

Sponsors

CDC

Cohen Foundation

“Humbled by the expertise and patient voices that are so powerful”

“Meet the challenges with tenacity, grace and wisdom”

“Partnership will last beyond the two days”



Patients

**Non-profit
Agencies**

**Academic
Institutions**

Many siloed
disciplines

**Pharmaceutical
Industry**

**Government
agencies**

CDC
FDA
NIH

Legislative branch

Cohen Foundation

CDC

NASEM

Patients

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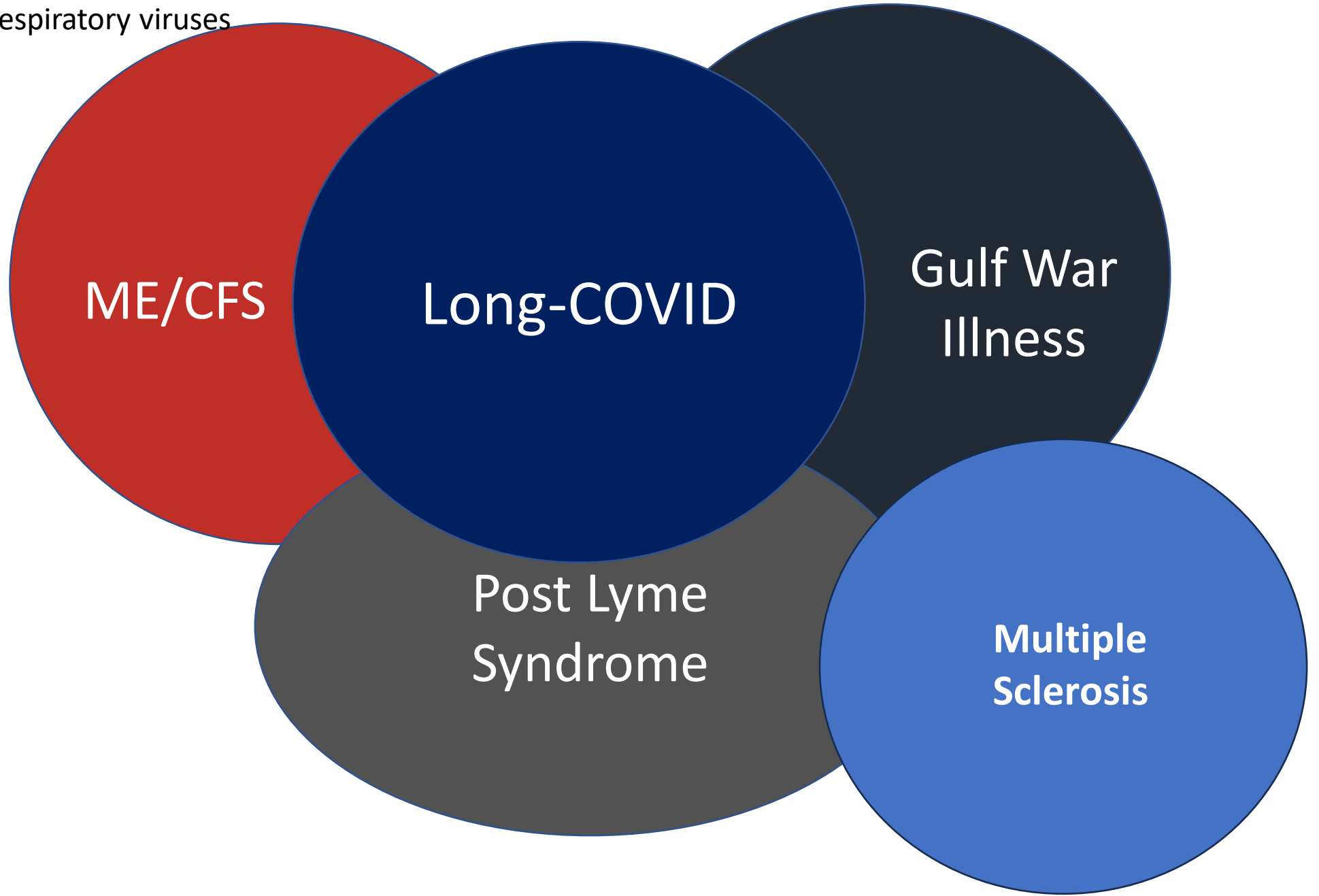
**Government
agencies**

