

COVID19



Keeping Up with a Moving Target

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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 monoclonal antibodies, baricitinib, and several vaccine platforms.

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Learning Objectives

- Discuss the implications of the Delta variant



Thank You

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What's Important About Viral Variants of Concern?

World Health Organization Designation: **VOC**

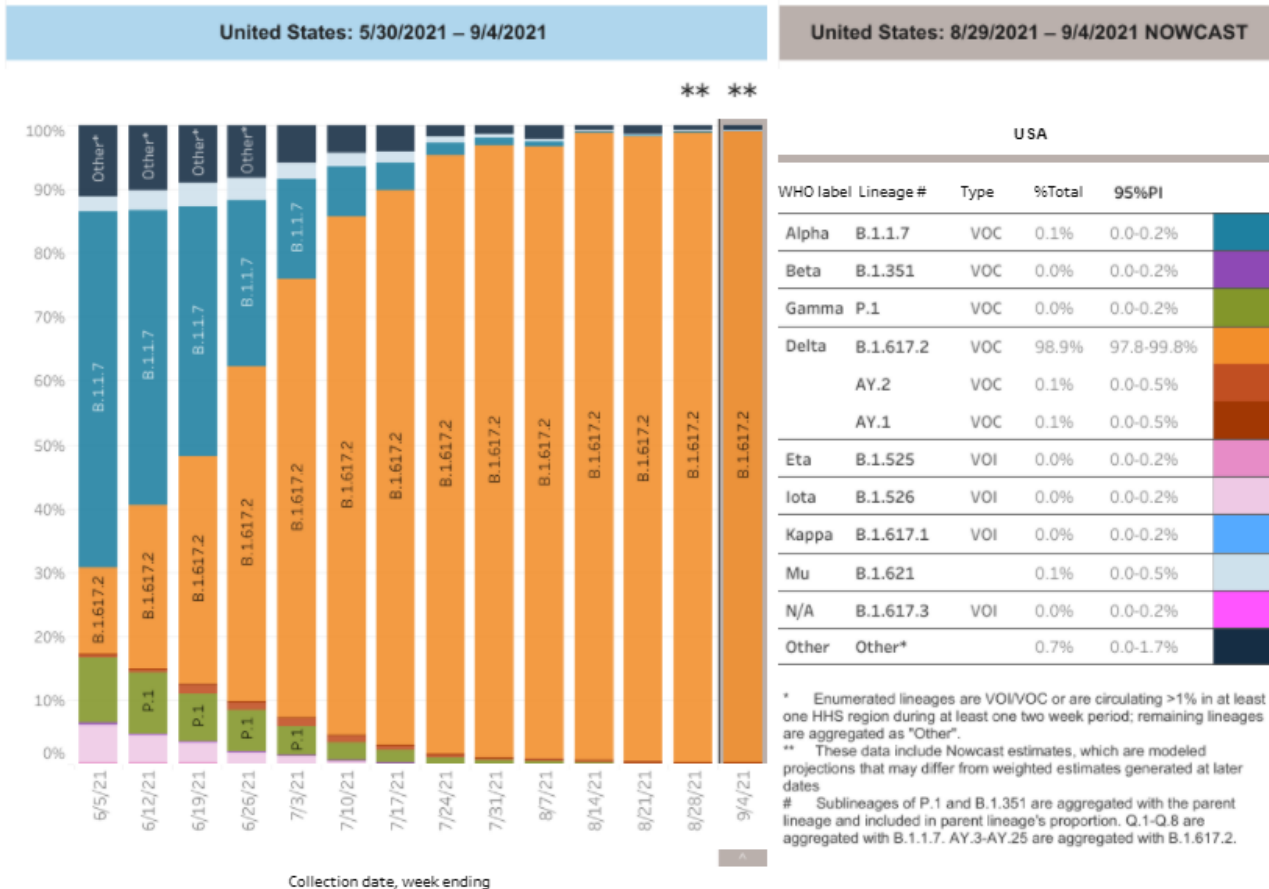
Increased transmissibility, virulence,
reduced effectiveness of vaccines, antibodies or diagnostics

Currently designated Variants of Concern:

