Rabies: Human Risk Assessment Presentation
November 4, 2013
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SLIDE 1 TITLE

SLIDE 2
Hello, my name is Marilyn Goss Haskell and I am one of the state's public health veterinarians with the North Carolina Division of Public Health, Communicable Disease Branch. This presentation is about Human Rabies Risk assessments.

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The learning objectives for this presentation are:

- To recognize the public health significance of rabies,
- To be able to explain what constitutes a rabies exposure, and
- To be able to explain the importance of the different vaccine regimens that are administered to prevent rabies: prior to an exposure called pre-exposure prophylaxis and after an exposure called postexposure prophylaxis.

SLIDE 4
Your key Rabies Resources are listed on this slide

- **The 2013 NC Rabies Public Health Program Manual** is a detailed and comprehensive guide for rabies prevention and control. You should take the time to become familiar with this manual. Important forms and algorithms are found in the appendix including the affidavit used to qualify indigent patients for free rabies biologics and the Rabies Algorithm for Human Risk Assessments for exposures to domestic and wild animals.
- The **Compendium of Rabies Prevention and Control** provides information related to prevention and control of rabies in animals that is not addressed in NC general statute, including guidance on rabies vaccinations in animals, and management of exotic animals and wild hybrids.
- The **Centers for Disease Control website** on Rabies has a variety of valuable resources including guidance for medical assessment, diagnosis and management of potential human cases of rabies and updates about shortages of human rabies biologics.
- And lastly, do not hesitate to call the Communicable Disease Branch Rabies On-Call public health veterinarians and epidemiologists for assistance. We are available (24/7) at 919-733-3419

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As public health practitioners in NC it is our mission to educate people in our state about the serious threat of rabies to humans and domestic animals and when there is a human exposure to ensure an accurate risk assessment and prompt referral for postexposure prophylaxis, if indicated.

- Rabies is the most important zoonotic disease risk for humans and domestic mammals in North Carolina.
- In North Carolina the rabies reservoir animals are raccoons and bats; each species may be infected with their own species-specific variant of the rabies virus.
- Rabies is nearly 100% fatal. However, if a person is exposed to a rabid animal, and receives prompt wound care and postexposure prophylaxis the disease is 100% preventable.

SLIDE 6

According to the World Health Organization, worldwide there are approximately 60,000 human deaths due to rabies each year, primarily in the developing countries of Africa and Asia. More than 99% of all human rabies cases are due to canine variant rabies and more than half of those cases and deaths are in children less than 15 years old. In the 1940s and 50s canine variant was the threat in the US, but canine variant was recently eradicated from the US in 2008, according to the CDC. The majority of indigenous human rabies cases and deaths in the US over the last 3 decades were caused by bat variant rabies.

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In the US between 2002 and June 2013, 27 domestically acquired human rabies cases were reported. Among the 18 patients that acquired bat variant cases, 16 patients died and two survived; 28 % did not recall an exposure to a bat, and 72% of the cases recalled direct contact or a bite exposure but did not realize the significance and did not seek timely postexposure prophylaxis. There have been only 3 reported cases of eastern raccoon variant rabies in humans acquired in the US, all since 2003. A 25 year old Virginia man died in 2003 with an unknown exposure. More recently, a Maryland man died of eastern raccoon variant rabies in 2013, 17 months after organ transplantation in 2011. The donor, a NC resident who died in 2011, was retrospectively diagnosed with ERV rabies through testing banked tissues, the variant was genetically linked to the recipient.

Slide 8

Rabies is enzootic in North Carolina. That means it is present in the wildlife and feral and stray animals throughout the state. Raccoons are the terrestrial or land reservoir for rabies in NC – they are the species that is most likely to be infected, spread and keep the rabies virus alive in NC. Domestic animals like dogs, cats, and livestock, though not likely to become infected and transmit if currently vaccinated, are susceptible to rabies because they are mammals. When domestic animals become infected with rabies, people are more likely to be exposed. Rabies virus is present in the saliva of mammals when they are shedding the virus, but, animals may not always appear sick if it is early in the shedding period.