CDC
FDA
NIH

Legislative branch

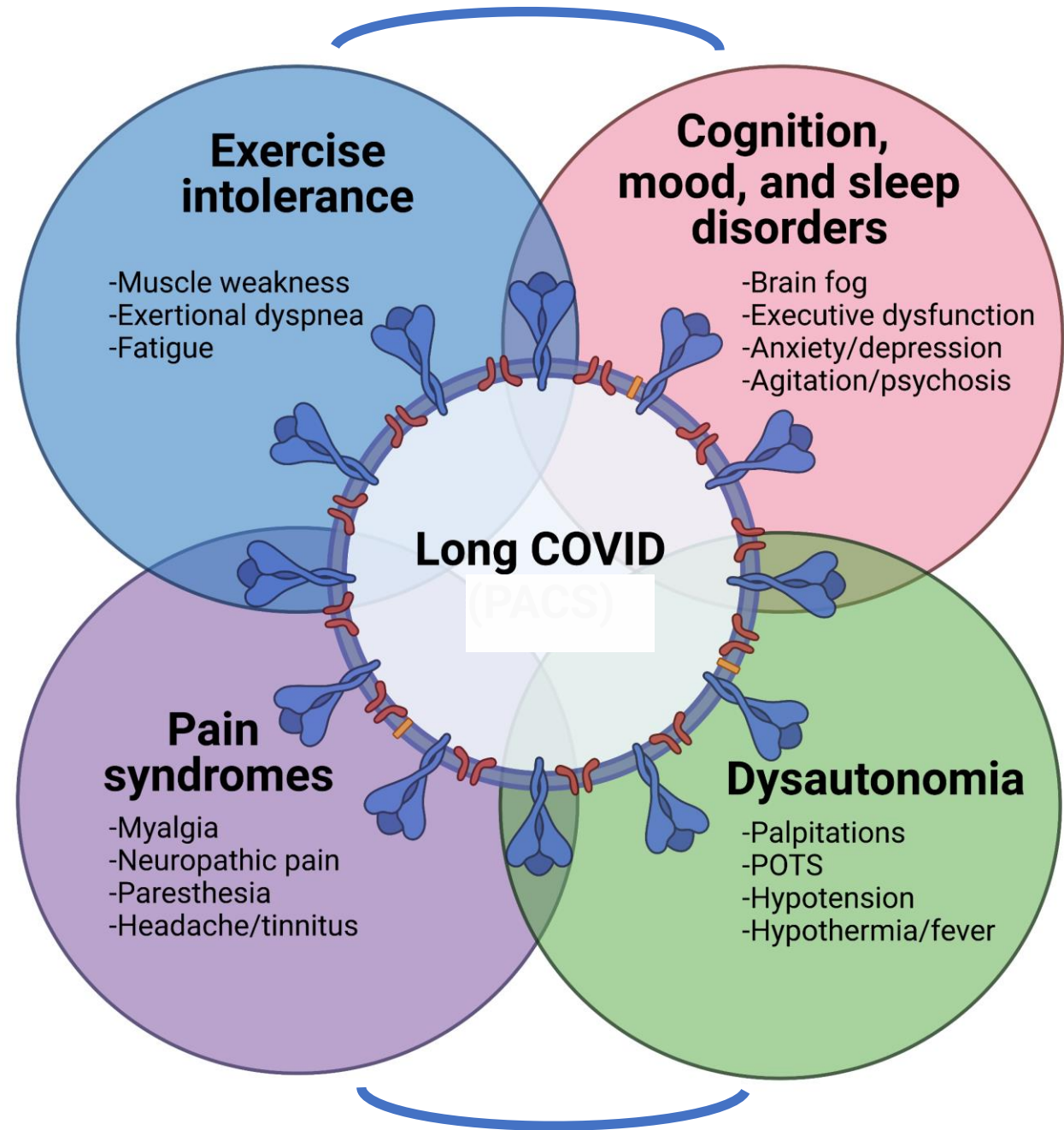
Biggest Mysteries of Medicine

Ebola
Enteroviruses
Respiratory viruses



Heterogeneity of Symptoms

(splitters and lumpers)



Challenges

- Epidemiology not clear
- No diagnostic tests (even documentation of infection)
- No treatment for altering disease course
- Gap in understanding of pathogenesis
- Lack of resources

Longitudinal analysis reveals high prevalence of Epstein-Barr virus associated with multiple sclerosis

