

NWX-DISEASE CONTROL & PREVENTI (US)

Moderator: Dale Babcock
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11:00 am CT

Coordinator: Welcome and thank you for standing by.

At this time, all participants are in a listen-only mode. During the question and answer session, you may press star and then 1 on your touchtone phone if you would like to ask a question.

Today's conference is being recorded. If you have any objections, you may disconnect at this time.

I'd now like to turn the meeting over to Dr. Andrew Kroger. You may begin.

Andrew Kroger: Thank you very much. Welcome to Current Issues in Immunization NetConference.

I'm Andrew Kroger. I'm a Medical Officer in the Immunization Services Division of the National Center for Immunization and Respiratory Diseases - or NCIRD at the CDC. And I'll be the moderator for today's session.

To participate in today's program, you need a telephone connection and a separate internet connection.

The learning objectives for this session are: to describe an emerging immunization issue; be able to list a recent immunization recommendation made by the Advisory Committee on Immunization Practices or ACIP; to locate resources relevant to current immunization practice; and to obtain, assess, and apply patient information to determine the need for immunization.

Today is August 12, 2015. We have two topics for today's NetConference. Ms. JoEllen Wolicki, a Nurse Educator in the Communication and Education Branch in the Immunization Services Division in NCIRD CDC, will discuss rotavirus and hepatitis A as presented in the CDC textbook Epidemiology and Prevention of Vaccine-Preventable Diseases -- also known as the Pink Book -- whose 13th edition was published this year.

A question and answer session will follow today's presentation. And we will offer another question and answer session on Thursday, August 20 at 10:00 am Eastern time for those who could not attend today's session or did not have time to ask a question.

Please make a note of the following information -- if you have technical trouble please dial star 0 on your telephone. If you would like to ask a question when we get to that segment, please press star 1 on the phone.

Continuing education or CE credit is available only through the CDC ATSDR Training and Continuing Education online system at www2a.cdc.gov/tceonline/. CE credit for this session today expires on September 14, 2015.

CDC, our planners, and our presenters wish to disclose that they have no financial interests or other relationships with the manufacturers of commercial products, suppliers of commercial services, or commercial supporters.

Presentations will not include any discussion of the unlabeled use of a product or a product under investigational use with the exception of Ms. Wolicki's discussion of the use of rotavirus vaccine in a manner recommended by the Advisory Committee on Immunization Practices, but not approved by the Food and Drug Administration. CDC does not accept any commercial support.

And so now I will turn the microphone over to JoEllen. You may begin.

JoEllen Wolicki: All right, thank you Dr. Kroger. Let's begin with rotavirus disease and vaccines. For those of you following along in the 13th edition of the Epidemiology and Vaccine-Preventable Disease text, the rotavirus chapter begins on page 311.

In 1973, a virus particle was observed in the intestinal tissue of children with diarrhea. By 1980, rotavirus was recognized as the most common cause of severe gastroenteritis in infants and young children in the United States. It is now known that the infection with rotavirus is nearly universal, with almost all children infected by five years of age. In the pre-vaccine era, rotavirus was responsible for 20 to 60 deaths per year in the United States and up to 500,000 deaths from diarrhea worldwide.

The virus was subsequently called the rotavirus because of its similarity in appearance to a wheel. Rota is Latin for wheel. Rotavirus is a double-stranded RNA virus. The virus is composed of three concentric shells that enclose 11 gene segments. The outermost shell contains two important proteins -- VP7, or G-protein, and VP4, or P-protein. VP7 and VP4 define the

serotype of the virus and induce neutralizing antibody that is probably involved in immune protection. From 1996 to 2005, five strains of rotavirus -- G1 through 4 and G9 -- accounted for 90% of the isolates from children younger than five years in the United States. Of these, the G1 strain accounted for more than 75% of isolates. Rotavirus is very stable and may remain viable in the environment for weeks or months if not disinfected.

The virus enters the body through the mouth. And viral replication occurs in the small intestine. Recent evidence indicates that up to two-thirds of children with severe rotavirus gastroenteritis show the presence of rotavirus antigen in serum. Infection may lead to isotonic diarrhea.

The immune correlates of protection from rotavirus are poorly understood. Serum and mucosal antibodies against VP7 and VP4 are probably important for protection from disease. Cell-mediated immunity probably plays a role in recovery from infection and in protection. Recovery from a first rotavirus infection usually does not lead to permanent immunity. After a single natural infection, 38% of children are protected against a subsequent rotavirus infection, 77% are protected against rotavirus diarrhea, and 87% are protected against severe diarrhea. Reinfection can occur at any age. Subsequent infections confer progressively greater protection and are generally less severe than the first.

The incubation period for rotavirus diarrhea is short -- usually less than 48 hours. The clinical manifestations of infection vary and depend on whether it is the first infection or reinfection. The first infection after three months of age is generally the most severe. Infection may be asymptomatic, may cause self-limited watery diarrhea, or may result in severe dehydrating diarrhea with fever and vomiting. Up to one-third of infected children may have a

temperature greater than 102 Fahrenheit. The gastrointestinal symptoms generally resolve in three to seven days.

