Learning from previous viral infections: From influenza to SARS, MERS and Zika

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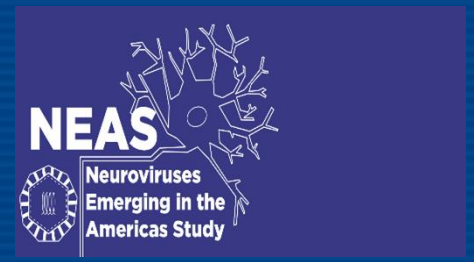
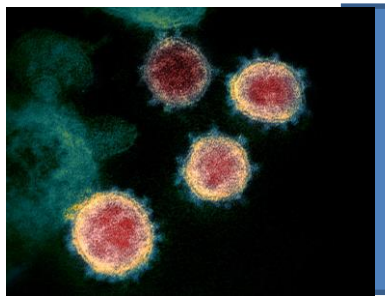


The long road to Post-COVID-19 Condition



SARS-CoV2
The virus and
Pathogenesis

Covid-19
Systemic Illness

COVID-19
Clinical
Neurological
Problems

Pneumonia
Systemic inflammatory
Disorder
Organ complications

Delirium
Encephalopathies
Cerebrovascular
Others

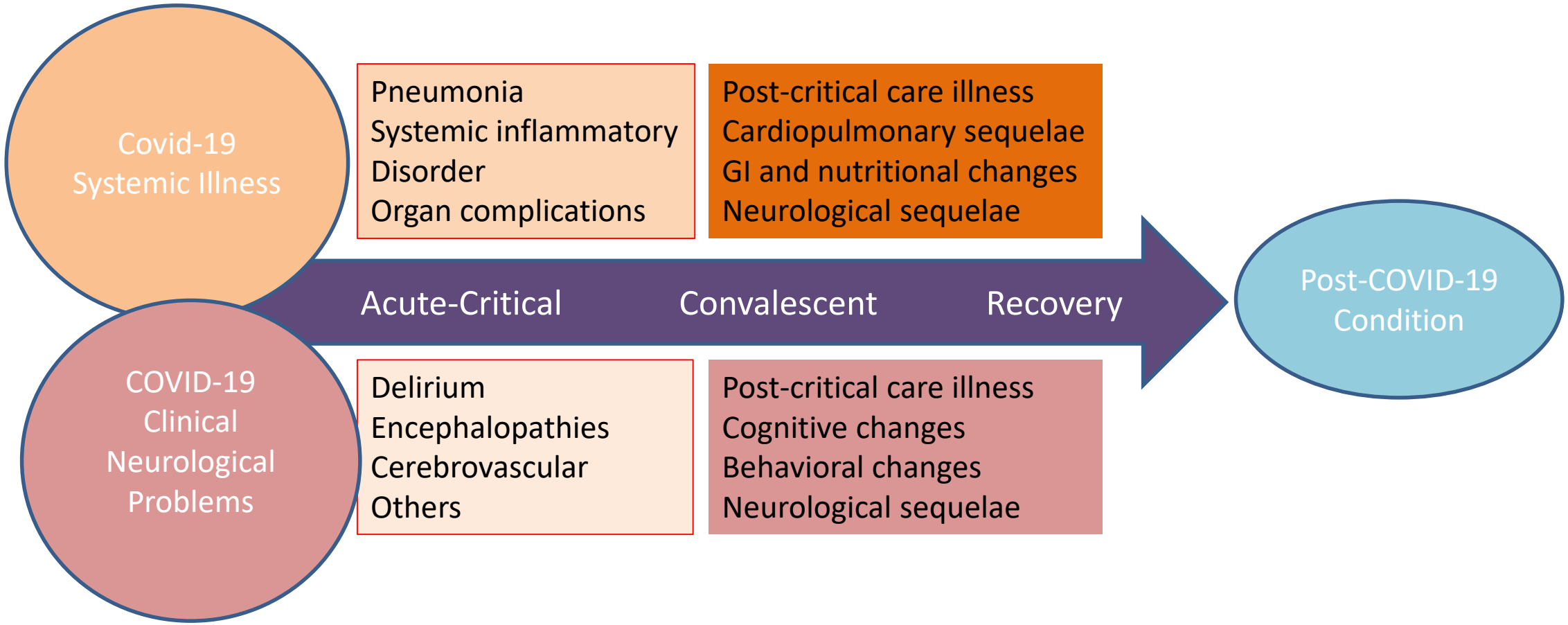
Acute-Critical → Convalescent → Recovery

Post-critical care illness
Cardiopulmonary sequelae
GI and nutritional changes
Neurological sequelae

Post-critical care illness
Cognitive changes
Behavioral changes
Neurological sequelae