Kjetil Bjornevik^{1†}, Marianna Cortese^{1†}, Brian C. Healy^{2,3,4}, Jens Kuhle⁵, Michael J. Mina^{6,7,8}, Yumei Leng⁶, Stephen J. Elledge⁶, David W. Niebuhr⁹, Ann I. Scher⁹, Kassandra L. Munger^{1†}, Alberto Ascherio^{1,10,11*†}


Clonally expanded B cells in multiple sclerosis bind EBV EBNA1 and GlialCAM

<https://doi.org/10.1038/s41586-022-04432-7>

Received: 6 August 2021

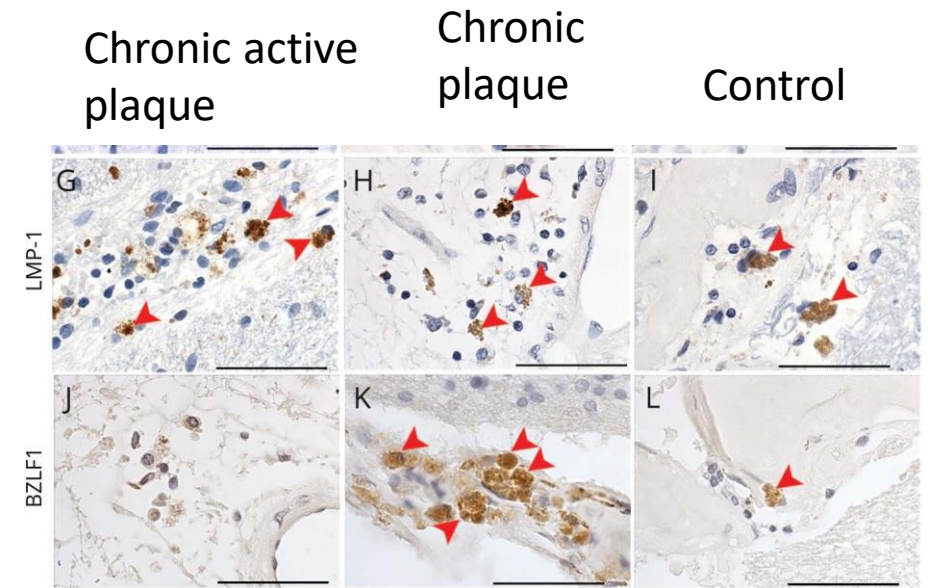
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 Check for updates

Tobias V. Lanz^{12,3,4}, R. Camille Brewer¹⁴, Peggy P. Ho⁵, Jae-Seung Moon¹⁴, Kevin M. Jude⁶, Daniel Fernandez⁷, Ricardo A. Fernandes⁶, Alejandro M. Gomez¹⁴, Gabriel-Stefan Nadj¹⁴, Christopher M. Bartley⁹, Ryan D. Schubert⁹, Isobel A. Hawes⁹, Sara E. Vazquez¹⁰, Manasi Iyer¹¹, J. Bradley Zuchero¹¹, Bianca Teegen¹², Jeffrey E. Dunn¹³, Christopher B. Lock¹³, Lucas B. Kipp¹³, Victoria C. Cotham^{14,15}, Beatrix M. Ueberheide^{14,15}, Blake T. Aftab¹⁶, Mark S. Anderson¹⁷, Joseph L. DeRisi^{10,18}, Michael R. Wilson⁹, Rachael J. M. Bashford-Rogers¹⁹, Michael Platten^{2,3,20}, K. Christopher Garcia⁶, Lawrence Steinman⁵ & William H. Robinson¹⁴✉

