

# A paradigm shift: Widespread SARS CoV-2 infection and persistence in humans

Daniel S. Chertow, MD, MPH

Critical Care Medical Department, Clinical Center

Laboratory of Virology, NIAID

February 17, 2022



# Disclosures

- None

# Objectives

- Describe the burden of SARS-CoV-2 infection within versus outside of the respiratory tract
- Define SARS-CoV-2 cellular tropism across the human body and brain
- Determine if SARS-CoV-2 persists in tissues and over what interval
- Assess if SARS-CoV-2 replicates and/or evolves in different anatomic compartments

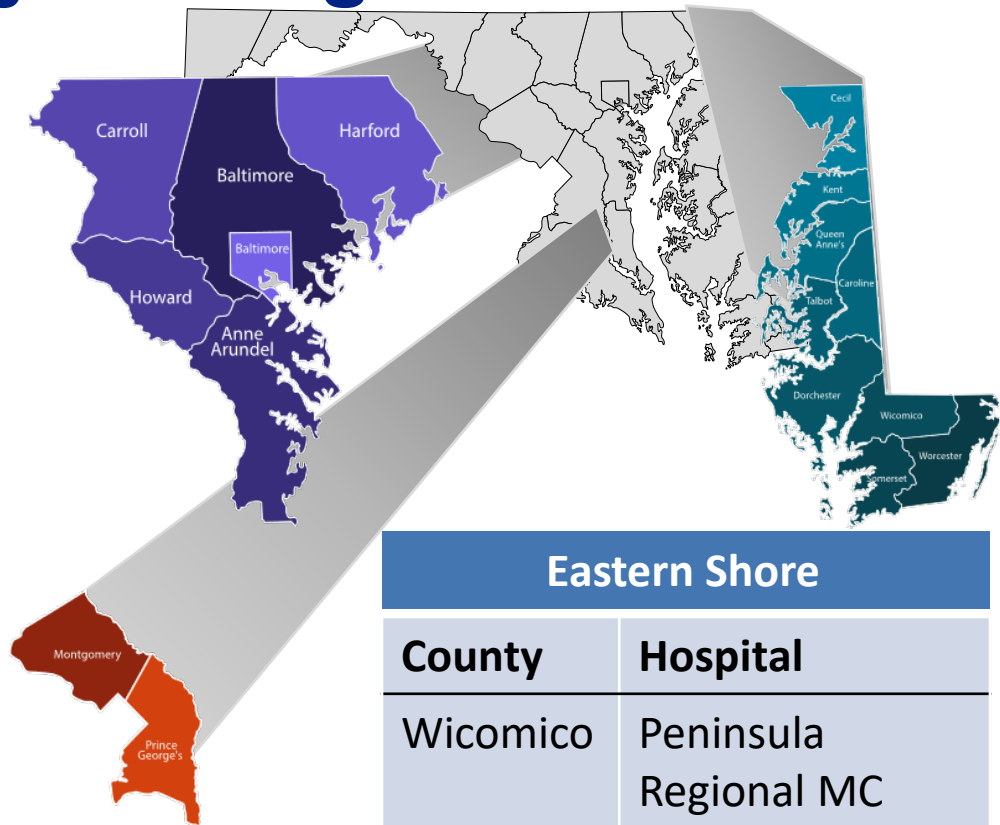
# Seven participating hospitals across three Maryland regions

## Central Maryland

County	Hospital
Baltimore	Greater Baltimore MC
Baltimore	UMD St. Joseph's MC
Baltimore city	UMD MC
Baltimore city	UMD MC Midtown
Anne Arundel	UMD BWMC

