Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Alzheimer's Biomarker Consortium for Down Syndrome and Horizon21).[10] In the past, adults with Down syndrome have not been included in Alzheimer's disease clinical trials. Such trials admittedly pose additional challenges for people with Down syndrome (and possible risks) compared with those for the general population regarding recruitment and feasibility of completing all the assessments. Therefore, Fortea and colleagues emphasise that people with Down syndrome are able and willing to participate in multimodal studies needed for clinical trials. Biomarker studies, as reported here and by other teams,[11] are crucial and will serve as a foundation for the design of clinical trials for Alzheimer's disease in people with Down syndrome.[12] Biomarker criteria can be used to streamline the recruitment of people with Down syndrome for clinical trials. Additionally, biomarker characterisation will be useful for future precision medicine approaches and important for the development of effective interventions within this high-risk population.[13] Biomarker research in people with Down syndrome has important contributions and implications for the general population, especially for individuals with late-onset Alzheimer's disease.

We declare no competing interests. We both contributed equally.

*Elizabeth Head, Beau Ances
heade@uci.edu

Department of Pathology and Laboratory Medicine, University of California, Irvine, CA 92697, USA (EH); and Department of Neurology, Washington University, St Louis, MO, USA (BA)

1 Lott IT, Head E. Dementia in Down syndrome: unique insights for Alzheimer disease research. *Nat Rev Neurol* 2019; **15:** 135–47.
2 Zigman WB, Devenny DA, Krinsky-McHale SJ, et al. Alzheimer's disease in adults with Down Syndrome. *Int Rev Res Ment Retard* 2008; **36:** 103–45.
3 Jack CR, Bennett DA, Blennow K, et al. A/T/N: an unbiased descriptive classification scheme for Alzheimer disease biomarkers. *Neurology* 2016; **87:** 539–47.
4 Fortea J, Vilaplana E, Carmona-Iragui M, et al. Clinical and biomarker changes of Alzheimer's disease in adults with Down syndrome: a cross-sectional study. *Lancet* 2020; **395:** 1988–97.
5 Head E, Phelan MJ, Doran E, et al. Cerebrovascular pathology in Down syndrome and Alzheimer disease. *Acta Neuropathol Commun* 2017; **5:** 93.
6 Wilcock DM, Griffin WS. Down's syndrome, neuroinflammation, and Alzheimer neuropathogenesis. *J Neuroinflammation* 2013; **10:** 84.
7 Schupf N, Lee JH, Pang D, et al. Epidemiology of estrogen and dementia in women with Down syndrome. *Free Radic Biol Med* 2018; **114:** 62–68.
8 Lee JH, Lee AJ, Dang LH, et al. Candidate gene analysis for Alzheimer's disease in adults with Down syndrome. *Neurobiol Aging* 2017; **56:** 150–58.
9 Cohen AD, McDade E, Christian B, et al. Early striatal amyloid deposition distinguishes Down syndrome and autosomal dominant Alzheimer's disease from late-onset amyloid deposition. *Alzheimers Dement* 2018; **14:** 743–50.
10 Strydom A, Coppus A, Blesa R, et al. Alzheimer's disease in Down syndrome: an overlooked population for prevention trials. *Alzheimers Dement* 2018; **4:** 703–13.
11 Mapstone M, Gross TJ, Macciardi F, et al. Metabolic correlates of prevalent mild cognitive impairment and Alzheimer's disease in adults with Down syndrome. *Alzheimers Dement* 2020; **12:** e12026.
12 Rafii MS. Improving memory and cognition in individuals with Down Syndrome. *CNS Drugs* 2016; **30:** 567–73.
13 Petersen ME, Zhang F, Schupf N, et al. Proteomic profiles for Alzheimer's disease and mild cognitive impairment among adults with Down syndrome spanning serum and plasma: an ABC-DS study. *Alzheimers Dement* 2020; published online April 17. DOI:10.1002/dad2.12023.

For the **Alzheimer's Biomarker Consortium for Down Syndrome** see https://www.nia.nih.gov/research/abc-ds

Vaccinating against mosquitoes: anticipating the unexpected

Mosquitoes act as vectors of a remarkable number of viruses and some parasites, which they transmit in their saliva while they feed on blood. Among these mosquito-borne agents are pathogens that cause some of the most medically devastating infectious diseases—malaria, lymphatic filariasis, dengue, yellow fever, Zika virus disease, chikungunya, Japanese encephalitis, and West Nile fever. Although some of these diseases have been around for centuries, in the past few decades epidemics caused by viruses such as West Nile, chikungunya, and Zika took many regions by surprise, overwhelming health systems.

COVID-19 has reminded the world how quickly a virus can cause havoc. The susceptibility of humans is compounded by a lack of available treatments. Increased handwashing, controlled coughing and sneezing, and physical distancing when appropriate will reduce the future incidence of directly transmitted viruses like coronaviruses, influenza viruses, and noroviruses. By contrast, vector-borne pathogens are unaffected by improved personal hygiene practices because their indirect transmission relies on infected arthropods (eg, mosquitoes, sandflies, ticks) or aquatic snails. According to WHO, vector-borne pathogens account for at least 17% of all infectious diseases and each year they cause more than 700 000 deaths.