Persistent EBV in brain



Moreno MA,et al., 2018

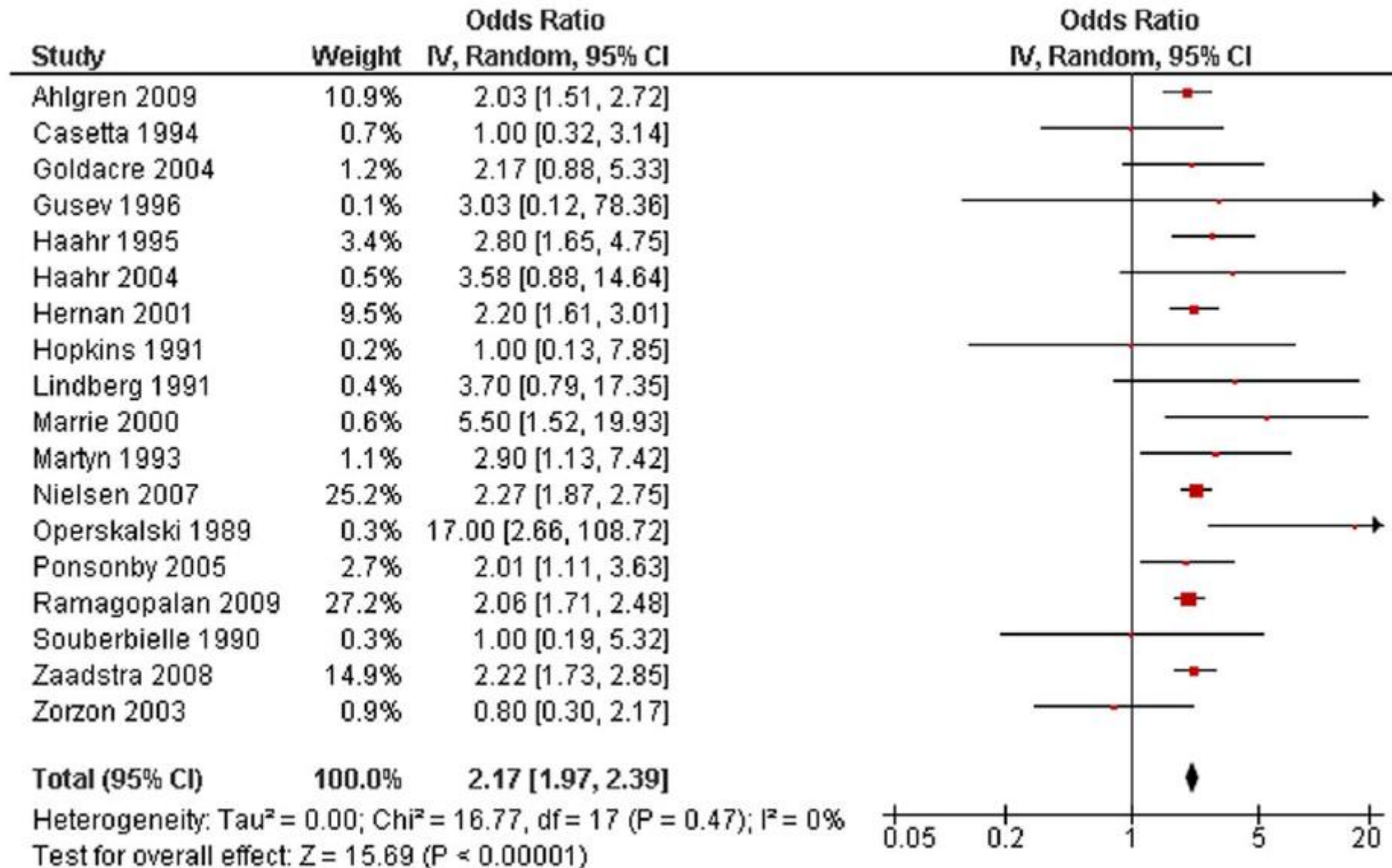
Sefarini 2013, 2014, 2017, 2019

Veroni et al., 2018

Tzartos et al., 2012

Hassini et al., 2018

Forest plot for risk of MS after EBV infection (Handel et al., 2010)



Viral/microbial etiology

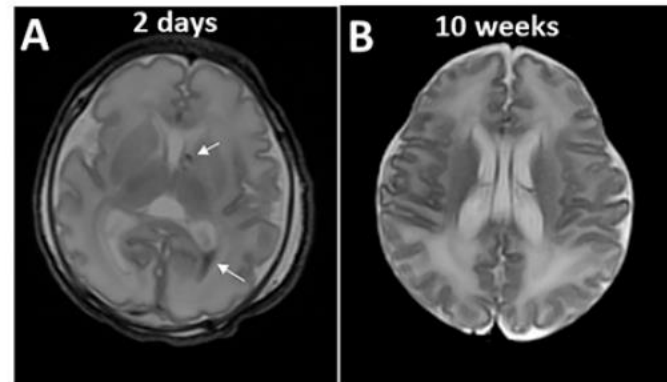
- Persistent infection
- Defective virus/ viral products
- Reactivation of latent viruses/co-infection
- Microbiome