## Capital Region

County	Hospital
Montgomery	NIH Clinical Center



## Eastern Shore

County	Hospital
Wicomico	Peninsula Regional MC

# Autopsy study design

24-hour interval

COVID-19 death



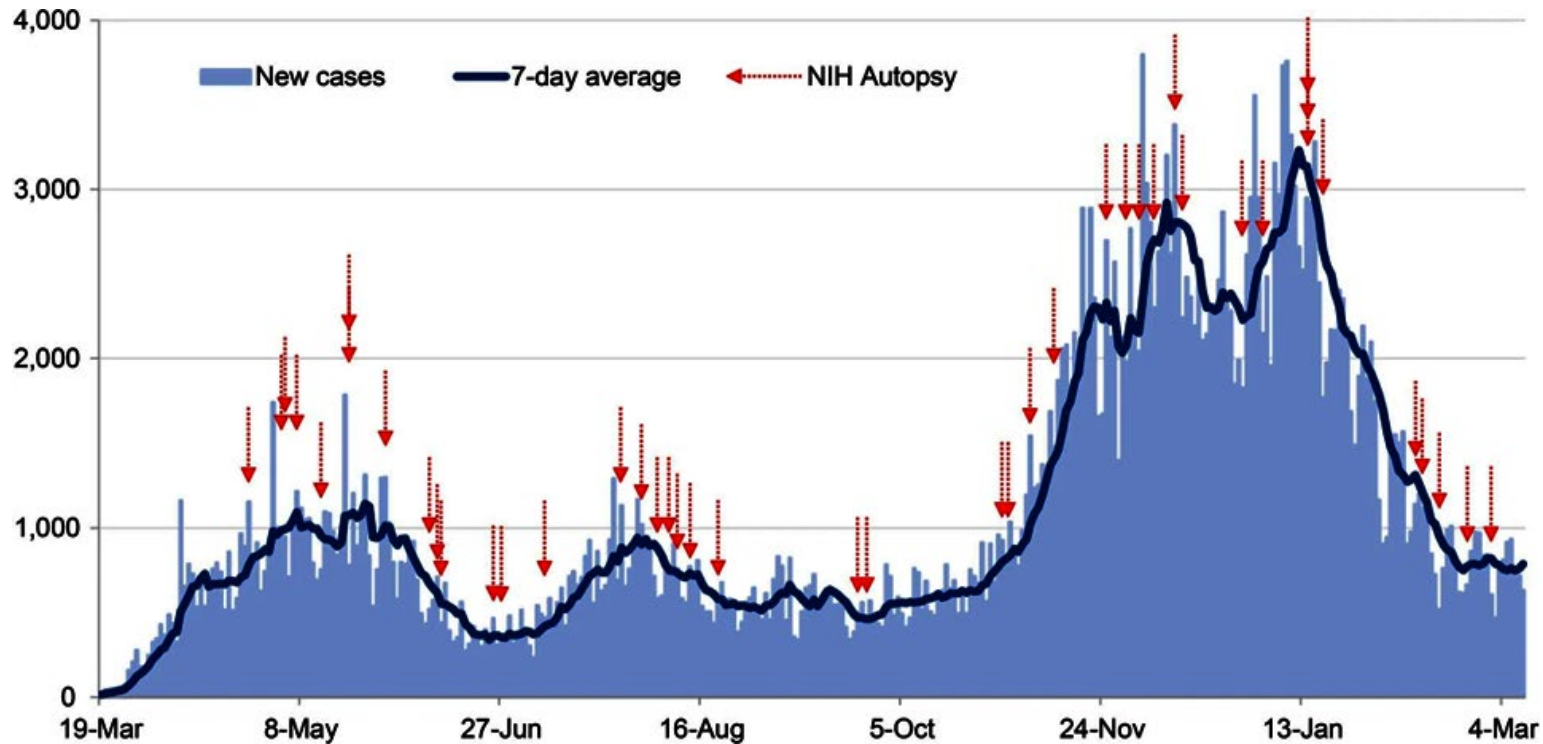
Consent and transfer



Autopsy and tissue procurement

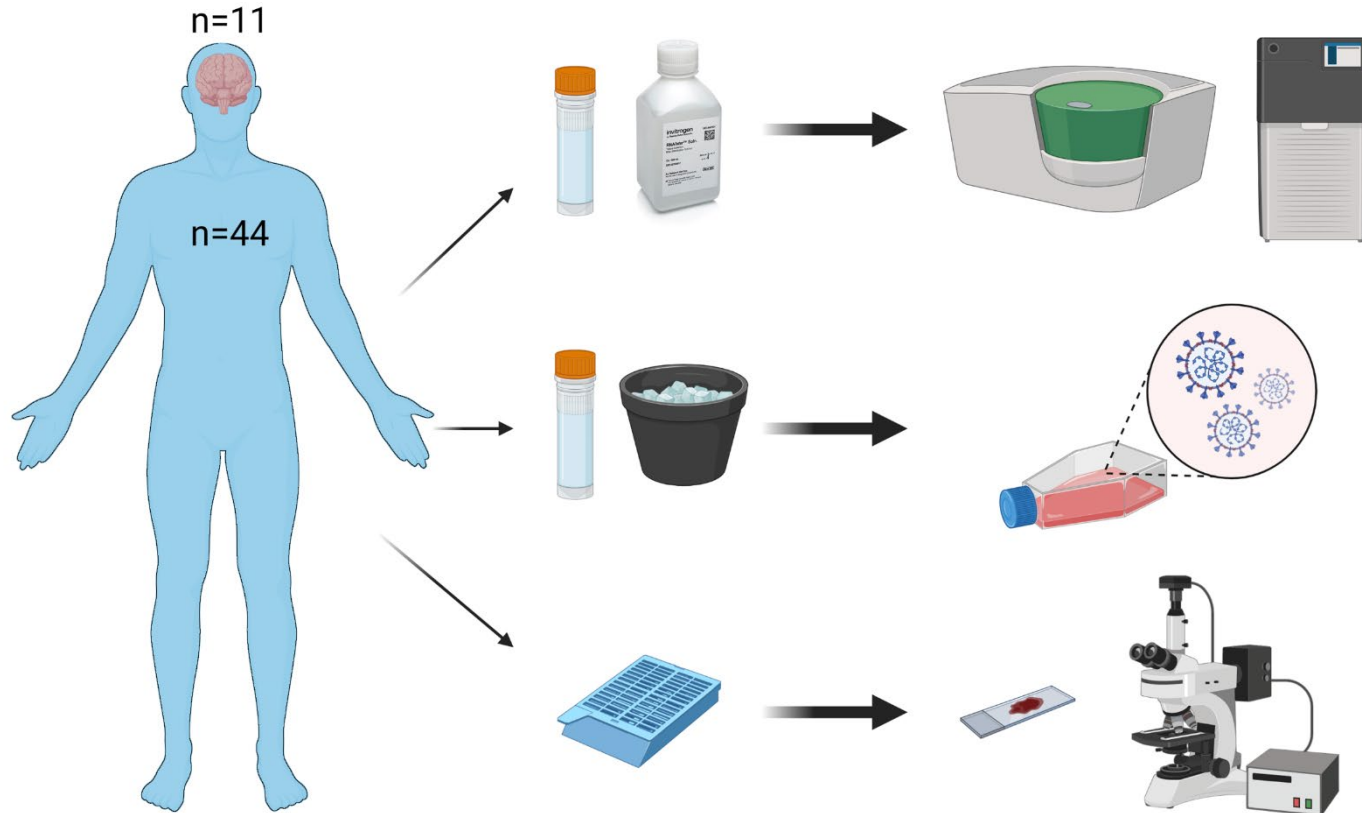


# Autopsy timing relative to Maryland COVID-19 cases, 3/2020 to 3/2021



[Stein et al. \*Nature\*. 2022; Dec 16.](#)

# Sample procurement



# Demographics

<b>Age (years)</b>	<b>(n=44)</b>
Mean (Min, Max)	<b>59.2 (6, 91)</b>
<b>Age by group (years)</b>	<b>n (%)</b>
0-17	1 (2.3)
18-24	1 (2.3)
25-34	2 (4.5)
35-44	6 (13.6)
45-54	4 (9.1)
55-64	11 (25.0)
65-74	11 (25.0)
75-84	5 (11.4)
≥85	3 (6.8)
<b>Sex</b>	
Male	<b>30 (68.2)</b>
Female	<b>13 (29.5)</b>
Intersex	<b>1 (2.3)</b>
<b>Race/Ethnicity</b>	
Non-Hispanic Asian	<b>1 (2.3)</b>
Non-Hispanic Black or African American	<b>18 (40.9)</b>
Non-Hispanic White	<b>18 (40.9)</b>
Hispanic or Latino	<b>7 (15.9)</b>

