

**NWX-DISEASE CONTROL & PREVENTI**

**Moderator: Andrew Kroger**  
**October 07, 2015**  
**11:00 am CT**

Coordinator: Welcome and thank you for standing by. At this time, all participants' lines will remain on a listen only mode. During the question and answer session, please press star one on your touch tone 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.

And now I would 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 Net Conferences. 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: one, to describe an emerging immunization issue; two, be able to list a recent immunization recommendation made by the Advisory Committee on Immunization Practices or ACIP; three, to locate resources relevant to current

immunization practice; and four, to obtain, apply, and assess the immunization information to determine the need for immunization.

So today is October 7, 2015. We have one topic for today's net conference. Meningococcal presented by Dr. Raymond Strikas, Team Lead in the Communication and Education Branch, Immunization Services Division in NCIRD CDC.

Topic corresponds to the chapter Meningococcal Disease as presented in the CDC text book Epidemiology and the Prevention of Vaccine-Preventable Diseases, also known as the Pink Book whose thirteenth edition was published this year.

A Question and Answer Session will follow today's presentation. Please make a note of the following information. If you have technical trouble, please dial star zero on your telephone, if you'd like to ask a question when we get to that segment, please press star one 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/](http://www2a.cdc.gov/tceonline/). CE credit for this session today expires on November 9, 2015.

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

Presentations will not include any discussions of the unlabeled use of a product or product under investigational use with the exception of Dr Strikas's discussion of the use of Meningococcal Vaccine in a manner recommended by

the Advisory Committee on Immunization Practices but not approved by the Food and Drug Administration.

CDC does not except any commercial support. And now I will turn the microphone over to Dr. Strikas. You may begin.

Raymond Strikas: Thank you very much Dr. Kroger. Welcome to this discussion of Meningococcal disease and the vaccines to prevent it. Meningococcal disease is an acute potentially severe illness caused by the bacterium *Neisseria meningitidis*.

Illness believed to be meningococcal disease was first reported in the 16th century. *Neisseria meningitidis* is a leading cause of bacterial meningitis and sepsis in the United States. It can also cause focal disease such as pneumonia and arthritis.

*Neisseria meningitidis* is also a cause of epidemics of meningitis and bacteremia in sub-Saharan Africa. The World Health Organization has estimated that Meningococcal disease was the cause of 171 thousand deaths worldwide in the year 2000. And although some disease counts have diminished since then, it's still a prominent problem.

Almost all invasive disease by *Neisseria meningitidis* here is caused by sera groups A, B, C, Y, and W. The relative importance of the serogroups depends on geographic location and other factors such as age.

Meningococci are transmitted by droplet aerosol or secretions by the nasopharynx of colonized persons. The bacteria attach to and multiply on the mucosal cells of the nasopharynx. In a small proportion, that is less than one

percent of colonized persons, the organism penetrates the mucosal cells and enters the bloodstream.

The bacteria spreads through the blood to many organs. In about 50 percent of bacteremic persons, the organism crosses the blood-brain barrier into the cerebrospinal fluid and causes purulent meningitis. An antecedent upper respiratory infection or URI may be a contributing factor.

The incubation period of meningococcal disease is 3 to 4 days, with a range of 2 to 10 days. Symptoms include abrupt onset of fever, meningeal symptoms, hypotension, and rash. The case fatality rate 10 percent to 15 percent but up to 40 percent meningococemia or blood born infection.

Meningitis is the most common presentation of invasive meningococcal infection and results from hematogenous dissemination of the organism.

Meningeal infection is similar to other forms of acute purulent meningitis, with sudden onset of fever, headache, and stiff neck, often accompanied by other symptoms, such as nausea, vomiting, photophobia or eye sensitivity to light, and altered mental status. Meningococci can be isolated from the blood in up to 75 percent of persons, 75 percent of persons with meningitis.

Meningococcal sepsis is the bloodstream infection, also called meningococemia, occurs without meningitis in five percent to 20 percent of invasive meningococcal infections. This condition is characterized by abrupt onset of fever and a petechial or purpuric rash, often associated with hypotension, shock, acute adrenal hemorrhage, and multiorgan failure.

Less common presentations of meningococcal disease include pneumonia in five percent to 15 percent of cases, arthritis in about two percent, otitis media

in one percent, and epiglottitis in less than one percent. This is the hand of a child with meningococcal sepsis. The child has disseminated intravascular coagulation or clotting and is at risk of losing this limb.

This is an adult with meningococcal sepsis who will lose the right arm because of the tissue not being oxygenated secondary to blood clotting. Risk factors for the development of meningococcal disease include deficiencies in the terminal common complement pathway, functional or anatomic asplenia, and underlying chronic disease.

Certain genetic factors such as polymorphisms in the genes for mannosebinding lectin and tumor necrosis factor may also be risk factors. Household crowding and both active and passive smoking are associated with increased risk as are persons who have had antecedent viral infections.

Early studies in the United States demonstrated that blacks and persons of low socioeconomic status were at higher risk for meningococcal disease than other persons. However, race and low socioeconomic status are likely markers for differences in factors such as smoking and household crowding than inherent risk factors for this disease.

As disease incidence has decreased, differences by race have also decreased and no difference in disease incidence exists now between blacks and whites. During outbreaks, bar or nightclub patronage and alcohol use have also been associated with higher risk for disease.

Microbiologists working with *Neisseria meningitidis* isolates are at increased risk of infection and should be vaccinated. Cases of meningococcal disease, including at least two fatal cases, have been reported among microbiologists.

These persons have worked with *Neisseria meningitidis* isolates rather than patient specimens.

Studies conducted in the 1990s that quantified the risks for the Meningococcal disease among college students demonstrated the overall incidents among college students was similar to, or somewhat lower than that observed among persons of approximately the same age in the general population.