Rotavirus infection in infants and young children can lead to severe diarrhea, dehydration, electrolyte imbalance, and metabolic acidosis. Children who are immunocompromised because of congenital immunodeficiency or because of a bone marrow or solid organ transplantation may experience severe or prolonged rotavirus gastroenteritis and may have evidence of abnormalities in multiple organ systems, particularly the kidney and liver.

The reservoir of a rotavirus infection is the gastrointestinal tract and the stool of infected persons. Rotaviruses are shed in high concentration in the stool of infected persons. Transmission is by fecal-oral route, both through close person-to-person contact and by fomites such as toys or other surfaces that are contaminated with stool. In temperate climates, the disease is more common during the fall and winter months. In the U.S., before vaccine was available, annual epidemics peaked in the Southwest during November and December and progressed to the Northeast by April or May.

This infection is highly communicable, as evidenced by the nearly universal infection of children by five years of age in the pre-vaccine era. Infected persons shed large quantities of virus beginning two days before the onset of diarrhea and for up to ten days after the onset of symptoms.

This slide shows the enormous disease burden of rotavirus in the United States before vaccines and the routine immunization of infants.

Although most infections -- especially the most severe cases -- occur primarily in young children, adults can also be infected with rotavirus. This slide shows an article about rotavirus infection among elderly adults in two

retirement communities in Illinois in 2011.00. Infection among adults does tend to occur more in the elderly and in adults who are traveling.

Currently, there are two rotavirus vaccines licensed for use in the United States. Both are live, attenuated vaccines. RV5, or RotaTeq, is manufactured by Merck and was licensed by the Food and Drug administration, or FDA, in February 2006. RV5 contains five reassortant rotaviruses developed from human and bovine parent rotavirus strains. RV1, or Rotarix, is manufactured by GlaxoSmithKline and was licensed by the FDA in April 2008. RV1 contains one live strain of live attenuated human strain type rotavirus. Neither vaccine contains preservatives or thimerosal.

In Phase III RV5 clinical efficacy evaluation, conducted in Finland and the US, the efficacy of the three-dose series against G1 through G4 rotavirus gastroenteritis of any severity was 75%, and against severe G1 to G4 rotavirus disease was 98% during the first full rotavirus season after vaccination. Severe rotavirus gastroenteritis is defined by the severity of the fever, vomiting, diarrhea, and changes in behavior. In a large healthcare utilization study evaluating children during the first two years of life, RV5 vaccine reduced the incidence of office visits for rotavirus gastroenteritis by 86%, ED visits or emergency department visits by 94%, and hospitalizations by 96%. The main Phase III clinical efficacy trials of RV1 were conducted in Latin America and Europe. In the Latin American study, the efficacy of the two-dose series against severe rotavirus gastroenteritis to age one year was 85%. In the European study, the efficacy against severe rotavirus gastroenteritis was 96% through the first rotavirus season and any rotavirus gastroenteritis was 87%. In the European study, RV1 reduced hospitalization for rotavirus gastroenteritis by 96% through the second season. Because of similar estimates of efficacy and safety, the Advisory Committee on Immunization Practices does not state a preference for one vaccine product over the other.

Rotavirus vaccination is routinely recommended for all infants without contraindications as you see here on the childhood immunization schedule. The red box highlights the rotavirus vaccine series. Remember when reading the schedule, the yellow bar indicates the vaccine is routinely recommended.

The vaccine should be administered as a series of either two doses of RV1 at ages two and four months, or three doses of RV5 at ages two, four, and six months. The vaccination series for both vaccines may be started as early as six weeks of age. ACIP developed age recommendations that vary from those of the manufacturers. ACIP recommendations state that the maximum age for the first dose of both vaccines is 14 weeks 6 days. This is an off-label recommendation for RV5 since the product information states a maximum age of 12 weeks. The maximum age for any dose of either rotavirus vaccine is eight months zero days. No rotavirus vaccine should be administered to infants older than 8 months 0 days of age. This is an off-label recommendation for both vaccines, because the labeled maximum age for RV1 is 24 weeks, and the labeled maximum age for RV5 is 32 weeks.

ACIP does not define a maximum interval between doses. It is preferable to adhere to the recommended interval of eight weeks. But if the interval is prolonged, the infant can still receive the vaccine as long as it can be given on or before the eight-month birthday. It is not necessary to restart the series or add doses because of a prolonged interval between doses. There are few data of the safety or efficacy of administering more than one dose -- even partial doses close together. ACIP recommends that providers do not repeat the dose if the infant spits out or regurgitates the vaccine. Any remaining doses should be administered on schedule. The minimum interval between doses is four weeks. In addition, ACIP recommends that rotavirus vaccine series should be completed with the same product whenever possible. But we know that sometimes providers do not know the product that was previously

administered, or do not have that product in their inventory. If this occurs, vaccination should not be deferred. In this situation, the provider should continue or complete the series with the product that is available. If any dose in the series was RV5 or RotaTeq or the vaccine brand is not known, a three dose schedule should be followed. Infants documented to have had rotavirus gastroenteritis before receiving the full course of rotavirus vaccination should still begin or complete the two or three dose schedule following the age recommendations. This is because the initial infection may provide only partial protection against subsequent rotavirus disease.