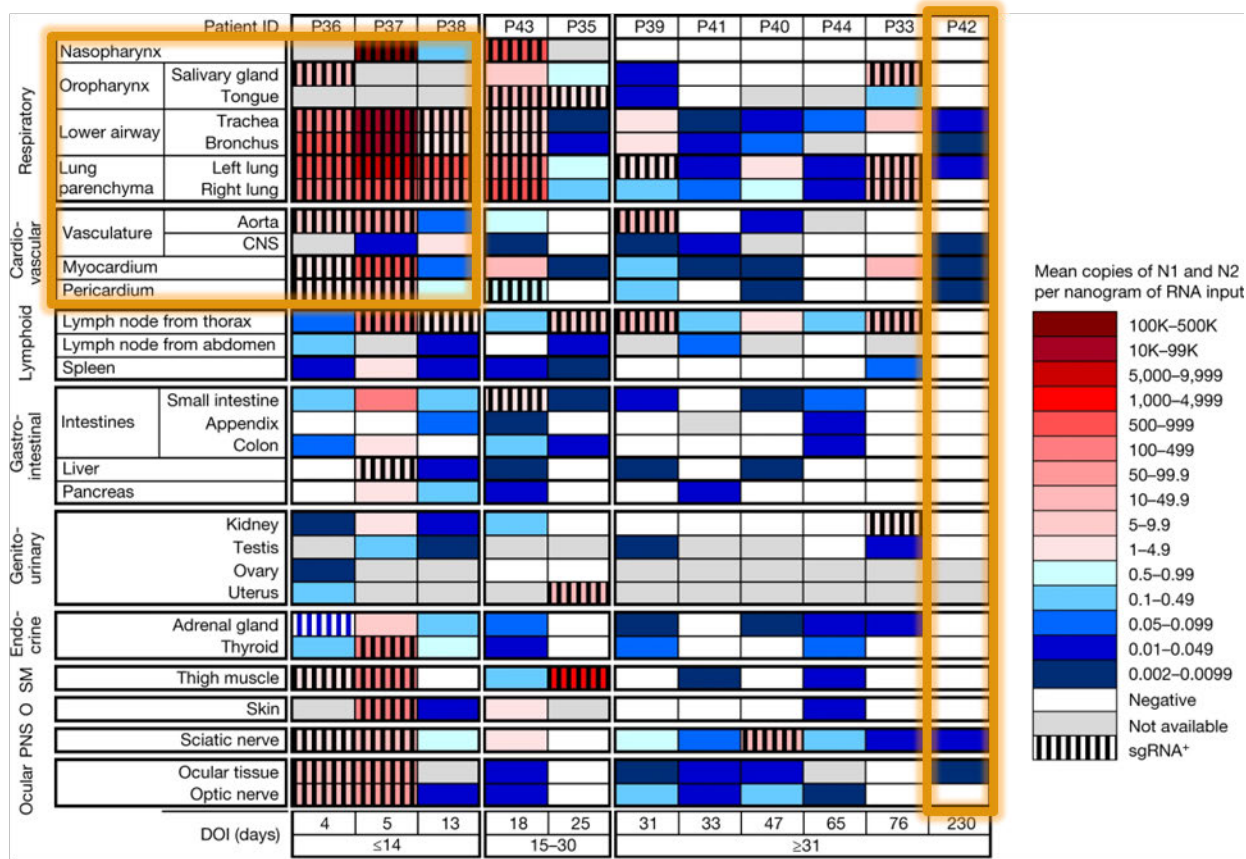


# Comorbidities

Comorbidities pre-COVID-19 diagnosis	n (%)
1+	43 (97.7)
2+	<b>34 (77.3)</b>
3+	27 (61.4)
Autoimmune disease	5 (11.4)
Cancer	7 (15.9)
Cardiovascular disease	<b>15 (34.1)</b>
Cerebrovascular disease	5 (11.4)
Chronic immunosuppression	4 (9.1)
Chronic respiratory disease	<b>16 (36.4)</b>
Diabetes mellitus	<b>14 (31.8)</b>
History of thromboembolic event(s)	4 (9.1)
Hypertension	<b>27 (61.4)</b>
Hyperlipidemia	14 (31.8)
Liver disease	3 (6.8)
Obesity (BMI $\geq$ 30)	<b>23 (52.3)</b>
Renal disease	8 (18.2)