However a later case control study that involved 50 cases of meningococcal disease among college students had multivariate analysis indicate that first year college students living in residence halls were at higher risk for meningococcal disease than other students with an odds ratio of about three point six or nearly a four fold increase in risk.

Other studies in later 1990s yielded similar results. Meningococcal disease is typically diagnosed by isolation of bacteria from a normally sterile site. However, sensitivity of bacterial culture may be low, particularly when performed after initiation of antibiotic therapy.

A gram stain of cerebrospinal fluid or CSF showing gram-negative diplococci strongly suggests meningococcal meningitis. Real-time polymerase chain reaction or rt-PCR detects DNA of meningococci in blood, cerebrospinal fluid, or other clinical specimens.

Although culture remains the criterion standard for diagnosis of meningococcal disease in the United States, PCR is useful for detection of other isolates from clinical samples in which the organism could not be detected by culture methods, such as when a patient has been treated with antibiotics before obtaining a clinical specimen for culture.

Kits to detect polysaccharide antigen of these bacteria in CSF are rapid and specific, but false negative results are common, particularly in serogroup B disease. Antigen tests of urine or serum are unreliable.

Serologic testing such as by enzyme immunoassay for antibodies polysaccharide may be used as part of the evaluation if meningococcal disease is suspected, but should not be used to establish the diagnosis.

The clinical presentation of meningococcal meningitis is similar to other forms of bacterial meningitis. Consequently initial empiric therapy with broad spectrum antibiotics such as third generation cephalosporins and vancomycin should be started promptly after appropriate cultures have been obtained.

Many antibiotics are effective for *Neisseria meningitidis* infection including penicillin and few penicillin resistant strains of meningococcus have been reported in the United States. Once *Neisseria meningitidis* infection has been confirmed, penicillin alone is usually the recommended therapy.

Meningococcal disease occurs worldwide in both endemic and epidemic form. The reservoir is humans. Humans are the only natural reservoir for the spectrum. In as many as 10 percent of adolescents and adults are asymptomatic transient carriers of *Neisseria meningitidis*, most strains of which are not pathogenic, that is strains that can't be classified into a group.

The transmission is primarily spread by respiratory droplet spread or by direct contact. The temporal pattern notes the disease occurs throughout the year but their incidence is highest in the late winter and early spring coinciding with circulation of respiratory viruses.

Communicability is generally limited. In studies of households in which a case of meningococcal disease has occurred, only three percent to four percent of households had secondary cases. Many households had only one secondary case. Estimates of the risk of secondary transmission are generally two to four cases per thousand household members at risk.

However, this risk is still five hundred to eight hundred times that in the general population. This graph demonstrates that between 2005 and 2011, an estimated eight hundred to 12 hundred cases of meningococcal disease occurred annually in the United States, a remarkable drop off from the 1990s and times before.

And this incidence of eight hundred to 12 hundred represents 0.3 cases per one hundred thousand population. Since 2005, declines have occurred among all age groups and in all vaccine contained serogroups.

In addition, incidence of disease attributable to serogroup B, a serogroup not included in the quadrivalent polysaccharide conjugate vaccine, declined for reasons that are not known.

Serogroups B, C, and Y are the major causes of meningococcal disease in the United States, each being responsible for approximately one third of cases. The proportion of cases caused by each serogroup varies by age group.

Approximately 60 percent of disease among children zero through 59 months is caused by serogroup B, for which no vaccine is licensed in the United States, at least for that age group. Serogroups C, W, or Y, which are included in conjugate vaccines available in the U.S. cause 73 percent of all cases of meningococcal disease among persons 11 years of age or older.

There are three peaks in the meningococcal disease incidence before one year of age, in adolescent and young adulthood, and lastly in persons aged 80 years and older. The incidence of serogroups C and Y, which represent the majority of cases of meningococcal disease preventable by the conjugate vaccines, are at historic lows.

However, a peak in disease incidence among adolescents and young adults 16 to 21 years, the second grey era on the slide, has persisted even after routine vaccination of adolescents was recommended in 2005.

From 2000, 2004 to the period 2005, 2009, the estimated annual number of cases of serogroups C and Y meningococcal disease decreased 74 percent among persons 11 through 14 years but only 27 percent decreased among persons age 15 through 18 years.

As mentioned, serogroups B, C, and Y are the major cause of Meningococcal disease in the U.S., and again each being responsible for about one third of cases and serogroup B is more common in children less than five years of age. Again, we do not have a vaccine licensed for that age group yet.

In the United States, meningococcal outbreaks account for only two percent of reported cases. So 98 percent of cases are sporadic. Recent outbreaks have been reported of serogroup B in several universities around the United States and serogroup C outbreaks have been reported amongst men who have sex with men.

Let's turn now to vaccines to prevent meningococcal disease. The first meningococcal vaccine licensed in the U.S. as the polysaccharide vaccine was licensed in 1974. The current quadrivalent A, C, W, Y containing

polysaccharide vaccine is Menomune, manufactured by Sanofi Pasteur and it was licensed in 1981.

Each dose of this vaccine consists of 50 micrograms of each of the four purified bacterial capsular polysaccharides. The vaccine contains lactose as a stabilizer. This vaccine, commonly abbreviated as MPSV4, is administered by subcutaneous injection. The vaccine is available in single dose and 10 dose vials.

Diluent for the single dose vial is sterile water without a preservative. Diluent for the 10 dose vial is sterile water with thimerosal added as a preservative. After reconstitution the vaccine is a clear, colorless liquid.

Polysaccharide vaccines for meningococcal disease as with pneumococcal disease and Hib vaccines in the past have an age related immune response. They're not consistently hemogenic in children less than two years of age.

There's little or no booster response with revaccination and the antibody has less functional activity in preventing disease and eliminating bacteria and the response to the vaccine has been improved by conjugation to a protein antigen which we'll talk about further.

