Vaccine Preventable Diseases/ Session 2
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Slide 1 Title

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Hello, I'm Susan Sullivan, Communicable Disease Branch Nurse Consultant for vaccine preventable diseases. This section of the VPD presentation will cover general information on the viral diseases varicella, measles, mumps, rubella, polio, and the bacterial diseases diphtheria, and tetanus. Essential data elements for reporting VPDs in NC EDSS will also be reviewed.

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Upon completion of this presentation the participant will be able to:
Locate control measures for less commonly seen VPDs
Identify appropriate clinical specimens for VPD testing, and
List key data elements for reporting VPDs in NC EDSS

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This presentation is an overview. For comprehensive coverage of this material, you can read the case definitions for each disease and review relevant chapters in the CDC Pink Book or on-line VPD surveillance manual, as well as the CDC immunization webinars available on the CDC Immunization webpage for questions about testing; you can also refer to the State Lab guide to services.

Remember that guidance published in the Morbidity and Mortality Weekly Report supersedes any previous CDC reference document. When in doubt, check with the CD Branch at 919 733 3419.

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First, I will discuss varicella.

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Unlike many vaccine preventable diseases I will discuss, varicella cases are not individually reportable in NC. However, because varicella can cause serious complications and is highly

contagious, a public health response is still warranted so that control measures can be implemented to prevent outbreaks and prevent infection of susceptible persons at high risk for complications.

Outbreaks of varicella (which CDC generally defines as 5 or more cases) are reportable to the CD Branch, as are outbreaks of any communicable disease. Varicella cases that occur within one incubation period (21 days) of a previous case are considered part of an outbreak if they are epidemiologically linked. The CDC Varicella Outbreak Manual is available on-line and provides detailed guidance in the control and investigation of single cases as well as varicella outbreaks.

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Primary varicella (usually called chickenpox) is a highly infectious febrile rash illness that starts with a mild prodrome of fever and malaise.

The prodrome is followed by a progressive rash that starts on the head, chest, and back then spreads outward to the rest of the body. The lesions are usually most concentrated on the chest and back. Lesions evolve from maculopapular to vesicular and then into noninfectious dried crusts over a 5- to 6-day period. Unvaccinated patients usually develop 200–500 itchy blisters in several successive crops, with maculopapular lesions, vesicles, and crusts all being present at the same time. The illness lasts about 5–10 days.

Complications of varicella can include bacterial skin infections, sepsis, pneumonia, encephalitis, cerebellar ataxia, Reye syndrome, and even death. Complications occur much more frequently in persons older than 15 years, and infants younger than 1 year of age.

Immunocompromised persons have the highest risk for disseminated disease. The onset of maternal varicella from 5 days before to 2 days after delivery may result in overwhelming infection of the neonate and a fatality rate as high as 30%.

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Primary infections with the varicella-zoster virus (VZV) results in chickenpox. The virus establishes latency in the dorsal root ganglia during primary infection. Reactivation results in herpes zoster, known as shingles. Varicella is highly infectious, with secondary infection occurring in 61%–100% of susceptible household contacts. Transmission occurs by airborne spread from respiratory secretions or lesions, or person to person by direct contact with secretions or lesion fluid. The incubation period for varicella is most commonly 14–16 days but can be up to three weeks. Varicella is infectious from 1-2 days before rash unset until crusting of all lesions.

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Varicella vaccine became available in the United States in 1995 and a recommendation for a second dose was made in 2006.

These graphs on this slide show the number of varicella cases in blue and the varicella vaccine coverage rates in red for two sites of the CDC's Varicella Active Surveillance Project. As you can see, the number of cases declined dramatically between 1995, when varicella vaccine first became available, through 2005, when varicella vaccine coverage was over 90%.

Before vaccine, varicella accounted for about 1.4 million cases, more than 11,000 hospitalizations, and about 100-150 deaths every year in the U.S. Most cases were previously healthy children less than 15 years of age. In the most recent report of the U.S. National Immunization Survey, estimated vaccination coverage among children aged 19–35 months for 1 or more varicella vaccine doses was over 90%. As a result of improved vaccine coverage rates, varicella deaths have declined by 98.5% in children and adolescents less than 20 years of age.