World Health Organization

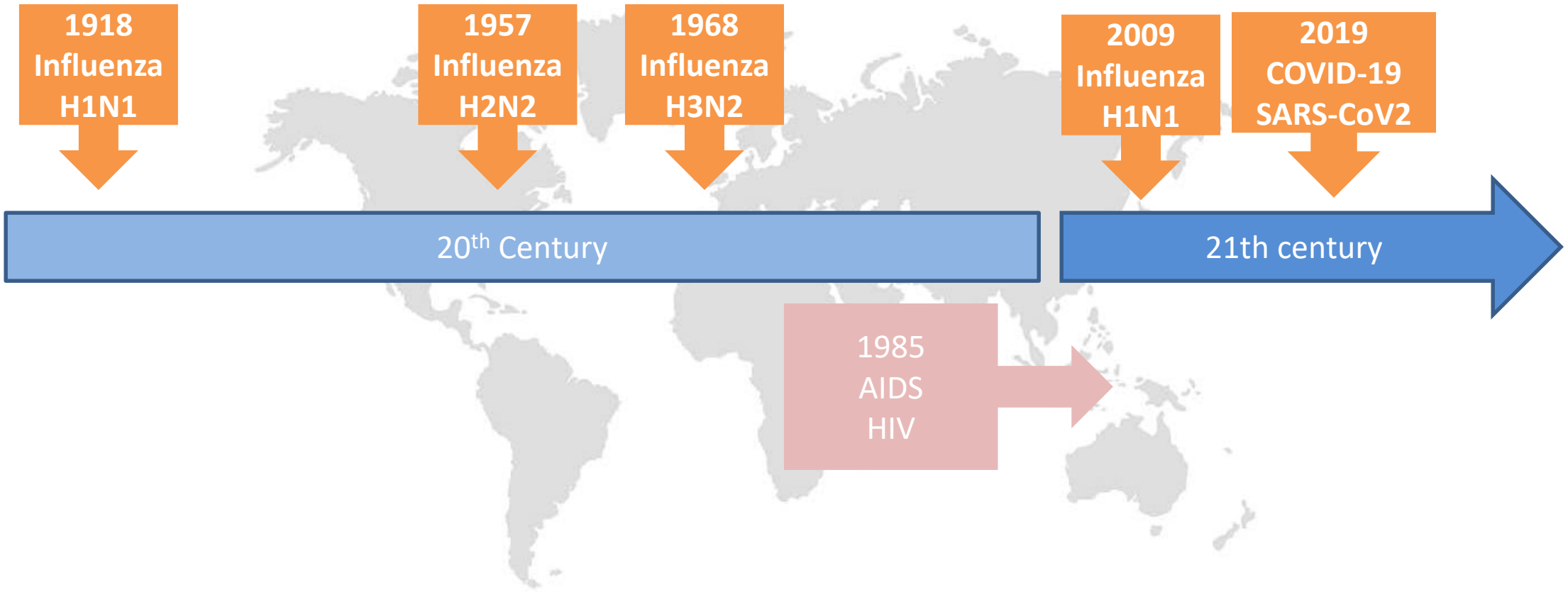
The long road to Post-COVID-19 Condition



World Health Organization

CA Pardo/Johns Hopkins Neurology

Infectious disease outbreaks in the 21st century



World Health Organization

Pardo CA/Johns Hopkins

Lessons from Influenza the 19th and 20th century: Long-term and after-effect of viral infections

- **1889-1892 flu pandemic,**
- **"Asiatic flu" "Russian flu"**
  - "neuralgia"
  - "neuroasthenia"
  - "nerve exhaustion"
  - "grippe catalepsy"
  - "post-grippal" numbness
  - "prostration"
  - "inertia"
  - paranoia

Wellcome Collection/Attribution 4.0 International (CC BY 4.0)/A man with influenza, taken in hand by a doctor, surrounded by dancing politicians. Wood engraving by Pépin (Guillaumin), 1889

558 THE LANCET,] [MARCH 7, 1891.

THE INFLUENZA OF 1890 AND A DEPRESSED TONE OF HUMAN VITALITY.

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The art of medicine

Taking pandemic sequelae seriously: from the Russian influenza to COVID-19 long-haulers

www.thelancet.com Vol 396 October 31, 2020

*Mark Honigsbaum, Lakshmi Krishnan
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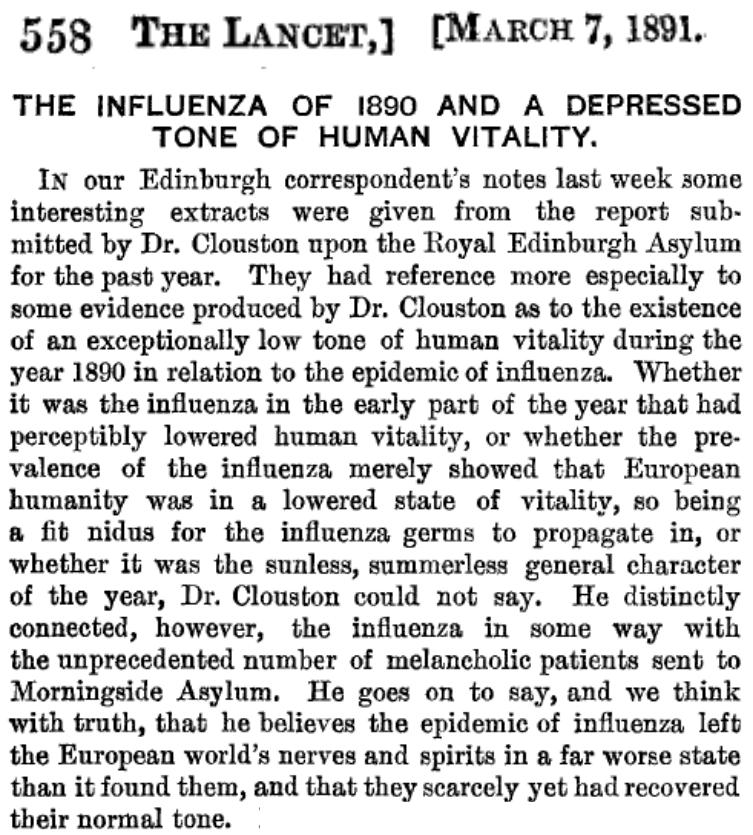
"the epidemic of influenza left the European world's nerves and spirits in a far worse state that it found them…"

- Influenza A virus subtype H2N2
- Influenza A virus subtype H3N8
- Coronavirus OC43 (?)