Currently MPSV4 is, while approved for persons two years of age and older, is not recommended for vaccination of civilians and it should only be used for persons at increased risk for *Neisseria meningitidis* infection or 56 years of age or older who are expected to need meningococcal vaccine only once.

Now, meningococcal conjugate vaccines are composed of meningococcal polysaccharides conjugated to a protein carrier. They elicit both T and B cell immunity they have a, therefore have a T cell dependent immune response.

There are three meningococcal conjugate vaccines currently licensed in the United States. Two single component vaccines, Menactra and Menveo, and one combination vaccine with Hib, MenHibrix.

Menactra, sometimes abbreviated MenACWY-D, produced by sanofi pasteur, was licensed in 2005. Each 0.5 milliliter dose of this vaccine contains 4 micrograms of each of meningococcal A, C, W, and Y polysaccharides conjugated to approximately 48 micrograms of diphtheria toxoid protein carrier hence the abbreviation D after the ACWY.

This vaccine is approved for use in persons 9 months through 55 years of age. It is administered by intramuscular injection. Menactra is supplied as a liquid in a single dose vial and does not contain a preservative or an adjuvant.

Menveo, sometimes abbreviated MenACWY-CRM produced by the Novartis company, was licensed in the United States in 2010. Menveo consists of two portions.

The first is 10 micrograms of lyophilized or freeze dried meningococcal serogroup A capsular polysaccharide conjugated to CRM 197, meningococcal surface protein, and 5 micrograms each of capsular polysaccharide of serogroup C, W, and Y conjugated to that same surface protein.

These meningococcal bacteria are kept in 0.5 milliliters of a phosphate buffered saline liquid which is used to reconstitute the lyophilized Meningococcal A component before injection.

Menveo is approved for use in persons two months through 55 years of age. It is administered also by intramuscular injection. And also, it does not contain a preservative or an adjuvant.

MenHibrix, produced by GlaxoSmithKline, was licensed in the United States in 2012. This vaccine is sometimes abbreviated, Hib-MenCY-TT, contains 5 micrograms of *Neisseria meningitidis* serogroups C and Y capsular polysaccharide also conjugated to tetanus toxoid hence the abbreviation TT, and two and a half micrograms of Hib serogroup, Hib capsular polysaccharide conjugated also to tetanus toxoid.

The vaccine is lyophilized and should be reconstituted with a 0.9 percent saline diluent. MenHibrix is approved as a four dose series for children at two, four, six, and 12 through 18 months. The first dose may be given as early as six weeks of age, the fourth dose may be given as late as 18 months.

CDC's recommendation with the ACIP published March 22, 2013 in the MMWR, notes that limited data suggests that different conjugate vaccine products can be used interchangeably.

The safety and immunogenicity of Menveo vaccination has been evaluated in adolescents three years after they receive a single dose of either conjugate vaccines, and that is Menactra or Menveo, administered at age 11 through 18 years.

Following revaccination with Menveo, 99 percent of more persons previously immunized with Menveo or Manactra had serum bactericidal titers of one to eight or greater. The solicited adverse event rates, including injection site reactions, reported after revaccination was similar to the rates reported after primary vaccination.

No data exists on the use of Menactra following primary vaccination with Menveo.

ACIP has recommended that either of two Meningococcal B vaccines be used for high risk persons ten years of age or older. They include Trumenba in a three dose series and Bexsero in a two dose series.

I will discuss provisional ACIP recommendations for high risk groups and age groups of adolescents and young adults for these two vaccines later. So now let's talk about routine adolescent vaccine recommendations with meningococcal vaccines.

This is the 2015 child and adolescence vaccination schedule. Meningococcal conjugate ACWY vaccines are listed on the schedule as outlined in red near the bottom. For high risk children beginning at two years of age, for routine vaccinations beginning at 11 to 12 years of age, with a booster dose at 16 to 18 years of age.

Again, ACIP recommends routine vaccination with either Meningococcal conjugate vaccine at 11 to 12 years of age, and a booster dose at 16 years of age or older. For adolescents who receive the first dose at 13 through 15 years of age, a onetime booster dose should be administered, preferably at age 16 through 18 years.

Healthy persons who receive their first routine dose of Meningococcal conjugate vaccine at or after 16 years of age do not need a booster dose unless they become at increased risk for Meningococcal disease.

Routine vaccination of healthy persons who are not at increased risk for exposure to *Neisseria meningitidis* is not recommended for anyone after age 21 years unless they develop a high risk condition and we'll talk about those later.

A booster dose is not recommended for healthy persons 22 years of age or older even if the first dose was administered 11 through 15 years because as I showed you in the graph, and we'll look at the graph again, the high risk period ends at about 21 years of age.

Although doses of meningococcal conjugate vaccines separated by 8 weeks can both be counted as valid it is preferable to use a longer interval between doses, three to five years if possible.

In its 2005 recommendation for meningococcal conjugate vaccine, the ACIP made no recommendations about revaccination or a booster dose, pending the availability of additional data. Immunologic data available from the manufacturer show that there's a significant decline in antibody three to five years after vaccinations with one dose. Although only a few break through cases have been reported.

Now here's the graph we showed you before from the CDC Active Bacterial Core Surveillance system, shows the rate of Meningococcal serogroups both C and Y by single year of age through 25 years of age in 1999 through 2008.

And note the increase in rates for both serogroups in ages 17 through 21 years of age. Antibody persistence studies performed since ACIP's initial recommendations in 2005 as I noted, indicating antibody after vaccination declines three to five years after one dose of either Menactra or Menveo.