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Close interactions with raccoons results in spread of rabies or "spillover" into other wild and domestic animals, and humans. Raccoons and other animals that may be infected, like foxes, have adapted well to urban and suburban areas that people live in with their pets. It is not uncommon to see raccoons around homes throughout NC. You should assume any raccoon or rabies vector species is infected with rabies. One of the most important Public Health messages we can deliver is for people and their pets to stay away from wildlife! Do not approach, handle or bring wildlife home. Do not feed wildlife. Do not feed your pets outside, or leave pets outside unsupervised.

There is a section in the Appendix of the Rabies Manual called "Information for the public" that provides talking points for a news release. All livestock are susceptible to rabies. It is not uncommon for skunks to be seen in pastures and paddocks with livestock, including goats, cattle and horses, and then test positive for rabies. When livestock are potentially exposed to rabid animals or are reported rabid, the SLPH and the CDB public health veterinarians will notify NCDA Veterinary Division, who then will take over the livestock part of the investigation.

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This slide lists the high risk rabies vector species that we expect to be infected with rabies in NC and transmit the disease. They include the reservoir species raccoons and bats and other wildlife that live and feed in the same environment as raccoons: skunks, foxes, beaver, groundhogs and large carnivores, like coyotes and bobcats.

If a human or a domestic animal (not currently vaccinated) is exposed to a high risk rabies vector, typically by a bite, then the wild animal should be submitted for testing to the state. Any human exposed to any of these animals listed will require rabies postexposure prophylaxis unless the animal is captured by animal control, submitted for testing to the SLPH, and tests negative *within 48 hours.*

SLIDE 11

Each year about 4,000 animals are tested at the SLPH. About 90% of the reported rabid animals each year are wildlife species. You can see from this pie chart that among 431 positive animals in 2012; raccoons represented about half of the positive animals, followed by skunks 19%, foxes 16%, and bats 6.5%. These data do not represent the percentage of rabies positive animals for a particular wildlife species population in North Carolina. Remember that these animals were submitted because there was an unusual circumstance of exposure or potential exposure to a human or not currently domestic animal; often these animals are sick or behaving unusually for the species. Among domestic animals, rabid cats consistently outnumber rabid dogs. Every year several livestock species test positive as a result of an encounter with a rabid species of wildlife. Low risk wild animals including small rodents (like mice, rats, squirrels, etc.) and rabbits are approved for testing typically because of a human bite. Small rodents are not

likely to be infected with rabies, but when the circumstances of the exposure are investigated, if the bite was unprovoked, the animal ill or behaving inconsistent for the species, it will be approved for testing. There have been 3 domestic pet rabbits that have tested rabies positive in NC, all were housed outside. Animal control is required to call one of the state's public health veterinarians to approve testing of low risk species through a risk assessment before they can be submitted to the SLPH for testing.

SLIDE 12

This graph displays the number of confirmed rabid animals in NC from 1952 to 2012 tested at the SLPH. Raccoon variant rabies in raccoons was first reported in NC in 1991 and has grown into a major epidemic in the state since the early 1990s. The first case of rabies in bats was reported by the SLPH in NC in 1963. In 2013 North Carolina reported the first human case of Eastern Raccoon Variant rabies in a young man who was an avid hunter of raccoons and other small game; he died in 2011. Prior to that, the last reported human rabies case in North Carolina was over fifty years ago, in 1955, a woman in Cherokee county was bitten by her own dog and died from canine variant rabies. There have been 26 human cases of rabies reported in North Carolina from 1918 to October 2013. There have been no reported human cases of bat variant rabies in NC, as of 2013.

SLIDE 13

How did raccoon variant rabies get into North Carolina?

This map shows the expanding epizootic of raccoon variant rabies in the Eastern United States. Two major epidemics of raccoon rabies converged on North Carolina' s wildlife population in the early to mid-1990s from the north and south as pictured by the light and dark aqua coloration on this map in NC. In the 1940s there was an epizootic of raccoon rabies in Florida. Raccoon to raccoon transmission resulted in spread of the disease North throughout FL, AL, GA, SC and then into NC in the early to mid-1990s. A second epizootic developed in the Mid-Atlantic States in the late 1970s – originating at the WVA-VA border as a result of translocation of rabid raccoons for hunting purposes. The mid-Atlantic epizootic rapidly spread north, and south and into NC in the mid-1990s. From that point in time rabies has spread from animal to animal to virtually every county throughout NC. Let's take a closer look at this disease…

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Rabies is caused by a RNA virus of the genus Lyssavirus. Rabies causes an acute meningoencephalitis that is nearly 100% fatal. After virus infected saliva is inoculated into a wound, the virus stays at the site of the bite wound for most of the incubation period. The virus replicates or multiplies in muscle tissue and binds to special receptors at the junction of nerves and muscles. Virus begins to travel quickly through peripheral nerves within nerve axons and muscles toward the spinal cord.

