Rabies pre-exposure prophylaxis: Summary of background information

ACIP WG meeting
October 29, 2020

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CAPT, US Public Health Service
Co-Lead rabies ACIP WG
Strategies to prevent rabies in the United States

- Avoidance of risky behaviors
- Vaccination of pets and wildlife
- Proper use of personal protective equipment
- Pre-exposure prophylaxis (PrEP)
- Post exposure prophylaxis (PEP)
“Recognized” and “unrecognized” exposures

- Exposures from terrestrial mammals (above): Canine tooth size 15-50mm and bite strength ~320 lbs of pressure causing “recognized” trauma when exposures occur
- Exposure from bats (below): Canine tooth size: 2-10mm and bite strength ~2 lbs of pressure which can cause both recognized and unrecognized exposures

Unrecognized bat exposure:
- Child
- Persons with altered mental status, e.g., due to intoxication or dementia
- Persons frequently rushed by bats, i.e., those who often enter heavily populated bat area like bat biologist
Role of PEP

- Timely PEP alone is effective in preventing rabies

- Challenges of relying on only PEP
  - Uncertain access to prompt PEP for some travelers
  - Potential for unrecognized or high concentration exposures for select populations
  - Risk for multiple rabies exposures for persons who work with rabies virus or suspect rabid animals

- PEP schedule
  - PrEP naïve persons: Rabies immune globulin (RIG) + rabies vaccine IM [0, 3, 7, 14 days]
  - PrEP vaccinated persons: Rabies vaccine IM [0, 3 days]
Role for PrEP in some populations

- Provide some coverage if PEP is delayed or is inadvertently not given
- Eliminate need for RIG which is expensive and is not always easily accessible
- Shorten PEP series

Current ACIP PrEP series: IM [0, 7, 21/28 days]

- First exposure to rabies virus
- PEP = rabies vaccines IM [0, 3 days]

Age (years) of hypothetical person

21
33
40
No role for PrEP in general U.S. population

- No rabies exposures
- PrEP not indicated
# Updated table with rabies pre-exposure prophylaxis (PrEP) recommendations

<table>
<thead>
<tr>
<th>Risk category</th>
<th>Nature of Risk</th>
<th>Typical Population</th>
<th>Disease Biogeography</th>
<th>Primary Immuneogenicity</th>
<th>Long-term Immuneogenicity</th>
</tr>
</thead>
<tbody>
<tr>
<td>#1: Elevated risk for unrecognized and recognized exposures including unusual / high risk exposures (e.g., aerosol exposures and high concentration exposures)</td>
<td>Risk of virus exposure is continuous. Exposure is often in high concentrations, may go unrecognized, and can be unusual (e.g., aerosolized virus).</td>
<td>Laboratory personnel working with live rabies virus in research, diagnostic, or vaccine production capacities (e.g., necropsy of suspect rabid animal or working with rabies virus cultures)</td>
<td>Laboratory</td>
<td>IM [0, 7 days]</td>
<td>Titers every 6 months (booster if titer &lt; 0.5 IU/mL)</td>
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<tr>
<td>#2: Elevated risk of unrecognized and recognized exposures</td>
<td>Risk of virus exposure is episodic. Exposure typically recognized but could be unrecognized. Unusual exposures do not occur.</td>
<td>Persons who frequently handle bats or at frequent risk for coming into contact with bats because of entry into high density bat environments (e.g., bat biologist)</td>
<td>All geographic regions where bats are a reservoir for rabies</td>
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<td>Titers every 2 years (booster if titer &lt; 0.5 IU/mL)</td>
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<tr>
<td>#3: Elevated risk of recognized exposures</td>
<td>Risk of virus exposure greater than population at large. Exposure is almost always a recognized one.</td>
<td>Persons who work with animals • Animal care professionals (e.g., veterinarians, technicians, animal control officers) • Others who repeatedly handle terrestrial reservoir species (e.g., wildlife biologists, rehabilitators, and trappers) • Speleologists • Veterinary students • Short-term / volunteer hands-on animal care workers where increased risk is expected for short time periods*</td>
<td>All geographic regions where terrestrial* and non-terrestrial mammals are reservoirs for rabies</td>
<td>IM [0, 7 days]</td>
<td>Titer once at 1-3 years (booster if titer &lt; 0.5 IU/mL) OR Booster no sooner than day 21 and no later than year 3</td>
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<tr>
<td>#4: Low risk of exposure / (i.e., general population)</td>
<td>Risk of virus exposure is uncommon. Bite or non-bite exposure</td>
<td>U.S. population at large</td>
<td>Nationwide</td>
<td>• No pre-exposure prophylaxis • No serologic monitoring</td>
<td>n/a</td>
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1For questions about the disease biogeography of the region where an exposure occurred, please contact your local or state health department
2Bats are reservoirs for rabies in all US states except Hawaii
3Terrestrial mammals are non-bat species (e.g., racoons, skunks, livestock)
Updated table with rabies pre-exposure prophylaxis (PrEP) recommendations