In addition, results from a vaccine effectiveness study demonstrated waning effectiveness, and many adolescents are not protected five years after vaccination. ACIP concluded that a single dose of Meningococcal conjugate vaccine administered at age 11 to 12 years is unlikely to protect most adolescents through the period of increased risk at ages 17 through 21 years.

On the basis of this information, ACIP recommended in 2010, adding a booster dose at age 16 years. Here's some other caveats about the new adolescent booster dose recommendation.

While the minimum interval between conjugated vaccine doses is eight weeks, they can be counted as valid. It is preferable to put a longer interval between doses, three to five years if possible. Now also, a booster dose is not recommended for healthy persons if the first dose of conjugate vaccines is administered at 16 through 21 years of age.

And a booster dose again is not recommended for healthy persons 22 years of age or older even if the first dose had been administered 11 to 15 years of age because they've aged out of the high risk period for this disease. Now let's talk about vaccine recommendations of persons who have increased risk of Meningococcal disease independent of age.

For children younger than 19 months of age with anatomic or functional asplenia including sickle-cell disease, one should administer an infant series of MenHibrix or Menvio at two, four, six, and 12 to 15 months of age.

For children now 19 through 23 months of age with anatomic or functional asplenia, one should administer two primary doses of Menveo at least 3 months apart. The doses are valid if they're at least eight weeks apart.

For children 24 months of age and older with persistent complement component deficiencies or anatomic or functional asplenia including sickle cell disease, who have not received a complete series of MenHibrix or Menveo, one can administer, could administer two primary doses of either vaccine at least 3 months apart.

Again, the doses are valid if they're at least eight weeks apart. Do not administer Menactra to a child with asplenia including sickle cell disease until after the second birthday, and at least four weeks after completion of all pneumococcal conjugate vaccine or Prevnar 13 doses.

This is because Menactra been demonstrated to interfere with sero-conversion and antibody production of some of the pneumococcal serotypes. And pneumococcal disease is a higher risk disease for children with asplenia than is meningococcal disease.

The complement pathway is important for preventing meningococcal disease and Neisseria meningitidis is the primary bacterial pathogen affecting persons with like complement components deficiency.

For children two through 18 months of age with persistent complement component deficiencies, you should administer either an infant series of either MenHibrix or Menveo at two, four, six, and 12 through 15 months or a two dose primary series of Menactra starting at nine months with at least eight weeks between doses.

Pneumococcal conjugate vaccine is not specifically indicated for these children but is recommended as it is for all other children. Children 19 through 23 months of age with persistent complement component deficiencies who have not received a complete series of MenHibrix or Menveo, they should receive two primary doses of meningococcal conjugate vaccine.

Either Menveo or Menactra can be given at least three months apart, again the minimum interval is eight weeks.

For children 24 months of age and older with persistent complement component deficiencies just as those with anatomic or functional asplenia who have not received a complete series of MenHibrix or Menveo, administer two primary doses of either Menveo or Menactra at least three months apart with a minimum interval of eight weeks.

So in summary, the infants and young children at increased risk are those with persistent complement component deficiencies, functional or anatomic asplenia and also children who are at risk for a community outbreak attributed to a vaccine serogroup, or who are traveling to or residing in regions where meningitis, meningococcal disease is epidemic or hyper endemic.

And for these traveling children, Menveo is the only approved suitable vaccine at that age. They should receive four doses of MenHibrix at two, four, six, and 12 to 15 months or Menveo. Booster doses should be administered, they continue to be at high risk and we'll talk about further.

For persons two through 55 years of age, the high risk groups include those who continue to have complement component deficiency, have functional or anatomic asplenia, and if they have HIV infection and one of the other conditions or have another high risk condition, all of these people need two doses of meningococcal conjugate vaccine at least eight to twelve weeks apart.

Let me emphasize, while HIV infection is not currently considered to be an indication for meningococcal conjugate vaccination by itself, these people do need a two dose series to receive proper protection if they have another high risk factor such as they've come to adolescence at 11 to 12 years or they're at high risk because of international travel or they happen to be microbiologists.

Again, they need two doses at least eight weeks apart.

Other persons at high risk include first year college students living in residential housing, 21 years of age or less.

Travel to or residence in countries where meningococcal disease is hyper endemic or epidemic, or microbiologists who are routinely exposed to isolates of *Neisseria meningitidis* or they are military recruits and these people need one dose of Meningococcal conjugate vaccine.

Both Meningococcal conjugate vaccines and MPSV4 are recommended for use of control of Meningococcal outbreaks caused by vaccines from vaccine serogroups. These again are serogroups A, C, W, Y. MenHibrix may be used for age appropriate persons, that is infants and young children in outbreaks if vaccines from serogroup C or Y are involved.

An outbreak is defined of the occurrence of at least three confirmed probably confined cases of the same serogroup of meningococcal disease during a period of three months or less with a resulting primary impact rate of 10 or more cases per hundred thousand persons.

The incidence of m disease is highest in the world in meningitis in sub-Saharan Africa. Highlighted in orange on this map, the incidence of meningococcal disease is several times higher than meningitis in the United States with periodic epidemics throughout the dry season which is December through June in that area.

During non-epidemic periods the rate of meningococcal disease in this region is roughly five to ten cases per hundred thousand population per year. During

epidemics, the rates can be as high as one thousand cases per hundred thousand population.

Although most common in the African meningitis belt, meningococcal outbreaks can occur anywhere in the world. Serogroup A dominates in the sub-Saharan belt although other serogroups are also found.

For international travelers, vaccination is recommended for those visiting the parts of this sub-Saharan African area known as the meningitis belt during that dry season December through June.

Infants and children who received MenHibrix and are travelling to areas with high endemic rates of meningococcal disease should receive a quadrivalent meningococcal conjugate vaccine usually Menactra or Menveo are effective against the other serogroups, particularly serogroup A.