Dependency on a vector could be the weakness of vector-borne pathogens, which is the view of

An anopheles mosquito (*Aedes aegypti*)/ Coloured drawing by A J E Terzi/Wellcome Collection, CC BY 4.0

Published **Online** June 11, 2020 https://doi.org/10.1016/S0140-6736(20)31319-2

See **Articles** page 1998

For **WHO data on vector-borne diseases** see https://www.who.int/news-room/fact-sheets/detail/vector-borne-diseases

Jessica Manning and colleagues,[1] who report in *The Lancet* their study of the safety and immunogenicity of a mosquito saliva peptide-based vaccine. Although blood-feeding vectors are known to induce an immune response when they feed, attempts to harness this knowledge have resulted in only two marketed vaccines, both for control of the cattle tick, but derived from midgut rather than salivary antigens.[2] One reason development of an antivector vaccine has been so challenging is the evolutionary tensions between vector and vertebrate host: responses of the host (nociceptive, inflammatory, and immune) to prevent the bloodletting are countered by bioactive molecules (mostly proteins and peptides) synthesised in vector salivary glands and secreted into the host as the vector attaches and feeds.[3,4]

For Manning and colleagues' clinical trial, a vaccine was prepared comprising four peptides of 32–44 amino acids in length. The peptide sequences are predicted T-cell epitopes of proteins from *Anopheles gambiae* salivary glands, conserved across *Anopheles*, *Aedes*, and *Culex* spp mosquitoes. 49 healthy participants (30 [61%] women; median age 30·5 years [IQR 24·5–35·0]) were recruited and randomly assigned to the vaccine with adjuvant (n=17) or without adjuvant (n=16) or placebo (n=16). Inoculation of this peptide vaccine (with or without adjuvant) had no untoward systemic effects in the 33 participants given at least one dose of vaccine, even when ten starved *Aedes aegypti* mosquitoes fed on them. This basic result is encouraging given the potential for severe allergic responses. The mosquito feeding challenge could be argued to be soft—ie, *Anopheles*-induced immunity challenged with *Aedes* saliva antigens. The outcome could have been different with *A gambiae* mosquitoes, although the vaccine was based on conserved antigens.

Although more safety testing needs to be done, the next big challenge is showing a mosquito peptide vaccine provides protection against mosquito-borne pathogens, which is unlikely, but not implausible. Extensive research on developing antisandfly vector vaccines to control leishmaniasis provides some design clues.[5,6] *Leishmania* parasites, inoculated into the skin when an infected sandfly bites, infect macrophages and form skin lesions (cutaneous forms) or migrate to the spleen, liver, and bone marrow (visceral forms). Preclinical studies showed that rhesus macaques immunised with a sandfly salivary protein (PdSP15) were protected against cutaneous leishmaniasis when exposed to sandflies infected with the parasite.[7] Protection correlated with accelerated *Leishmania*-specific $CD4^{+}IFN\text{-}\gamma^{+}$ lymphocyte production. A similar effect was observed when mice immunised against a tick salivary protein survived an otherwise lethal challenge with ticks infected with tick-borne encephalitis virus.[8] Immune responses to the vector create an environment in the skin that is hostile to pathogens that are injected during feeding, promoting a protective antipathogen response.[6]

The great attraction of antivector vaccines is the prospect of one vaccine protecting against all the different pathogens, known and unknown, transmitted by one vector (or even related vectors). This approach compares favourably with conventional antipathogen approaches—eg, yellow fever vaccine protects against yellow fever virus transmitted by *A aegypti* but not against chikungunya, dengue virus, Zika virus, or as yet unrecognised pathogenic viruses transmitted by the same mosquito species. Relying on an antivector vaccine is risky and a combined antipathogen and antivector vaccine approach is considered safer. However, as a first line of defence, an effective mosquito peptide vaccine could save lives and buy time to develop a targeted vaccine.[9]

I declare no competing interests.

Pat Nuttall
pat.nuttall@zoo.ox.ac.uk
Department of Zoology, University of Oxford, Oxford OX1 3SZ, UK

1 Manning JE, Oliveira F, Countinho-Abreu IV, et al. Safety and immunogenicity of a mosquito saliva peptide-based vaccine: a randomised, placebo-controlled, double-blind, phase 1 trial. *Lancet* 2020; published online June 11. https://doi.org/10.1016/S0140-6736(20)31048-5.
2 Willadsen P. Anti-tick vaccines. *Parasitology* 2004; **129** (suppl)**:** S367–87.
3 Ribeiro JMC. Role of saliva in blood-feeding by arthropods. *Annu Rev Entomol* 1987; **32:** 463–78.
4 Vogt MB, Lahon A, Arya RP, et al. Mosquito saliva alone has profound effects on the human immune system. *PLoS Negl Trop Dis* 2018; **12:** e0006439.
5 Peters NC, Kimblin N, Secundino N, Kamhawi S, Lawyer P, Sacks DL. Vector transmission of *Leishmania* abrogates vaccine-induced protective immunity. *PLoS Pathog* 2009; **5:** e1000484.
6 Reed SG, Coler RN, Mondal D, Kamhawi S, Valenzuela JG. *Leishmania* vaccine development: exploiting the host-vector-parasite interface. *Expert Rev Vaccines* 2016; **15:** 81–90.
7 Oliveira F, Rowton E, Aslan H, et al. A sand fly salivary protein vaccine shows efficacy against vector-transmitted cutaneous leishmaniasis in nonhuman primates. *Sci Transl Med* 2015; **7:** 290ra90.
8 Labuda M, Trimnell AR, Licková M, et al. An antivector vaccine protects against a lethal vector-borne pathogen. *PLoS Pathog* 2006; **2:** e27.
9 Wang Y, Marin-Lopez A, Jiang J, Ledizet M, Fikrig E. Vaccination with *Aedes aegypti* agbr1 delays lethal mosquito-borne Zika virus infection in mice. *Vaccines (Basel)* 2020; **8:** e145.