WHAT YOU NEED TO KNOW ABOUT RABIES

ASSOCIATION OF IMMUNIZATION MANAGERS
FEBRUARY 2021

Bavarian Nordic is a fully integrated, leading biotechnology company focused on the research, development, innovation, manufacturing and commercialization of vaccines for the prevention and treatment of life Threatening diseases
**VIRAL DISEASE ALMOST ALWAYS FATAL IF UNTREATED**

- **Paralytic rabies**
  Ascending spread of flaccid muscle weakness, bilateral weakness of facial muscles, sphincter involvement

- **Classical (furious) rabies**
  Hyper-excitability, periods of confusion, hallucinations, agitation and hydrophobia

- **Onset of coma**

- **Death**
  Coma (0-14 days)

  - Acute neurological phase (2-7 days)
  - First neurological signs (>10 days)
  - Prodromal phase (2-10 days)

- **Incubation of virus**
  (20-90 days)

- **Nonspecific symptoms**
  Fever, malaise, chills, fatigue, insomnia, anorexia, headache, anxiety, irritability

- **Exposure**
  Bite or scratch from, or mucosal contact with, a rabid animal

Rabies transmission in dogs has been virtually eliminated in the USA, in part due to widespread canine vaccination programs\(^5\)

- As a result, **wildlife has accounted for >90%** of rabid animals reported in the USA since 1980\(^5-7\)
  - Primary vectors in this region are skunks, foxes, raccoons, bats and mongooses (in Puerto Rico)\(^5-7\)
  - In the US, the primary rabies vector is the bat due to encounters with bats that may be less recognized e.g. saliva/small scratch

41 cases of human rabies have been reported in the USA from 2003-2017\(^3\)

- 11 cases were infected outside the USA\(^7\)
- 24 cases were caused by bat exposure\(^7\)

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PRIMARILY TRANSMITTED FROM ANIMALS TO HUMANS

• Rabies virus is transmitted in saliva via bites, scratches and direct contact with mucosal membranes
• Rabies infection causes behavioral changes in animals
• Every mammal studied to date is susceptible to rabies; dogs are the source of 99% of human rabies infections worldwide
• Bat rabies has recently emerged as a public health threat
• Rare categories of rabies virus infection:
  • Inhalation of aerosolised rabies virus in caves containing millions of bats or in laboratories
  • Transmission via infected organ transplantation

CHILDREN ARE AT GREATER RISK

- Children are at greater risk of rabies exposure than adults because they:
  - Tend to play with animals
  - May not report bites
  - May receive more severe bites and are often bitten around the hands or face
  - These areas have a high density of nerve endings, so bites to these areas may increase the risk of developing encephalitis more rapidly

Rabies disproportionately affects poor, rural communities, and, particularly, children

# ACIP RECOMMENDATIONS FOR PRE-EXPOSURE VACCINATION

<table>
<thead>
<tr>
<th>Risk Category</th>
<th>Nature of Risk*</th>
<th>Typical Population</th>
<th>Preexposure Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Continuous</td>
<td>Virus present continuously. Specific exposures likely to go unrecognized</td>
<td>• Rabies research lab workers</td>
<td>Primary course. Serologic testing every 6 months; booster if antibody titers are below acceptable level</td>
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<tr>
<td></td>
<td></td>
<td>• Rabies biologics production workers</td>
<td></td>
</tr>
<tr>
<td>Frequent</td>
<td>Exposure episodic, with source known, but exposure also might be unrecognized</td>
<td>In rabies-enzootic areas:</td>
<td>Primary course. Serologic testing every 2 years; booster if antibody titers are below acceptable level</td>
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<tr>
<td></td>
<td></td>
<td>• Rabies diagnostic lab workers</td>
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<tr>
<td></td>
<td></td>
<td>• Spelunkers</td>
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<tr>
<td></td>
<td></td>
<td>• Veterinarians/staff</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>• Animal-control and wildlife workers</td>
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<tr>
<td></td>
<td></td>
<td>• All persons who frequently handle bats</td>
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</tr>
<tr>
<td>Infrequent</td>
<td>Exposure usually episodic with source recognized</td>
<td>• Veterinarians and terrestrial animal-control workers where rabies is uncommon to rare</td>
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<tr>
<td></td>
<td></td>
<td>• Veterinary students, travellers visiting areas where rabies is enzootic and immediate access to care is limited</td>
<td>Primary course. No serologic testing or booster needed</td>
</tr>
<tr>
<td>Rare (population at large)</td>
<td>Exposure always episodic with source recognized</td>
<td>• U.S. population at large, including persons in rabies-epizootic areas</td>
<td>No vaccination necessary</td>
</tr>
</tbody>
</table>

https://www.cdc.gov/vaccines/hcp/acip-recs/vacc-specific/rabies.html#recs

* Exposure can be from a bite, non-bite or aerosol
Pre-Exposure Prophylaxis

• Eliminates the need for passive immunization (RIG)
• Decreases the number of doses of vaccine needed after exposure\textsuperscript{14-15}
• Provides partial immunity for individuals whose PEP may be delayed\textsuperscript{14-15} or who are at continual, frequent or increased risk of unapparent or unrecognized

\begin{itemize}
  \item Day 0
  \item Day 7
  \item Day 21 or day 28
\end{itemize}

3 dose intramuscular

Post-Exposure Prophylaxis

- Rabies immunization is achieved through rabies vaccination AND rabies immunoglobulin (RIG)
- If PrEP was previously given to an exposed individual, RIG is not needed, and fewer PEP vaccine doses are required

Doses given IM

RIG also administered, if required

Potential exposure

Day 0  Day 3  Day 7  Day 14  Day 21  Day 28

PEP if patient previously vaccinated

Bavarian Nordic has been an important player in the area of infectious diseases for 25 years worldwide
  - Longstanding partnerships with various governments
    - Provided smallpox vaccine for US, EU, and CA National Stockpiles under Emergency Use Programs
    - Recent FDA and Health Canada approvals for smallpox and monkeypox vaccines

Expert in producing vaccines using CEF cells
  - 28 million doses produced for the US and other governments
  - Produced Ebola vaccine within one year; 2 million doses donated to DRC and Rwanda in collaboration with Janssen
  - Strategic collaborations with Janssen for vaccine development in HIV, HBV and HPV
  - BN acquired Encepur® (TBE) and Rabavert® from GSK in August 2020
  - Current development plans include oncology vaccines for several pathologies and ID vaccines for RSV and three strains of equine encephalitis

As a small company, we are dedicated to providing full service for our commercial vaccines and support at the public health level
### Support for Increased Rabies Education in the US

- Embarking on various educational partnerships with healthcare providers to increase public awareness of rabies risks through proper treatment protocols
  - AIM Corporate Alliance Silver Partner 2021

### Support for State-Level Immunization Managers

- We made it a priority to align with *Minnesota Multistate Infuse* to ensure a seamless transition of ownership from GSK (no pricing disruption)
- Support Program-Level and Local Health Departments
  - Dedicated Sales Force to support Health Departments in all 50 states
  - High priority attention to any sudden need for increased vaccine supply
  - Create and provide materials to support educational needs (coming soon)
## CONTACTS

<table>
<thead>
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<th>Function</th>
<th>Email</th>
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<tr>
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<td>Partnerships</td>
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**Other Company Resources:**

Customer Service: 1-844-4BAVARIAN or bavarian-nordicUS@medcomminc.com

Corporate Website: [https://www.bavarian-nordic.com/](https://www.bavarian-nordic.com/)
Infectious Disease Website: [https://loweringtherisk.com/](https://loweringtherisk.com/)

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