Children who received primary immunization and remain at increased risk should receive booster doses and if the primary vaccination series was completed by seven years of age, the first booster dose should be three years after the last primary immunization and every five years thereafter if they stay at increased risk.

If the primary immunization series is completed on or after seven years of age, the first booster dose should be five years after primary immunization and every five years thereafter again, if they stay at increased risk.

ACIP also recommended in 2009 routine revaccination of other persons at high risk of exposure and these groups again include microbiologists, with prolonged exposure to the *Neisseria meningitidis* and frequent travels to or persons living in areas of high rates of meningococcal disease such as sub-Saharan Africa or traveling through the Hajj pilgrimage in Saudi Arabia.

These persons should be revaccinated at least every five years as long as they remain at increased risk. Meningococcal conjugate vaccine should be administered to the persons two through 55 years of age.

For persons now age 56 years or older who are vaccinated previously for meningococcal conjugate vaccine and are recommended for revaccination, or for whom multiple doses are anticipated such as persons with asplenia or microbiologists, meningococcal conjugate vaccine is preferred. This is an off label recommendation by ACIP.

International travelers should receive a booster dose of meningococcal conjugate vaccine if the last dose was administered five or more years previously. And again, vaccination the three years before the date of travelers is required by the government of Saudi Arabia for all travelers to Mecca during the annual Hajj.

So we have some polling questions for you now: a six month old child with asplenia comes into your office today, and you had all of the following vaccines in stock, which one of these would you give? And there may be more than one answer. Let's wait a few more seconds to see what you say.

Okay so the slide has the correct answers. Most of you chose ManHibrix which is correct and others of you chose Menvio which is also correct. Both of those vaccines are recommended for high risk children down to two months of age.

Let's go to the next question. A six month old child with asplenia comes to your office today. He is accompanying his family on a vacation to South

Sadan, which is in the meningococcal belt. If you have all of the following vaccines in stock, which one would you give?

Let's wait some time for some answers. OK the correct answer, and there's only one correct answer, is Menveo because as I mentioned in the sub-Saharan meningitis belt, serogroup A is the most common meningococcal serogroup prevalent there causing disease and serogroup A is not contained in MenHibrix but it is contained in Menveo.

And Menveo is the only appropriate vaccine for this child even if this child received MenHibrix earlier. The child does need a dose or more of Menveo to protect the child adequately. Thank you and let's move on to the rest of the presentation. Now let me talk about meningococcal serogroup B vaccine recommendations.

In June, the MMWR published ACIP and CDC recommendations for either of the license vaccines Bexsero or Trumenba and stated that either vaccine should be administered to a person 10 years of age or older who are increased risk of meningococcal disease,

including persons with persistent complement component deficiencies that include people that are taking a drug called Soliris, or eculizumab which impairs complement function, people who have atomic or functional asplenia, people who are microbiologist and are exposed to the Neisseria meningitidis.

Or people identified to be at an increased risk because of a serogroup B Meningococcal disease outbreak. These recommendations are essentially the same as those for meningococcal conjugate ACWY vaccine and the same high risk groups.

At the June 2015 ACIP meeting, the ACIP voted to make a permissive recommendation for the use of Meningococcal B vaccination for adolescents and young adults ages 16 through 22 years of age, which provides short term protection for most strains of serogroup B Meningococcal disease.

The preferred age for Meningococcal B vaccination is 16 through 18 years of age. This recommendation is labeled as category B meaning that clinicians who discuss this on an individual basis with their patients to decide about the risks and benefits of vaccination.

Serogroup B disease is uncommon but it can be very severe as we discussed as any Meningococcal infection can be and therefore we recommend that the clinicians discuss these issues of vaccination with their patients. But the recommendation is there and the vaccination may be used as decided by the clinician and the patient.

This is a draft recommendation. It will not be an official recommendation until approved by the CDC director and published in the MMWR. We anticipate publication of this recommendation in the near future.

ACIP recommends the same vaccine should be used for all doses in the Meningococcal B series. So if MenB-4C which is Bexsero is used, that would be a two dose series. If MenBFHP which is Trumenba, would be a three dose series given that each vaccines target different proteins, a mixed schedule is not recommended or considered valid.

So this is in contrast to what I said earlier of m conjugate vaccines where interchangeability is not deemed a problem and it is not deemed a problem for most other inactivated vaccines. But for meningococcal B vaccines, one should complete the series with the vaccine started.

Both of these inactivated vaccines are inactivated vaccines and based on available data and expert opinion, they can be administered at the same time as other age appropriate vaccines such as Meningococcal ACWY conjugate vaccine, Tdap or HPV if one is vaccinating adolescents.

Meningococcal B vaccine should be administered in a separate syringe and at a separate site than other vaccines if feasible. At present, no booster dose of Meningococcal B vaccines are recommended for any group including high risk persons, and ACIP did not state a preference for one vaccine over the other.

Now let's talk about adverse events. For meningococcal polysaccharide vaccine fever between 100 degrees and 103 degrees Fahrenheit within seven days of vaccination was reported in up to three percent of recipients. Systemic reactions, such as headache and malaise, within seven days of vaccination are reported in up to 60 percent of recipients.

Fewer than three percent of recipients reported these systemic reactions as severe. Meningococcal conjugate vaccines post-licensure data from the Vaccine Adverse Reporting System or VAERS demonstrate to the most frequently reported adverse events for Menactris in adolescents and adults includes fevers in about 17 percent, headache in about 16 percent, injection site erythema in about 14 to 15 percent, injection site pain approaching 60 percent, and dizziness in about 13 percent. Syncope (unintelligible) was reported in about 10 percent of these reports about Menactra. Of all reported events, about six percent was coded as serious.

That means they resulted in life threatening illness, hospitalization, prolonged hospitalization, informative disability or death. Serious events included

headache, fever, vomiting, and nausea. Higher estimates for local and systemic reactions on the slide come from pre-licensure studies, not VAERS, which are cited on the vaccine packaging insert.

