Hepatitis B Virus
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SLIDE 1
I'm Elizabeth Draper, a Nurse Consultant with the Immunization Branch for the NC Division of Public Health. I'll be presenting today's lecture on hepatitis B.

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After this lecture, you should be able to recognize the common modes of hepatitis B virus (or HBV, as it's often referred to) transmission; apply your knowledge of hepatitis B serologies and their possible interpretations to help you determine case definition; locate the web-based DPH guidance for use in HBV case investigation; and finally, apply the HBV NC EDSS algorithms that you find on the site when reporting cases.

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In the mid-1980's, approximately 26,000 new acute cases of hepatitis B were reported in the US each year. Due in part to successful screening and vaccination programs and the implementation of universal precautions, that number has been decreasing. In 2007, 4,519 new cases were reported. Because symptoms can be very mild, many infected individuals may not seek medical attention. The CDC estimates that only around 10% of new acute cases are reported, and the actual number of new cases occurring in 2007 was probably closer to 43,000. Some of these acute infections do not resolve and will become chronic infections. According to CDC estimates, there are 800,000 to 1.4 million chronic carriers in this country. Many of these carriers are unaware that they have hepatitis B and are able to infect others. Chronic infection is responsible for most HBV-related morbidity and mortality, including cirrhosis and liver cancer. In the US, approximately 3,000 people die of hepatitis B-related chronic liver disease each year.

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Because the early strategies of the 1980's to prevent HBV were not very effective, the CDC developed national strategies to eliminate HBV transmission. These strategies were published in the early 1990's. North Carolina's Hepatitis B Prevention Program incorporated these strategies through the Perinatal Hepatitis B Prevention Program for tracking and prophylaxing infants born to infected mothers (1990); a universal statewide children's immunization program that offers hepatitis B vaccine to all children 0-18 years of age at no charge (1994); collaborative immunization initiatives to vaccinate at-risk adults (2001); and, the Sixth-Grade school-site Hepatitis B Immunization Initiative, an 11 year initiative for vaccination of susceptible adolescents prior to the age when risk of exposure is the greatest. We completed this program in May 2006.

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HBV is a blood-borne pathogen and can be transmitted percutaneously by way of contaminated sharps and non-intact skin entry. It can also be transmitted perinatally from an infected mother to her infant, or by sexual and other mucous membrane

exposures, such as splashes to the eyes, nose and mouth, or by indirect transmission of virus that is shed on inanimate objects, then touched and transferred to mucous membranes, open wounds, or abrasions. Hepatitis B virus is much more contagious than HIV. This is probably due to more hepatitis B viral particles being present in the blood of an infected person and also the resiliency of the hepatitis B virus. Studies show hepatitis B virus may be viable and infectious for at least 7 days at room temperature on environmental surfaces.

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After exposure, incubation may take anywhere from 6 weeks to 6 months. If symptoms occur, they can include fever, malaise, headache, loss of appetite, nausea and vomiting, abdominal pain, skin rashes, and myalgias and arthralgias. With jaundice, which usually develops after onset of other symptoms, there may be light or gray-colored stools, as well as dark urine. All forms of viral hepatitis (A, B, & C) have similar symptoms. Usually, infants and young children with newly acquired hepatitis B will be asymptomatic, while older children and adults will be symptomatic in 30 to 50% of the cases. Hepatitis B surface antigen (HBsAg), is the serologic marker for infectiousness and may be present in the blood for several weeks before the onset of symptoms. It can be present for days to months after an acute infection and persists in chronic infections.

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These are some of the hepatitis B labs that appear in the case definitions and their basic interpretations:

HBsAg is hepatitis B surface antigen. As I said earlier, this is considered a marker of infectivity when found in the serum.

Anti-HBc is the total hepatitis B core antibody and indicates a previous or ongoing infection at an unknown time.

HBeAg stands for hepatitis B “e” antigen. This is the marker of a high degree of infectivity and viral replication.

Anti-HBs, or hepatitis B surface antibody, is generally interpreted as an indicator of recovery and immunity from infection. You may also see this in individuals who have been vaccinated against hepatitis B.