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Once in the spinal cord the virus moves rapidly to the brain where it infects neurons and causes swelling or inflammation, medically called encephalomyelitis. Dysfunction of neurons is what causes all of the central nervous system symptoms of the disease. Once the virus reaches the brain of an infected person or animal, it simultaneously spreads rapidly through nerves to the salivary glands, and like a centrifuge to virtually every nerve in the body (cornea, skin, and organs). Coma and death usually occur shortly thereafter. The incubation period in people is the time from exposure to development of clinical signs of disease and is usually around 3 weeks to 3 months, although incubation periods as short as 5 days and up to years have been documented.

SLIDE 16

Bites from rabid animals are the most common way that people and animals become infected with rabies. There are other modes of possible transmission called non-bite exposures that are listed on this slide that may be less likely to transmit rabies. Any person who has had contact with a rabid or potentially rabid animal, particularly to the saliva, tears, or nervous tissue, should have a risk assessment to determine the need for PEP. Any direct or suspected direct contact with a bat is considered an exposure. Bat bites may go unrecognized or not be taken seriously, as we have learned from the history of humans that have succumbed in the US.

SLIDE 17

An exposure to rabies, is defined by the CDC in the 2008 ACIP guidelines as “any bite, scratch or other situation in which saliva or central nervous system (CNS) tissue from a potentially rabid or confirmed rabid animal enters an open wound, or comes in contact with a mucous membrane by entering the eye, mouth or nose”. Rabies can also be transmitted through tears of a rabid mammal, and this body fluid should be included in the assessment, according to the WHO 2013 guidelines.

SLIDE 18

Bat exposure assessments are more complex. Any potential exposure to a bat requires a thorough evaluation and history of exposure. When multiple bats (greater than one) are found in an inhabited building, call Rabies On-Call for guidance and refer to the 2013 Rabies Manual – Human Rabies chapter, sections on Bat Exposure Assessments and Bats in Building for investigative steps in these situations. If a single bat is involved in a potential human or animal exposure, it should be safely collected and submitted by Animal Control to the SLPH for rabies diagnosis. According to the 2008 CDC ACIP guidelines, “Any direct contact between a human and a bat should be evaluated for an exposure. If the person can be reasonably certain a bite, scratch, or mucous membrane

exposure did not occur, or if the bat is available for testing and is negative for presence of rabies virus, postexposure prophylaxis is not necessary." Other situations that might qualify as exposures include: finding a bat in the same room as a person who might be unaware that a bite or direct contact had occurred. Examples include a deeply sleeping person awakens to find a bat in the room, or an adult witnesses a bat in the room with a previously unattended child, mentally disabled person, or intoxicated person. These situations should not be considered exposures if rabies is ruled out by diagnostic testing of the bat or circumstances suggest it is unlikely that an exposure took place.

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These pictures help to illustrate the reasons why bats bites may go unrecognized or may seem insignificant:

- There may be a limited injury inflicted by a bat bite. See how tiny the bite marks are in the picture.
- There is evidence that some bat-variant rabies viruses are inoculated into superficial epidermal (skin) layers and result in infection. These bat variant viruses have evolved special pathogenicity factors.
- Patients may not be able to recall a bat encounter that might have occurred several weeks or months earlier, and
- Some people may not be aware that bats can transmit rabies and that exposure to a bat is risky business.

Education about bats and rabies is an important part of our job in public health!

SLIDE 20

Within a 7 day period in 2010 we had 3 major bat investigations as shown on this slide! You will undoubtedly receive calls about bat exposures and bat infestations in dwellings. It is important to become familiar with how to assess bat exposures and what recommendations to make. In the Rabies Manual, Human Rabies chapter, follow the guidelines in the *Bats in Buildings* document. We receive calls about bats in homes, rental and HUD housing, daycare, at summer camps, universities, hospitals and churches, and so on. Contact summer camps leaders in your county prior to camp opening and recommend inspection of buildings for bat infestations and exclusion of bats from living quarters by a professional entity if found to be infested.