Maternal SARS-CoV-2, Placental Changes and Brain Injury in 2 Neonates

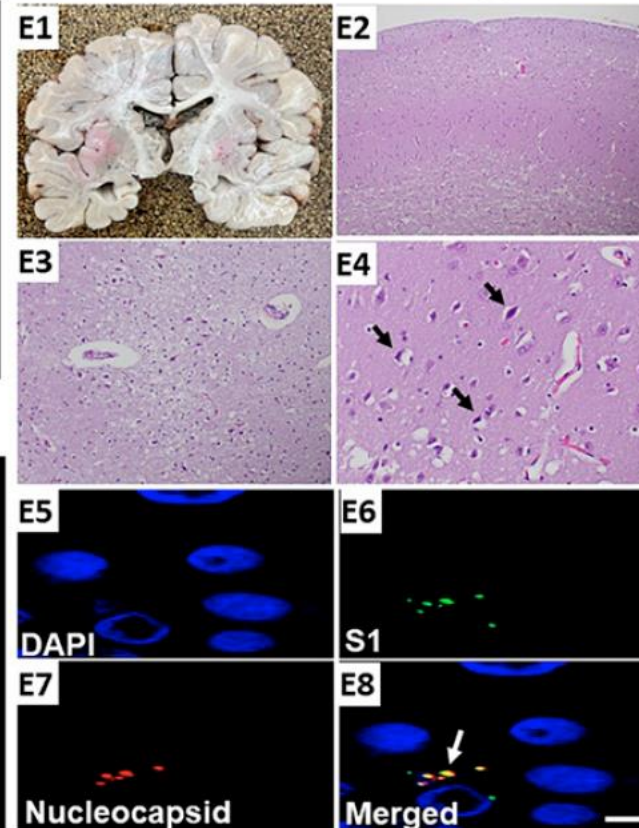
Merline Benny, MD,^a Emmalee S. Bandstra, MD,^a Ali G. Saad, MD,^b Roberto Lopez-Alberola, MD,^c Gaurav Saigal, MD,^d Michael J. Paidas, MD,^e Arumugam R. Jayakumar, PhD,^e Shahnaz Duara, MD^a

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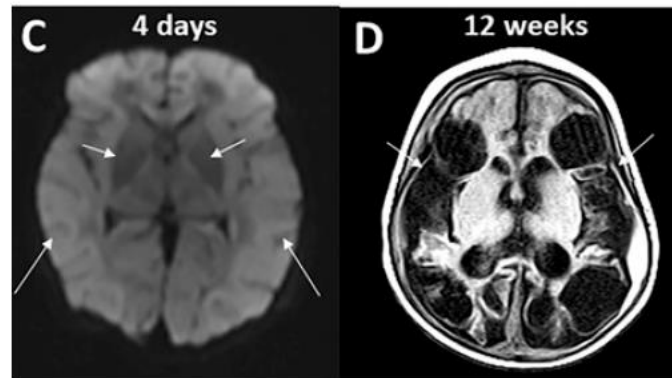
Case-1 Brain MRI