RV5 comes in a manufacturer filled oral dosing tube. RV1 is supplied as a lyophilized vaccine that requires reconstitution. Only the diluent supplied by the manufacturer should be used to reconstitute Rotarix or RV1. Both vaccines are administered orally. There are no restrictions related to eating or drinking, including breastfeeding, after rotavirus vaccine is given. Breastfeeding does not appear to diminish the immune response to rotavirus vaccines. Rotavirus vaccines can be given at the same visit as other routinely recommended vaccines.

In 2014, a review of vaccine administration error reports that were submitted to the Vaccine Adverse Event Reporting System involving rotavirus vaccines was published in the Morbidity and Mortality Weekly Report -- or MMWR. Between 2006 and 2013, there were 39 reports of rotavirus vaccines being injected. Most of these errors were associated with Rotarix vaccine. As you can probably guess, adverse health effects reported included irritability and injection site reactions. In addition, eye splashes were reported during vaccine administration. The healthcare provider was the person most commonly affected. Administering the vaccine slowly into the side of the infant's cheek can decrease the likelihood the infant will spit out the vaccine back at the provider. Staff who administer vaccines, including rotavirus vaccines, should

be knowledgeable regarding proper administration techniques and routes of administration for the vaccines in their facility's inventory.

As with other vaccines, rotavirus vaccine is contraindicated for infants who are known to have had a severe allergic reaction to a vaccine component or following a previous dose of vaccine. Latex rubber is contained in the oral applicator of RV1 or Rotarix, so infants with a severe allergy to latex should receive RV5 or RotaTeq. The RV5 dosing tube does not contain latex. Some post marketing studies of these vaccines have detected an increased risk for intussusception following rotavirus vaccine administration, particularly during the first week following the first dose. As a result of this, in October 2011, ACIP added a history of intussusception to the list of contraindications for rotavirus vaccine. ACIP also added severe combined immunodeficiency -- often abbreviated as SCID -- as a contraindication to rotavirus vaccine in response to reported cases of vaccine-acquired rotavirus infection in infants with SCID.

Limited data are available from clinical trials on the safety of rotavirus vaccines in infants known to be HIV-infected; these infants were clinically asymptomatic or mildly symptomatic when vaccinated. The limited data available do not indicate that rotavirus vaccines have a substantially different safety profile in HIV-infected infants as compared to infants that are not HIV infected. Other considerations, including HIV diagnosis, might not be established by the time the first dose of rotavirus vaccine is indicated. Only 3% or less of HIV-exposed infants in the US will be determined to be HIV infected. And the vaccine strains are considerably attenuated or weakened. Rotavirus vaccine should generally not be administered to infants with acute moderate or severe gastroenteritis. However, infants with mild acute gastroenteritis or other mild illnesses may be vaccinated.

For children with preexisting, chronic gastrointestinal condition, ACIP considers the benefit of vaccination to outweigh the theoretical risks, and vaccination is recommended. We frequently receive questions asking if rotavirus vaccine can be administered through a gastrostomy tube. The manufacturers have not addressed this, but CDC considers administration of rotavirus vaccine via a gastrostomy tube to be acceptable practice. There should be no problem flushing the tub after the vaccine has been administered.

Available data suggests that preterm infants -- those born less than 37 weeks' gestation -- are at increased risk for hospitalization from rotavirus during the first one to two weeks of life. In clinical trials, rotavirus vaccine appeared to be generally well tolerated in preterm infants, although relatively small numbers of preterm infants were evaluated. ACIP considers the benefits of rotavirus vaccination to outweigh the risks of adverse events. ACIP supports vaccination of a pre-term infant according to the same schedule and precautions as a full-term infant, provided the following conditions are met: the infant's chronological age is at least six weeks, the infant is clinically stable, and the vaccine is administered at the time of discharge or after discharge from the neonatal intensive care unit or nursery.

Infants living with persons with immunodeficiency or impaired immune systems can be vaccinated. ACIP believes that the indirect protection an immunocompromised person receives from a vaccinated infant outweighs the small risk associated with transmitting vaccine virus to an immunocompromised household member. We are often asked a similar question about pregnant women. Because the majority of women of childbearing age have pre-existing immunity to rotavirus, the risk of infection by vaccine is very low. And of course, it is always prudent to remind parents and other caregivers and all household members to employ good handwashing

after changing a diaper or otherwise coming in contact with feces of a vaccinated infant.

The Phase III clinical trials of both vaccines were very large -- over 60,000 infants each -- to be able to study the occurrence of intussusception in vaccine recipients as compared to placebo recipients. No increased risk for intussusception was observed for either vaccine. Post-licensure evaluations of RV1 in Mexico identified a low level risk of intussusception in week one after dose one. In Australia, a possible risk was identified with both RV5 and RV1, although based on small numbers of cases. US data on RV5 -- available through February 2010 from the Vaccine Safety Datalink System -- did not identify an increased risk of intussusception, but were not able to exclude a risk of the magnitude observed in these other settings. The VSD was unable to assess RV1 at that time because too few doses had been administered. Monitoring in the United States is ongoing. Parents and health care providers should be aware of possible low-level increased risk of intussusception following rotavirus vaccine.