SLIDE 21

On December 19, 2011 a South Carolina woman died from bat variant rabies. The patient did not report a history of an animal bite, but family members revealed later that bats had been observed in the patient's home during the previous summer. The patient had sought information on bat removal from a local county service, but was not advised of the risk of rabies associated with bat exposures and was not referred for public health consultation. This case highlights the importance of strong partnerships among state and

local public health officials, animal control, and state wildlife agencies to ensure prompt referral of persons potentially exposed to bats to public health officials for appropriate risk assessments and postexposure prophylaxis (PEP) recommendations.

SLIDE 22

This graph shows the seasonality of bats that have tested positive at the SLPH by month from 2002 through 2012. It is important to note that during the months April to October there is an increase in the number of positive bats tested corresponding with increased submissions and bat encounters, primarily in buildings. If a single bat is found in a dwelling and people or pets could have been exposed, it should be safely captured and submitted for testing. If more than one bat is found in a dwelling, then the building may be infested. Recommend that the owner or manager of the building have the building inspected by a Wildlife Damage Control Agent who will determine the points of entry into the living space and building and how to appropriately exclude the bats.
If there is an infestation in the building with the potential for exposures to multiple bats, some not captured, then those persons exposed should be assessed for postexposure prophylaxis and animal control should assess the pets.

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As a CD Nurse at the LHD you will receive calls from animal control, bite victims, attending physicians, Hospital EDs and veterinarians reporting animal bites and possible rabies exposures. Risk assessments for PEP are based on many factors and questions posed to the bite victim. Look in the appendix section of the Rabies Control Manual at the Algorithms for Rabies Risk Assessments to assist you in assessing risk of human exposures and the need for PEP. Some of the key questions to answer are:
Is it a true exposure according to ACIP guidelines?
Is the animal species low risk or high risk, domestic or wild?
If a Low Risk animal:
Was the behavior consistent with the species and were there signs of illness?
Were there bite wounds on the exposing animal?
Was it a provoked or unprovoked attack?
What was the severity of attack on the victim, and location of bite wounds?

It is important to get to know your animal control officers and develop good communications and working relationships, regardless where Animal Control is housed (sheriff or police, environmental health, or other department). Most rabies investigations involve both animal control and CD Nurses. Animal control plays an important role in rabies prevention and control; they enforce the NC Rabies laws, capture the biting animals, implement 10 day confinements and 6 month quarantines, euthanize, prepare and submit animals for rabies testing, and conduct the animal part

of rabies exposure investigations. Animal Control in turn, should refer all human rabies risk assessments to the LHD CD Nurses.

SLIDE 24
Rabies is enzootic in every NC county. If your county does not report an animal rabies case in a particular year, rabies is still present in the wildlife in your county; we can't let our guard down. Enforcement of the rabies laws is ongoing for all counties in NC. The NC Rabies Laws are regulated by the state and enforced at the local level, usually by animal control as delegated by the local health director. There are several North Carolina Rabies Laws that you should become familiar with.

SLIDE 25
All owners of dogs, cats and ferrets are required by NC statute to have their pets vaccinated against rabies by 4 months of age and keep the vaccination current. Vaccination of livestock is not required by NC state rabies laws. The decision to vaccinate livestock is a decision made by the farmer or rancher in consultation with their veterinarian. Animals in public settings (petting zoos, horseback riding, exhibitions or sanctioned agricultural fairs) should be vaccinated against rabies according to the 2011 Rabies Compendium. There are USDA licensed rabies vaccines for horses, cattle, and sheep. There are no currently approved vaccines for goats, swine or donkeys.

SLIDE 26
North Carolina General Statute 130A-196 requires that attending physicians report all animal bites to the local health director within 24 hours. Also the person bitten, parent or guardian and the person that owns or is in control of the biting animal are required to report the bite. Then the bite investigation begins.