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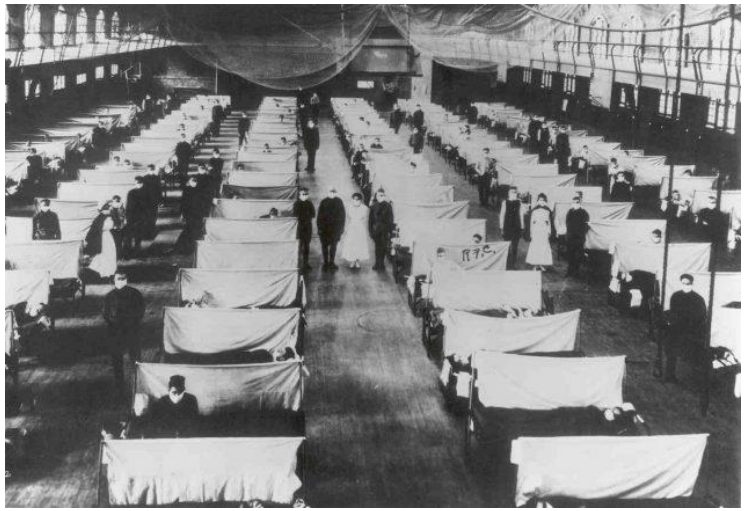
World Health Organization

Lessons from Influenza the 19th and 20th century: Long-term and after-effect of viral infections

- **1918-1919 flu pandemic,**
- **"Spanish flu"**
  - Neurological effects
  - Encephalitis lethargica (?)
  - Post-infectious syndrome
  - Asthenia

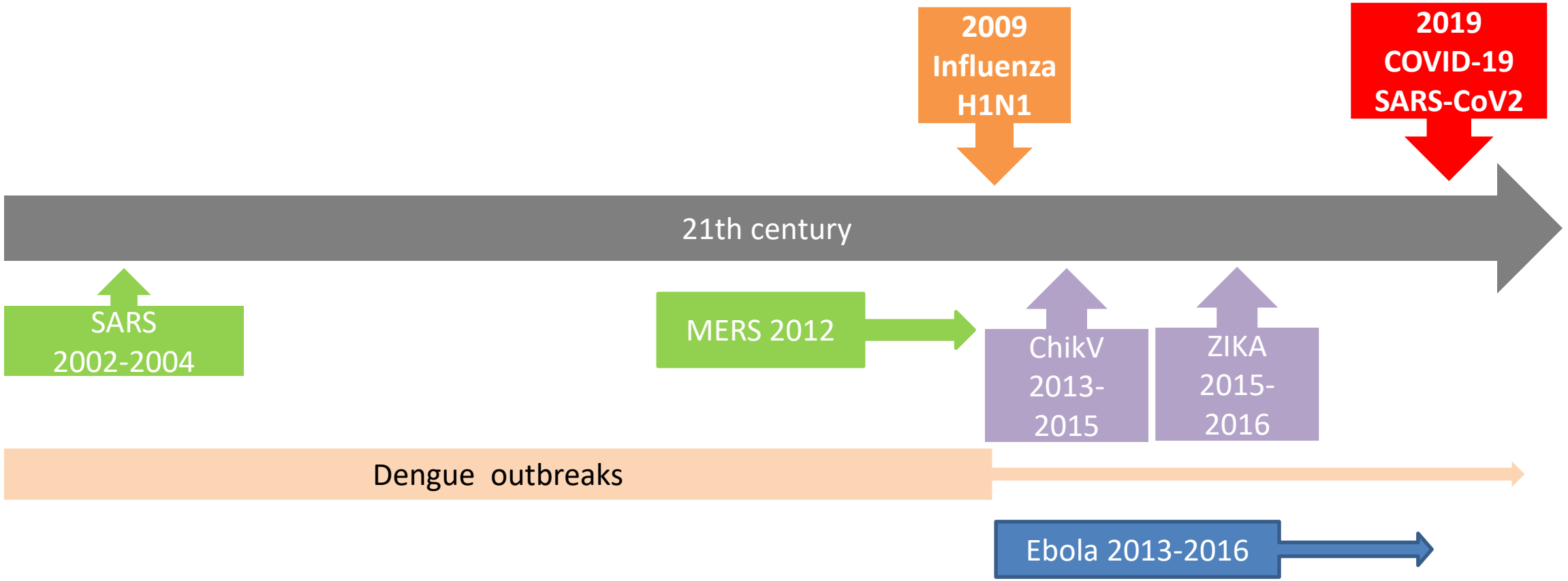
➢ **Influenza A virus subtype H1N1**



J Neurol Neurosurg Psychiatry 1998;64:5

Post-encephalitic Parkinsonism or *Von Economo's* Encephalitis:
The link with the "Spanish flu" remains controversial

Viral disease outbreak in the 21st century



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Pardo CA/Johns Hopkins

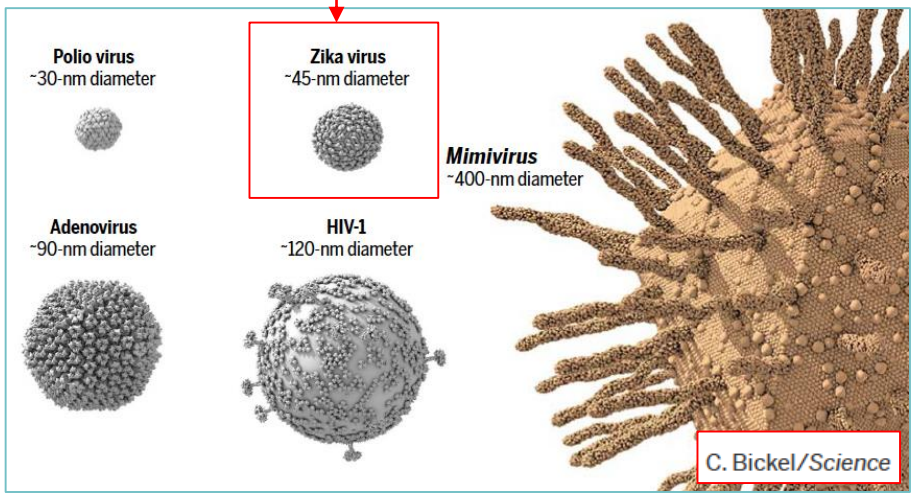
Flavivirus Associated with Epidemic Diseases