IgM anti-HBc indicates a recent infection with HBV (usually 6 months or less).

HBV DNA, which you may also see referred to as “viral load,” carries the genetic blueprint of the virus. High levels of HBV DNA indicate a high rate of virus replication.

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Since 1991, North Carolina communicable disease law has mandated that pertinent hepatitis B serologic test results and all diagnosed acute and chronic HBV cases, be reported to the local health director. You may receive hepatitis B reports from physicians and medical facilities. The NC Administrative Code also states that laboratories are responsible for reporting “Hepatitis B virus or any component thereof, such as hepatitis B surface antigen.” Local communicable disease staff investigate cases and report to the NC Division of Public Health for state and national surveillance. This reporting is done through NC EDSS, the NC Electronic Disease Surveillance

System. Detailed information on the reporting and follow-up of hepatitis B can be found in the on-line NC Communicable Disease Manual, in the NC EDSS section, under "Disease Specific Guidance." The URL for this site is listed at the end of this slide presentation in the "Resources" section.

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Once you've accessed this section, you will find the following resources: Hepatitis B Rules for Investigation and Reporting in NC EDSS, also including guidance on who is responsible for investigating an event and how to determine which previously reported events do not require further investigation; Hepatitis B ELR Generated Event Decision Tree; Hepatitis B Paper Copy Lab Decision Tree; NC EDSS Hepatitis B Pregnancy Tracking and Perinatal Tracking are easy to follow decision trees or algorithms; Contacts provide guidance on how to enter contacts into NC EDSS.

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When you receive a report for a case of acute hepatitis B, the first thing you will do is look at the case definition. The clinical case definition describes an acute illness with a discrete (or distinct) onset of symptoms, AND jaundice or elevated serum aminotransferase levels (which are ALT or AST levels, also known as SGPT and SGOT). The laboratory criteria for diagnosis consists of IgM antibody to hepatitis B core antigen (anti-HBc) positive, OR hepatitis B surface antigen (HBsAg) positive, and IgM anti-HAV negative (if done). A confirmed case meets the clinical case definition and is lab confirmed. If you have only received a lab, or the CD report is not complete, you should contact the physician's office for additional information. This is also a good opportunity to ask what information has been discussed with the patient. Is the patient pregnant? Has the physician discussed control measures? This information will help you to determine what follow-up is needed. If the information meets case definition, you would report it as an acute case of hepatitis B.

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This graph shows the course of a resolving acute infection and the sequence of serologic markers. HBsAg, shown here as the red line, usually becomes detectable at 1-2 months after exposure. Symptoms, with ALT elevation and jaundice, occur several weeks later. The blue, yellow, and orange lines show the course of antibody responses that occur after infection. In a resolving case, HBsAg (the red line) is usually not detectable after 6 months. As acute HBV resolves, the anti-HBs may take up to 8 months to show positive serologically. Note the 8 week "window" between HBsAg becoming negative and HBV surface antibody becoming positive. Because many cases of acute HBV do not produce significant symptoms, clinicians will probably only see 10% of the cases that actually occur.

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The case definition for chronic hepatitis B addresses both probable and confirmed carriers. The chronic carrier is asymptomatic, but may have a discrete, or a vague,

onset of symptoms. Elevated ALT/AST may be present due to a compromised liver with onset of fibrosis or cirrhosis.
A probable carrier has a single positive hepatitis B surface antigen, hepatitis B e antigen or HBV DNA test result when no hepatitis B core antibody IgM results are available. A confirmed carrier is hepatitis B surface antigen or HBV DNA or hepatitis B e antigen positive two times, at least 6 months apart. Any combination of these tests performed at least 6 months apart meets the confirmed *chronic* (carrier) case definition, OR they can be IgM antibody to hepatitis B core antigen negative and have a positive test for hepatitis B surface antigen, hepatitis B e antigen or HBV DNA. Most of the serious complications, such as fibrosis, cirrhosis, liver failure and hepatocellular carcinoma occur in chronically infected individuals. Again, you would want to contact the physician's office to ask the pregnancy question and to find out what information has been shared with the patient about hepatitis B.