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<tr>
<th>Risk category</th>
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<th>Primary Immunogenicity PrEP</th>
<th>Long-term Immunogenicity</th>
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<td>Risk of virus exposure is epidemic. Exposure typically recognized but could be unrecognized. Unusual exposures do not occur</td>
<td>Persons who frequently handle bats or at frequent risk for coming into contact with bats because of entry into high density bat environments (e.g., bat biologist)</td>
<td>All geographic regions where bats are a reservoir for rabies2</td>
<td>IM [0, 7 days]</td>
<td>Titer every 2 years (booster if titer &lt;0.5 IU/mL)</td>
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<td>Geographic regions internationally with canine rabies</td>
<td>IM [0, 7 days]</td>
<td>Titer once at 1-3 years (booster if titer &lt;0.5 IU/mL) OR Booster no sooner than day 21 and no later than year 3.</td>
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3Terrestrial mammals are non-bat species (e.g., racoons, skunks, livestock)
## Current ACIP PrEP recommendations

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<th>Risk group</th>
<th>Populations</th>
<th>Primary immunogenicity</th>
<th>Long-term immunogenicity</th>
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<tbody>
<tr>
<td>#1</td>
<td>Research laboratorians</td>
<td></td>
<td>Titer check ever 6 months</td>
</tr>
<tr>
<td></td>
<td>Diagnostic laboratorians</td>
<td></td>
<td>Titer check every 2 years</td>
</tr>
<tr>
<td>#2</td>
<td>Persons who frequently handle or come into contact with bats because of entry into high density bat regions</td>
<td></td>
<td>Titer check every 2 years</td>
</tr>
<tr>
<td>#3</td>
<td>Animal care professionals and others who frequently handle terrestrial mammals in regions with terrestrial rabies&lt;sup&gt;2&lt;/sup&gt;</td>
<td>IM [0, 7, 21/28 days]</td>
<td>Titer check every 2 years</td>
</tr>
<tr>
<td></td>
<td>Animal care professionals and others who frequently handle terrestrial mammals in regions without terrestrial rabies&lt;sup&gt;2&lt;/sup&gt;</td>
<td></td>
<td>No titer checks</td>
</tr>
<tr>
<td></td>
<td>Students, spelunkers, travelers, and short-term animal care professionals</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Actions taken in response to titer checks for #1 Risk Category

- PrEP
- Titer checked
  - Titer ≥ 0.5 IU/mL
  - No booster
- Titer checked
  - Titer < 0.5 IU/mL
  - Booster given

Days [0, 3, 7, 14 days]  6 months  12 months

Time
## Proposed changes

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<th>Long-term immunogenicity</th>
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<tr>
<td>#1</td>
<td>Research laboratorians</td>
<td>IM [0, 7 days]</td>
<td>Titer check ever 6 months(^1)</td>
</tr>
<tr>
<td></td>
<td>Diagnostic laboratorians</td>
<td></td>
<td>Titer every 6 months</td>
</tr>
<tr>
<td>#2</td>
<td>Persons who frequently handle or come into contact with bats because of entry into high density bat regions</td>
<td></td>
<td>Titer check every 2 years(^2)</td>
</tr>
<tr>
<td>#3</td>
<td>Animal care professionals and others who frequently handle terrestrial mammals in regions with terrestrial rabies(^2)</td>
<td></td>
<td>Titer once (1-3 years after primary series) OR Booster no sooner than day 21 and no later than year 3</td>
</tr>
<tr>
<td></td>
<td>Animal care professionals and others who frequently handle terrestrial mammals in regions without terrestrial rabies(^2)</td>
<td></td>
<td></td>
</tr>
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<td>Students, spelunkers, travelers, and short-term animal care professionals</td>
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## Implications of proposed changes