***Flaviviridae* Family**

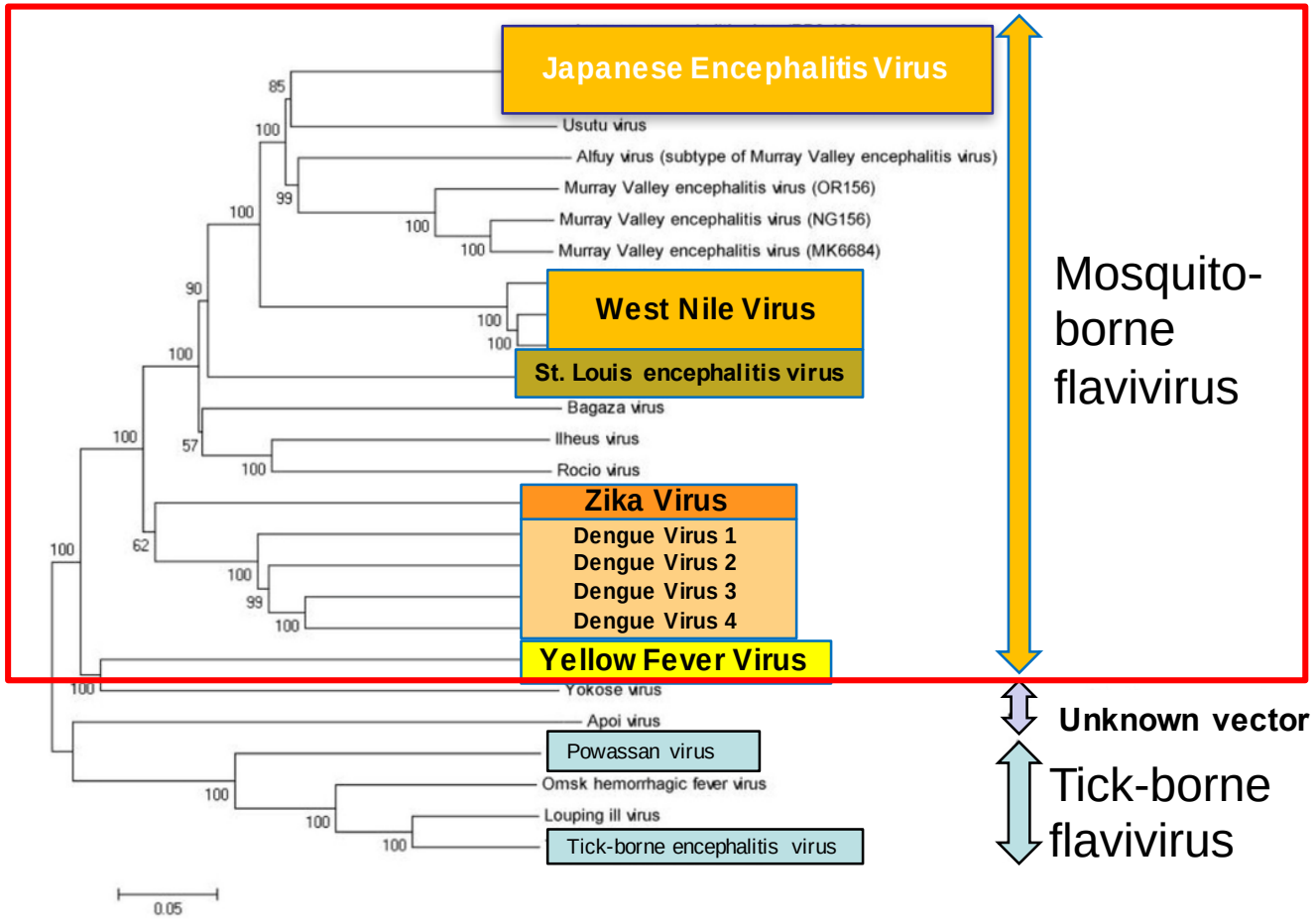
Hepacivius genus

Flavivirus genus

- (+)ssRNA
- Enveloped
- Icosahedral/spherical
- 40-60 nm



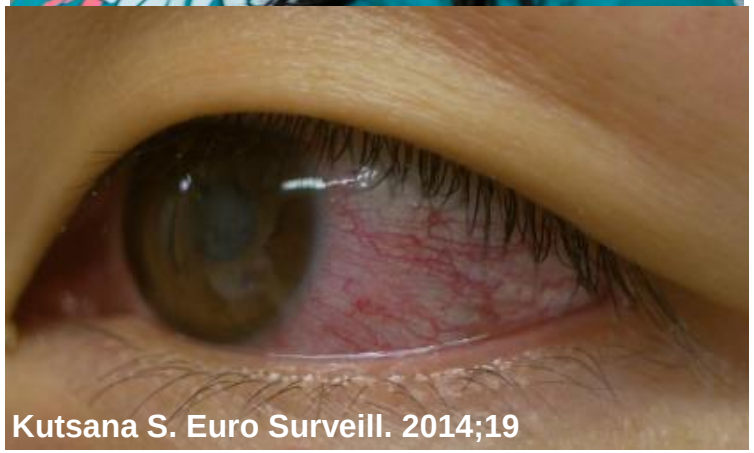
Flavivirus



Zika virus has been in many areas of the world since 1950 and spread only until recent years to the French Polynesia and Latinamerica

