

COVID 19



Keeping Up with a Moving Target



CME Information

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Name of Faculty or Presenter	Reported Financial Relationship
Paul G. Auwaerter, MD, MBA, FIDSA	JNJ: Ownership equity Scientific Consulting: Verily, EMD Serono DMSB: Humanigen

Dr. Auwaerter has indicated that he will be referencing the unlabeled or unapproved use of agents currently being investigated in on-going studies and trials, including a remdesivir, baricitinib, and several vaccine platforms.

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CME Information

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Learning Objectives

- Discuss implications of the Delta variant
- Describe the COVID-19 clinical trial experience of ivermectin



Thank You

This activity is supported by educational grants from Gilead Sciences, Inc., Regeneron Pharmaceuticals, and Eli Lilly and Company.

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Please see **COVID19.DKBmed.com** for additional resources and educational activities



Paul Auwaerter, MD, MBA, FIDSA

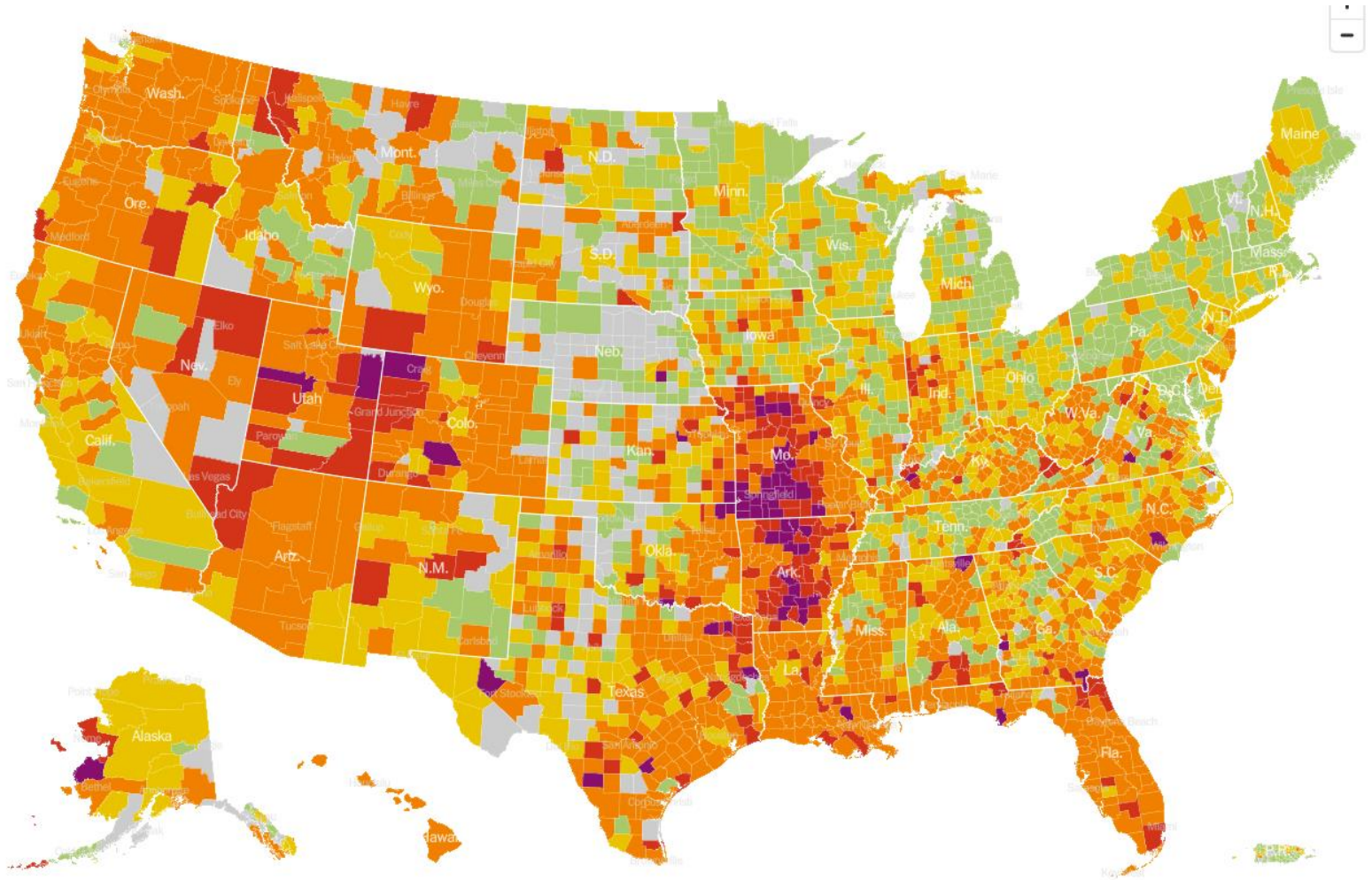
Clinical Director, Division of Infectious Diseases

