QUO VADIS? Variants, Sick Kids, Vaccines and the Unvaccinated

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Where I.C.U. Beds Are Nearly Full Now

Occupancy by hospital referral region for week ending Aug. 12

After a winter surge, I.C.U. capacity remained stable into summer
## SARS-CoV-2 Variants

### Variants of Concern

<table>
<thead>
<tr>
<th>Name</th>
<th>Lineage</th>
<th>Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alpha</td>
<td>B.1.1.7</td>
<td>Emerged in Britain in December and thought to be roughly 50 percent more infectious. Now dominant in the U.S.</td>
</tr>
<tr>
<td>Beta</td>
<td>B.1.351</td>
<td>Emerged in South Africa in December. Reduces the effectiveness of some vaccines.</td>
</tr>
<tr>
<td>Gamma</td>
<td>P.1</td>
<td>Emerged in Brazil in late 2020. Has mutations similar to B.1.351.</td>
</tr>
<tr>
<td>Delta</td>
<td>B.1.617.2</td>
<td>Prevalent in India. Carries the L452R spike mutation, among others.</td>
</tr>
</tbody>
</table>

### Variants of Interest

<table>
<thead>
<tr>
<th>Name</th>
<th>Lineage</th>
<th>Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>Epsilon</td>
<td>B.1.427, B.1.429</td>
<td>Common in California and thought to be about 20 percent more infectious. Carries the L452R mutation.</td>
</tr>
<tr>
<td>Zeta</td>
<td>P.2</td>
<td>First documented in Brazil.</td>
</tr>
<tr>
<td>Eta</td>
<td>B.1.525</td>
<td>Spreading in New York. Carries some of the same mutations as B.1.1.7.</td>
</tr>
<tr>
<td>Theta</td>
<td>P.3</td>
<td>First documented in the Philippines.</td>
</tr>
<tr>
<td>Iota</td>
<td>B.1.526</td>
<td>Spreading in New York. One version carries the E484K mutation, another carries S477N.</td>
</tr>
<tr>
<td>Kappa</td>
<td>B.1.617.1</td>
<td>Prevalent in India. Carries the L452R spike mutation, among others.</td>
</tr>
</tbody>
</table>
**Delta, Kappa: The B.1.617 Lineage**

B.1.617 carries more than a dozen mutations, but is sometimes called a “double mutant” because of two prominent mutations: **E484Q** and **L452R**.

The B.1.617 lineage has continued to evolve, splitting into new lineages including B.1.617.1, known as **Kappa**, and B.1.617.2, known as **Delta**. It has emerged as a fast-growing virus, **outpacing other variants of concern**.

**E484Q** lies at the same location as **E484K**, the “Eek” mutation that might help the virus **evade some types of antibodies**.
The first report of local transmission of the SARS-CoV-2 Delta variant in mainland China.

All 167 infections could be traced back to the first index case.

Daily sequential PCR of quarantined subjects indicated that the viral loads of Delta infections, when they first become PCR+, were on average ~1000 times greater compared to A/B lineage infections during initial epidemic wave in China in early 2020.

They occur on day 4 after infection

This suggests faster viral replication, viral load and greater infectiousness of Delta.

medRxiv preprint doi: https://doi.org/10.1101/2021.07.07.21260122; this version posted July 23, 2021
A viral video asserts falsely that the pandemic is supported by an animal reservoir.
Delta variant may cause more severe disease than Alpha or ancestral strains: Published evidence

- Canada: Higher odds of hospitalization [aOR 2.20 (CI 1.93-2.53)], ICU admission [aOR 3.87 (CI 2.98-4.99)], and death [aOR 2.37 (CI 1.50-3.30)]\(^1\)

- Singapore: Higher odds of oxygen requirement, ICU admission, or death [aOR 4.90 (CI 1.43-30.78)] and pneumonia [aOR 1.88 (CI 0.95-3.76)]\(^2\)

- Scotland: Higher odds of hospitalization [HR 1.85 (CI 1.39-2.47)]\(^3\)
# VACCINES