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Because of the high vaccine coverage, the majority of varicella cases now occur in vaccinated persons following exposure to wild-type virus. This "breakthrough infection" usually results in mild illness of shorter duration with less than 50 lesions and little to no fever. The mild symptoms can make breakthrough infections difficult to diagnose.

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CDC recommends two doses of varicella vaccine for children, adolescents, and adults. Children should receive the first dose at 12 through 15 months old and a second dose at 4 through 6 years old. Varicella vaccine is available alone or in combination with the measles-mumps-rubella vaccine.

A vaccine for herpes zoster, also called shingles, was licensed in 2006. A single dose of shingles vaccine is recommended for adults 60 years of age and older.

In a large clinical trial, shingles vaccine reduced the risk of disease by about half (51%) and the risk of post-herpetic neuralgia by 67%. While the vaccine was most effective in people 60-69 years old, it also provided some protection for older groups.

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This table lists various tests available for varicella. As varicella disease declines and fewer clinicians have direct experience with breakthrough infections, the need for laboratory confirmation has grown. Varicella hospitalizations, deaths, or other severe or unusual disease, should routinely be laboratory confirmed. While viral culture and DFA can be used, PCR is the faster, most reliable and sensitive method for confirming infection. In vaccinated persons, serologic results should be interpreted carefully. For example, the fourfold rise in IgG that we look for may not occur in vaccinated persons. Consult the CD Branch and SLPH for guidance if needed.

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Evaluating immunity is an important step in any vaccine preventable disease investigation. Evidence of immunity to varicella includes any of the following:

- Documentation of age-appropriate vaccination
- Lab evidence of immunity or disease confirmation, keeping in mind that some assays lack sensitivity to always detect vaccine induced immunity
- Being born in the U.S. before 1980, although this does not apply to healthcare personnel, pregnant women or immunocompromised persons
- Clinician diagnosis of disease or history of disease with lab confirmation when indicated or
- History of clinician diagnosed herpes zoster

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The decision to use antiviral medications should be determined by specific host factors, extent of infection and initial response to therapy. Most viral replication stops within 72 hours after rash onset so treatment is not considered clinically beneficial for most otherwise healthy children. However, the American Academy of Pediatrics recommends considering treatment for persons at risk for more serious disease including

- Persons over 12 years of age
- Persons with chronic skin or pulmonary disorders
- Persons receiving long term aspirin therapy and certain kinds of corticosteroid therapy, and
- Secondary case-patients who are in the same household as infected children

Once a decision is made, treatment should begin as soon as possible. Antiviral medication administered within 24 hours of rash onset has been shown to decrease the duration and severity of clinical illness.

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This table summarizes control measures for varicella cases and contacts. Vaccination is recommended as post-exposure prophylaxis for persons without evidence of immunity if it can be given within 3-5 days post exposure. A two dose policy is recommended for outbreak control in congregate and high risk settings. Vaccination for non-immune postpartum women is also key to preventing neonatal varicella.

Prophylaxis with antivirals may be indicated for those at higher risk as previously discussed.

Varicella immune globulin may be used up to 10 days post exposure for persons who are non-immune, at higher risk of severe disease, and vaccine ineligible.

Traditional measures of isolation and quarantine are still used to manage varicella and are tailored to the setting and immune status of the affected persons. More in depth discussion can be found in the CDC VPD Manual and CDC Varicella Outbreak Manual, both online. The CD Branch is always available for any questions.

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Next, I will discuss measles, mumps and rubella.

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Measles (also called rubeola) is a highly contagious rash illness that is transmitted from person to person by direct contact with respiratory droplets or airborne spread. The classic presentation of measles begins with a prodrome of fever which increases in a stepwise fashion often peaking as high as 103-105, followed by the onset of cough, coryza (runny nose) and conjunctivitis. Koplik spots, a rash on the mucous membranes, are considered pathognomonic for measles. These occur 1-2 days before the rash to 1-2 days after the rash and appear as punctate blue-white spots on the bright red background of the buccal mucosa.