# SARS-CoV-2 RNA throughout the body...

n=11



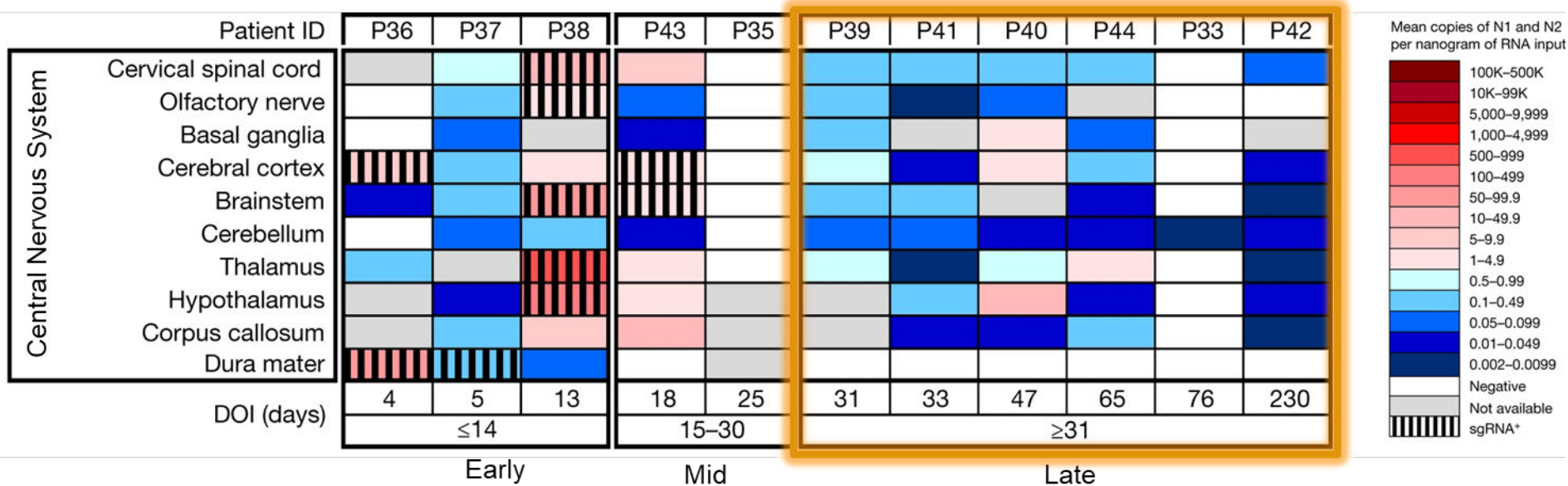
Early

Mid

Late

[Stein et al. Nature. 2022; Dec 16.](#)

# ...and brain



# Isolation of SARS-CoV-2 in respiratory and non-respiratory tissues in Vero E6 cells

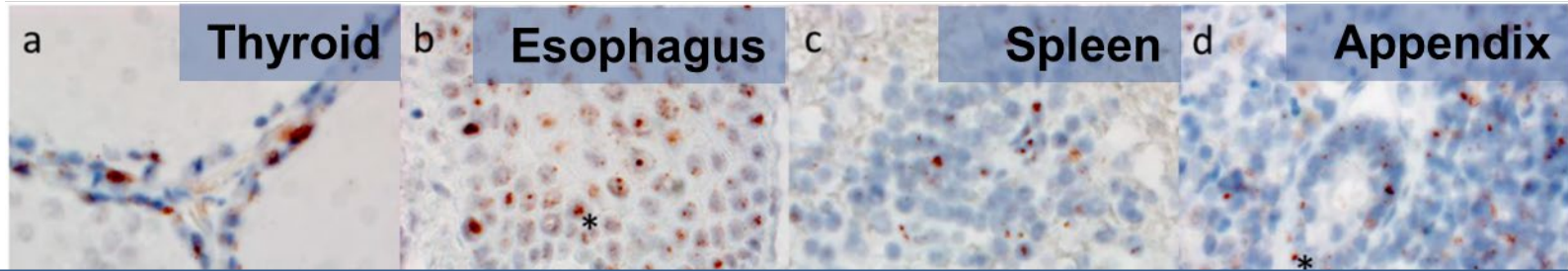
- Virus isolation on 55 samples
  - 25/55 (45%) of tissues with CPE
  - 9/20 patients + up to D12