Published by AAAS

Courtesy Dr. Jairo Lizarazo

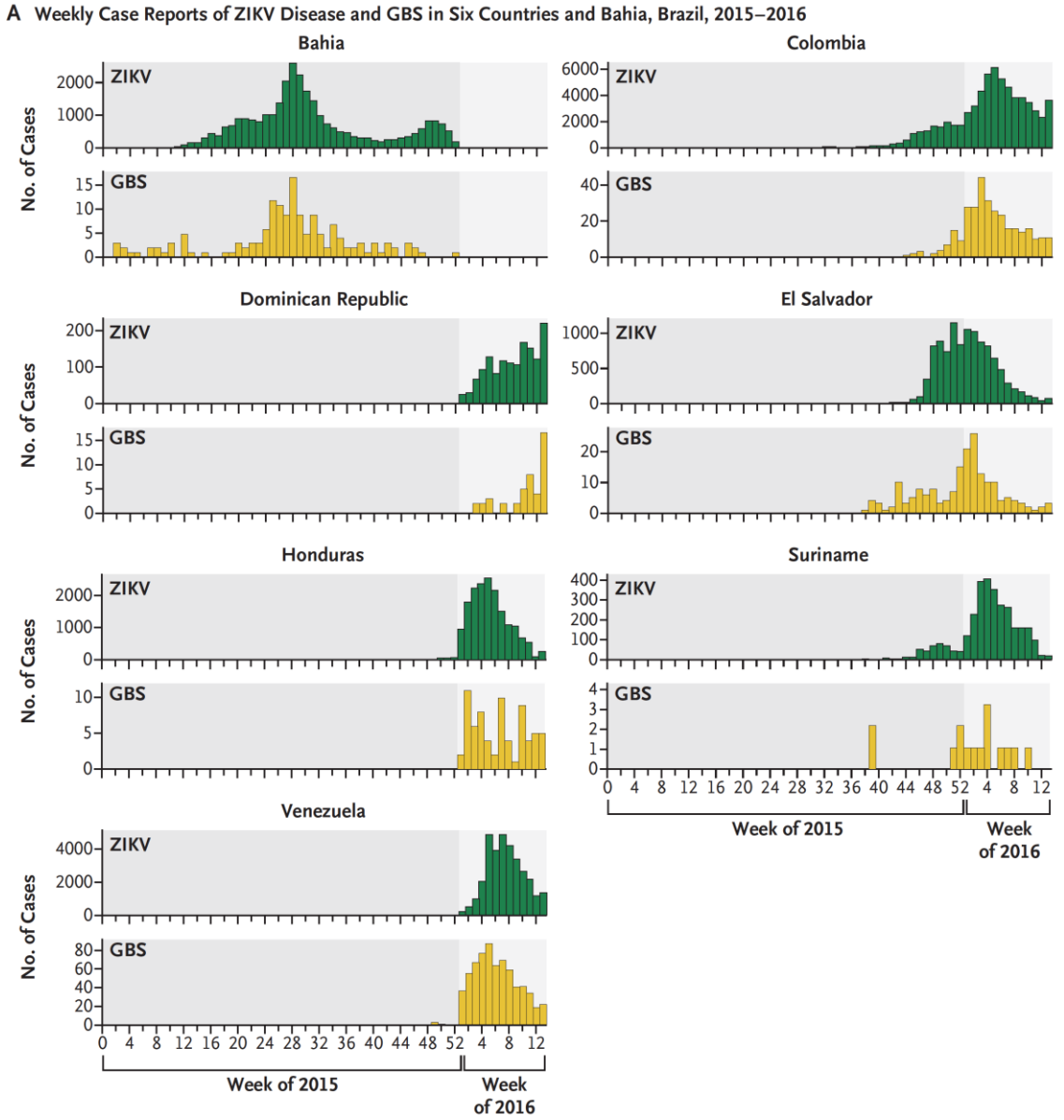


Kutsana S. Euro Surveill. 2014;19

Clinical Manifestations of Zika infection

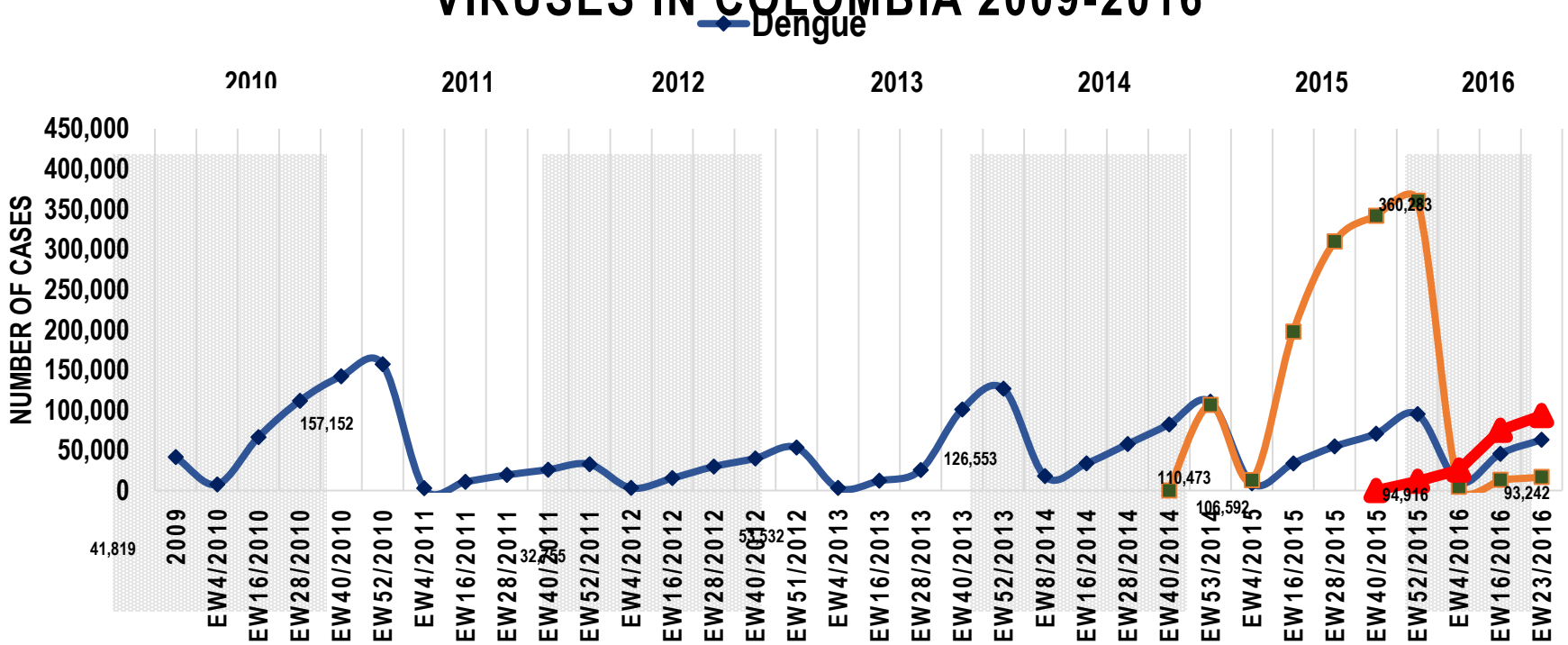
- Exanthema and rash
- Fever
- Headache
- Myalgias
- Arthralgias
- Conjuntivitis
- Diarrhea
- **80 % infected people remain asymptomatic**