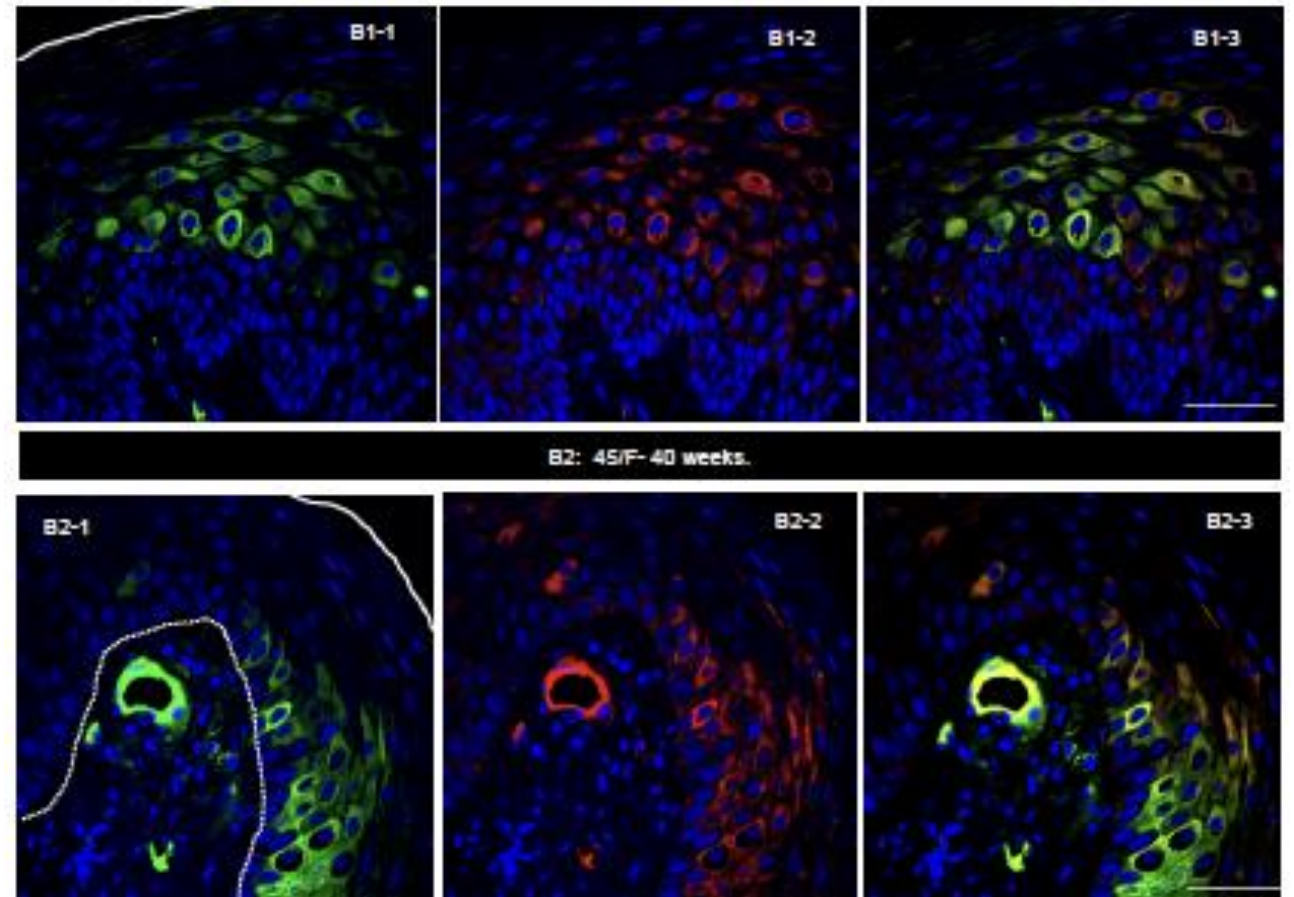
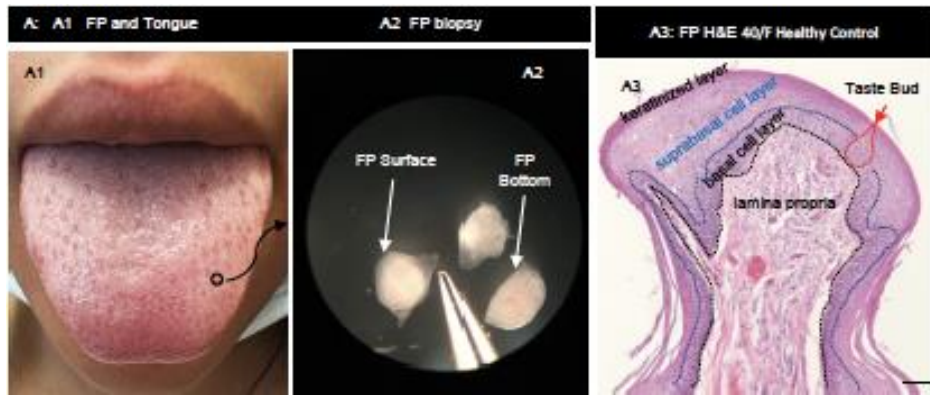
Case-1 Brain Pathology