The measles rash is maculopapular, begins at the hairline, then spreads to the face and upper neck, initially blanching with pressure. Over the next 3 days, the rash gradually proceeds downward and outward to the hands and feet. The rash fades in the same order it appears.

Complications occur in one third of cases, mostly in children <5 and adults over 20. Severe complications include pneumonia, encephalitis and even death.

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The graph on the right shows the decline in measles in the United States between 1980 and 2010. In 2000, endemic measles was declared "eliminated" from the United States, meaning endemic transmission no longer occurs here. However, ongoing measles outbreaks in other countries continue to occur and imported cases are only a plane ride away from your county. Gathering a thorough travel history from a suspect case can help can help in determining the likelihood of exposure.

All reports of suspected measles cases should be investigated immediately. If it is discovered that the case patient was traveling by plane or ship while infectious, the CD Branch should be notified immediately for assistance with contact tracing. The potential for further transmission should be evaluated for anyone exposed during the case-patient's infectious period, which is 4 days before to 4 days after rash onset. The N.C. 2013 outbreak, as an example, began with a returning traveler and resulted in 23 cases and considerable expenditure of public health resources. For the most reliable information about diseases and travel, consult the CDC Yellow Book, which is online and also listed in the concluding references.

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Laboratory confirmation is essential for all outbreaks and all sporadic measles cases. Viral culture and PCR are available if specimens can be collected within 3 days of rash onset.

Detection of measles-specific IgM antibody and measles RNA by PCR are the most common methods for confirmation of measles infection.

A serum sample and throat swab (or nasopharyngeal swab) should be obtained from suspected cases at first contact. Collection of both respiratory and urine samples can increase the likelihood of detecting virus.

Staff at both the CD Branch and state laboratory are available for consultation and can assist with confirmatory testing as needed. Keep in mind that negative culture or PCR do not rule out measles because both methods are affected by the timing of specimen collection as well as the quality and handling of clinical specimens.

Genotyping by a CDC reference lab is also available to distinguish wild type from vaccine strain if a person has been vaccinated within 18 days of rash onset.

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This slide summarizes measles control measures. The primary control strategy is achieving a high level of immunity in the affected population.

MMR can be used if eligible contacts can receive it within 72 hours of initial exposure. Except for healthcare personnel, unvaccinated persons who receive their first dose of MMR within 72 hours post exposure may return to child care, work or school. Non-immune contacts who are not able to receive MMR should receive immune globulin.

Case patients should be isolated for 4 days post rash onset (day 0). Exposed susceptible contacts who did not receive MMR within 72 hours after initial exposure should be excluded until 21 days after rash onset in the last case in the affected setting.

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Mumps is an acute viral illness caused by a paramyxovirus. The classic symptoms of mumps usually begin with a nonspecific prodrome including low-grade fever, myalgia, anorexia, malaise, and headache. Parotitis –the acute onset of unilateral or bilateral, tender swelling of parotid glands – is the most common manifestation. The parotitis typically develops 16 to 18 days after exposure to mumps virus. It usually lasts at least two days, but may persist longer than ten days. Mumps infection may present with only nonspecific or primarily respiratory symptoms, or may be a subclinical infection.

Serious complications can occur, including aseptic meningitis and orchitis (or testicular swelling), which occurs in more than 50% of post-pubertal males. Mumps deaths are rare and mostly attributable to meningitis.

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Sporadic cases of acute parotitis are most often due to causes other than mumps, including Epstein-Barr virus and other viral infections. If mumps is suspected, laboratory testing should be performed. Clinical specimens should ideally be obtained within three days and not more than eight days after parotitis onset.

Acute mumps infection can be detected by PCR, mumps virus culture, the presence of serum mumps IgM, or a significant rise in IgG antibody titer in acute and convalescent serum specimens.