Sherrilyn and Ken Fisher Professor of Medicine

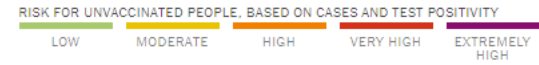
Fisher Center for Environmental Infectious Diseases

Johns Hopkins University School of Medicine

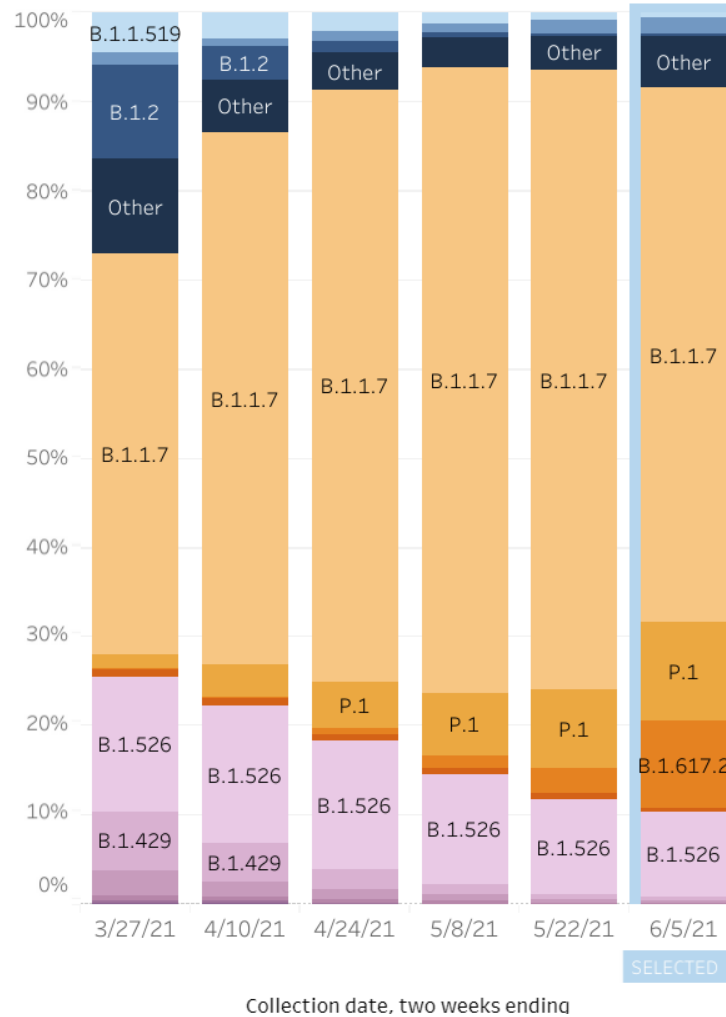
US COVID-19 Risk Levels



Risk levels



Delta: Increasing Percentage of US Cases



USA

	Lineage	Type	%Total	95%CI
Most common lineages #	B.1.1.7	VOC	60.0%	56.4-63.5%
	P.1	VOC	11.0%	8.6-13.8%
	B.1.617.2	VOC	10.0%	7.2-13.6%
	B.1.526	VOI	9.5%	7.6-11.9%
	B.1		2.0%	1.3-3.2%
	B.1.1.519		0.5%	0.3-0.7%
Additional VOI/VOC lineages #	B.1.2	†	0.1%	0.0-0.2%
	B.1.351	VOC	0.4%	0.2-0.8%
	B.1.429	VOI	0.4%	0.2-0.7%
	B.1.427	VOI	0.3%	0.1-0.6%
	B.1.525	VOI	0.1%	0.0-0.3%
	B.1.617.1	† VOI	0.0%	0.0-0.1%
	P.2	† VOI	0.0%	0.0-0.1%
	B.1.617.3	† VOI	0.0%	NA
Other*	Other		5.8%	4.6-7.4%

* Other represents >200 additional lineages, which are each circulating at <1% of viruses
 † Fewer than 10 observations of this variant during the selected time/location context
