TICK-BORNE ENCEPHALITIS (TBE) VACCINE

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Chair, ACIP TBE Vaccine Work Group
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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

ACIP

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CDC Lead

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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

1. https://www.fda.gov/patients/fast-track-breakthrough-therapy-accelerated-approval-priority-review/priority-review

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
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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

Ixodes ricinus (Photo credit: ECDC/Guy Hendrickx)

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 next few days. On admission to the hospital, the patient was disoriented and stuporous. Cerebrospinal fluid (CSF) showed lymphocytic pleocytosis and elevated protein; bacterial cultures, herpes simplex

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, DrPH (COL, MC, USA); Sara Bazaco, PhD, MPH; Shauna Stahlman, PhD, MPH; Shawn S. Clausen, MD, MPH (CDR, MC, USN); Angelia A. Cost, PhD, ScM

The risk of tick-borne encephalitis (TBE) among U.S. military service mem-

WHAT ARE THE NEW FINDINGS?

The risk of TBE among U.S. military service members and beneficiaries is low but not

Mancuso J et al. MSMR 2019

TBE vaccines in Europe and Russia*

Trade name	Manufacturer (Location)	Age group
FSME-IMMUN, TicoVac	Pfizer (Austria)	≥1 year
Encepur	Bavarian Nordic (Denmark)	≥1 year
EnceVir	Microgen (Russia)	≥3 years
TBE-Moscow	Chumakov Institute (Russia)	≥3 years

*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