Mumps diagnostic tests have many limitations. Serologies may be falsely positive because of other conditions that cause parotitis. Serum mumps IgM test results may be falsely negative or IgG test results may already be positive at the initial blood draw in people who have had previous contact with mumps virus, either through vaccination or natural infection. Viral detection by PCR or culture may have low yield if the buccal swab is collected more than three days after parotitis onset. For all of these reasons, mumps cases can't be ruled out by negative lab results.

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Treatment for mumps is supportive only. Because sporadic acute parotitis cases are rarely mumps, consider vaccination status, epi links and results of testing for other etiologies when deciding which control measures are appropriate.

Unlike measles, MMR vaccine and immune globulin are not indicated for post-exposure prophylaxis. However, susceptible contacts should still be vaccinated to protect against future exposures.

Isolation and quarantine are important tools for mumps control. Recent outbreaks have shown that mumps can spread even among vaccinated people in settings with close contact, such as among students living in dormitories.

Mumps case patients should be isolated for 5 days after parotitis onset. Droplet precautions should be used when caring for mumps patients in healthcare settings.

Guidance for quarantine of exposed persons depends on the setting. In a healthcare setting, susceptible contacts should be excluded from the 12th day after the 1st unprotected exposure through the 25th day after the last exposure.

In a school setting, exclude susceptible contacts until the 26th day after onset in the last case in the affected school. Once vaccinated, students can immediately be readmitted.

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Rubella is a viral illness characterized by a mild, maculopapular rash. Children usually develop few or no constitutional symptoms, but adults may experience a 1–5-day prodrome of low-grade fever, headache, malaise, mild coryza, and conjunctivitis. Post auricular, occipital and posterior cervical lymphadenopathy is characteristic, and precedes the rash by 5–10 days.

The rubella rash occurs in 50%–80% of rubella-infected persons. It begins on the face and progresses downwards. Rubella is sometimes misdiagnosed as measles or scarlet fever. Other symptoms can occur, including arthralgia or arthritis in up to 70% of adult women with rubella. Severe complications include thrombocytopenic purpura and encephalitis. These are not common and mostly seen in adults.

Rubella is transmitted through direct or droplet contact from nasopharyngeal secretions and has an average incubation period of 17 days. Persons with rubella are most infectious when the rash is erupting, but they can shed virus from 7 days before to 7 days after rash onset.

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When rubella infection occurs during pregnancy, serious consequences can result. These include miscarriages, fetal deaths, and a constellation of severe birth defects known as congenital rubella syndrome (CRS). Infection early in pregnancy is most severe. Up to 85% of fetuses infected in 1st trimester will be affected, but defects are rare with infections after 20 weeks gestation. The most common congenital defects are hearing impairment, cataracts, heart defects and neurologic abnormalities.

As shown in this graph, both rubella and CRS have become much less frequent in the US due to vaccination efforts over the past several decades. Elimination of endemic rubella was verified in the United States in 2004. However, because of international travel and countries without routine rubella vaccination, imported cases of rubella and CRS cases are likely.

Prevention of CRS is the main objective of the rubella vaccination program.

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Clinical diagnosis of rubella is unreliable, therefore, suspected cases should be laboratory confirmed. PCR is most often used to detect rubella virus. Serology interpretation is challenging. Because rubella incidence is low, a high proportion of IgM-positive tests will likely be false positives and may occur due to the presence of rheumatoid factors, cross-reacting IgM, or infection with other viruses.

To detect a significant rise in rubella-specific IgG, the first serum should be obtained as soon as possible after onset of illness and the second serum should be collected about 7–21 days after the first specimen. In most rubella cases, rubella IgG is detectable by 8 days after rash onset. Tests for IgG antibody should be conducted on both acute-and convalescent specimens at the same time with the same test.

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As with mumps, post exposure MMR vaccination doesn't prevent or alter the clinical severity of rubella and is not recommended. The same is true with immune globulin (IG).

Any direct contact with a patient with rubella during the infectious period (7 days before to 7 days after rash onset) is defined as an exposure. Every effort should be made to identify all pregnant women who might have been exposed to a patient and evaluate them serologically for rubella-specific IgM and IgG antibodies.

Isolation and quarantine should be implemented as outlined here- Cases should be isolated for 7 days after rash onset.