## Leading vaccines

<table>
<thead>
<tr>
<th>Developer</th>
<th>How It Works</th>
<th>Phase</th>
<th>Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pfizer-BioNTech</td>
<td>mRNA</td>
<td>2, 3</td>
<td>Approved in several countries. Emergency use in U.S., E.U., other countries.</td>
</tr>
<tr>
<td>Moderna</td>
<td>mRNA</td>
<td>3</td>
<td>Approved in Switzerland. Emergency use in U.S., E.U., other countries.</td>
</tr>
<tr>
<td>Gamaleya</td>
<td>Ad26, Ad5</td>
<td>3</td>
<td>Emergency use in Russia, other countries.</td>
</tr>
<tr>
<td>Oxford-AstraZeneca</td>
<td>ChAdOx1</td>
<td>2, 3</td>
<td>Approved in Brazil. Emergency use in U.K., E.U., other countries.</td>
</tr>
<tr>
<td>CanSino</td>
<td>Ad5</td>
<td>3</td>
<td>Approved in China. Emergency use in other countries.</td>
</tr>
<tr>
<td>Johnson &amp; Johnson</td>
<td>Ad26</td>
<td>3</td>
<td>Emergency use in U.S., E.U., other countries.</td>
</tr>
<tr>
<td>Vector Institute</td>
<td>Protein</td>
<td>3</td>
<td>Early use in Russia. Approved in Turkmenistan.</td>
</tr>
<tr>
<td>Novavax</td>
<td>Protein</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Sinovac</td>
<td>Inactivated</td>
<td>3</td>
<td>Approved in China. Emergency use in other countries.</td>
</tr>
<tr>
<td>Sinopharm-Wuhan</td>
<td>Inactivated</td>
<td>3</td>
<td>Approved in China. Limited use in U.A.E.</td>
</tr>
<tr>
<td>Bharat Biotech</td>
<td>Inactivated</td>
<td>3</td>
<td>Emergency use in India, other countries.</td>
</tr>
</tbody>
</table>
A viral video asserts, falsely, that vaccines do not protect against the SARS-CoV-2.

In addition antibody mediated enhancement would reverse this graphic with more cases in Vaccinated. A false viral video assertion.
They both caught Covid, but one was vaccinated

She got the shot. Her vaccine hesitant husband didn't. Now he's in a Mississippi ICU bed battling coronavirus.
They Spurned the Vaccine. Now They Want You to Know They Regret It.

People who once rejected the vaccine or simply waited too long are now grappling with the consequences, often in raw, public ways.

Glen Arnell, right, and Mindy Greene visited her husband, Russ Greene, at Utah Valley Specialty Hospital. Mr. Greene was hospitalized with complications from Covid-19 after choosing not to receive a vaccination for the virus. Kim Raff for The New York Times
New 32 year old mother dies from Covid-19 before she can hold her newborn

My 16 month old son was lucky to get a pediatric ICU bed when he needed one. He shouldn't have needed luck
Vaccination of people after prior COVID disease

The study was funded in part by NIH (NCI and NHLBI). Published on April 1, 2021, in Nature Medicine.

- More than 1,000 people at Cedars-Sinai had received two doses of the vaccine at the time of the study.
- Overall, those previously infected with SARS-CoV-2 had higher levels of antibodies at all three time points.
- The levels of antibodies taken before vaccination in people who were previously infected by the virus were similar to those seen in uninfected people after their first shot.
- Antibody levels in previously infected people after their first shot were as high as those from uninfected people after their second shot.
- The researchers used two different tests to see whether the antibodies in people’s blood had the potential to neutralize the virus.
- After a single vaccine dose, antibodies from previously infected people performed similarly to those from uninfected people after two doses.
- “Overall, individuals who were previously infected with COVID-19 developed an antibody response after a single vaccine dose that was comparable to that seen after a two-dose vaccination course administered to individuals without prior infections.
- “It appears that a single booster dose given to previously infected individuals offers the same benefit as two doses given to people without prior infection.”

A viral video falsely asserts that having prior infection ‘did not result in vaccine response’
Greater risk of disease, hospitalization and death among unvaccinated vs. vaccinated people: National estimates

At current incidence, 35,000 symptomatic infections per week among 162 million vaccinated Americans

Data from COVID Tracker as of July 24, 2021. Average incidence 100 cases per 100,000 persons per week. Vaccine effectiveness against symptomatic illness = 88% (Lopez Bernal et al. NEJM 2021) where risk is [1 – VE] or 12%. Vaccine effectiveness hospitalization (or death) = 96% (Bowen et al. NEJM 2021), where risk is [1 – VE] or 4%. Rate in unvaccinated = Community rate / [1 – fully vaccinated coverage] + [1 VE] * fully vaccinated coverage. Rate in fully vaccinated = [1 – VE]. Rate in unvaccinated. Fully vaccinated coverage proportions were from COVID Data Tracker as of July 24, 2021 (50% for US).
• Israel is experiencing a Delta variant surge.
  ▪ 78% of the elderly most of the population in Israel had received 2 doses of the Pfizer vaccine February 2021.
  ▪ Consequently all preventive measures had been lifted.
  ▪ Fears are that more severe disease is being seen in the elderly who were vaccinated early
  ▪ The reason booster doses are now being recommended in the US at 8 months post 2\textsuperscript{nd} dose.
  ▪ In the last few days, booster doses are now recommended in the US, 8 months out from the second dose to counteract waning immunity.
  ▪ The elderly and those with underlying conditions appear most at risk from waning immunity.
A viral video falsely asserts that vaccine does not stop infection.
Who's not vaccinated?

