Centers for Disease Control and Prevention
Clinician Briefing
Pregnancy and Smallpox Vaccination
SARS
May 2, 2003

SMALLPOX

Dr. Walt Orenstein, CDC, Director, National Immunization Program:

***Please note:** Data and analysis discussed in these presentations were current when presented. Data collection and analysis are ongoing in many cases, therefore updates may be forthcoming elsewhere on this website, through publications such as CDC's Morbidity and Mortality Weekly Report or other venues. Presentations themselves will not be updated. Please bear this in mind when citing data from these presentations*

- Smallpox vaccination is contraindicated in women who are pregnant, and women who are vaccinated are urged not to become pregnant within four weeks following vaccination. We have developed a registry for women who are inadvertently vaccinated while pregnant or become pregnant shortly after vaccination. In this week's MMWR we report our experience with three groups: the military, vaccine trials, and the civilian vaccination program. From these programs 103 women were put into the registry.
- In the military program over 52,000 women of child-bearing age were vaccinated, and 85 have been assigned to the registry. Of these, 62 conceived before vaccination and 23 conceived within four weeks following vaccination. We do not yet have data on their outcome, but we understand that to date, no cases of fetal vaccinia have been detected.
- Of the women in the clinical trials, 12 have been assigned to the registry. At the moment we have no outcome data on these women. Each had a negative pregnancy test before she was vaccinated.
- In the civilian program we vaccinated 6,174 women of reproductive age. Six were exposed to a smallpox vaccine during pregnancy. Based on the date of last menstrual period, two of these six were probably pregnant at the time of vaccination, and four became pregnant after vaccination. The two pregnant before vaccination probably became pregnant in the week before vaccination and hence any pregnancy testing on the day of vaccination is unlikely to detect their condition. Two of the six women exposed to the vaccine had miscarriages. The rest are planning to carry their pregnancies to term as far as we know. Because we did not have the products of conception for the two who miscarried, we are unable to determine either histologically or by culture whether vaccinia virus was present.
- There are fewer than 50 cases of fetal vaccinia reported in the medical literature. In the US there have been three cases. In two of the three, the child either died shortly after birth or there was spontaneous abortion. The third had scarring and otherwise appeared to be normal.
- We have tried to make estimates of what the incidence rate of fetal vaccinia may be in the US based on experience between 1967 and 1971 when there was one case among somewhere between 90,000 and 280,000 pregnant women who were vaccinated. We

estimate that this is an extremely rare event. What we are going to do now is look at our materials to see if we can enhance our message and make it more effective.

- At the present time, we have warned women not to get vaccinated if they are pregnant and not to become pregnant within four weeks of vaccination. The Advisory Committee on Immunization Practices has fairly strong recommendations, which include questioning about the possibility of pregnancy before vaccination, asking about the date of the last menstrual period, providing education about fetal vaccinia, counseling women not to become pregnant, recommending abstinence or highly effective contraception, and advising women who believe they might be pregnant to perform a urine pregnancy test on the day of vaccination. We feel our current materials are adequate at the moment. However, we are likely to make some revisions in the next several weeks that we hope will raise consciousness even more.
- It is important to point out that based on fertility patterns in women of about the same age group, we would have expected somewhere between 8 and 12 per 1,000 to have been pregnant if there had been no pregnancy screening whatsoever. The fact that we had 1 per 1,000 suggests that the program that we are currently using is quite effective. So we see no reason to make a change in the program at the moment. However, we will try to enhance our educational materials sometime in the next several weeks.

Questions and Answers:

James August, APSME:

Can you could be a little more specific about what can be done to tighten up the screening process?

Dr. Orenstein:

I think there are potentially several things that could be considered. One is that although none of the civilian cases would have been detected by pregnancy tests on the day of pregnancy, it still may be reasonable to have the tests available at the vaccination sites should there be any questions. Another thing that could be done would be to actually ask the woman for the date of her last menstrual period and whether she had unprotected sex during that period, in which case we would recommend against her being vaccinated. We could offer information on effective contraceptive methods if abstinence is not a possibility, such as hormonal contraceptives being more effective than barrier contraceptives and the like. The military has made a few changes with regard to their questions. I do not know exactly what they are, but there are just a few questions dealing with asking about the last menstrual period, trying again to raise the consciousness of the woman, and giving her a better timeframe for understanding when she might become pregnant and how long she has to avoid becoming pregnant.