Quarantine depends on the setting. In a healthcare setting, exclude non-immune for 7 days after exposure and continuing through either 23 days after last exposure or 7 days after rash appears. Exposed healthcare personnel who are vaccinated as part of control measures should be excluded from direct patient care for 23 days after the last exposure to rubella.

In a school setting, exclude until 23 days after the onset of rash of the last reported case-patient in the outbreak setting.

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This table provides a quick summary reference of key information for measles, mumps and rubella regarding transmission, incubation and infectious periods, levels of communicability and exposure.

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Since licensure in the 1960s and 1970s, MMR vaccine has been an important tool in the prevention of measles, mumps rubella and congenital rubella syndrome. MMR is a live, attenuated vaccine given in a two-dose series at 12-15 months and 4-6 years. Effectiveness against all three infections is high, as shown here, and immunity is considered lifelong.

For more detailed information on MMR vaccine recommendations, please refer to the most recent CDC MMWR Report from the Advisory Committee on Immunization Practices (ACIP).

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Next, I will discuss polio.

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Polio is an infectious disease characterized by acute flaccid paralysis and caused by 3 serotypes of virus that lives in the throat and intestinal tract. It is most often spread through person-to-person contact with stool of an infected person, and may also be spread through oral/nasal secretions. Most people infected with the polio virus have no symptoms; however, for the less than 1% who develop paralysis, it may result in permanent disability and even death.

Although the last U.S. case occurred in 1979, polio used to be very common in the United States and caused severe illness in thousands of people each year before polio vaccine was introduced in 1955. In the U.S., children now receive 4 doses of inactivated polio vaccine (IPV), at 2 months, 4 months, 6-18 months, and a booster shot at 4-6 years. Oral polio vaccine (OPV) is still used in many parts of the world.

Global eradication efforts are underway in Pakistan, Afghanistan and Nigeria, the three remaining polio endemic countries. In October, 2013, the World Health Organization (WHO) announced that polio had been detected in Syria for the first time since 1999. This resurgence illustrates the challenges of disease elimination in places where there is civil unrest, frequent population movements and gaps in immunity. The risk of further spread of wild poliovirus type 1 across the region is considered to be high, according to WHO. For North Carolina, as well as other states, the potential for importation remains as long as polio exists anywhere.

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Specimens for culture from stool, pharyngeal swab or CSF are acceptable for testing. Virus isolation is highest from stool and less so for other specimens. Labs should forward virus isolates to CDC for intratypic differentiation to determine whether the isolate is wild or vaccine-related. Serology plays a supporting diagnostic role. Identification of wild poliovirus is a public health emergency and paralytic polio requires immediate reporting. Testing and recommendations would be made in consultation with CDC, state and local public health.

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Like polio, diphtheria and tetanus are diseases that you will probably never see; however they continue to be global public health concerns.

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Diphtheria, now uncommon in the United States, is a disease caused by infection with toxigenic strains of Corynebacterium diphtheriae. The disease is transmitted from person to person by

respiratory droplets or direct contact with respiratory secretions, discharges from skin lesions or, rarely, fomites.

The onset of respiratory diphtheria is insidious and begins 2–5 days after exposure with sore throat, malaise, and low-grade fever. The hallmark of respiratory diphtheria is the presence of an exudate that forms into a tough, grayish-white pseudomembrane over the tonsils, the pharynx, or larynx. The pseudomembrane is strongly adherent, and attempts to dislodge it usually result in bleeding. The membrane may progress and cause airway obstruction, which, if left untreated, can be fatal. Accompanying inflammation of the cervical lymph nodes and surrounding soft-tissue swelling of the neck give rise to a "bull-neck" appearance, as shown in this picture.

Absorption of diphtheria toxin from the site of infection can cause systemic complications, including damage to the myocardium, nervous system and kidneys. Untreated respiratory diphtheria lasts for one to 2 weeks, but complications can persist for months. The case-fatality rate is about 10%.

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Diphtheria was once a major cause of illness and death among children in the United States. The graph on the right shows the remarkable decline in the number of cases in the United States from 1940 through 2010 that has occurred as a result of vaccination.

