TICK-BORNE ENCEPHALITIS (TBE) VACCINE

Katherine Poehling, M.D.
Chair, ACIP TBE Vaccine Work Group
October 29, 2020
Formation of ACIP TBE Vaccine Work Group

- TBE Vaccine Work Group formed in September 2020
- Followed notification that Pfizer planned to submit Biologics License Application (BLA) to Food and Drug Administration (FDA) for their TBE vaccine
- Several TBE vaccines manufactured and licensed internationally, but none produced or licensed in the United States and no existing ACIP TBE vaccine recommendations
## TBE Vaccine Work Group members and participants

<table>
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<tr>
<th>ACIP</th>
<th>ACIP liaisons</th>
<th>Technical advisors (cont’d)</th>
<th>CDC participants (cont’d)</th>
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<tr>
<td>Kathy Poehling (Chair)</td>
<td>David Shlim, ISTM</td>
<td>Bruce McClenathan, DOD</td>
<td>Stacey Martin, DVBD</td>
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<td>José Romero</td>
<td>Mark Sawyer, AAP</td>
<td>Steven Schofield, CATMAT</td>
<td>Michael McNeil, DHQP</td>
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<th>ACIP Secretariat</th>
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<tr>
<td>Susan Hills, DVBD</td>
<td>Alan Barrett, Univ Texas Galveston</td>
<td>Mary Wilson, Univ Calif SFO</td>
<td>Steve Waterman, DVBD</td>
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<td>Lin Chen, Mount Auburn Hosp</td>
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<tr>
<td>Wilbur Chen, Univ Maryland</td>
<td>Grace Appiah, DGMQ</td>
<td>Jessica MacNeil</td>
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<td>Katherine Kinder, DOD</td>
<td>Susan Chu, GID</td>
<td>Amanda Cohn</td>
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<tr>
<td>Tony Marfin, PATH</td>
<td>Caitlin Cossaboom, DHCPP</td>
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Possible timeline for licensure of TBE vaccine

- If Pfizer’s TBE vaccine receives priority review designation, FDA’s goal to take action on an application within 6 months\(^1\)
- Licensure possible by 3rd quarter of 2021

Purpose of ACIP TBE Vaccine Work Group

- To discuss use of TBE vaccine in
  - U.S. adults and children visiting or living in TBE endemic areas
  - Laboratory workers
Terms of Reference for TBE Vaccine Work Group

- To review information on TBE, including its epidemiology, clinical presentation, diagnosis, treatment, and outcome
- To review data on infection risk and burden for U.S. civilian and military travelers and laboratory workers
- To review data on vaccine safety, immunogenicity, and effectiveness
- To provide evidence-based recommendation options for ACIP
- To identify areas in need of further research for informing potential future vaccine recommendations
- To publish ACIP recommendations in the Morbidity and Mortality Weekly Report (MMWR)
Today’s topics

- Background on TBE disease and vaccines
  - Susan Hills (CDC/NCEZID)

- Immunogenicity and safety of Pfizer’s TBE vaccine
  - Heinz-Joseph (Joe) Schmitt (Pfizer)

- Next steps for TBE Vaccine Work Group
  - Susan Hills (CDC/NCEZID)
BACKGROUND ON TBE DISEASE AND VACCINES

Susan Hills, MBBS, MTH
Arboviral Diseases Branch
Division of Vector-Borne Diseases
Fort Collins, Colorado
TBE virus and transmission

- Flavivirus
  - European, Siberian, and Far Eastern subtypes

- Transmitted to humans by *Ixodes* species ticks
  - Infections usually acquired in wooded areas during recreational or occupational activities
Other TBE virus transmission modes

- Unpasteurized dairy products
- Slaughter of animals
- Laboratory exposure
- Transfusion or transplantation
- Breastfeeding
Geographical range and risk

- 5,000 to 13,000 cases reported annually in endemic areas
- Most cases occur April to November
- Most exposures occur < 2,500 ft

Source: Dobler et al, Wien Med Wochenschr 2012
Clinical features of TBE

- Incubation period: 7–14 days (range: 4–28 days)
- About 25% infected persons develop clinical symptoms
- Febrile or neurologic illness (e.g., meningitis, encephalitis, or meningoencephalomyelitis)
- Monophasic or biphasic course
  - Monophasic illness (Far Eastern, Siberian subtypes)
  - Biphasic illness with febrile then neurologic illness (European subtype)
- Clinical management consists of supportive care
Outcome of TBE

- Neurologic sequelae
  - 30% (European subtype)
  - 80% (Far Eastern subtype)

- Case fatality rates
  - 1–2 % (European subtype)
  - 20% (Far Eastern subtype)

- Incidence and severity of disease highest in older persons
Cases among U.S. travelers

- Cases only occasionally reported among US civilian and military travelers
- Recent publications:

Tick-Borne Encephalitis Among U.S. Travelers to Europe and Asia — 2000–2009

Tick-borne encephalitis virus (TBEV) is the most common arbovirus transmitted by ticks in Europe. Approximately 10,000 cases of tick-borne encephalitis (TBE) are reported annually in Europe and Russia. The cases usually present as a mild febrile illness, but can become serious, with symptoms of encephalitis and meningitis with signs of meningeal irritation, generalized weakness, fever, headache, and meningismus.

CDC. MMWR Morb Mortal Wkly Rep 2010

Tick-borne Encephalitis Surveillance in U.S. Military Service Members and Beneficiaries, 2006–2018

James D. Mancuso, MD, DPH (COL, MC, USA); Sara Battrico, PhD, MPH; Shanna Stahlschmidt, PhD, MPH; Shawn S. Clauser, MD, MPH (CDR, MC, USN); Angela A. Cost, PhD, S.M

The risk of tick-borne encephalitis (TBE) among U.S. military service members and beneficiaries is low but not negligible.

Mancuso J et al. MSMR 2019
## TBE vaccines in Europe and Russia*

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<tr>
<th>Trade name</th>
<th>Manufacturer (Location)</th>
<th>Age group</th>
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<tr>
<td>FSME-IMMUN, TicoVac</td>
<td>Pfizer (Austria)</td>
<td>≥1 year</td>
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<tr>
<td>Encepur</td>
<td>Bavarian Nordic (Denmark)</td>
<td>≥1 year</td>
</tr>
<tr>
<td>EnceVir</td>
<td>Microgen (Russia)</td>
<td>≥3 years</td>
</tr>
<tr>
<td>TBE-Moscow</td>
<td>Chumakov Institute (Russia)</td>
<td>≥3 years</td>
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*Also 1 vaccine in China
Pfizer’s TBE vaccine

- Inactivated vaccine
- Pediatric and adult formulations
- Current vaccine formulation used since 2001
- Licensed in > 30 countries in Europe
Summary of TBE and TBE vaccine

- Focally endemic disease with risk extending from western and northern Europe through to northern and eastern Asia
- Primarily tick transmitted to persons visiting or working in wooded areas
- Clinical disease can be severe and high case fatality and sequelae rates with some TBE virus subtypes
- Cases among travelers rare
- One TBE vaccine (Pfizer) soon to be submitted for licensure in the United States
  - Vaccine used for about 20 years in Europe
- Vaccine never previously licensed in US
- No existing TBE vaccine ACIP recommendations