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The rabies timeline begins when an animal is exposed to rabies. In this case a dog has killed a rabid raccoon and has mucous membrane exposure to nervous tissue as it bites and chews on the raccoon. The raccoon may have also bitten the dog. The incubation period begins with the exposure and lasts until the onset of viral shedding in an animal. "Shedding" occurs late in the incubation period about the same time virus enters the brain. It is important to remember that rabid animals can shed and transmit rabies virus in their saliva for a short time and still appear normal and healthy, before they develop clinical signs of disease. That period is maximally 10 days, and that is the basis for the 10 day confinement period after a dog, cat or ferret bites a human. You will use this shedding information to determine the time frame of potential human exposures to a rabid animal. You will interview all people potentially exposed to a rabid animal during the shedding period, tracing backwards in time 14 days from the first day the animal

exhibited clinical signs or behavior changes. You will conduct human exposure assessments to determine who will or will not need postexposure prophylaxis.

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The NC statutes 130A-196 and 197 are based on the shedding and incubation periods for rabies in dogs, cats and ferrets. NCGS 130A-196 requires a 10 day confinement period for any dog, cat and ferret that bites a person. Based on guidelines from the CDC and 2011 Rabies Compendium, one of your key references, the 10 day confinement is sufficient time to observe an animal for clinical signs of rabies after a bite to a human. If the animal had been shedding rabies at the time of the bite or exposure, you can be certain the dog, cat or ferret would be dead or very ill with clinical signs of rabies within 10 days of the exposure. If the animal is normal and healthy after 10 days confinement, then it was not shedding rabies virus in the saliva at the time of the bite and no PEP will be required for the victim. GS 130A-197 requires either up to a 6 month quarantine or euthanasia for all dogs, cats and ferrets that are not currently vaccinated when they are exposed to a rabid animal or animal reasonably suspected to be rabid. An infected dog, cat or ferret may incubate rabies as long as 6 months, but typically develops rabies 3 weeks to 3 months after the bite. The quarantine period covers the entire potential incubation period.

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According to NC statute 130A-197 if a currently vaccinated dog, cat or ferret is exposed to a potentially rabid animal, then all that is required is a rabies booster administered within 5 days of the exposure.

SLIDE 30

If a person or not- currently vaccinated animal are exposed to a potentially rabid animal, then the animal should be submitted to the SLPH for rabies testing.

SLIDE 31

This is a true story and we receive calls of this sort more often than we like or should. A pet dog fights with a raccoon or a dead raccoon is found in the yard where a pet was left unsupervised. The dog then licks a family member or the family member handles and cleans wounds inflicted by the raccoon, with bare hands and there are fresh cuts on their hands or they cannot recall if they wiped their eyes or nose with their wet hands. If wet saliva, tears or neurological tissue from a rabid or potentially rabid raccoon were transferred onto a mucous membrane or open wound of a person, then that is considered an exposure to rabies. PEP would be recommended unless the raccoon were captured and tested negative for rabies. People should always be warned not to handle and to keep their children away from wild animals or animals recently exposed to wild animals. If necessary to handle the pet, thick impermeable rubber or latex gloves should

be worn and don't let children near. What happens to the dog in this situation? Animal Control should always be called to assist in the assessments of dog, cat or ferret exposures to potentially rabid animals. Animal control will determine if the dog was currently vaccinated against rabies and if so, then a rabies booster is required within 5 days of date of exposure. If no humans or unvaccinated animals were exposed - the raccoon will not have to be submitted for testing. If the raccoon escapes or tests positive or UNSAT and the dog is unvaccinated or not currently vaccinated against rabies the dog will be placed in 6 month quarantine at the discretion of the LH Director or euthanized. If a person or unvaccinated animal is exposed to a potential rabies vector, ALWAYS call animal control to capture the wild animal if possible and submit for testing. This is one reason why it is so important to keep dogs, cats and ferrets currently vaccinated.

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If a domestic dog, cat or ferret bites a person, and is not captured by animal control and placed in a 10 day confinement within 72 hours, then the patient should begin PEP.

SLIDE 33

There are currently 2 cellular derived rabies vaccines available for rabies vaccination of humans. The two manufacturers are Novartis and Sanofi Pasteur. There are also 2 companies that manufacture human rabies immune globulin --Sanofi Pasteur and Grifols (formerly Talecris). There is an affidavit to qualify indigent patients for free rabies vaccine and HRIG through our SLPH located in the Appendix of the Rabies Control Manual. You may contact Veterinary Public Health to find out more about this program.

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Pre-exposure Immunization is recommended for people "at risk" for rabies exposures in their line of work or hobby.