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This graph shows the serologic picture of a chronic infection. Notice that HBsAg (the red line) persists past 6 months and there is no production of anti-HBs.

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LHD follow-up of acute and chronic cases of hepatitis B consists of testing contacts through the State Laboratory of Public Health, instruction of cases and contacts in control measures, administering vaccinations to contacts and referring them for hepatitis B immune globulin (or HBIG), if indicated. For acute cases of hepatitis B, sexual, blood, mucosal, and needle-sharing contacts need to be tested, referred for prophylaxis with HBIG if appropriate, and vaccinated. Additionally if the acute case is the primary caregiver for an infant less than 1 year of age, the infant should be referred for prophylaxis. Until the results of testing are known, contacts should be instructed to follow control measures to prevent possible transmission of the virus. Prophylaxis with a single dose of HBIG within 14 days of the last sexual exposure or 7 days past the last blood, mucosal or needle sharing exposure may prevent a contact from developing hepatitis B. Although testing is recommended before prophylaxis, treatment should not be delayed past these windows of opportunity waiting on test results. Refer contacts within these windows immediately. Hepatitis B vaccine is available from the state at no cost for recognized contacts to a hepatitis B case. All contacts who test negative should be vaccinated against hepatitis B as quickly as possible. Because of the lag time in obtaining test results, local health departments may obtain the blood sample and provide the first vaccination in the same visit. Person-to-person transmission of HBV can occur in settings involving nonsexual interpersonal contact over a long period of time, although it isn't often documented. For this reason, follow up of a chronic case follows the same course as an acute case, with the addition of testing and vaccinating all household contacts, not just those with sexual, blood, mucosal or needle-sharing history. Finally, any contact tested for acute or chronic hepatitis B should be referred to their private physician if test results are positive for the disease.

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An important part of the follow-up of hepatitis B cases includes control measures. Detailed control measures for hepatitis B can be found in the NC Administrative Code cited on the slide. There is also a form addressing control measures in the Hepatitis B Manual that you can discuss with the patient and request that they sign. These resources can be easily accessed from the online NC Communicable Disease Manual. Section (a) of the hepatitis B control measures deals with the hepatitis B infected person and section (b) addresses control measures for "persons reasonably suspected of being exposed." Section (b) also addresses the prophylaxis for infants born to HBsAg positive mothers and HBsAg unknown status mothers.
Administration of hepatitis B immune globulin, or HBIG, provides immediate, "passive" protection and would be indicated in certain post-exposure settings (within 7 days of blood exposure or within 14 days of sexual exposure). Hepatitis B vaccine produces an "active" immune response in approximately 50% of vaccinated persons after one dose. If an active immune response occurs after vaccination, antibodies develop in approximately 2 weeks. Proper spacing of doses is usually at 0, 1 – 2 months and 6 months. The single antigen hepatitis B three-dose vaccination series is administered intramuscularly to help ensure optimum immune response and long-term protection. As a CD nurse in a local health department, an important part of your job will be to follow-up with hospitals and providers to make sure that the infants born to HBsAg positive mothers receive this critical prophylaxis.

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Perinatal transmission (from infected mother to infant at birth) and horizontal transmission from infected household contacts are two primary sources for HBV infection for infants and children. The younger a person is at the time of infection, the more likely he will develop chronic HBV. The risk of developing the chronically infected state is inversely related to age at the time of infection. While greater than 90% of infected adults will resolve the infection and be immune for life, more than 90% of acutely infected infants will become chronic carriers with the risk of lifelong liver disease and early death. (For children 1-5 years of age, it's 25 to 50%).

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This is the case definition is for Hepatitis B, Perinatally Acquired. Again, we see the positive hepatitis B surface antigen. Perinatal hepatitis B in the newborn may range from asymptomatic to fulminant hepatitis. Additionally, these infants must be greater than 1 – 24 months of age, and born in the U.S. or U.S. territories to an HBsAg positive mother. Initially, when an infant is born to a HBsAg positive mother, the event is entered into the NC Electronic Disease Surveillance System as Hepatitis B, Perinatally Acquired, with a case classification of "contact."