This slide outlines adverse reactions following vaccination. RV5 recipients had a small but statistically significant increased rate of diarrhea and vomiting in the first week following vaccination as compared to the placebo group. RV1 recipients had a small but statistically significant increased rate of cough or runny nose in the first week after vaccination as compared to the placebo group.

Rotavirus vaccine should be stored in the refrigerator between 35 and 46 degrees Fahrenheit, or two to eight degrees Celsius. Rotarix vaccines have different lot numbers on the vaccine cartons, the diluent, and the box. If space is limited -- and it often is -- frequently there is only one field in an electronic

health record or in the immunization information system. Document the lot number on the box, as the other lot numbers can be determined from this one.

And here are some rotavirus resources for providers and patient information - and for information for patients on rotavirus vaccination.

We will use the rest of our time to discuss hepatitis A disease and vaccine. For those of you following along in the Pink Book, the hepatitis A chapter begins on page 135.

The first descriptions of hepatitis A are generally attributed to Hippocrates. Outbreaks of jaundice, probably hepatitis A, were reported in the 17th and 18th century. Hepatitis A, which was formerly called infectious hepatitis, was first differentiated from hepatitis B in the 1940s. In the 1970s, identification of the virus and the development of serologic testing helped differentiate hepatitis A from the other types of non-B hepatitis. Hepatitis vaccines were licensed in 1995 and 1996.

Hepatitis A virus is acquired by the mouth and replicates in the liver. After ten to twelve days, the virus is present in the blood and is excreted via the biliary system into the feces. Peak titers occur during the two weeks before onset of illness. Although virus is present in serum, its concentration in serum is much less than that in feces. Virus excretion begins to decline at the onset of clinical illness. Most infected persons no longer excrete virus in the feces by the third week of illness. Children may excrete virus longer than adults.

The incubation period of hepatitis A is approximately 28 days, although it can range from 15 to 50 days. The clinical course of acute hepatitis A is indistinguishable from that of other types of acute viral hepatitis. The illness typically has an abrupt onset of fever, malaise, anorexia, nausea, and

abdominal discomfort, dark urine and jaundice. Clinical illness usually does not last longer than two months, although in 10 to 15% of persons may have prolonged or relapsing signs and symptoms for up to six months. The likelihood of symptomatic illness is directly related to age. Children younger than six years of age, about 70% of those infections are asymptomatic. In older children and adults, infection is usually symptomatic, with jaundice occurring in more than 70% of patients.

Humans are the only natural reservoir for the virus. There are no insect or human vectors. Hepatitis A infection is acquired primarily through the fecal-oral route by either person-to-person contact or ingestion of contaminated food or water. There is no seasonal variation in incidence. Viral shedding persists for one to three weeks. Infected persons are most likely to transmit hepatitis A virus one to two weeks before the onset of illness, when hepatitis A virus concentration in the stool is highest.

In 1996, ACIP recommended hepatitis A vaccination for persons at increased risk of disease. Hepatitis A disease rates have been declining since vaccination initiation and since 1998 have been at historically low levels. The rate of hospitalization for hepatitis A in the United States declined more than 68% from pre to post-vaccine era for all age groups. Medical costs for both hospitalization and ambulatory care visits are estimated to have declined by more than 68% from 29.1 to 9.3 billion dollars.

Inactivated hepatitis A vaccines are available from two manufacturers. HAVRIX vaccine is manufactured by GlaxoSmithKline, and Merck manufactures VAQTA. Both are available in two formulations -- pediatric and adult. The pediatric formulation are approved for persons one through eighteen, and the adult formulation is approved for persons 19years of age and older. And this is consistent for both products.

Both hepatitis A vaccine products are highly immunogenic. More than 95% of adults will develop protective antibody within 4 weeks of a single dose, and nearly 100% will seroconvert after receiving two doses. Among children and adolescents, more than 97% will be seropositive within a month of the first dose. In clinical trials, all recipients had protective levels of antibody after two doses.

This table outlines the ages, doses, schedule, and route for both vaccines. The vaccine is a two-dose series for both children and adolescents. These doses should be separated by at least six calendar months. The route of administration is an intermuscular, or IM, injection.

Both vaccines are effective in preventing clinical hepatitis A. The efficacy of HAVRIX in protecting against clinical hepatitis A was 94% among 40,000 Thai children one to 16 years of age who received two doses while living in villages with high rates of disease. The efficacy of VAQTA in protecting against clinical hepatitis A was 100% among 1,000 New York children two to 16 years of age who received one dose while living in a community with a high HAV disease rate.

In 2001, the Food and Drug Administration approved a combination hepatitis A - hepatitis B vaccine. Twinrix is manufactured by GlaxoSmithKline. Each dose of Twinrix contains 720 EL.U. of hepatitis A vaccine, which is equivalent to a pediatric dose, and 20 micrograms of hepatitis B surface antigen protein, equivalent to an adult dose of hepatitis B vaccine. The vaccine is administered in a three-dose series at zero, one, and six months. Appropriate spacing of the doses must be maintained to ensure long-term protection from both vaccines. The first and second doses should be separated by at least four weeks, and the second and third doses should be separated by

at least five months. Twinrix is approved for persons aged 18 years and older and can be used in persons in this age group with indications for both hepatitis A and hepatitis B vaccines.

