.5 per 1000 live births among unvaccinated women ($p=0.05$). Club foot is a condition in which the foot is twisted and turned inward. These women received a strain of vaccinia virus potentially more pathogenic (harmful) than the New York City Board of Health strain used in the United States. Naderi S. Smallpox vaccination during pregnancy. *Obstet Gynecol* 1975 Aug;46(2):223-6.

⁵ Of 91 pregnant women treated with VIG, 42 had a “good” outcome, none had an adverse outcome, and the outcomes in the balance are unknown. Feery JB. The efficacy of vaccinia immune globulin: A 15-year study. *Vox Sang* 1976;31(Suppl 1):68-76.

⁶ A CDC website notes that the woman “should be counseled regarding the basis of concern for the fetus. However, vaccination during pregnancy should not ordinarily be a reason to terminate pregnancy.”
www.bt.cdc.gov/agent/smallpox/vaccination/contraindications-clinic.asp

⁷ There is no major difference in risk based on trimester. Levine MM, Edsall G, Bruce-Chwatt LJ. Live-virus vaccines in pregnancy: Risks and recommendations. *Lancet* 1974;2:34-8.

⁸ Thousands of immune-deficient women have received immune globulin IV replacement therapy during pregnancy. Millions of Rh-negative women have received Rho(D)IG during pregnancy.

⁹ Note, in contrast, that varicella-zoster immune globulin (VZIG) is not recommended for pregnant women inadvertently given varicella vaccine, even though a rare condition called congenital varicella syndrome is known to exist.

¹⁰ Fenner F, Henderson DA, Arita I, Jezek Z, Ladnyi ID. *Smallpox and Its Eradication*. Geneva: World Health Organization, 1988.

<http://www.who.int/emc/diseases/smallpox/Smallpoxeradication.html>.

See also Polack MF. Complications of smallpox vaccination in the Netherlands, 1959-1970. International Symposium on Smallpox Vaccine, Bilthoven, 1972. *Symposium Series Immunobiol Standard* 1972;19:235-42.

¹¹ In one case series, 3 of 22 pregnant women given VIG aborted their fetuses, two within a week and one within 5 weeks of vaccination. Sharp JC, Fletcher WB. Experience of anti-vaccinia immunoglobulin in the United Kingdom. *Lancet* 1973;1:656-9.

¹² Stenchever MA, Droegemuller W, Herbst AL, Mishell DR. *Comprehensive Gynecology*, Mosby, 2001: p. 414.

¹³ For additional assistance, contact the following resources:

* Vaccine safety issues, case management, ethical advice: Vaccine Healthcare Center Network, c/o Walter Reed Army Medical Center, Washington, DC, 202-782-0411 (DSN 662)

* Maternal-fetal medicine expertise: Department of Obstetrics & Gynecology, Division of Maternal-Fetal Medicine, Madigan Army Medical Center, Tacoma, WA, (253) 968-1710 or -1252 (DSN 782).

* VIG information for clinicians: US Army Medical Research Institute of Infectious Diseases (USAMRIID), Fort Detrick, MD, 301-619-2257 (DSN 343), 888-USA-RIID.