People at risk include:

- Veterinarians and Staff
- Laboratory Workers
- Animal Control Officers
- Animal Shelter Workers
- Wildlife Workers
- Travelers to rabies endemic countries

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The regimen for Pre-exposure consists of 3 doses of rabies vaccine, one dose given on Days 0, 3 and 21 or 28 consisting of 1.0 mL IM in the Deltoid muscle; alternating Deltoids.

Vaccinations can be given by the local health department or a health care provider. A Rabid Fluorescent Foci Inhibition Test (RFFIT) is recommended by the ACIP to determine there is an adequate rabies virus or neutralization antibody titer: every 2 years for those at moderate risk and every 6 months for those at high risk (laboratorians). This test is available at Kansas State University and Atlanta Health Associates and is the only test recommended by the CDC and ACIP for assessment of rabies titers.

SLIDE 36

The Postexposure Rabies Vaccination regimen for unvaccinated people that are not immunocompromised requires 4 doses of rabies vaccine administered, one each on Day 0, 3, 7, and 14: 1.0 ML IM in the Deltoid muscle (Day 0 on the opposite side as the HRIG then alternating right and left deltoids). Human Rabies Immune Globulin is given on Day 0 (20 IU/kg) into and round the wound sites as is feasible and any additional dosage is inoculated into the deltoid and anterolateral thigh on the opposite side of vaccine administration. HRIG provides immediate passive immunity until the patient's active immunity begins; a significant antibody titer is usually evident about 7 days after the initial rabies vaccine.

Remember if the patient is immunocompromised, a five dose regimen is administered: one dose of vaccine on Days 0, 3, 7, 14 and an additional dose of vaccine is given on Day 28. Corticosteroids, other immunosuppressive agents, antimalarials, and immunosuppressive illnesses might reduce immune responses to rabies vaccines substantially, for persons with immunosuppression, with the understanding that the immune response still might be inadequate. Postvaccination rabies virus-neutralizing antibody titers, the Rapid Fluorescent Foci Inhibition Antibody Test, may be checked one to two weeks after the last vaccine dose. Titer values might be less than adequate among immunosuppressed persons with HIV or other infections. Always consult Veterinary Public Health with any questions.

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On June 24, 2009 the Advisory Committee on Immunization Practices (ACIP) voted in favor of accepting a recommendation from the ACIP rabies working group to reduce the number of rabies vaccine doses for postexposure prophylaxis (PEP), from 5 doses as recommended in the 2008 ACIP document on Human Rabies Prevention, to 4 doses for most individuals that are healthy and not immune compromised. These recommendations became official on March 19, 2010 when they were accepted by the CDC Director and published in the MMWR.

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Postexposure Rabies Vaccination regimen for previously-vaccinated people. Wound Cleansing is the single most important and necessary first action – all bite wounds, scratches or contaminated wound areas should be thoroughly cleansed for 15 minutes with soap and running water. A physician visit is recommended for wound care and assessing the need for antibiotics and administration of Tetanus vaccine. Two doses of rabies Vaccine are administered, one each on Day 0 (the first day of the regimen) and Day 3: 1.0 ML IM in the Deltoid muscle (alternating right and left deltoids). No HRIG required for previously vaccinated persons!

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I would like to emphasize a couple of points about delays in postexposure prophylaxis and Anatomical Location of the Exposure: Severe wounds to the face, head, neck and upper body provide ready access of the virus to the central nervous system through rapid viral neurotropism. In this situation PEP should be provided immediately. Substantial delays between exposure and initiation of prophylaxis are of concern with any exposure. It is so important for animal control to be engaged to capture any biting domestic, feral or wild animal and have it confined or tested promptly. If the patient has sustained an aggressive attack to the face and upper body by any animal, or if we don't have the rabies test results for a wild, feral, or abnormal domestic animal within 24-48 hours, then PEP should begin immediately. These situations are evaluated on a case by case basis.

SLIDE 40
Thank you for your attention and I hope you have a better understanding of rabies and human risk assessments now. Please don't hesitate to call us at NC Veterinary Public Health for assistance anytime.

SLIDE 41
We are available 24/7 at the numbers on this slide. The following two slides contain lists of rabies resources and references. Remember the 2013 NC Rabies Public Health Program Manual is your main resource.