	Patient	DOI (days)	Tissue	sgRNA (RNA/ater)		CPE	sgRNA (Flash Frozen)	
				Cq	Copies/ $\mu$ L RNA		Tissue homogenate	Tissue culture supernatant
Cq 15 to <20 n = 11	P37	5	Nasal Placode	15.96	1,592,517.55	+	23.57	17.84
	P18	9	R Superior Lobe	16.20	1,038,562.68	+	21.81	20.76
	P27	1	L Inferior Lobe	16.56	941,521.52	+	27.06	18.36
	P18	9	R Middle Lobe	16.68	751,163.28	+	21.45	19.11
	P27	1	L Superior Lobe	16.74	840,216.22	+	24.05	19.88
	P27	1	R Superior Lobe	17.55	605,097.14	+	25.54	19.03
	P18	9	L Inferior Lobe	17.61	399,355.23	+	26.07	19.15
	P18	9	R Inferior Lobe	18.28	252,263.17	+	21.96	19.59
	P24	12	R Middle Lobe	19.55	176,024.58	+	27.14	19.50
	P24	12	R Inferior Lobe	19.56	175,035.32	+	26.07	18.62
	P27	1	R Inferior Lobe	19.79	119,393.37	+	24.64	19.44
Cq 20 to <25 n = 14	P16	8	R Middle Lobe	20.52	140,774.62	+	29.87	18.68
	P19	7	Distal Trachea	20.61	51,758.95	+	23.91	21.58
	P37	5	Sinus Turbinate	21.02	51,430.26	+	29.88	18.33
	P32	6	L Bronchus	21.44	42,994.30	+	31.91	13.80
	P7	7	R Superior Lobe	21.52	30,890.52	+	27.27	17.93
	P32	6	Proximal Trachea	22.08	26,122.49	+	29.75	17.85
	P16	8	R Bronchus	22.42	25,076.22	+	33.77	17.39
	P22	4	R Middle Lobe	22.65	14,095.29	-	30.18	--
	P24	12	L Bronchus	23.68	10,796.93	-	--	--
	P38	13	L Inferior Lobe	23.69	6,419.78	-	35.09	--
	P36	4	L Inferior Lobe	24.03	5,030.85	+	34.08	19.28
	P43	18	Sinus Turbinate	24.29	6,828.27	-	30.83	--
	P22	4	R Superior Lobe	24.31	4,449.02	-	37.05	--
	P7	7	R Inferior Lobe	24.42	4,147.43	+	33.22	16.94

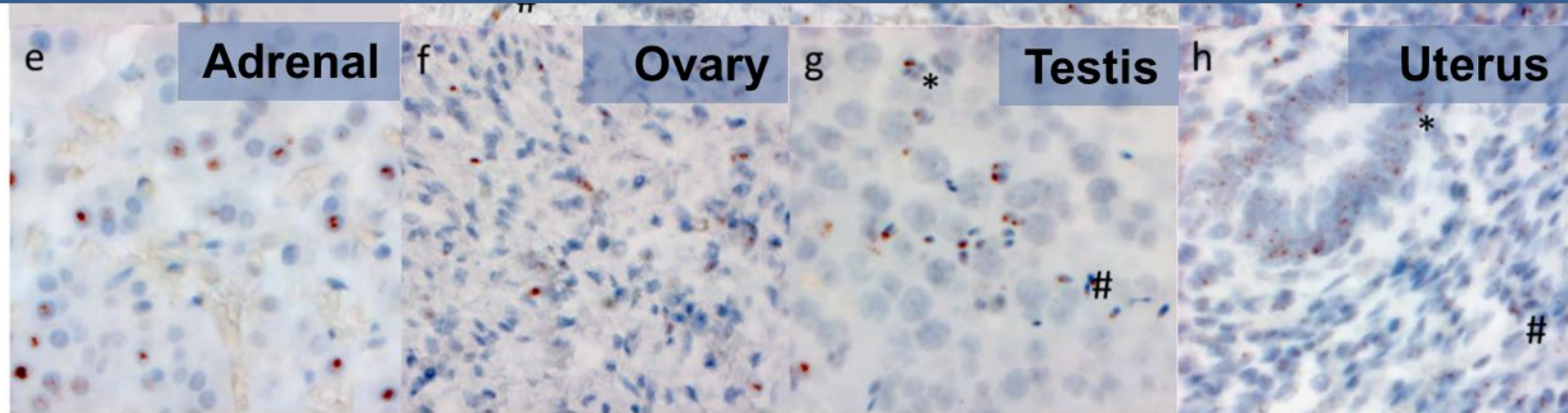
	Patient	DOI (days)	Tissue	sgRNA (RNA/ater)		CPE	sgRNA (Flash Frozen)	
				Cq	Copies/ $\mu$ L RNA		Tissue homogenate	Tissue culture supernatant
Cq 25 to <30 n = 16	P38	13	Thalamus	25.25	2,474.15	-	--	--
	P32	6	Choroid/Sclera	25.31	1,871.99	+	--	17.44
	P35	25	Skeletal Muscle	25.59	1,598.27	-	--	--
	P38	13	Hypothalamus	25.68	1,821.09	-	--	--
	P37	5	Thyroid	26.50	863.87	-	31.58	--
	P27	1	Pericardium	26.68	1,449.89	-	35.98	--
	P18	9	Abdominal Aorta	27.26	566.91	-	--	--
	P32	6	Liver	27.40	422.10	-	34.25	--
	P32	6	Jejunum	27.44	416.89	+	32.94	14.73
	P19	7	Mediastinal LN	27.96	353.22	+	--	16.29
	P27	1	R Ventricle	28.04	608.73	+	--	15.28
	P32	6	Thyroid	28.51	196.07	-	35.10	--
	P37	5	Optic Nerve	28.63	219.51	-	32.68	--
	P33	76	L Inferior Lobe	28.92	137.49	-	--	--
	P32	6	R Adrenal Gland	29.41	104.26	+	34.60	16.01
	P33	76	Thoracic LN	29.72	83.96	-	--	--