 # Sublineages of P.1 and B.1.351 (P.1.1, P.1.2, B.1.351.2, B.1.351.3) are aggregated with the parent lineage and included in parent lineage's proportion. AY.1 and AY.2 are aggregated with B.1.617.2.

Delta Variant: Variant of Most Concern?

First described in India (B.1.651.2)

- 90% of infections in the UK
- 20% in the US

Increased transmissibility

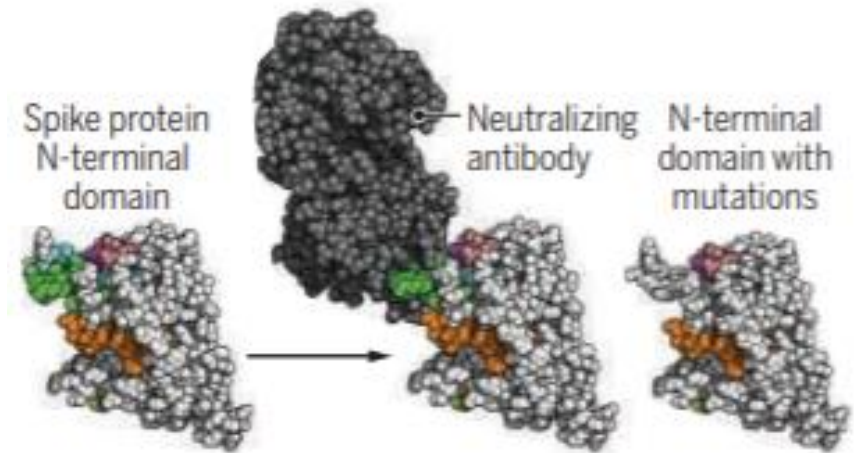
- 50-100% compared to alpha variant
- 2x increased risk of hospitalization?

Reduced protection

- If only 1 shot of mRNA vaccine or AstraZeneca
- Pfizer, AstraZeneca
 - Slightly less protection

Evasive maneuver

The spike protein's N-terminal domain (left) includes a "supersite" where powerful antibodies latch on to the virus (middle). Mutations there (right) can prevent them from binding.



Kupferschmidt, Wadman, Science 6/24/21

Why is Delta the Current Variant of Most Concern?

Nine mutations with potential

P681R

- Site adjacent to furin site cleavage
- Human enzyme affects ability of virus to enter cells