The most frequently reported adverse events for Menveo in adolescents and adults were injection site erythema in about 20 percent and injection site swelling in about 14 percent. Syncope was reported in about 8.8 percent of reports involving Menveo. There was no pattern among the serious adverse events and reports for either vaccine including in the few reported deaths.

Rates of local and systemic adverse events observed after administration of MenHibrix, which is not on the slide, were comparable to rates observed after administration of Hib vaccine. Therefore, Hib was found to be, that is MenHibrix is found safe and immunogenic for both Hib and Meningococcal serogroups C and Y.

Early reports to VAERS, and CDC and FDA suggested an increased risk of Guillain-Barre Syndrome or GBS after receiving Menatrac. Subsequent studies have not demonstrated an increase risk.

After reviewing these safety studies, ACIP voted in 2010 to remove the history of Guillain-Barre Syndrome or GBS, as a precaution for vaccination because the benefits of meningococcal vaccination outweigh the risks for recurring GBS in these persons.

However the history of GBS continues to be listed as a precaution in the package inserts for meningococcal conjugate vaccines. Not on the slide, but it's important to mention breastfeeding and immunosuppression are not contraindications to vaccination.

And also pregnancy should not preclude vaccination with meningococcal conjugate vaccine or polysaccharide vaccine if indicated.

Vaccination with meningococcal conjugate vaccine or polysaccharide vaccine or MenHibrix is contraindicated for persons known to have a severe allergic anaphylactic reaction to the vaccine or to a vaccine component including diphtheria toxoid.

Recommended vaccinations can be administered to persons with minor acute illnesses such as diarrhea or mild upper respiratory tract infection with or without fever. Vaccinations should be deferred for persons with moderate or severe acute illness until the condition has improved.

I will not discuss chemoprophylaxis antibiotic use for close or household context meningococcal disease. This topic is discussed in detail in the Pink book and also in the reference cited on this slide from the MMWR in March of 2013.

Now let's talk about meningococcal vaccine administration errors. Some providers have inadvertently administered Meningococcal conjugate vaccines by the subcutaneous route. There are few data on the efficacy or safety of these vaccines given by the subcutaneous route. Sanofi Pasteur from Menactra recommends repeating the dose given subcutaneously.

CDC does not recommend revaccination if subcutaneous vaccination was used for either Meningococcal conjugate vaccines.

Now what about errors with Menveo given it comes with two components you're supposed to mix together?

The liquid CYW135 component was administered without using it to reconstitute the A component. We don't recommend revaccination routinely because serogroup A disease is rare in the United States so revaccination is not needed if the person does not plan to travel outside the U.S.

However, if this person is planning to travel to an area where serogroup A disease is common such as sub-Saharan Africa, revaccination with an appropriate meningococcal conjugate vaccine including serogroup A is recommended and there is no minimum interval between the errant dose and the follow up dose to give them serogroup A.

The information for this presentation is obtained from the sources listed on the slide including The Prevention and Control of Meningococcal Disease recommendations of the ACIP from 2013, 2014, and 2015 as well as from the Pink book.

Other resources for meningococcal disease are ACIP's meningococcal vaccines' recommendation webpage, CDC's meningococcal infection webpage, CDC's Meningococcal vaccination webpage, the Immunization Action Coalition, as well as the Children's Hospital of Philadelphia. Thank you very much, let me turn the microphone back to Dr. Kroger.

Andrew Kroger: Thank you very much Dr. Strikas. Now we're going to move to a Question and Answer session and while the queue fills I'll give you some information about continuing education. If you do have a question, please dial star one to get in the queue for the operator. And please be sure your question is related to today's content.

We will have a recast of this program available on the internet at our web site at [www.cdc.gov/vaccines/ed/ciinc](http://www.cdc.gov/vaccines/ed/ciinc). This will be available the week of October

12, 2015. The slides will be there as will the audio portion and other resource information.

For continuing education credit, go to [www2a.cdc.gov/tceonline/](http://www2a.cdc.gov/tceonline/). The course number for this program is E as in Edward, C as in cat, 2064-100715. Note that 100715 is today's date and that this course number is specific to today's course.

You'll need this course number when completing CE requirements. You will also need the verification code which is Mening9 and this also applies to today's program only, I'll repeat that verification code, M-E-N-I-N-G nine. The numeral nine with no space. CE credit for this program expires November 9, 2015.

I'll 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 please let us have all participants ask the questions they wish to ask. Operator?

Coordinator: We have one question in queue and that comes from XXXXXX.

XXXXXX: Hi, so when I hear Pfizer talking about their Meningococcal B vaccine, they claim that it was developed to respond better to the Meningococcal B strains here in the United States versus the GSK vaccine that was developed for European strains. Can you talk a little more about the epidemiology, understanding that there is no preference by the ACIP?

Raymond Strikas: Yes my understanding, and this is detailed in the June 12, 2015 MMWR reference at the end of the presentation is that the immunogenicity which is how the vaccines were licensed is deemed similar enough that there is no

preference and there is so far no evidence that I'm aware of vaccine effectiveness that affects this evidence.

And if Pfizer has some or you have some I'd be happy to hear about it, that demonstrates increased effectiveness of one vaccine over the other in any setting where they've been used. So I'm not aware that there's a difference for the United States for these vaccines.

XXXXXX: OK. Thank you.

Andrew Kroger: Thank you, we'll take the next question in queue?

Coordinator: At this time there are no questions in queue. Once again, if you would like to ask a question please press star one and record your name.

Andrew Kroger: Well while we wait for a question, I'll ask Dr. Strikas a question we often receive. Sometimes we hear about healthy adolescents and they may receive two doses of quadrivalent meningococcal vaccine at 11 years of age. The two doses are more than eight weeks apart but will this help the adolescent need another dose of quadrivalent Meningococcal vaccine after the 16th birthday?