2016:
GBS in times of Zika



dos Santos T. et al. August 31, 2016
The NEW ENGLAND JOURNAL of MEDICINE
DOI: 10.1056/NEJMc1609015

INCIDENCE OF DENGUE, CHIKUNGUNYA AND ZIKA VIRUSES IN COLOMBIA 2009-2016



NEAS Neuroviruses Emerging in the Americas Study

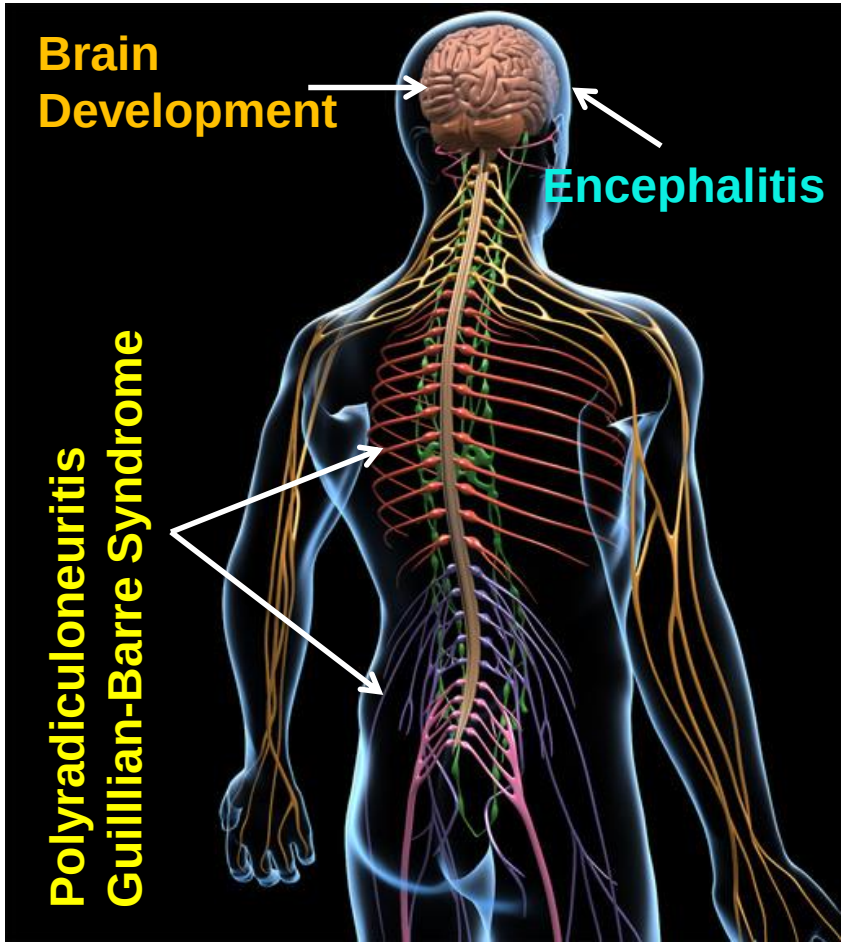
Based on data from the Colombian National Institute of Health (Boletin Epidemiologico Semanal)

Parra B et al., N Engl J Med 2016;375:1513-23.

Neurological Problems Presumed to be Associated with Zika Infection

Peripheral Nervous System Involvement:

- **Guillain-Barre Syndrome**
  - ➢ Acute Demyelinating Polyneuropathy
  - ➢ Acute Motor Axonal Neuropathy
  - ➢ Miller-Fisher variant
- **Neuropathies**