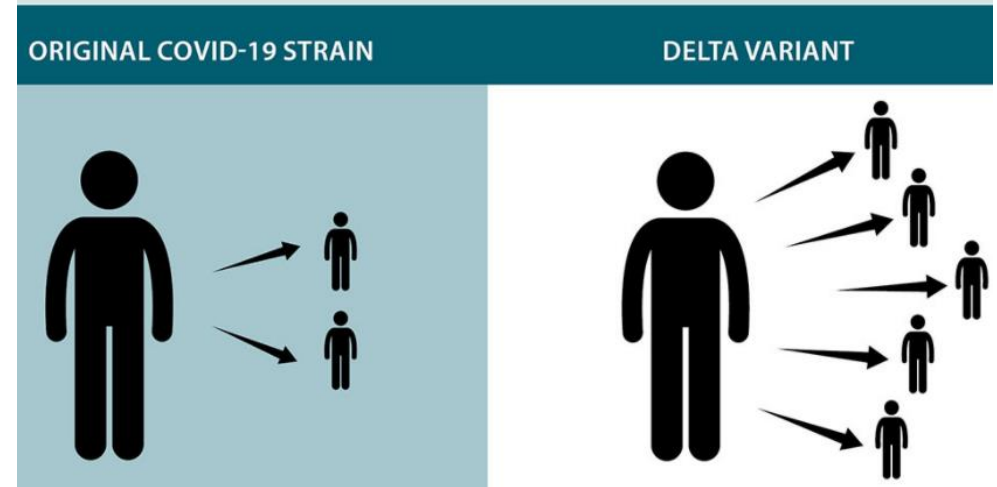
WHO label	Pango lineage*	GISAID clade	Nextstrain clade	Additional amino acid changes monitored°	Earliest documented samples	Date of designation
Alpha	B.1.1.7 #	GRY	20I (V1)	+S:484K +S:452R	United Kingdom, Sep-2020	18-Dec-2020
Beta	B.1.351	GH/501Y.V2	20H (V2)	+S:L18F	South Africa, May-2020	18-Dec-2020
Gamma	P.1	GR/501Y.V3	20J (V3)	+S:681H	Brazil, Nov-2020	11-Jan-2021
Delta	B.1.617.2§	G/478K.V1	21A	+S:417N	India, Oct-2020	VOI: 4-Apr-2021 VOC: 11-May-2021

- Variants are a normal consequence of viral infections
- Quick replacement by viruses with increased fitness (Delta, *i.e.* B.1.617.2)
- Delta: increased transmissibility (50-70%)
- Trend toward infecting younger people

What's Important About Viral Variants



The Delta variant is more contagious than previous strains—it may cause more than **2x as many infections**



As of Sept 4, Delta = ~ 99% sequenced virus

Delta Variant: Variant of Most Concern

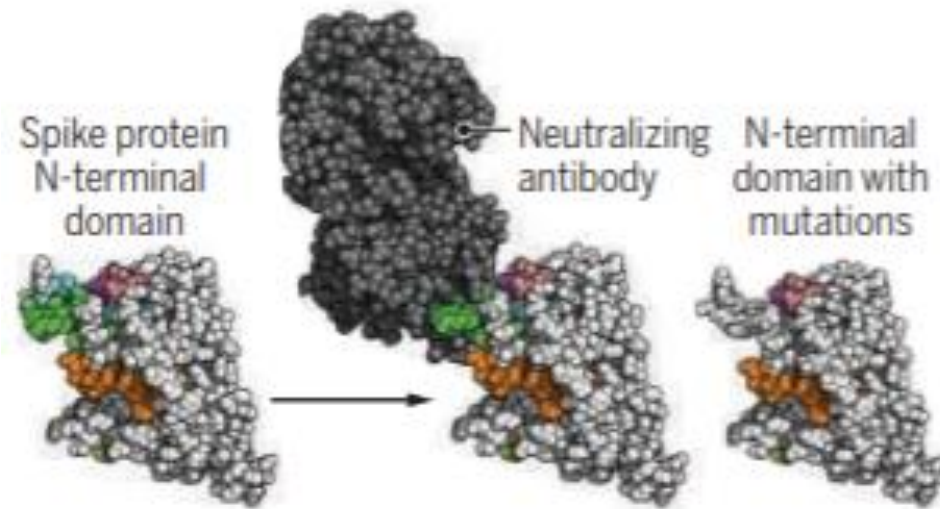
First described in India (B.1.651.2)

Reduced protection

- If only 1 shot of mRNA vaccine or AstraZeneca = little effect
- Pfizer, Moderna, AstraZeneca (2 doses)
 - Reports of less efficacy against infection
 - Remains effective against severe illness

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

What is Delta Plus (AY.3)?