SARS

Dr. Tonji Durant, Ph.D., SARS Epidemiology Team Leader:

- This week the Centers for Disease Control and Prevention released an updated interim case definition for SARS, Severe Acute Respiratory Syndrome. Two revisions to the case definition expand the clinical criteria to include or to address the spectrum of disease associated with SARS infection and the lab component. I will go through the clinical criteria of the case definition as well as the laboratory criteria.
- The revised version includes clinical criteria:
  -Asymptomatic or mild respiratory illness
  -Moderate respiratory illness characterized by a temperature of 100.4 or greater, with the issue of subjective fever, and one or more of the clinical findings of respiratory illness, including for example, coughs, shortness of breath, difficulty breathing or hypoxia
  -Severe respiratory illness characterized by a temperature of 100.4 or greater, again, exercising clinical judgment, and one or more clinical findings of respiratory illness as I mentioned before, and additionally, radiographic evidence of pneumonia or respiratory distress syndrome or autopsy findings consistent with pneumonia or respiratory distress syndrome without an identifiable cause.
- Those are the three categories of clinical criteria. We have retained the epidemiologic link in this case definition because most cases of SARS infection have been related to travel exposure and some among contacts.
- In terms of laboratory criteria, we have two case classifications, suspect or probable, and within each of these there may be laboratory criteria, laboratory confirmed negative, or undetermined infection. So classifications of probable and suspect still exist. In terms of confirming laboratory presence of the infection, it includes the detection of antibody of SARS-CoV and specimens obtained during acute illness or greater than 21 days after illness onset, or detection of SARS-CoV RNA by RTPCR confirmed by a second PCR assay using a second aliquot of the specimen and a different set of PCR primers or isolation of SARS-CoV.
- Those are the components of laboratory criteria. But I think it is important for us to clarify what the lab tests are. They are PCR acute serology, chronic serology, or culture for the virus itself. When we say something is laboratory confirmed, we mean there is actually evidence of SARS coronavirus infection. So a laboratory result or finding is evidence of the SARS coronavirus infection via any of these confirmation criteria that I laid out earlier. A laboratory finding does not mean that you have SARS; it indicates a coronavirus infection. A negative PCR or a negative viral culture does not exclude coronavirus infection and is not considered a definitive laboratory result. In these instances a convalescent serum specimen obtained greater than 21 days after illness is needed to determine infection with SARS CoV. And again, all of the SARS CoV assays are now under evaluation.
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Dr. Susan Maloney, CDC, Chief, Epidemiology and Special Studies, Division of Global Migration and Quarantine:

- I would like to discuss travel alerts and travel advisories, first the rationale behind CDC issuance of these travel alerts and advisories, and second, the distinctions or the

differences between the two types of notices. Then I will review the current CDC travel alerts and advisories in place for SARS and discuss in particular recent changes to the Vietnam and Taiwan alerts. This information is all available on the CDC website – www.cdc.gov/ncidod/sars/travel.

- A travel alert is a notification by CDC that an outbreak of disease is occurring in a geographic area. The purpose of the alert is to provide accurate information to travelers and resident expatriates about the status of the outbreak, to help them identify ways they can reduce their risk of infection, and to tell them what to do if they should become ill while they are in the area. In an alert, the risk for the individual traveler is felt to be definable and very limited. For example, transmission has occurred in defined settings associated with specific risk factors such as transmission in a healthcare or hospital setting where ill patients are being cared for. For a travel alert there is no recommendation against nonessential travel to the area.
- In distinction, a travel advisory is notification by CDC that disease is occurring in a region. The purpose of the advisory is to provide accurate information as with the alert, but an advisory also serves to try to reduce the volume of travel to the affected area, which can in turn reduce the risk of translocating the disease to previously unaffected sites. For a travel advisory there is a recommendation against nonessential travel to the area because the risk to the traveler is considered to be higher than for a simple travel alert notice. For example, the risk is increased because there is evidence of community transmission and/or inadequate containment of the outbreak. In short, we have outlined four criteria for instituting alerts and advisories, and these criteria include:

  (1) Transmission and the magnitude and scope of the outbreak in an area affect the decision to issue a travel alert or advisory. We look at both the presence and absence of community transmission and evidence that cases have been exported from the area.
  (2) We look at containment measures. The presence or absence of acceptable outbreak control measures in the affected area will impact the decision to issue an advisory or an alert. Areas where disease is occurring that are considered to have poor containment measures in place may have the potential for higher risk of transmission to exposed persons or translocation to other sites.
  (3) The third criterion is the quality of surveillance. The criterion used is whether health authorities in the area have the ability to accurately detect and report cases and conduct appropriate contact tracing of exposed persons.
  (4) The fourth criterion is the quality and accessibility of medical care. For example, areas where disease is occurring that are considered to have suboptimal infection control procedures or medical services in place or remote locations without access to medical evacuation may be considered to present a higher risk level to the traveler.