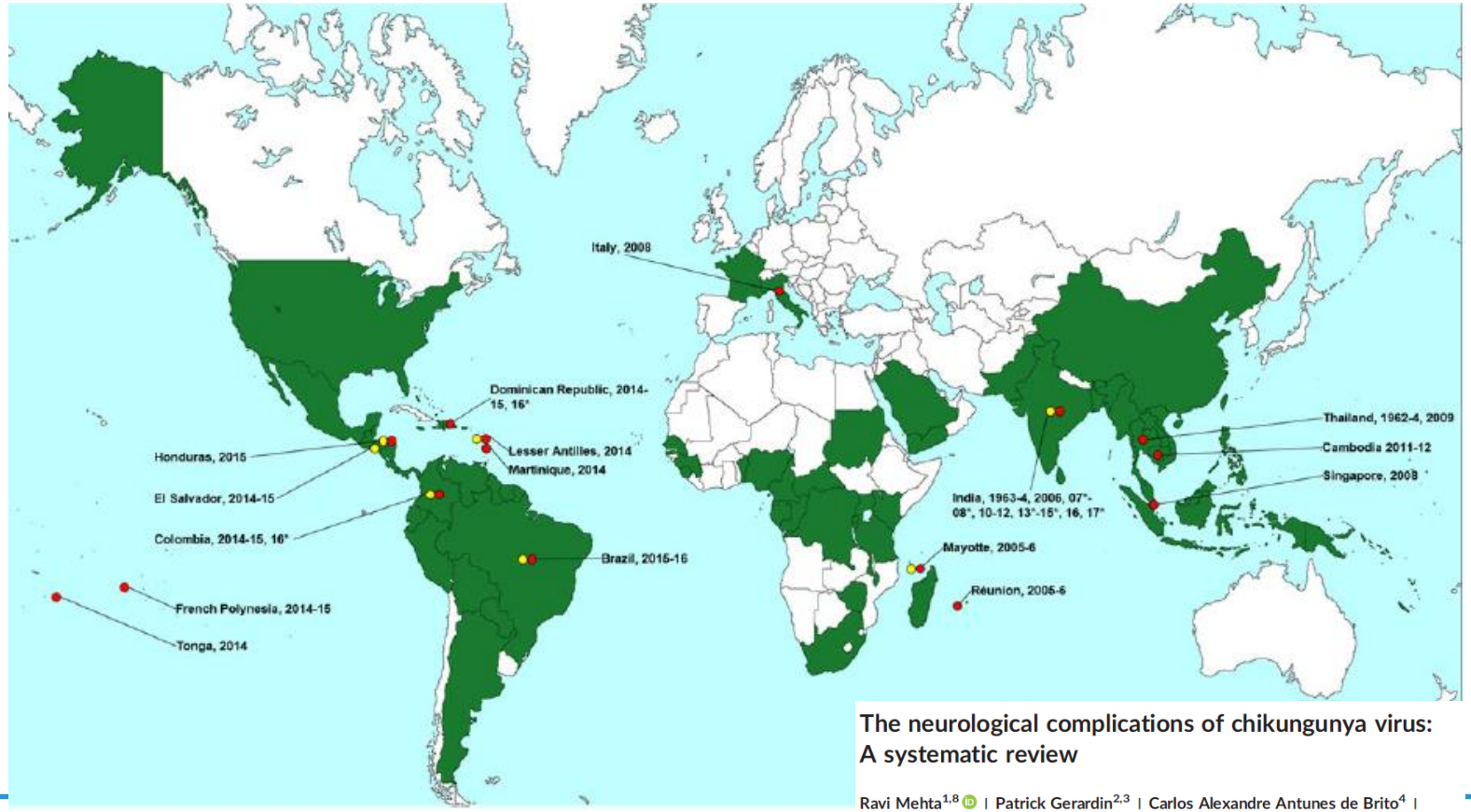


Central Nervous System Involvement:

- Encephalitis
- Myelitis
- Optic neuritis

Immune Mediated Pathogenesis vs Direct Viral Neuropathogenicity or Both

Chikungunya virus: emergent y re-emergent



The neurological complications of chikungunya virus: A systematic review

Ravi Mehta[1,8] | Patrick Gerardin[2,3] | Carlos Alexandre Antunes de Brito[4] | Cristiane Nascimento Soares[5] | Maria Lucia Brito Ferreira[6] | Tom Solomon[1,7,8]

Rev Med Virol. 2018;e1978.
https://doi.org/10.1002/rmv.1978

World Health Organization

	Mono-infection (n=98)				Dual infection (n=50)				All cases (n=201)		
	ZIKV (n=41)	CHIKV (n=55)	DENV (n=2)	p value*	ZIKV + CHIKV co-infection (n=13)	ZIKV + CHIKV (n=33)	CHIKV + DENV (n=4)	p value†	Laboratory evidence of acute arbovirus infection (n=148)	No laboratory evidence of acute arbovirus infection (n=53)	p value‡
Systemic features of infection											
Fever	21 (51%)	47 (85%)	1 (50%)	0·0003	11 (85%)	31 (94%)	4 (100%)	0·0063	114 (77%)	33 (62%)	0·037
Rash	37 (90%)	43 (78%)	0	0·12	10 (77%)	31 (94%)	2 (50%)	0·36	123 (83%)	43 (81%)	0·75
Pruritus	13 (32%)	18 (33%)	2 (100%)	0·92	5 (38%)	14 (42%)	3 (75%)	0·29	55 (37%)	15 (28%)	0·25
Non-purulent conjunctivitis	13 (32%)	15 (27%)	0	0·64	4 (31%)	8 (24%)	3 (75%)	0·70	43 (29%)	16 (30%)	0·88
Myalgia	20 (49%)	37 (67%)	2 (100%)	0·068	7 (54%)	25 (76%)	3 (75%)	0·24	94 (64%)	32 (60%)	0·69
Joint oedema	16 (39%)	36 (65%)	0	0·010	4 (31%)	20 (61%)	1 (25%)	0·82	77 (52%)	18 (34%)	0·024
Arthralgia	25 (61%)	47 (85%)	1 (50%)	0·0061	8 (62%)	28 (85%)	3 (75%)	0·67	112 (76%)	28 (53%)	0·0019
Vomiting	8 (20%)	16 (29%)	0	0·29	6 (46%)	13 (39%)	1 (25%)	0·048	44 (30%)	19 (36%)	0·41
Diarrhoea	3 (7%)	9 (16%)	0	0·19	4 (31%)	5 (15%)	0 (0%)	0·27	21 (14%)	10 (19%)	0·42
Sore throat	5 (12%)	4 (7%)	0	0·64	1 (8%)	3 (9%)	1 (25%)	>0·99	14 (9%)	4 (8%)	0·92
Difficulty breathing	7 (17%)	4 (7%)	0	0·24	5 (38%)	3 (9%)	0	0·33	19 (13%)	10 (19%)	0·29
Cough	9 (22%)	3 (5%)	0	0·016	2 (15%)	6 (18%)	2 (50%)	0·43	22 (15%)	4 (8%)	0·17