Single-antigen hepatitis A vaccine may be used to complete a series begun with Twinrix and vice versa. A person 19 years of age and older who receives one dose of Twinrix may complete the hepatitis A series with two doses of the adult formulation of hepatitis A vaccine separated by at least five months. A person who receives two doses of Twinrix may complete the hepatitis A series with one dose of adult formulation hepatitis A vaccine five months after the second dose. A person who begins the hepatitis A series with single-antigen hepatitis A vaccine may complete the series with two doses of Twinrix or one dose of the adult formulation hepatitis A vaccine. What helps to understand this is to remember that Twinrix contains the pediatric formulation of hepatitis A vaccine.

Here is the routine childhood schedule and the hepatitis A immunization recommendations are outlined in the red box.

All children without contraindications should be given hepatitis A vaccine. The first dose is routinely recommended at age one year. Vaccination should be completed according to the licensed schedule. Remember there should be at least six calendar months between the doses and integrated into routine childhood vaccination schedule. Children who are not vaccinated by age two can be vaccinated at subsequent healthcare visits.

States, counties, and communities with existing hepatitis A vaccination programs age two through 18 years of age are encouraged to maintain these programs. In these areas, efforts should focus on routine vaccination of children 12 months of age and should enhance, not replace, ongoing programs

directed at a broader population of children. In areas without existing hepatitis A vaccination programs, catchup vaccination of unvaccinated children aged two through 18 years may be considered. Such programs might especially be warranted in the context of increasing incidents or ongoing outbreaks among children or adolescents.

Adults should be assessed if they are at increased risk for hepatitis A and offered vaccine accordingly. Hepatitis A vaccine is highlighted here on the adult immunization schedule by the red text box. Remember, a purple bar indicates vaccine recommendations are based on risk factors or for certain populations.

Here is figure two of the adult immunization schedule which outlines high risk persons.

This slide outlines the risk groups included in the adult schedule for hepatitis A. Persons at increased risk for hepatitis A should be identified and vaccinated during healthcare visits.

All susceptible persons traveling to or working in countries that have high or intermediate risk of hepatitis A infection should be vaccinated. These areas are in red, blue, and green on this map. Vaccination is not indicated for travelers to countries in which disease rate is low, and these areas are outlined or shown in yellow on this map. Data are not available regarding the risk of hepatitis A for persons traveling to certain areas of the Caribbean. Although vaccine or IG should be considered if travel to areas that have questionable sanitation is anticipated.

The first dose of hepatitis A vaccine should be administered as soon as travel is considered. For unvaccinated healthy persons one through 40 years of age

or younger, one dose of vaccine administered any time before departure can provide adequate protection. The series should be completed following the recommended schedule.

Unvaccinated adults older than 40 years of age, immunocompromised persons, and persons with chronic liver disease planning to travel in 2 weeks or sooner should receive the first dose of vaccine and also can receive immune globulin at the same visit. Administer IG and vaccine using separate needles at different anatomic sites. Pre-vaccination testing may be considered for older travelers or for younger persons of certain populations.

In 2009 ACIP recommended hepatitis A vaccination for all unvaccinated persons who anticipate close person contact -- such as a household contact or regular babysitting -- with an international adoptee from a country of high or intermediate risk during the first 60 days after arrival. The first of the two-dose series should be administered as soon as the adoption is planned -- ideally at least two weeks prior to the arrival of the adoptee.

Other groups that should be offered vaccine include men who have sex with other men, persons who use illegal drugs, and persons who have clotting factor disorders. Persons with occupational risk include only those who work with hepatitis A-infected primates or with hepatitis A virus in a laboratory setting. No other groups have been shown to be at increased risk for hepatitis A infection due to occupational exposure. Persons with chronic liver disease are not at increased risk for acquiring a hepatitis A infection because of their liver disease alone. However, these persons are at increased risk for fulminant hepatitis A and complications should they become infected. Susceptible persons who have chronic liver disease should be vaccinated.

Hepatitis A vaccination is not routinely recommended for healthcare personnel, persons attending or working in child care centers, or persons who work in liquid or solid waste management such as sewer workers or plumbers. These groups have not been shown to be at increased risk for hepatitis A infection based on their occupation. ACIP does not recommend routine hepatitis A vaccination for food service workers, but vaccination may be considered based on local epidemiology and state or local requirements.

Hepatitis A infection produces lifelong immunity so there is no benefit for vaccinating someone with serologic evidence of a hepatitis A infection. But the risk for adverse events following vaccination for these persons is not higher than serologically negative persons.

As a result of this, the decision to conduct prevaccination testing should be based on the prevalence of immunity, the cost of testing and vaccinating, and the likelihood that the testing will interfere with initiating vaccination if needed. Testing of children is not indicated, as the expected prevalence of infection is low. Serologic testing may be cost-effective for adults who were born in or lived for extensive periods in areas with high rates of infection, older adolescents and adults in certain populations -- such as American Indians and Alaskan Natives and Hispanics -- adults in certain groups with high prevalence of infection, and adults 40 years of age and older. Post-vaccination testing is not indicated because of the high rate of vaccine response in children and adults.