Raymond Strikas: Yes you should plan on giving this adolescent another dose. And the optimal thing to remember is the data I discussed in the presentation is it's been demonstrated after one dose of conjugate vaccine particularly for serogroups C and Y which has most of the disease adolescence immunity and you want to protect that young person through the 21 year.

So if you vaccinated a person at 11 years of age or twelve years of age and the second dose was given only eight weeks later, one does not anticipate protection much beyond the 15th and 17th birthday. The high risk period

continues hence the recommendation to vaccinate them between 16 and 18 years of age to protect them through 21 years of age.

So this person should get another dose and in this case a third of the conjugate vaccine.

Andrew Kroger: Thank you very much. Do we have any other questions in the queue now?

Coordinator: Yes. So our next question comes from XXXXXXXX.

XXXXXXXX: Hi, my question is about Menomune given for patients over age 55. I guess I need some clarification. If a patient is traveling to Africa, the Meningococcal belt there, and needs a Menomune is that only a one time dose versus patients who are asplenia over 55 getting them every five years?

Raymond Strikas: That's correct. If the anticipation is that this older person having reached that age though I don't consider them that old, but anyways, that person, if that person does not plan to travel but once to a high risk area meningococcal polysaccharide in this case Menomune vaccine is appropriate.

If the person anticipates traveling regularly or, and or if the person has a high risk condition or situation and that is asplenia as you mentioned, complement component condition, happens to be a microbiologist that person then would be getting, we would be recommending meningococcal conjugate vaccine every five years to protect them.

Of if the person says, "I plan to go back to Africa sometime in the future." It's better to give them conjugate vaccine based on that prediction even then if they choose later to not go. But polysaccharide vaccines tend to offer better protection in that population.

So if it's a onetime thing and you would prefer to give them the polysaccharide, the concern is that if you give them the polysaccharide first, the response to conjugate vaccine later may not be as good in someone who needs repeated vaccination. Does that answer your question?

XXXXXXX: Yes I think so. Thank you very much.

Raymond Strikas: Thank you.

Andrew Kroger: Thank you. We'll take the next question if there's one in the queue?

Coordinator: Yes, our next question comes from XXXXXXXXXXXXXXXX.

XXXXXXXXXXXXXXXXXX: Hello? Hello there, can you hear me?

Andrew Kroger: Yes, we can hear you.

XXXXXXXXXXXXXXXXXX: So my question is, pertains to the map of Ethiopia on the belt. Is there any particular reason why half of the country pretty much has a vertical line through it? Is it just because there's no meningococcal disease reported from the Eastern half or not enough providers on the western half?

Raymond Strikas: I'm not absolutely sure and I don't pretend to know the epidemiology of Meningococcal disease in Africa that well. My understanding from colleagues who work there is surveillance can be difficult to do and not all cases are reported so it may well have to do with limitations of surveillance. Not to say there isn't disease there. And so if one was concerned about traveling to that area I think one would want to consult the latest guidelines on CDC's travel website its [cdc.gov/travel](http://cdc.gov/travel) and or the world health organization

and make sure it's up to date. But there may be some limitations of surveillance as you suggest.

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

Coordinator: Question is from XXXXXXXXXXXXXXXXXXXX.

Raymond Strikas: Hello?

XXXXXXXXXXXXXXXXXXXX: Am I on?

Andrew Kroger: You're on, we can hear you.

XXXXXXXXXXXXXXXXXXXX Thank you very much. My question is, Menomune in single dose vials is not available and has not been available in quite some time. I don't know when it will be made available. If we have someone that is older than six years of age coming in for their initial meningitis shot and they've never had one before, they don't expect to ever need one again, what do we do?

Raymond Strikas: Yes, that's a challenge and we've had that question regularly. And we haven't had a - I haven't had a conversation with the vaccine company to try to understand when they think this vaccine supply issue may be resolved.

If there's still some time, a month or more before the person plans to travel and the company believes they'll get vaccine to you, although that hasn't been the case for several months, at least.

Than one would prefer to wait for the polysaccharide vaccine, because as I say, it works a little bit better or at least the immune response seems to be better on a one time basis in older persons.

However, if the person can't wait, they're traveling soon or one doesn't anticipate receiving Menomune soon, then using the meningococcal conjugate vaccine as a reasonable alternative even if they're only going on need it once because it offers some protection, reasonably good protection we believe.

And which is much better than no protection in that part of the world.

Woman: Can I ask a follow up?

Raymond Strikas: Yes.

Woman: Would have be written anywhere? Where would we find that documentation?

Raymond Strikas: Oh, well it's what we received from Meningococcal expert staff, in which we've been responding to when we get individual emails. Let us check and see if that can be put somewhere on our Travel Website, or someplace else prominent and have a link from today's program to that.

So I'm not sure it's on Travel Website as yet, and we'll check on that for you.  
Thank you.

Andrew Kroger: Thank you. We'll take the question that's in the queue.

Coordinator: Next question is from XXXXXXXXXXXX.

XXXXXXXXXXXXXXXX Hi, this is...

Andrew Kroger: Hello?

XXXXXXXXXXXXXXXX: Hi. Can you hear me okay?

Andrew Kroger: Yes.

XXXXXXXXXXXXXXXX: We've actually been hearing some feedback where because there's been so much press coverage of Meningococcal B vaccine outbreak -- I mean Meningococcal B outbreaks, you know, some people saying, well why should I need the Meningococcal Conjugate.

It sounds like B is the strain that, that risk. So would you have any messages to emphasize that, you know, it might not get as much attention but, you know, AC, you know, WY are still important?