**SARS-CoV-2 isolated from choroid/sclera, jejunum, lymph node, heart, adrenal gland, and brain.**

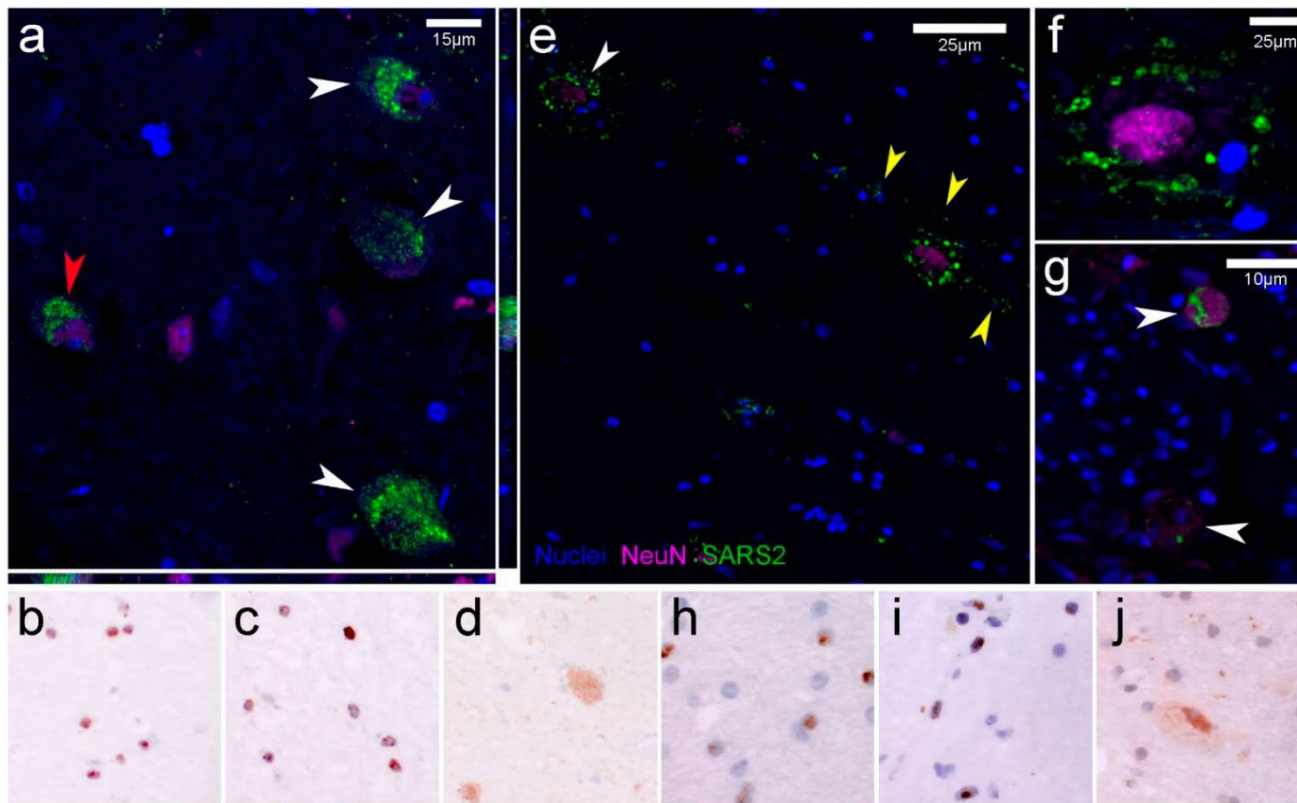
# SARS-CoV-2 spike RNA detected across multiple tissues and cell types