As with other vaccines, hepatitis A vaccine should not be administered to persons with a history of a severe allergic reaction (e.g. anaphylaxis) to a vaccine component or following a prior dose of vaccine. Vaccination of persons with moderate or severe acute illness should be deferred until the person is no longer moderate to severely ill.

Most commonly reported adverse reactions following vaccination is a local reaction at the injection site, including pain, redness, or swelling. These reactions were reported by 20 to 50% of recipients. The symptoms were mild and self-limiting.

Hepatitis A containing vaccine should be stored in the refrigerator between 35 and 46 degrees Fahrenheit or two to eight degrees Celsius. We frequently hear about vaccine administration errors related to the wrong formulation being administered to the wrong age group -- so for example, the pediatric formulation administered to an adult and vice versa. Strategies which may help prevent these errors include storing the vaccine formulations separately in the original packaging. When pediatric and adult formulations are mixed together in the same bin or area of the storage area, it is easy for staff to grab and administer the wrong formulation.

Here is a list of hepatitis A resources for providers, parents, and adult patients.

I want to thank you very much for your attention and turn the program back to Dr. Kroger.

Andrew Kroger: Thank you very much, JoEllen. We're now going to move to a question and answer session. And while the queue fills, I'm going to give you some information about continuing education. But if you have a question, please dial star 1 to get into the queue for the Operator, and please be sure that your question is related to today's content.

We will have a recast of this program available on the internet on our Web site at www.cdc.gov/vaccines/ed/ciinc. This will be available the week of

August 17th. The slides will be there as well as the audio portion and other resource information.

For continuing education credit, go to www2a.cdc.gov/tceonline/. The course number for this program is date specific and reads as follows -- E as in Edward C as in cat 2064-081215. So that last part's today's date 081215. You will need this course number when completing CE requirements.

You will also need the verification code, which is ROTA12 with no space, and this applies to today's program only. I'll repeat the verification code, ROTA12 with no space.

CE credit for this program expires September 14, 2015.

I'm going to repeat this information at the end of the question and answer period as well.

So now, let me turn it over to the Operator and let our participants ask the questions they wish to ask. Operator?

Coordinator: At this time, there are currently no questions in the queue. Once again, if you'd like to ask a question press star 1 and record your name.

Andrew Kroger: Ok. Well while we wait for the question to come in, I'll ask Miss Wolicki a question we often receive. It's a rotavirus question. So if the first dose of a rotavirus vaccine happens to be administered as an administration error -- it spilled and there's a partial dose -- does that dose need to be repeated, and when?

JoEllen Wolicki: That's a really good question, Dr. Kroger. We get that one a lot. If the partial dose is due to the provider error, the dose is invalid and should be repeated.

There should be some discretion on the part of the provider to make this determination. If the error is identified the same day, give the repeat dose that day. If a day has passed, then generally for live vaccines we routinely recommend a 28 day waiting period before giving that repeat dose. This can be somewhat problematic though with rotavirus vaccines, since we know we have maximum ages for doses. So we do not want to wait to repeat the dose -- especially if this is the first valid dose. So this is one of those few circumstances where you're not going to wait the 28 days, but administer the dose at an interval as wide as you can make it but earlier than that 15 week zero days of age.

Commented [KA(1)]: This sentence sounds fine to me

Commented [WJ(2)]: I think so but would have to listen to it to be sure.

Andrew Kroger: Thank you very much, JoEllen. That's a very challenging question that we've received and we've spent a lot of time coming up with an answer to that one. So thank you.

Are there any other questions in the queue?

Coordinator: We have several questions in queue. And the first one comes from ().

(): Hi. Thank you for taking my question. Why is Twinrix hep A a pediatric dose but the hep B portion is not?

JoEllen Wolicki: That's a really good question. Thank you so much for it.

So the hepatitis A series is a two-dose series. And the way that they tested Twinrix, they used the pediatric dose because they knew they would be giving three doses, so they tested the pediatric formulation because they knew they would have to give three doses because hepatitis B -- which we're going to talk about a little later on in this series -- is a three-dose series.

So the Twinrix schedule is based off the hepatitis B schedule and that's why the pediatric formulation is in the Twinrix.

(): Thank you.

Andrew Kroger: Thank you very much. We'll take the next question in the queue.

Coordinator: Our next question comes from ().

(): Hi. Thank so much. I've been having to go through CVX codes recently and have come across - keep coming across this hepatitis A adolescent three dose series. I don't ever remember a three dose series for pediatric. Do you know anything about that?

Andrew Kroger: This is Dr. Kroger. I've heard similar questions. When the vaccine was first being in pre-licensure period there was a time when there were some alternate dosing schedules for that vaccine. I don't know if that's why perhaps that's still appearing on some forms. I don't really have a direct answer to your question. Maybe you can send that one to NIP Info and I can kind of hunt it down.

But I do know that we've gotten the question about alternative schedules and sometime it's been an old investigational use. I don't know why that would be showing up on current codes, but - or there are formulations of Twinrix in other countries that are used for other patients, but again I don't see why that would be showing up as a code.

So maybe if you could send that question to NIP Info, we can kind of hunt down what's going on.

(XXXX): Ok I'll do that. Thank you.

Andrew Kroger: Thank you. We'll take the next question.

Coordinator: Next question comes from ().