Subvariant of Delta

- Isolated in India, UK, USA and other countries
- UK and India: Variant of Concern
- ~15% of US variants

Additional mutation (also seen in Beta variant)

- K417N, spike protein = ↑ cell entry
- Affects efficacy of some monoclonal antibody therapy and vaccine-induced immunity

WHO Variants of Interest (VOI)

Currently designated Variants of Interest:

WHO label	Pango lineage*	GISAID clade	Nextstrain clade	Earliest documented samples	Date of designation
Eta	B.1.525	G/484K.V3	21D	Multiple countries, Dec-2020	17-Mar-2021
Iota	B.1.526	GH/253G.V1	21F	United States of America, Nov-2020	24-Mar-2021
Kappa	B.1.617.1	G/452R.V3	21B	India, Oct-2020	4-Apr-2021
Lambda	C.37	GR/452Q.V1	21G	Peru, Dec-2020	14-Jun-2021
Mu	B.1.621	GH	21H	Colombia, Jan-2021	30-Aug-2021

CDC definition:

1. Changes to receptor binding
2. Reduced neutralization by antibodies from previous infection or vaccination
3. Reduced efficacy of treatments
4. Potential diagnostic impact
5. Predicted increase in transmissibility or disease severity

Mu: 0.1% of global cases, some features similar to Beta
— may evade coronavirus-specific antibodies

Mu: Mutations with Causes for Concern

B.1.621, VOI

Similar to Beta

- E484K (also seen in Delta+, facilitates tighter binding to receptor, immune evasion too, need higher antibody levels)
- K417N (immune evasion)

And an Alpha mutation

- P681H (spike cleavage site → virus-cell fusion)

And a Delta mutation

- D950N (N-terminal domain change)

Detected in all 50 US states

As of 9/7, detected in 46 countries

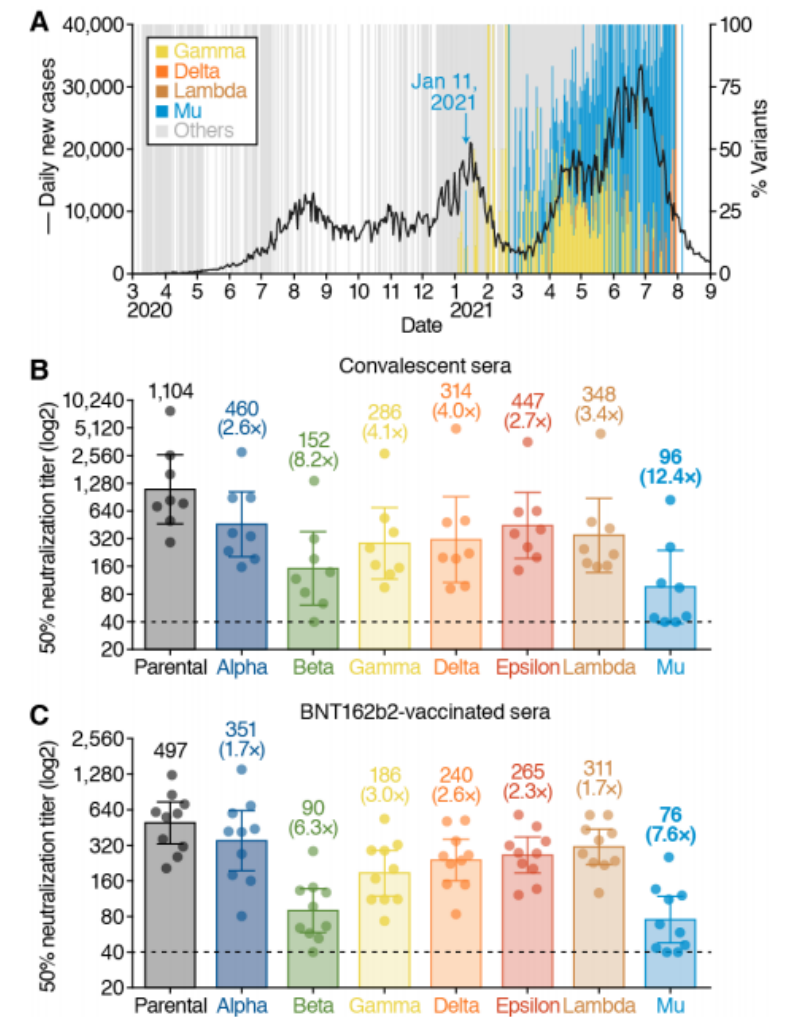
Less circulating worldwide?