Raymond Strikas: Yes, as I said, the epidemiology as far as I know up to the present is that the B outbreaks have gotten a lot of note but as I said, B disease -- an outbreak disease is a small percentage of sporadic disease. And the more common disease is C and Y. And so both vaccines are important to consider.

We have a routine recommendation for ACWY, because C and Y comprise about two-thirds or more of the cases in adolescents and young adults and B comprises less. They [type B] just happen to have been the cause of outbreaks for reasons that are not fully understood.

Some B outbreaks in universities that have led to, you know, relatively small number of cases but any case is potentially very severe and it had severe outcomes, and many people have been vaccinated in those university settings.

But you know, the epidemiology is still that there's more disease caused by the other serogroups and so vaccination with, you know meningococcal conjugate vaccines for ACWY prevention is if anything more important because there's more disease caused by those, it just hasn't had the press because those are sporadic cases.

And I don't know how else to characterize it for you. I hope that's helpful.

XXXXXXXXXXXXXXXXX: That is. Thank you.

Andrew Kroger: Thank you. Why don't we take one last question if we have one.

Coordinator: We have a vacs question from XXXXXXXX.

XXXXXXXXX): Hi...

Andrew Kroger: Hello?

XXXXXXXXX: ...my question has already been answered. Thank you.

Raymond Strikas: All right. Thank you.

Andrew Kroger: Any others in the queue?

Coordinator: We have one more in queue and that comes from XXXXXXXXXXXXXXXX.

Andrew Kroger: Hello?

Raymond Strikas: Hello?

XXXXXXXXXXXXX: Hello. Can you hear me?

Andrew Kroger: Please go ahead.

XXXXXXXXXXXXX: Oh, okay. I am interested in having you just review very quickly with me, just so that I have this right. We have - I am at a hospital and we are reviewing our vaccination of our microbiology staff.

And I feel like I need to have just repeated to me quickly if you would, the dosing of which vaccine how many of those they need, how many doses they need, and do they need both the A and the B?

Raymond Strikas: Yes, so the recommendations are that if the microbiologist is deemed - is regularly - particularly those regularly working with or expected to regularly come in contact with (*Neisseria meningitidis*) bacteria, if it's a regular microbiology lab the odds of that are probably small.

But then one needs to make a judgment about their level of risk because the cases that mentioned were people who regularly work with those bacteria on a daily or weekly basis, as opposed to routine micro lab where you handle a lot of different bacteria.

And you uncommonly come into contact with (*Neisseria meningitidis*), so level of risk is a judgment call to be made by the institution and the people working in charge of that laboratory.

But if the judgment's made that they have people who are at risk of (Neisseria meningitidis) infection, including the serogroups that are in the vaccine than at present, both vaccines are recommended the meningococcal conjugate, ACWY vaccine, a single dose.

And then every five years, so long as the person is at risk, that is they stay in the business of microbiology and are expected to come into contact with (Neisseria meningitidis) bacteria.

And serogroup B, Meningococcal B vaccines where a series is recommended at present, either the two-dose series or the three-dose series. And since we don't know much about the duration of protection, right now no booster doses are recommended for the Meningococcal B vaccine.

But microbiologists are recommended to receive that if they're deemed to have an increased risk of (Neisseria meningitidis) bacteria contact in the course of their work. Does that help?

XXXXXXXXXXXXXXXXX-----: That does, extremely. And you don't want to give them both at the same time, or can you?

Raymond Strikas: You can. There's the data that you can read what resources I've sent you. The June 12th, 2015 meningococcal B recommendations indicate that as far as we know giving Men B vaccine in one arm and the conjugate vaccine in the other arm is fine.

Or if you're giving three vaccines you can use the anterior lateral thigh for a third vaccine in an adult as well. But they can be given at the same time in different sites.

XXXXXXXXXXXXX: Okay. I appreciate that. Thank you so much.

Raymond Strikas: Thank you.

Andrew Kroger: Thank you. Well that's all the time we can devote to questions, now. So I'll repeat the continuing education information. For CE credits you can see the web site, [www2A.CDC.gov/TCEonline/](http://www2A.CDC.gov/TCEonline/). The course number is E as in Edward, C as in Cat, 2064-100715.

Again note that's 100715, is today's date. The code applies to today's program. The verification code is MENING 9, MENING and then the numeral 9 with no space. CE credit expires November 9, 2015.

For help with the online system, available 8:00 a.m. to 4:00 p.m. Eastern Time, please dial 1-800-41TRAIN, that corresponds to 1-800-418-7246, or you can email, [ce@cdc.gov](mailto:ce@cdc.gov).

You can email immunization questions to us, if you did not get to ask them today at [nipinfo@cdc.gov](mailto:nipinfo@cdc.gov), and we'll try to respond to those as quickly as possible.

You can also call immunization questions to 1-800-CDCinfo, or 1-800-232-4636 from 8:00 a.m. to 8:00 p.m. Eastern Time, Monday through Friday. Additional resources you can use include the Pink Book, and the web site for the Pink Book, [www.cdc.gov/vaccines/pubs/pinkbook/index.html](http://www.cdc.gov/vaccines/pubs/pinkbook/index.html).

It's available online or you can purchase a hardcopy at the link for the Public Health Foundation Learning Resource Center. Our CDC vaccine and immunizations home page is [www.cdc.gov/vaccines/default.htm](http://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](http://www.cdc.gov/vaccines/ed/downloads/imz-resources.pdf).

Follow us on Twitter for immunization news, information and resources for private and public health care personnel, that's @cdcizlearn on Twitter. So that concludes our program.

I want to thank Dr. Raymond Strikas for the presentation covering the topic in great detail and for answering all of the questions. Thank you very much and have a great day from Atlanta. Goodbye.

Coordinator: That concludes today's conference. Thank you for your participation. You may now disconnect.

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