- I would also like to outline the criteria for downgrading or removing travel alerts and advisories. To downgrade a travel advisory to a travel alert we need to see adequate surveillance data from the area reported on a regular basis and no evidence of ongoing community transmission for two incubation periods after the date of onset of symptoms of the last case. For SARS this period would be 20 days. To remove a travel alert there

should be adequate surveillance data from the area and no evidence of new cases for three incubation periods after the date of onset of symptoms for the last case. For SARS this period would be 30 days, and there should be limited or no instances of unintentional exported cases from the area.

- Right now the CDC has travel alerts in effect for Hanoi, Vietnam, and Toronto, Canada. And we have travel advisories for Taiwan, Mainland China, Hong Kong, and Singapore.
- The travel advisory that has been in effect for Hanoi, Vietnam, was downgraded to a travel alert on April 29, 2003, and the reasons for this are several. The first is that monitoring by the Vietnamese Ministry of Health indicates that there are no new outbreaks of illness in Vietnam, and there is adequate surveillance for SARS in place. The second is according to Vietnam and the WHO, the onset of symptoms of the last reported case in Vietnam was on April 7, 2003, which is more than 20 days or two SARs incubation periods, and data from the WHO indicate that no new cases of exported SARS illness can be traced to Vietnam.
- A new travel advisory was posted for Taiwan on April 30, 2003, based on the magnitude and scope of the evolving outbreak, which includes a rapid increase in the number of reported suspect and probable SARS cases. In addition there are several cases without apparent links raising concern about community transmission. The Taiwan Department of Health in conjunction with CDC is currently investigating these cases and implementing measures to limit the spread of SARS in Taiwan. CDC advises that people planning elective or nonessential travel to Taiwan may wish to postpone their trips. This travel advisory also states that travelers to Taiwan should be aware of possible restrictions upon arrival in Taiwan. At the time of this notice and through today the Taiwan government has imposed a mandatory 10 day quarantine requirement on all travelers arriving by air from Mainland China, Hong Kong, Vietnam, Singapore, and Toronto.

Questions and Answers:

Dr. L.J. Tan, American Medical Association:

Is there a little more information on the reports about relapses? Do we know that when these people were released and pronounced cured, they were truly viral free, or was it just a premature release, and that is the reason for the relapse reports?

Dr. Umesh Parashar, CDC, Medical Epidemiologist, Respiratory and Enteric Viruses Branch:

We have seen reports in the media from the Associated Press relating to cases, specifically from Hong Kong, in which some patients might have suffered a clinical relapse. At this point there really are no details on how many patients have suffered these relapses, what kind of symptoms they are experiencing during relapses, and other details related to their initial illness or any data on viral shedding or infection during relapses. These are obviously all key questions that we will continue to monitor, but very limited information is available to us at this point.

John Bondage, Federation of State, County and Municipal Employees:

During the last conference call there was some information about theories of transmission, whether it was via a droplet, airborne, fomite, etcetera. Is there any updated information on transmission?

Dr. Parashar:

We continue to look at the role of various modes of transmission including the ones you mentioned. The general feeling based on data that are being reported is that in most instances probably droplet and close contact are the modes of transmission. There are certain instances, such as a cluster in an apartment building in Hong Kong and some other clusters in hospitals, that suggest that there might be other routes of transmission, especially with some patients who are believed to be super spreaders and are highly efficient in transmitting the disease and have caused several secondary cases. But the evidence to support any other role of transmission at this point remains mainly anecdotal and conjectural. So close contact and droplets probably remain key. We are looking at other modes of transmission including airborne and the role of fomites, especially in hospital settings.

James August, American Federation of State, County, Municipal Employees:

Part of my question ties into the previous question about the evaluation. During the last call we raised a number of questions about the adequacy of respiratory protection, in particular guidelines that were being followed with N95 respirators and whether or not a higher level of protection is warranted. I will hold off until we get word on that. There was also during the last call a concern about recommendations to more quickly raise the index of suspicion, if you will, and to isolate and mask patients with respiratory symptoms and what recommendations might be coming out of that. And then as a connected question, as we are talking about worker protection issues, it occurred to me after the last call and it occurs to me now, why isn't the Occupational Safety and Health Administration involved in these calls? And if they are not, what coordination is going on with OSHA?