Neurological disease in adults with Zika and chikungunya virus infection in Northeast Brazil: a prospective observational study

Maria Lúcia Brito Ferreira, Maria de Fatima Pessoa Militão de Albuquerque, Carlos Alexandre Antunes de Brito, Rafael Freitas de Oliveira França, Álvaro José Porto Moreira, Maria Íris de Morais Machado, Roberta da Paz Melo, Raquel Medialdea-Carrera, Solange Dornelas Mesquita, Marcela Lopes Santos, Ravi Mehta, Rafael Ramos e Silva, Sonja E Leonhard, Mark Ellul, Anna Rosala-Hallas, Girvan Burnside, Lance Turtle, Michael J Griffiths, Bart C Jacobs, Maneesh Bhojak, Hugh J Willison, Lindomar José Pena, Carlos A Pardo, Ricardo A A Ximenes, Celina Maria Turchi Martelli, David W G Brown, Marli Tenório Cordeiro, Suzannah Lant, Tom Solomon

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Inpatient progress and outcome											
Intubated	1 (3%; n=31)	1 (2%)	0	>0·99	2 (17%; n=12)	3 (9%; n=32)	0	0·087	7 (5%; n=136)	4 (9%; n=47)	0·40
Admitted to intensive treatment unit	3 (9%; n=33)	1 (2%)	0	0·29	2 (17%; n=12)	3 (9%; n=32)	0	0·27	9 (7%; n=138)	6 (13%; n=46)	0·28
Number of days in hospital	17 (9–23)	17 (9–22)	20 (14–25)	0·94	19 (13–23)	22 (8–29)	12 (7–17)	0·34	17 (9–24)	18 (9–27)	0·73
Disability at discharge¶	37 (93%; n=40)	47 (92%; n=51)	2 (100%)	>0·99	11 (85%)	26 (81%; n=32)	3 (100%; n=3)	0·15	126 (89%; n=141)	43 (91%; n=47)	0·92
Died	0	1 (2%)	0	>0·99	0	0	0	>0·99	1 (1%)	1 (2%)	0·45

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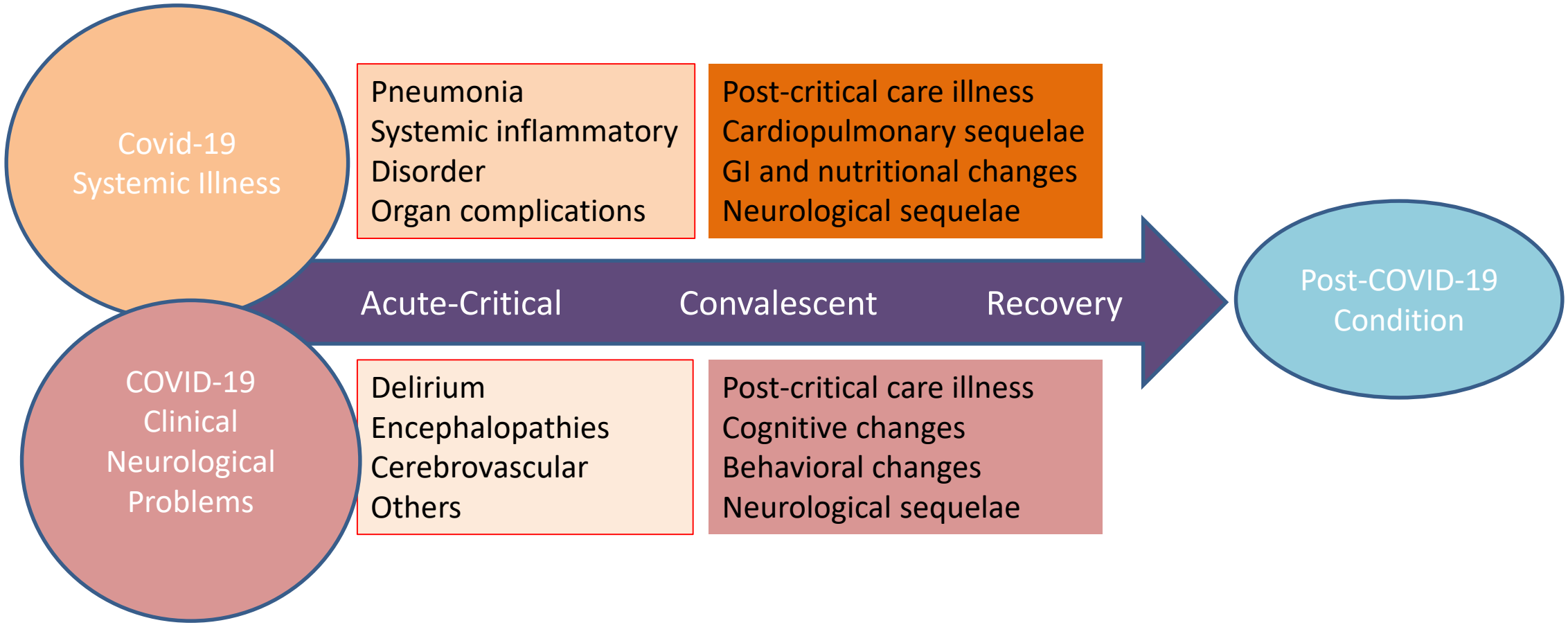

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NEAS
Neuroviruses Emerging in the Americas Study

ACN
Asociación Colombiana de Neurología

Universidad del Valle

Preparedness Latin American Network
ZikaPLAN

The Johns Hopkins
PROJECT RESTORE

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