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The Advisory Committee on Immunization Practices (ACIP) developed strategies to prevent cases of perinatal & early childhood HBV. They recommend that prenatal providers test all pregnant women for hepatitis B surface antigen with each pregnancy during an early prenatal visit, and transfer a copy of the ORIGINAL hepatitis B surface

antigen lab report to the delivery hospital so every pregnant woman has accurate documentation of her hepatitis B surface antigen status at the time of delivery. Errors in documentation, transcription and/or interpretation of the mother's hepatitis B surface antigen status occur each year in N.C. *(Results of the 2007 birth cohort showed that out of 216 infants tracked, 6 missed HBIG due to errors in interpretation, transcription, or communication of maternal Hepatitis B surface antigen test results. All 6 infants did receive hepatitis B vaccination within 1 day of birth. Of the 264 infants tracked in the 2008 birth cohort, 7 missed HBIG within the first day of birth, but all 7 did receive hepatitis B vaccination within 1 day of birth.)* Implementing this measure will help prevent errors like this from occurring. Additionally, hospital and obstetrical staff should review the hepatitis B surface antigen status of every pregnant woman upon admission for delivery. If the pregnancy status is unknown at the time of admission for delivery, testing should be done as soon as possible. Hepatitis B surface antigen test results should be included on all forms that transmit information about pregnancy care. All infants born to hepatitis B surface antigen positive and hepatitis B surface antigen unknown status mothers should receive appropriate, timely post-exposure prophylaxis and complete follow-up and, newborns should receive hepatitis B vaccine prior to discharge.

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Because 90% of acutely infected infants may become carriers, we want to do all that we can to prevent them from getting this virus. The ACIP also recommends that prenatal care providers

report the hepatitis B surface antigen POSITIVE woman to the local health department for infant tracking, contact investigation, and prophylaxis. (The testing and vaccination of contacts is provided at no charge and the infants are followed by the local health department to ensure completion of the vaccination series and post-vaccination testing is done). The second recommendation is for providers to counsel the hepatitis B surface antigen positive woman and give medical evaluation, or make a referral to a provider who can evaluate her HBV infection; and finally, providers should also inform the hepatitis B surface antigen positive woman of the need for prompt infant post-exposure prophylaxis, also known as PEP, at the time of delivery. The N. C. Immunization Program Contract Agreement Addendum REQUIRES local health departments to provide or assure case-management services to ensure that 100% of pregnant women in NC are tested for hepatitis B surface antigen during pregnancy, and 100% of infants born to hepatitis B surface antigen positive women and infants born to women with unknown hepatitis B surface antigen status receive recommended immunoprophylaxis and follow-up.

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PEP, consists of hepatitis B vaccine and HBIG, and is administered to the infants of hepatitis B surface antigen positive and hepatitis B surface antigen unknown status mothers within 12 hours of birth. Additionally, ALL medically stable infants weighing ≥ 2000 g at birth and born to hepatitis B surface antigen negative women should receive the hepatitis B vaccine prior to discharge. If the infant weighs less than 2000 g at birth AND the mother is hepatitis B surface antigen positive, the infant should receive PEP

(both HBIG and the first dose of vaccine) within 12 hours of birth. This birth dose would not be considered as part of the vaccine series, and repeated at one month of age or start the HBV vaccine series at one month of age. If the infant weighs less than 2000 g at birth AND the mother is hepatitis B surface antigen negative, the first dose may be delayed until 1 month after birth or until hospital discharge. If the mother's hepatitis B surface antigen status is unknown, the first dose of vaccine would be given within 12 hours of birth and the mother tested as soon as possible. If the mother's test result is hepatitis B surface antigen positive, HBIG would be administered ASAP – preferably within 3 days, but definitely less than 7 days. We would not consider this birth dose as part of the vaccine series. The series would start at 1 month of age or at discharge if the infant was gaining weight. Vaccine given at less than 2000 g may not be as effective, but it gives every possible chance for disease prevention.