N-terminal domain supersite

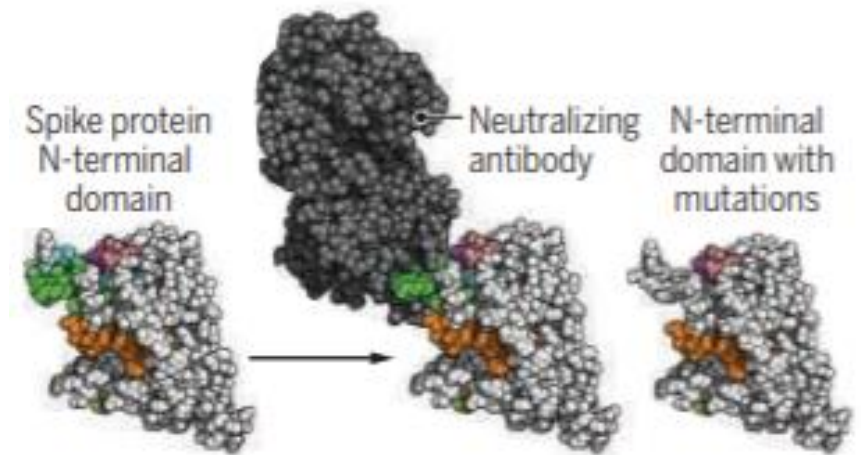
- Important site for antibody binding
- Amino acids 156 & 157 deleted
 - 158 AA change from arginine to glycine
- Elimination of antibody direct binding site

Other changes w/ potential

- Much unknown

Evasive maneuver

The spike protein's N-terminal domain (left) includes a "supersite" where powerful antibodies latch on to the virus (middle). Mutations there (right) can prevent them from binding.



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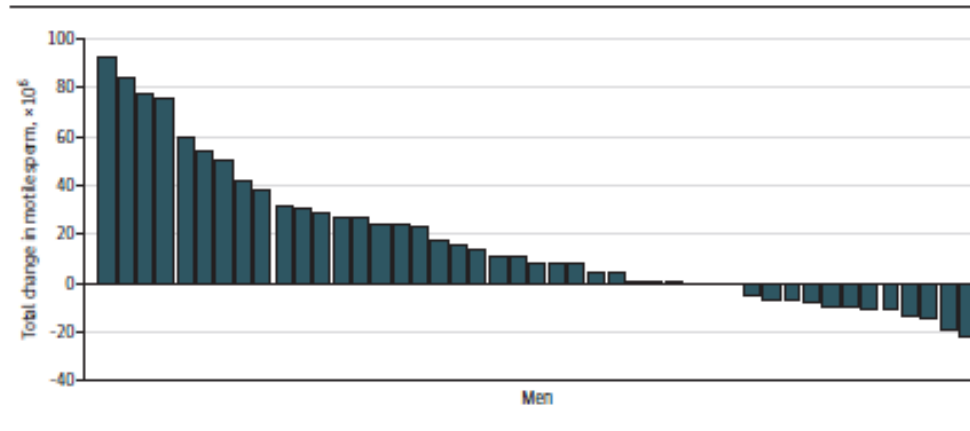
Does mRNA Immunization Affect Male Fertility?

Table. Change in Semen Analysis Parameters Before and After COVID-19 Vaccination

Parameter	Normal value	Median (IQR)		P value
		Baseline	Follow-up	
No. of participants		45	45	
Volume, mL	>1.5	2.2 (1.5-2.8)	2.7 (1.8-3.6)	.01
Sperm concentration, million/mL	>15	26 (19.5-34)	30 (21.5-40.5)	.02
Total motility, %	>40	58 (52.5-65)	65 (58-70)	.001
TMSC, million	>9	36 (18-51)	44 (27.5-98)	.001

Abbreviations: IQR, interquartile range; TMSC, total motile sperm count.

Figure. Waterfall Plot Showing Changes in Total Motile Sperm Count Parameters Within Participants Before and After COVID-19 Vaccination



Each bar represents an individual participant.

jama.com

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Is Ivermectin Effective for COVID-19?

10 RCTs, COVID-19, 5 vs. SOC, 5 vs. placebo

- Mild (8)
- Mild-moderate (1)
- Moderate (1)

All cause mortality: RR 0.37, 95%CI 0.12-1.13, very low QoE

LOS: median 0.72 days, 95%CI -0.86-2.29, very low QoE

No effect on viral clearance

Three trials suggesting mortality benefit, at high risk of bias

Conclusion: no impact on mortality, illness or viral clearance



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**Are monoclonal antibodies still effective
against the Delta variant?**



What other antivirals are being looked at for treatment of COVID-19?



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