(XXXXX): Can you tell us why we're not able to give the rotavirus after age eight months?

JoEllen Wolicki: So that's a really good question,. It's because of safety concerns in theoretical risks and the risk of intussusception, and that was the way that the vaccine was tested. So that's why we do not give the vaccine after eight months of age.

(XXXXX): Ok thank you very much.

Andrew Kroger: Thank you. We'll take the next question.

Coordinator: The next question is from ().

(XXXXX): I was just asking about the Twinrix, which you partially answered the question regarding how if the Twinrix is administered, how the hepatitis B portion is affected in terms of the recommendations and the requirements for the children attending school.

JoEllen Wolicki: Twinrix in this country is not licensed for children, so it shouldn't be given to children. We wouldn't necessarily ask you to repeat the dose, but if Twinrix was given to a child, we would say that that was a vaccine administration error.

You should determine how or why that practice happened in your clinic and then put strategies in place to prevent it from happening again, such as maybe moving where it is in the storage unit so it's not easily grabbed next to a pediatric formulation. Or maybe your staff wasn't as knowledgeable about that vaccine and maybe you need to do an education session about it. But in this country, Twinrix should not be given to children.

(XXXXX): Ok. All right. Thank you.

Andrew Kroger: Thank you. We'll take the next question.

Coordinator: Next question is from ().

(): Hello. Can you hear me?

Andrew Kroger: Yes we can hear you.

JoEllen Wolicki: Yes we can () thanks.

(): Excellent, thank you. I just had a question about rotavirus vaccine spacing between other live virus vaccines. Seems like I've read that there's a pretty universal like, you know, if you don't give them on the same day, you give them 28 days apart.

But it also seems like that maybe I've read that does not apply to rotavirus as a live virus vaccine.

JoEllen Wolicki: That's a really great question and we get that one frequently. That spacing that you're talking about, which sometimes we call like the live-live rule, means that live attenuated vaccines need to be given on the same day or separated by

28 days does not apply to oral, to live attenuated vaccines that are administered orally.

So that rule would not apply to rotavirus vaccines.

(XXXXXX): Ok thank you very much.

JoEllen Wolicki: Thank you.

Andrew Kroger: We'll take the next question.

Coordinator: Excuse me. The next question comes from ().

(XXXXXXX): Hello. To piggyback on the Twinrix schedule question from earlier, you said that there's a pediatric dose of hep A in Twinrix because of the third dose schedule of hep B. But the schedule options that were listed were two Twinrix and one adult hep A and one Twinrix and two adult hep A I believe.

Neither of the schedule options have three Twinrixes. And so I was wondering if you could provide a little bit more clarity on the pediatric dose schedule .

JoEllen Wolicki: Sure. That's - I'm sorry if it was - I know Twinrix can be confusing.

So Twinrix itself -- if you're just going to administer Twinrix and all of the doses are going to be Twinrix -- it is a three-dose series, all right? So it's a zero, one, six month series. All right.

But often what happens is that we know that people go from place to place and they go from provider to provider. And they may have gotten a dose of

Twinrix and then the next provider that they go to only has the single component hepatitis A vaccine and does not have Twinrix.

Or maybe they started the series with single component vaccine. They need hepatitis A and hepatitis B and the provider that they're going to does not have Twinrix.

So the schedule that I outlined showed that you can use Twinrix and start a series with Twinrix and complete it with single component vaccine, or you can start with single component vaccine and complete it with Twinrix.

So if you start with one dose of Twinrix, you need two doses of the adult formulation of hepatitis A vaccine to complete it if you have two doses of Twinrix and you need one dose of the hepatitis A vaccine to complete the series. Does that make sense?

(XXXX): Yes. Thank you for the clarification.

Andrew Kroger: Thank you. We'll take the next question.

Coordinator: Next question is from (XXXXXX).

(XXXXX): Hi and thank you for taking my question. We had a patient who is 18 and received his first dose of his hepatitis A at 0.57 ml. And then he turned 19 and the nurse only gave 0.5.

How - would you repeat that first dose to give him full immunity, and how long after the error was caught?

JoEllen Wolicki: That's a great question. So one of the general rules that I always like to remember when I'm talking about vaccines is we always vaccinate based on the age that they are for that visit. So once that child has turned to an adult, you're going to administer the adult formulation.

So it's great that you caught this error.

(XXXXX): Ok.

JoEllen Wolicki: So and it sounds like you've determined how it happened and you're going to put strategies in place to prevent it. So I'm really thrilled about that. Now repeating the dose, yes this considered when you look in the general - ACIP's general recommendations on immunization; this is considered a substandard dose. So it's not enough vaccine. So the dose does need to be repeated.

It can be repeated any time after that dose. You don't have to wait any interval because it is a substandard dose.

Andrew Kroger: Do we have any more questions in the queue?

Coordinator: No at this time there are no further questions.

Andrew Kroger: Let me ask a question we receive commonly about rotavirus vaccine. Can rotavirus vaccine be given down a G-tube?

JoEllen Wolicki: Yes. We get this question a lot, Dr. Kroger. And I'm glad you asked it. So yes, if there are no contraindications in the child -- such as the child is not moderate to severely acutely ill -- the vaccine can be given down a G-tube. Chronic gastrointestinal illness is considered a precaution to rotavirus vaccine,

but often G-tubes are placed in the context of other circumstances, such as an upper airway obstruction.