Dr. John Jernigan, CDC, Co-Leader, SARS Clinical and Infection Control Team:

We still think that the epidemiology of this illness suggests that most transmission occurs through large aerosol drops and through contact, either direct or indirect, and possibly through fomite transmission. We know that the organisms can survive for some period of time on environmental surfaces, so we are concerned about that. You may have seen that in Atlanta today results were released from a new case control study from Hong Kong that suggested that actually surgical masks were protective, which would go along more with droplet aerosol precautions, etcetera. However, there are these episodes, albeit rare, where there are patterns of transmission in which an airborne route of transmission can be ruled out. And specifically these tend to be a recurring thing that we are seeing around aerosol-generating events, such as intubation of patients, and so forth. I think somebody alluded that there might have been a cluster in Canada associated with that, and we are looking at that very carefully. We have a team that is helping investigate that, but we do not have any answers yet. There are some issues

around fit testing, whether the equipment was used appropriately, etcetera. However, in light of that epidemiologic observation, we are considering strengthening the recommendations about respiratory protection around aerosol-generating procedures. In fact we are drafting a new guidance today. So we probably are going to be recommending for those specific situations in which healthcare workers are going to be performing a high risk aerosol generating procedure that higher levels of protection be employed than an N95.

I should make the point that fit testing probably is critically important. There is really not that much meaningful difference in protection between something like an N95, N99, N100 if things are fit tested properly. So fit testing may be crucial, may be the most important thing, more important than going to a higher level of protection. So stay tuned, because the recommendations for protection around aerosol generating events may change. For others, it will not. Again, we think that the vast majority of transmission occurs by large aerosol droplet or contact. I have forgotten the second part of your question.

James August:

Let me follow-up on the first part of the question first, which is that your current recommendations on aerosol generating procedures make a lot of sense, which is to delay any of these procedures unless deemed medically necessary. I think that becomes the key. But as far as fit testing, I am glad you raised it. It is a critically important issue. I have been participating in the CDC Advisory Group on Tuberculosis and updating those guidelines, and there have been a fair number of disparaging remarks made about the need to do fit testing there. I am glad to hear it, but it is contradicting what some of the discussion has been regarding TB precautions.

Dr. Jernigan:

I am basing all my comments on SARS and the epidemiology that we are observing on SARS, so I would rather not get into TB.

James August:

What I am saying is that since we are talking about the same type of respirators and the same type of respiratory program, I am glad that the need for, or the emphasis on, fit testing is being raised here. The second part of my question, again related, is what role does OSHA have in this, because the respirator protection, the respirator program, the fit testing, has already been quantified by OSHA, and I have not seen their participation in these discussions to date.

Dr. Baden:

We do have representatives from NIOSH on the SARS teams. Unfortunately they are not in the room here with us, so I cannot answer more directly about the connection with OSHA. I am sorry for that.

Dr. Jernigan:

Actually I remember what the second part of your question was – identifying patients early. And I would say that I agree that this is critically important for control. I think that recognizing patients early and isolating them is probably the most important factor in controlling this illness. So I think that emergency rooms, ambulatory care clinics-- any place that expects patients to walk in--should be thinking through both the administrative and the logistical measures that are necessary in early recognition. This includes even educating your patients to let you know ahead of time if they have respiratory illness and they think they might have been exposed to SARS; or putting signs in the waiting rooms to say, "If you have a respiratory illness, let somebody know so you can put a mask on"; and having your triage people educated about asking very early, "Are you here for respiratory symptoms?"; and if so, asking quick screening questions about possible exposure to SARS so that appropriate infection control measures can be taken. I think that thinking about that ahead of time, before the first SARS patient walks through your door, is going to save a lot of headache down the road.

Bill Borwegian, Service Employees International Union:

Thanks for all your hard work on this epidemic. I have actually been playing around with the website a little bit trying to get a very clear and concise message to folks on how to do respirator fit testing, and it gets kind of convoluted. The link goes to different places, and to really get to the meat of what you are looking at is very difficult. And my recommendation is to clarify how an employer can do fit testing, perhaps boil it down to a one- or two- page fact sheet as you have done such an excellent job on with all your other information. I think that would be very helpful. I am just trying to make it more practical, more user friendly to explain to people how fit testing is actually done from a logistical standpoint.