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It's important that the local health department follow-up with the hospital to ensure that hepatitis B vaccine and HBIG were administered within 12 hours of birth. If the HBIG was not given within 12 hours of birth, the reason why should be documented in NC EDSS. After infant discharge, pediatric care providers should complete the HBV vaccination series by 6 months of age. Local health departments should contact the pediatrician's office to verify that hepatitis B vaccine doses were given on schedule, (usually at 0, 1-2 months and 6 months of age) and that post-vaccination serologies (hepatitis B surface antigen and antibody to hepatitis B surface antigen (anti-HBs) were drawn at 9-18 months of age, as recommended. If the infant is hepatitis B surface antigen positive, they will be reported as Hepatitis B, Perinatally Acquired and the case classification of "contact" in NC EDSS, would be changed to "confirmed." If the infant is hepatitis B surface antigen negative, but the infant's anti-HBs is less than 10mIU/ml, the health department CD nurse should work with the pediatrician's office to ensure that the infant receives a second hepatitis B vaccination series and is tested again. All of this information should be entered into NC EDSS as it becomes available. If the infant is hepatitis B surface antigen negative and his or her anti-HBs level is greater than or equal to 10mIU/ml, they are considered protected. These results would be entered into NC EDSS and the case classification would be changed to "does not meet criteria." Once complete, you would reassign the event to the State Disease Registrar.

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We've focused a lot on women who test positive for hepatitis B surface antigen (HBsAg), but we also need to address those pregnant women who test negative for HBsAg. It's important for the prenatal provider to assess for behaviors that increase her risk of HBV exposure. These risk factors include more than 1 sex partner in the previous 6 months, evaluation or treatment for an STD, recent or current injection drug use (IDU), or a sexual partner who is HBsAg positive. If a risk factor is present during the pregnancy, the provider should vaccinate the woman against HBV and counsel her about ways to prevent infection. This is also a good opportunity for prenatal care providers to inform the HBsAg negative pregnant woman of the importance of newborn HBV vaccination.

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Many at-risk adults may be seen in your STD Clinic. This provides an additional opportunity for vaccination and education. Settings where all unvaccinated adults should be offered vaccine are STD clinics, drug abuse treatment sites, HIV/AIDS testing sites, and correctional facilities for all inmates incarcerated 6 months or more. The NC Immunization Branch currently offers Twinrix®, a combination hepatitis A and hepatitis B vaccine, to at-risk adults via local health departments, federally qualified health centers, and rural health centers actively participating in the NC immunization program.

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As I mentioned earlier, the ACIP recommends post-vaccination testing for infants born to HBsAg POSITIVE mothers. They also recommend testing for dialysis patients and staff, persons with HIV, those at occupational risk, and sexual or needle-sharing partners of HBV cases. Revaccination is also indicated for anti-HBs non-response. Health care workers should be tested 1-2 months after administration of the final dose in the hepatitis B vaccination series. Otherwise, there are no recommendations for periodic testing, or for booster doses. Post-exposure prophylaxis would involve testing if the exposed health care worker's response status was unknown. Persons who do not respond to the first series should be given a second series. If the immune response is not sufficient after the second series, no further doses are recommended, but testing for HBsAg should be considered. True non-responders should be counseled about their risks of exposure and their susceptibility. The post-exposure prophylaxis for non-responders would consist of HBIG (passive antibody) ASAP after exposure and again at 1 month.

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Efforts to reduce the incidence of hepatitis B are working. This CDC chart illustrates the estimated acute case count of 53,000 in 1980, the peak in 1985 of 74,000, followed by a decrease to 13,000 by the year 2007. The number of reported acute cases for this time period starts at 19,014 in 1980 and decreases to 4,519 by the year 2007. Your efforts in the reporting and follow-up of hepatitis B are essential if we are to continue this successful downward trend. The following 2 slides contain some references and resources that you may find helpful. If you have specific questions or need additional guidance, please call the Immunization Branch. Thank you for your time and your participation in today's lecture.

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References

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Resources