And in any case, there may be circumstances where the provider decides that the risk of withholding vaccine is too great, even if there is a precaution. So the vaccine can be administered into the G-tube. And we get this question a lot.

Andrew Kroger: Thank you very much for that answer. Are there any more questions in the queue?

Coordinator: One more, and this one comes from ().

(XXXXXX): Hi. My question is about the spacing after the substandard dose. And in a previous webinar, it was mentioned that you have to wait the minimum interval period after an invalid dose. And I thought that JoEllen just said something different. So can you clarify please?

JoEllen Wolicki: Sure. I did say something different. So an invalid dose generally refers to a dose that the error was made in the timing of the vaccine. So the minimum interval wasn't met or the minimum age wasn't met. And so when it's a timing or a schedule error, we recommend that you wait that minimum interval before administering the next dose.

Now, when you give less than the dose, as the example of the pediatric formulation to an adult that is less vaccine than that adult needs and that's what we consider a substandard dose. And the rule is different for those. If it's a substandard dose, the dose can be repeated as soon as possible. There's no waiting period to wait to repeat that dose.

Andrew Kroger: Thank you for those questions. Is there - we'll take one last question, if they're in the queue.

Coordinator: We've got one more question and this one comes from ().

(XXXXXX): Hi. Sorry to beat a dead horse here. I had a previous email from NIP Info on the issue of when an adult is given a pediatric dose of the hepatitis A vaccine, do you revaccinate immediately or wait six months. And the email I'm looking at currently that I received said you may give it immediately if it was the first dose, but if it was the second dose you have to wait six months.

Is the number of the dose truly an issue?

Andrew Kroger: You know, it is, and there's a couple iterations to this over time that we've made some changes to it. First of all, the way that our policy on forecasting the next dose when the invalidation is due to a narrow interval, too short an interval, right? We say you have to forecast one minimum interval after that dose.

But the minimum interval that's used by most of the programs, in the computer programs that we use -- COCASA or most registries -- use the minimum interval that preceded the dose. Well, there is no minimum interval that precedes a first dose. There's no interval before a first dose. It's a first dose.

So we used to say that for hepatitis A you can get away with, if you violate an age on the first dose, you don't have to wait a full six months to give the first dose of hepatitis A vaccine if the person is old enough, you know, has surpassed the minimum age. So that's an example.

We didn't want people to kind of automatically have to put that interval in place. I'll give you a little bit of a teaser. You're going to see some evolution in terms of our how strict we are with invalidating doses kind of akin to what we do with hepatitis B and Pediarix. Sometimes we allow some shortened intervals, just to avoid this process of having to push that dose later and later six months away. Coming in the next general recs, the importance is that the first and the last dose of the series needs to be separated by at least six months. And that's coming.

So in the interest of time, I think we're going to move onto some continuing education information.

First of all, before I talk about this, we're going to have a Q&A session 10:00 am Eastern Time next Thursday, August 20. And we will stay on the line as long as we continue to receive questions for up to an hour.

So now let me get into the CE information. For CE credits, you can see our Web site www2a.cdc.gov/tceonline. The course number, which is date specific, reads as E as in Edward C as in cat 2064-081215. So please note that this date varies by our courses. So this one is August 12, 2015.

The verification code is ROTA12 with no space. Write this down. R-O-T-A no space the numeral one the numeral two. ROTA12.

CE credit expires September 14, 2015.

For help with the online system, available 8:00am to 4:00pm Eastern Time, please dial 1(800)41TRAIN. This corresponds to the number 1(800)418-7246. Or you can email ce@cdc.gov.

You can email immunization questions to us if you did not get to ask them today or if you cannot participate in the question and answer session next week at nipinfo@cdc.gov. And we'll try to respond to these as quickly as possible.

You can also call in your immunization questions at 1(800) CDC-INFO between 8:00am to 8:00pm Eastern Time Monday through Friday.

Additional resources that you can use include the Pink Book. And the Website for the Pink Book is [www.cdc.gov/vaccines/pubs -- P-U-B-S -- /pinkbook/index.html](http://www.cdc.gov/vaccines/pubs--P-U-B-S--pinkbook/index.html). This is available online, or you can purchase a hard copy at a link that you will see at this site, a link for the Public Health Foundation Learning Resource Center.

Our CDC Vaccines and Immunization Home Page is www.cdc.gov/vaccines/default.htm.

Our resource guide for healthcare personnel entitled CDC Immunization Resources for You and Your Patients is listed at www.cdc.gov/vaccines/ed/downloads/imz-resources.pdf.

Follow us on Twitter for immunization news, information, and resources for private and public healthcare personnel. That's at CDCIZLearn on Twitter.

So that concludes our program. I want to thank Ms. JoEllen Wolicki for the presentation covering the two topics in great detail and for answering your questions.

Thank you very much, and have a great day from Atlanta. Goodbye.

NWX- DISEASE CONTROL & PREVENTI (US)
Moderator: Dale Babcock
08-12-15/11:00 am CT
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Coordinator: This concludes today's conference. Thank you for joining us. You may now disconnect.

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