Overview of vaccines for epizootic henipaviruses

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- Opinions expressed here are those of the presenter and do not necessarily represent the views of NIAID or the United States government.
Henipaviruses associated with human disease

• Hendra virus (HeV) (originally equine morbillivirus)
  - Discovered in 1994 in horses and people associated with a stables outside Brisbane Australia
  - Cases primarily affect horses but spillover to people in direct contact with affected horses has occurred
  - Black-headed and grey-headed flying foxes (*Pteropus spp.*) are the suspected reservoir
  - New HeV genotype identified in grey-headed flying foxes in 2021

• Nipah virus (NiV)
  - Discovered in 1998-1999 during large epizootic outbreak in pigs and humans in contact with affected pigs
  - Regular outbreaks in India and Bangladesh
  - Transmitted by *Pteropus spp.* flying foxes
  - About 700 total cases to date; CFR ~55%
  - Two major genotypes: Nipah virus-Malaysia (NiV-M) and Nipah virus-Bangladesh (NiV-B)

• Mojiang virus (MojV)
  - Identified in 2012 in three fatal cases presenting with severe pneumonia
  - Surveillance suggests *Rattus flavipectus* rats as the reservoir species

• Langya virus (LayV)
  - Identified in febrile patients in China in 2022 during surveillance of patients with animal exposure
  - Virus detected primarily in shrews which are the proposed reservoir
Identified henipaviruses not associated with human disease

- Cedar virus (CedV)
  - Isolated during routine surveillance of an Australian flying fox colony outside Brisbane, Australia
    - Predominantly *Pteropus alecto* (black-flying fox) with some *P. poliocephalus* (grey-headed flying fox) in a mixed population

- Angavokely virus (AngV)
  - Identified in fruit bats in Madagascar
  - Genome structure suggests this virus could be pathogenic in humans

- Daeryong virus (DARV)
  - Isolated along with GAKV during field epidemiology studies collecting shrews in Korea
  - Detected in animals from a single collection site; primarily *Crocidura shatungensis* (Asian lesser white-toothed shrew)

- Gamak virus (GAKV)
  - Isolated from kidney of *Crocidura lasiura* (Ussuri white-toothed shrew)
  - Identified in animals from multiple collection sites in Korea

- Ghanaian bat virus (GhV)
  - Agent sequenced but not isolated
  - Binds Ephrin B2 (NiV receptor) but only seems to infect bat cells
Historical Outbreaks of Henipavirus associated disease

Henipavirus structure and genome

Binds to host cell receptor

Facilitates virus fusion to the host cell membrane

Hendra vaccine

• Hendra vaccine (EquiVac HeV) licensed for horses in Australia
  - Subunit vaccine containing soluble G protein
  - Two doses given 6 weeks apart with booster required at 6 months and annual boosters thereafter
  - Vaccinated horses develop high neutralizing Ab titers
  - Vaccine uptake is low despite low adverse reactions and evidence suggesting good protective efficacy

• No licensed HeV vaccine for humans
Henipavirus vaccine clinical trials (ClinicalTrials.gov)

- vVSV-NiV vaccine (PHV02)-Phase 1 (NCT 05178901) (Recruiting)
  - VSV expressing NiV-M G
  - 4 dose groups (2x10^5, 2x10^6, 2x10^7; prime-boost with 2x10^8)
  - Target 60 participants
  - Crozet BioPharma/CEPI

- mRNA vaccine (mRNA-1215)-Phase 1 (NCT 05398796) (Active)
  - mRNA encodes stabilized prefusion F (preF) and G from NiV-M
  - Four dose groups
  - Prime-boost at 1 or 4 months between vaccinations
  - Moderna/NIAID VRC

- Subunit vaccine (HeV-sG-V; HenipaVax™)-Phase 1 (NCT 4199169) (Completed)
  - Soluble Hendra virus G protein with Alum adjuvant
  - Three doses (concentration)
  - Multiple vaccine frequency (prime-boost with varying duration between vax)
  - Auro Vaccines/CEPI
Henipavirus vaccine clinical trials (ISRCTN registry)

- ChAdOx1 NipahB-Phase 1 (ISRCTN87634044) (Recruiting)
  - ChAdOx1 vector expressing NiV-B G
  - 3 dose groups (prime, prime/boost, placebo)
  - Target 51 participants
  - Oxford University/CEPI
Vaccines under development (preclinical, virus vector)

- ChAdOx expressing NiV-B G protective against NiV-B challenge in hamsters using prime only and prime-boost strategies

- Inactivated RABV expressing NiV G induces immune response in mice
  - (Vaccines (Basel). 2023 Nov 26;11(12):1758. doi: 10.3390/vaccines11121758. PMID: 38140162)

- RABV-based vac induces immune response in mice
  - (NPJ Vaccines. 2019 Apr 15;4:15. doi: 10.1038/s41541-019-0109-5. eCollection 2019. PMID: 31016033)

- Adenovirus expression NiV F protective in hamsters
  - (JCI Insight. 2023 Dec 8;8(23):e175461. doi: 10.1172/jci.insight.175461. PMID: 37917215)
Vaccines under development (preclinical, non-vectored)

- **HeV-sG-V; HenipaVax™**
  - Recombinant soluble HeV G (sG) protein with alhydrogel adjuvant.
    - Similar to EquiVac HeV
  - Demonstrated protection against NiV-B and HeV challenge in AGM IT exposure model
  - Single dose and prime/boost strategies.
  - Protection provided with vaccination 7 days prior to challenge
  - (NPJ Vaccines. 2021 Feb 8;6(1):23. doi: 10.1038/s41541-021-00284-w. PMID: 33558494)

- **mRNA vaccine expressing HeV G partially protective in hamster model**
  - mRNA for HeV sG (sHeVG) in the context of lipid nanoparticles
  - Two dose groups (10 or 30 ug) 30 days prior to IP challenge with NiV-M
  - Partial protection in both dose groups
  - Survivors had lower viremia (RNA) than nonsurvivors
Vaccines under development (preclinical, non-vectored)

- **NiVΔF.**
  - Complete NiV-M genome but lacking the fusion protein
  - Safe, immunogenic (IN and IM vax) in hamsters
  - Also safe in IC suckling mouse model
  - Protective (IN vax) in hamsters following IN or IP challenge
  - Currently being evaluated in AGM at IRF Frederick using IN and IM inoculation routes and IT NiV-M challenge

- Trivalent (NiV-HeV-EBOV) VLPs and VSV-pseudotype virus
  - Dr. Aguilar-Carreno will discuss
  - Ithinji et al., NPJ Vaccines. 2022 Dec 17;7(1):166

- Multiple mouse studies using various vaccine platforms/approaches and demonstrating serological responses but not protective efficacy
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