However, the disease continues to circulate globally, with occasional importations into the US. In 2011, 4,887 cases of diphtheria were reported worldwide to the World Health Organization (WHO), but many more cases likely go unreported. Although few cases of respiratory diphtheria have been reported in the United States in the past 2 decades, the disease is not considered eliminated. A carrier state may persist in asymptomatic persons.

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Diagnostic tests used to confirm infection include isolation of C. diphtheriae by nasal, throat or membrane culture and toxigenicity testing. CDC can perform a PCR test on clinical specimens to confirm infection with a toxigenic strain.

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Treatment includes administration of diphtheria antitoxin plus antibiotics and age appropriate vaccination. CDC can authorize Diphtheria Antitoxin (DAT) for use under Investigational New Drug (IND) protocol. Patients are usually not contagious 48 hours after antibiotics begin.

Contact investigations include testing, prophylactic treatment, vaccination, and monitoring for symptoms.

No discussion of diphtheria can fail to mention the historic Alaskan Iditarod. The original “Great Race of Mercy” occurred in 1925 when dog mushers from around Alaska joined forces to carry life-saving diphtheria serum to Nome in an effort to control a diphtheria outbreak.

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Tetanus is different from other vaccine-preventable diseases because it does not spread from person to person. The bacteria are usually found in soil, dust and manure and enter the body through breaks in the skin - usually cuts or puncture wounds caused by contaminated objects. The incubation period may range from 1 day to several months, depending on the wound type. Most cases occur within 14 days. In general, shorter incubation periods are seen with more heavily contaminated wounds, more severe disease, and a worse outcome of the disease.

The most common initial sign of generalized tetanus is spasms of the muscles of the jaw, or "lockjaw". Spasms continue for 3-4 weeks and complete recovery may take months.

Today, tetanus is uncommon in the United States, with an average of 29 reported cases per year from 1996 through 2009. The graph on the right shows the decreasing number of cases in the United States from 1947 through 2010. Nearly all cases of tetanus are among people who have never received a tetanus vaccine, or adults who don't stay up to date on their 10-year booster shots. Diabetes and intravenous drug use may be risk factors for tetanus. Maternal and neonatal tetanus are still public health challenges in places where unhygienic standards still exist. WHO estimates that in 2010, 58,000 newborns died from neonatal tetanus.

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Diagnosis of tetanus is based on the clinical presentation. History of an injury or apparent portal of entry may be lacking. The organism is rarely recovered from the site of infection, and there are no confirmatory lab tests.

Tetanus is a medical emergency requiring hospitalization and immediate treatment with human tetanus immune globulin (TIG), a tetanus toxoid booster, agents to control muscle spasm, and aggressive wound care and antibiotics.

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Approval from the CD Branch is necessary for testing through the State Lab for suspect and probable vaccine preventable diseases with the exception of pertussis. Keep in mind that for diseases you will probably never see, testing and recommendations are likely to be updated before you will ever need them, so checking for the latest CDC guidance and consultation with the CDB is necessary.

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Timely and complete electronic case reports are important for routine surveillance. The expectation is that case reports are transmitted to CDC within one month of diagnosis. To meet this CDC Program Performance Measure, the information listed here is needed for each NC EDSS vaccine preventable disease entry-

Administrative Package
Initial source and date of report to public health, county of residence, investigation trail

Clinical Package
Symptom onset date, all case definition data, treatment, hospitalization, outcome

Lab Package
Specimen date, type, result, ordering provider, and facility. It should be noted that some diseases require that the local lab send isolates from sterile sites to the SLPH for serotyping. These are Haemophilus influenzae, Neisseria meningitidis (meningococcal disease), and group A Streptococcus pyogenes.

Risk History Package
Exposure information, epidemiological links

Vaccine Package
Shot history dates, reason for refusal.

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The resources listed on these final slides are used frequently in your CD work. Thank you for your attention. I hope this has been helpful, and please feel free to contact the CD Branch with any questions you have.

Slide 43 CDC Resources

Slide 44 NC Resources