Case-2 Brain MRI



SARS-CoV-2 in taste papillae

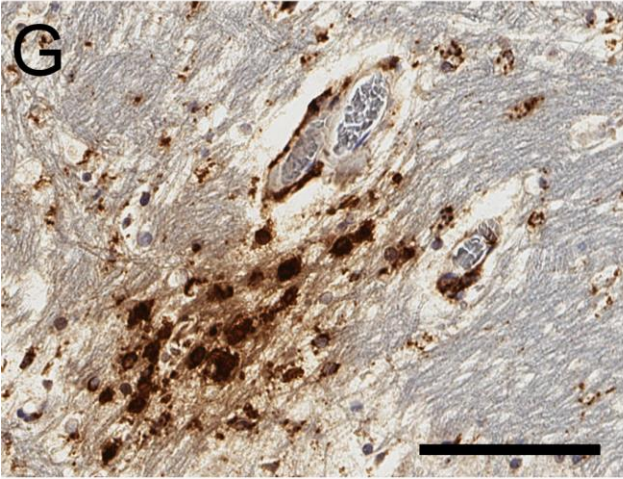


Yao Q,----Egan JM. NEJM
Evidence in press

Persistent Immune activation

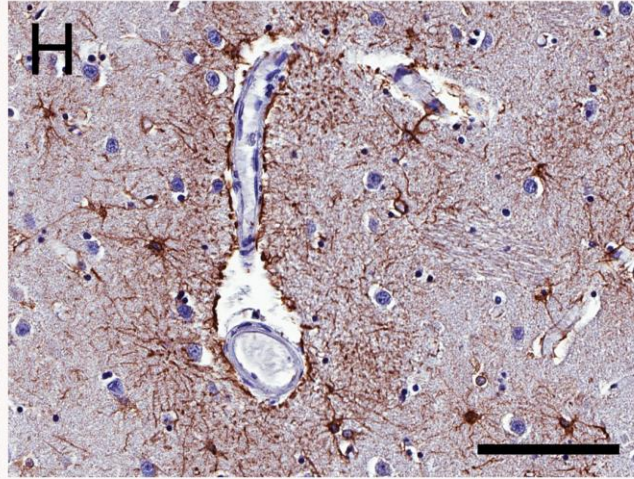
- Innate immune activation
- Autoimmune antibodies
- Immune exhaustion
- ?Genetic factors