Across the country, about 30 percent of adults have yet to receive a dose of the vaccine. But a recent survey shows how certain groups had a much higher or lower percentage unvaccinated than the national average.

By The New York Times | Source: Census Bureau Week 33 Household Pulse Survey (June 23 to July 5)
West Virginia is off the map only achieving 70% in late October 2022.
CAN WE CREATE A UNIVERSAL VACCINE FOR ALL COVID-10 VARIANTS

• Research is in progress

• Current vaccines based on the original spike sequences may need boosters

• Knowing which regions of the spike proteins are highly conserved might allow design of a universal SARS-CoV-2 vaccine for all variants

• The spike protein receptor binding domain also flips between up and down positions. Significance uncertain, but demonstration of plasticity of the virus

• Researchers have using cryogenic electron microscope to visualize the two most potent antibodies, say that these skirt around locations lower on the tip where the mutation spots are found and avoid them. This sees to allow them to identify other sites which are highly conserved, not appreciably affected by variations in sequence.
“SUPER ANTIBODY” to SARS-CoV-2

Scientists have uncovered an antibody that can fight off not only a wide range of SARS-CoV-2 variants, but also closely related coronaviruses.

Researchers examined antibodies isolated from people who had been infected with either SARS-CoV-2 or its close relative SARS-CoV.

One antibody, S2H97, stood out for its capacity to adhere to a protein fragment known as the receptor binding domain on multiple SARS-CoV-2 variants and dozens of coronaviruses belonging to a group called the sarbecoviruses.

S2H97 was able to prevent a range of SARS-CoV-2 variants and other sarbecoviruses from spreading among cultured cells.

It was also powerful enough to protect hamsters against SARS-CoV-2 infection.

A closer examination of its molecular structure revealed that it targets a previously unseen and well-hidden region of the ACE2 binding domain.

Molecules targeting this binding-domain region could provide protection against multiple viruses, and might one day be used to produce broad-ranging vaccines and treatments, the researchers say.
TREATMENT

MONOCLONAL ANTIBODY THERAPY IS AFFECTED BY THE VARIANTS

• Two monoclonal antibody therapies are already sidelined:
  • the first was Lily’s bamlanivimab so Lily transitioned to a combination of bamlanivimab plus etesevimab.
  • However the beta and gamma variants have reduced susceptibility to these drugs.

• Thus only two are currently generally recommended
  • Regeneron’s asirivimab plus imdevimab
  • GlaxoSMithKine and Vir Biotechnology sotrovimab

A viral video assertion that ivermectin, zinc and 25 hydroxyl vitamin D prevent infection has no credible data to support. Ivermectin is a compound to treat parasites in cows and is toxic if ingested in large quantities. Big problem in Mississippi, Alabama
Fig. 3 Impact of individual mitigation measures.
Data collected during two time periods in 2020 and 2021 from over 2 million respondents in 50 US states and Washington DC
Risk of in-person schooling by strata of number of reported mitigation measures. Figure shows estimated risk associated with full and part time in-person schooling by outcome and number of mitigation measures implemented.
A viral video assertion that masks to not stop virus Particles is false based on basic science and Epidemiology data.

Fig. 3. Droplet transmission through face masks. (A) Relative droplet transmission through the corresponding mask. Each solid data point represents the mean and standard deviation over 10 trials for the same mask, normalized to the control trial (no mask), and tested by one speaker. The hollow data points are the mean and standard deviations of the relative counts over four speakers. A plot with a logarithmic scale is shown in Supplementary Fig. S1. (B) The time evolution of the droplet count (left axis) is shown for representative examples, marked with the corresponding color in (A): No mask (green), Bandana (red), cotton mask (orange), and surgical (blue – not visible on this scale). The cumulative droplet count for these cases is also shown (right axis).
COVID-19 IN CHILDREN

Hospitalization of children with COVID-19

United States | 0 - 17 Years

New Admissions per 100,000 Population

Oct 2020 | Jan 2021 | Apr 2021 | Jul 2021
Long COVID syndrome in children

The graph illustrates the proportion of children experiencing various symptoms over a 28-day period. The symptoms include:

- Blisters
- Red welts
- Eye soreness
- Dizziness and light-headedness
- Anosmia
- Persistent cough
- Fever
- Diarrhoea
- Confusion
- Hoarse voice
- Headache
- Myalgias
- Loss of appetite
- Dyspnoea
- Sore throat
- Chest pain
- Abdominal pain
- Fatigue