<table>
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<tr>
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<th>Population</th>
<th>Primary immunogenicity</th>
<th>Implications</th>
<th>Long-term immunogenicity</th>
<th>Implications</th>
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<tbody>
<tr>
<td>#1</td>
<td>Research laboratorians</td>
<td>IM [0, 7 days]</td>
<td>Fewer vaccine doses but equivalent efficacy</td>
<td>Titer check every 6 months</td>
<td>No change</td>
</tr>
<tr>
<td></td>
<td>Diagnostic laboratorians</td>
<td></td>
<td></td>
<td></td>
<td>Makes sense to consider all laboratorians equally</td>
</tr>
<tr>
<td>#2</td>
<td>Bat biologists</td>
<td></td>
<td></td>
<td>Titer check every 2 years</td>
<td>No change</td>
</tr>
<tr>
<td>#3</td>
<td>Animal care professionals in terrestrial rabies regions</td>
<td></td>
<td></td>
<td>Titer once (1-3 years after primary series)</td>
<td>No change, fewer vaccine doses, fewer titer checks</td>
</tr>
<tr>
<td></td>
<td>Animal care professionals in non-terrestrial rabies regions, students, spelunkers, persistent travelers</td>
<td></td>
<td></td>
<td>OR</td>
<td>Same number of vaccine doses OR instead of 3rd vaccine, a titer</td>
</tr>
<tr>
<td></td>
<td>Short-term animal care professionals and persons without sustained risk for rabies</td>
<td></td>
<td></td>
<td>Booster no sooner than day 21 and no later than year 3</td>
<td>No additional vaccine and no titer</td>
</tr>
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Policy question #1

Should a 2 dose pre-exposure prophylaxis (PrEP) series involving HDCV* or PCECV† IM [0, 7 days] replace the 3 dose series IM [0, 7, 21/28 days] for all those for whom rabies vaccine PrEP is recommended?

*Human diploid cell vaccine
† Purified chick embryo cell vaccine
Policy question #2

Should an IM booster dose of rabies vaccine (*PCECV or †HDCV) be recommended as an alternative to a titer check no sooner than day 21 and no later than 3 years after the two-dose pre-exposure (PrEP) series IM [0, 7 days] for those in the #3 risk category who receive PrEP?

*Human diploid cell vaccine
† Purified chick embryo cell vaccine
Actions taken in response to titer check for #3 risk group

- Titer checked
- Titer ≥ 0.5 IU/mL
- No booster
- Considered to have had pre-exposure prophylaxis for any future exposures

Days [0, 7 days]  1-3 years  10+ years

- 2-dose PrEP
- Rabies exposure
- 2-dose PEP
Actions taken in response to titer check for #3 risk group

- **2-dose PrEP**
- **Titer checked**
- **Titer < 0.5 IU/mL**
- **Booster given**
- **Considered to have had pre-exposure prophylaxis for any future exposures**
- **Rabies exposure**
- **2-dose PEP**

Days [0, 7 days] | 1-3 years | 10+ years
--- | --- | ---

Time
Actions taken in response to titer check for #3 risk group

- 2-dose PrEP
- Booster - Considered to have had pre-exposure prophylaxis for any future exposures
- Rabies exposure - 2-dose PEP

Days [0, 7 days]  Day 21 - year 3  10+ years

Time
## Implications of proposed changes

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<td>No change</td>
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<tr>
<td>#2</td>
<td>Bat biologists</td>
<td></td>
<td></td>
<td>Titer every 6 months</td>
<td>Small population Makes sense to consider all laboratorians equally</td>
</tr>
<tr>
<td>#3</td>
<td>Animal care professionals in terrestrial rabies regions</td>
<td></td>
<td></td>
<td>Titer check every 2 years(^2)</td>
<td>No change</td>
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<td></td>
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\(^1\) Titer check every 6 months

\(^2\) Titer check every 2 years
Next presentation

- Summarize the Evidence to Recommendations Framework

- Show wording of 2 recommendations that will be voted on today
Acknowledgements

- ACIP rabies WG
- Ryan Wallace
- Jesse Blanton
- Doug Campos-Outcalt
- Rebecca Morgan
- Jessica MacNeil
- Whitni Davidson
Thank you

For more information, contact CDC
1-800-CDC-INFO (232-4636)

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