Detected SARS-CoV-2 RNA within >30 cell types across 35 tissues



# SARS-CoV-2 nucleocapsid RNA and protein detected in multiple CNS regions



# Summary

- SARS-CoV-2 burden is highest in respiratory tissues, but is widely disseminated in the body and brain
- SARS-CoV-2 RNA can persist in multiple anatomic compartments for over 7 months
- SARS-CoV-2 infects multiple cell types and replicates in multiple tissues including brain
- We observed a paucity of inflammation or direct viral cytopathology outside of the lung

# Acknowledgments

## University of Maryland

Daniel Herr	Kimberly Bowers	<b>SJMC</b>
Ronson Madathil	Anne Weichold	Michael McCurdy
Kapil Saharia	Douglas Tran	Kristen Sudano
Joseph Rabin	Eric Krause	Diane Blume
Nicole Hays	Joseph Herrold	Bethany Radin
Madeleine Purcell	Ali Tabatabai	Madhat Arnouk
Shreya Singireddy	Justin Richards	James Eagan Jr.
Jocelyn Wu	Erich Hochberg	
Katherine Raja	Christopher	<b>BWMC</b>
Ryan Curto	Cornachione	Mustafa Abdulmahdi
Jean Chung	Andrea Levine	Sabrina Sopha
Amy Borth	Michael McCurdy	Tyler Goldberg
Kapil Saharia	Thomas Scalea	
Zackary Chancer	Paula Minor	
Michael Mazzeffi	Mir Ahmad Moshref	
John Elder	Anthony Harris	
Mohammad Sajadi	Siamak Dahi	
Robert Christenson	Kristopher Deatrick	
Emily Kelly	Allen Burke	

### PRMC

Shahabuddin Soherwardi  
Yashvir Sangwan

### GBMC

Robert Palermo

## National Institutes of Health

<b>CCMD, CC</b>	<b>NCI</b>	<b>NIDCR</b>
Daniel Chertow	David Kleiner	Peter Burbelo
Kevin Vannella	Stephen Hewitt	
Junfeng Sun	Martha Quezado	<b>NIBIB</b>
Sabrina Ramelli	Willie Young	Thomas Pohida
James Dickey	Sarah Young	Marcial Garmendia-
Marcos-Ramos-Benitez	Billel Gasm	Cedillos
Andrew Platt	Michelly Sampaio De	
Izabella Lach	Melo	<b>NIMH</b>
Ashley Babyak	Sabina Desr	George Dold
Shelly Curran	Saber Tadros	Eris Saglio
Luis Valencia Perez	Xueting Jin	Phuoc Pham
Mary Richert	Sharika Rajan	
	Esra Dikoglu	
<b>NIAID</b>	Neval Ozakaya	
Emmie de Wit	Kris Ylaya	
Vincent Munster	Joon-Yong Chung	
Manmeet Singh	Sefania Pittaluga	
Claude Kwe Yinda	Grace Smith	
Karin Peterson		
Clayton Winkler	<b>NIDDK</b>	
Eli Boritz	Alison Grazioli	
Sung Hee Ko	Robert Star	
Frida Belinky	Megan Blawas	
Jeffrey Cohen	Justin Olivera	
Brian Kelsall		
Elizabeth Emmanuel		

**Special thanks to  
the NIH Clinical  
Center Admissions  
Staff**