- Ecuador/Colombia)w/ ~ 40% mu in past months than now
- Argument against replacing Delta

Mu Variant of Interest

No clear picture yet on transmissibility or virulence
Impact on vaccines or natural immunity? Colombia data

- Convalescent sera (8 pts)
 - 12.4x reduction
- Pfizer/BNT (10 pts)
 - 7.6x reduction
- Note: few delta or lambda isolates



WHO: Variants of High Consequence

Current number of variants: None

Definition:

- Clear evidence that prevention measures or medical countermeasures have significantly reduced effectiveness relative to previously circulating variants.

Vaccines Remain Effective Protecting Against Severe Infection

Protection from ED/Hospitalization Need

Based on 32,867 encounters, Delta predominant

Overall vaccine efficacy: 86% (95% CI = 82-89%)

18-75 yrs: 89%

≥ 75 yrs: 76%

Moderna 92%

JNJ 65%

Pfizer 77%

Limitations: timing of receiving vaccine, no assessment for partial vaccination

Vaccination Protects Against Infection and Severe Disease

CDC Centers for Disease Control and Prevention
CDC 24/7: Saving Lives, Protecting People™

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Morbidity and Mortality Weekly Report (MMWR)

CDC



Monitoring Incidence of COVID-19 Cases, Hospitalizations, and Deaths, by Vaccination Status — 13 U.S. Jurisdictions, April 4–July 17, 2021

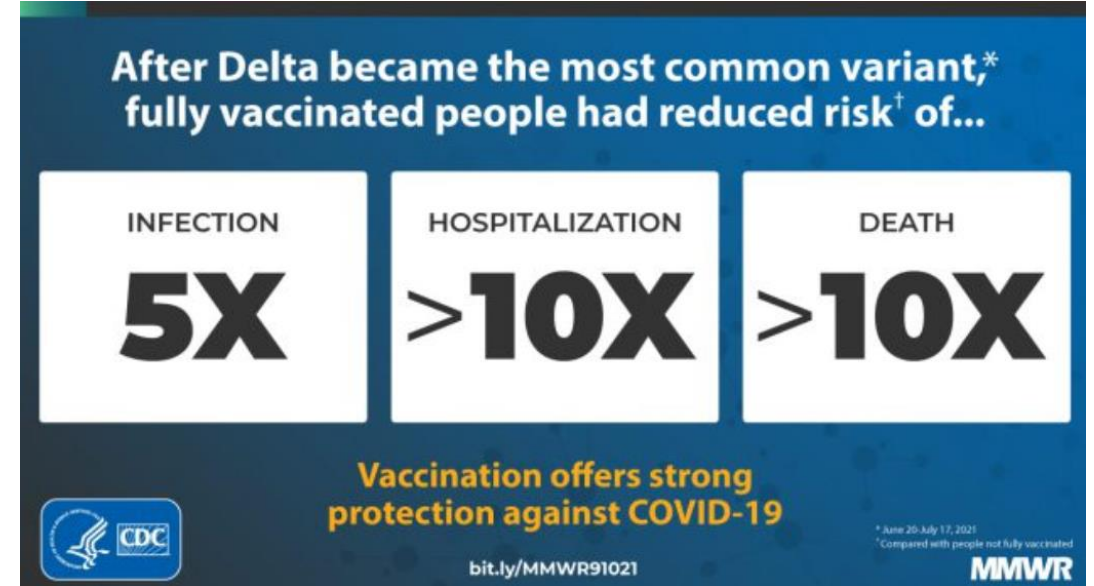
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Surveillance data

Little change regarding hospitalization/death compared to earlier reports in protection with introduction of Delta, more for ≥ 65 yrs

Some reduction in prevention





In light of the US campaign to administer booster shots for the Pfizer mRNA vaccine, our J&J recipients have questions about a booster of the same vaccine or transitioning to the mRNA vaccine platform altogether. When should we expect guidance for these patients?



**Is it possible to differentiate between
naturally acquired antibodies versus
vaccinated antibodies on a serology test?**



As we enter flu season, what is the recommendation about concurrent flu and COVID-19 vaccination?



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