CD68: Macrophages



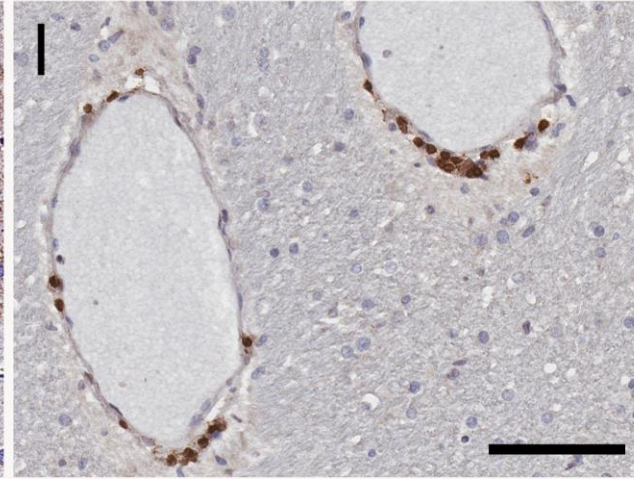
Perivascular activated
macrophages

GFAP: Astrocytes



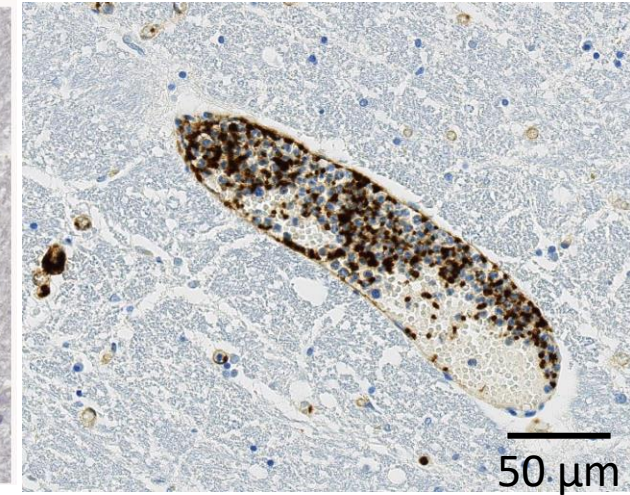
Perivascular activated
astrocytes

CD3 T cells



Very few T cells and
confined to the blood
vessels

CD61: Activated platelets

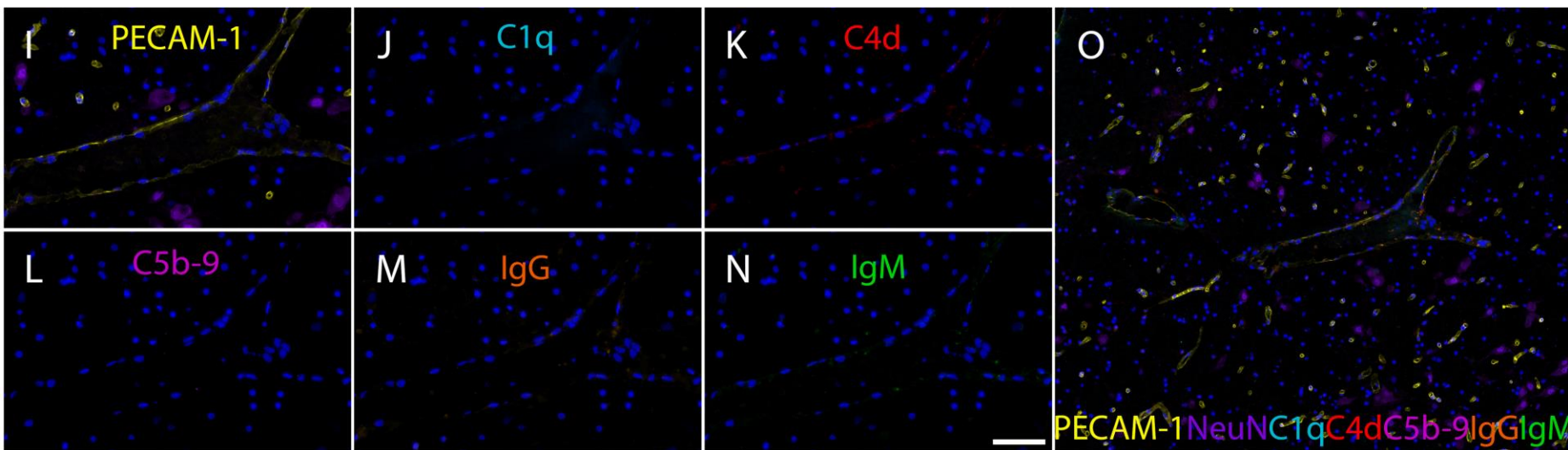


Platelets are sticking to
endothelial cells and
forming clots

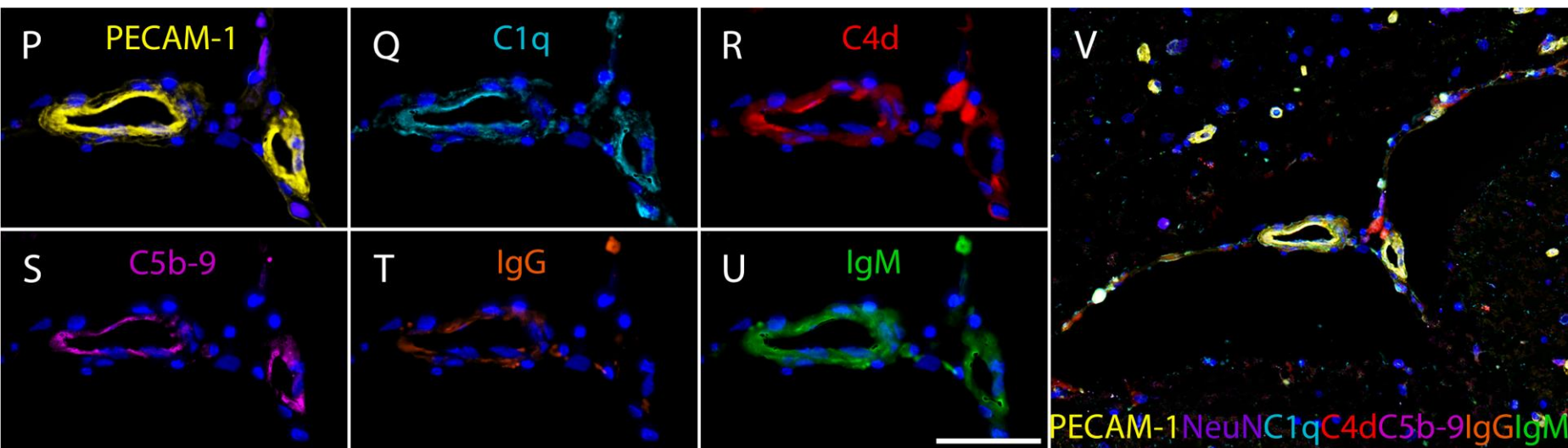
Lee et al. Brain 2022

Lee et al., NEJM 2021

Control



COVID-19



Activation of endothelial cells
(PECAM-1)

Deposition of complement

Deposition of IgG and IgM

Suggestions

Infection associated chronic illnesses: An entity

Patient engagement at every step of research process

Development of diagnostics/ biomarkers

In vitro organoids or in vivo animal models

Multidisciplinary clinics

Study pathogenesis in the context of clinical trials

Innovative design of clinical trials

Keystone Symposia
Long-COVID
Aug 27-30, 2023