The proportion of children experiencing these symptoms is color-coded, with darker colors indicating a higher proportion.
Evidence for a natural source

1. SARS-CoV-2 is derived from a betacoronavirus from horseshoe bats in south China
2. The original SARS virus was a betacoronavirus which probably passed through palm civets
3. Palm civets are a delicacy and traded live at the Wuhan wet market
4. The first SARS cases were in the wet market in Wuhan

5. No intermediate host has been identified for SARS-CoV-2 which is required
6. The virus is a modified version of the horseshoe bat virus
7. The horseshoe bat lives in caves many thousands of miles from Wuhan, and is not eaten or traded for food.
8. Unlike SARS, none of the original cases of SARS-CoV-2 were from the Wuhan wet market but from a different part of this large city.
Evidence for a laboratory source

1. The Wuhan laboratory worked on horseshoe bat viruses, isolated from bats they captured in the south China cave
2. The original SARS virus was a betacoronavirus which probably passed through palm civets.
3. Palm civets are a delicacy and traded live at the Wuhan wet market, bats are not,
4. No intermediate host has been identified for SARS-CoV-2
5. The virus is a modified version of the horseshoe bat virus, so requires intermediate hosts.
6. The horseshoe bat lives in caves many thousands of miles from Wuhan, and is not traded or eaten.
7. The Wuhan laboratory was recipient of an NIH grant to study ‘gain in function’ experiments in Wuhan with US collaborators. (Gain in function means that viruses are manipulated genetically to see whether they can be made more pathogenic for humans, with the objective of understanding what might happen. This process is controversial)
8. The SARS-CoV-2 has genetic coding not found naturally in bats, but is a human code for an important amino acid which affects binding of the virus to human cells.
9. There were rumors of a respiratory outbreak at the Wuhan laboratory conducting this work in November 2019, requiring hospitalization of young people.
10. The Chinese have destroyed or suppressed all laboratory data and all data associated with the possible November 2019 outbreak. They also closed the wet market, destroyed all animals etc.
11. Equally there has been silence from the US virology community.
12. The Chinese are spreading widely misinformation that the virus was an escape from Fort Detrick, Maryland.

DRAW YOUR OWN CONCLUSIONS
REASONS FOR GETTING A VACCINE

Getting vaccinated is both common sense and a civic responsibility

PERSONAL
• To avoid getting sick,
• To avoid being hospitalized
• To avoid ending up in Intensive Care, intubated.
• To avoid dying
• To avoid the disabling, long-COVID syndrome
• If you are pregnant, to protect the mother from severe, possibly fatal disease and to protect the baby, which could be lost

COMMUNITY
• To spare overworked and stressed nurses and medical staff the burden of your care
• To limit your ability to spread a deadly infection to vulnerable people
• To protect your community
• To protect your family
• To protect your workplace
• To help control and limit this deadly pandemic.
WHAT A VACCINE DOES NOT DO

Some myths debunked, and some solid science.

• No, there is no chip. (Why would anyone want to do this since you already have a cellphone???)
• No, it has no effect on fertility for men or women
• No, It does not lead to so called ‘enhancement’. This is a rare phenomenon only so far associated with dengue virus, and not with any respiratory viruses, and only occurring in children.
• Seasonality only affects certain respiratory viruses not SARS coronaviruses.
• No, it cannot possibly cause COVID disease itself because it only contains a part of the virus, and not the internal mechanisms the virus uses to replicate itself.
• SARS type coronavirus pandemics depend on human behavior, not seasons.
• Induce ‘enhancement’ of subsequent infections
SUMMARY OF KEY POINTS

- Vaccinate Vaccinate Mask Mask!!!
- Unvaccinated people comprise 90%+ of hospitalizations from COVID
- The Delta variant of SARS-Cov-2 replicates in humans much more than the original alpha variant and produces about 1000 times more viral load on average by day 4 after exposure
- While vaccinated people are far less likely to be infected with Delta variant than the unvaccinated, nevertheless when infected they can transmit the virus to others
- Vaccinated people infected with Delta variant harbor the virus for shorter periods than the unvaccinated.
- Vaccinated people infected with Delta variant are frequently asymptomatic or with only mild symptoms, resolving quickly.
- The very few vaccinated people with Delta infections (3-8% of all hospitalizations) who do badly or die have multiple underlying conditions.
- Younger unvaccinated infected people are now being hospitalized (over 180,000 infected in one week in August) at high rates including children
- Immunity may be waning 8 months after full vaccination, especially in the elderly, necessitating a booster.