Coping with COVID: Research, Risks and Patient Resistance to Vaccines: Latest Insights

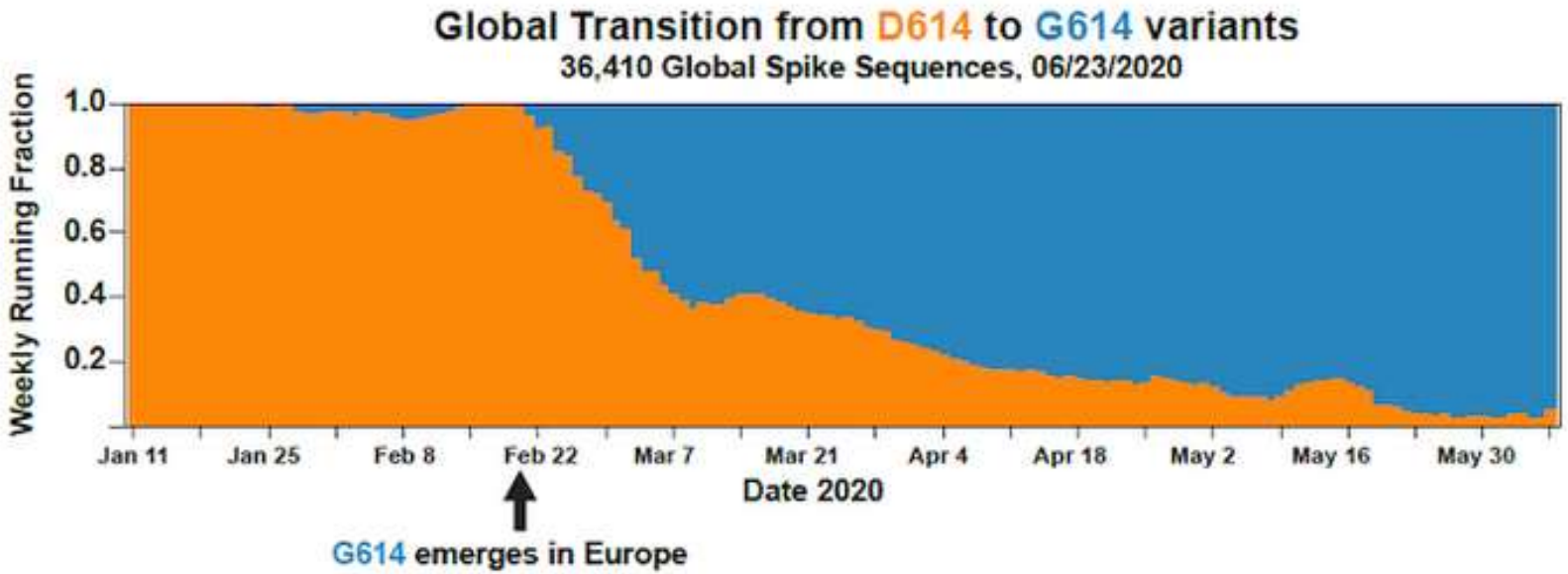
Angelo DeLucia, PhD

Newer variant of COVID-19-causing virus dominates global infections

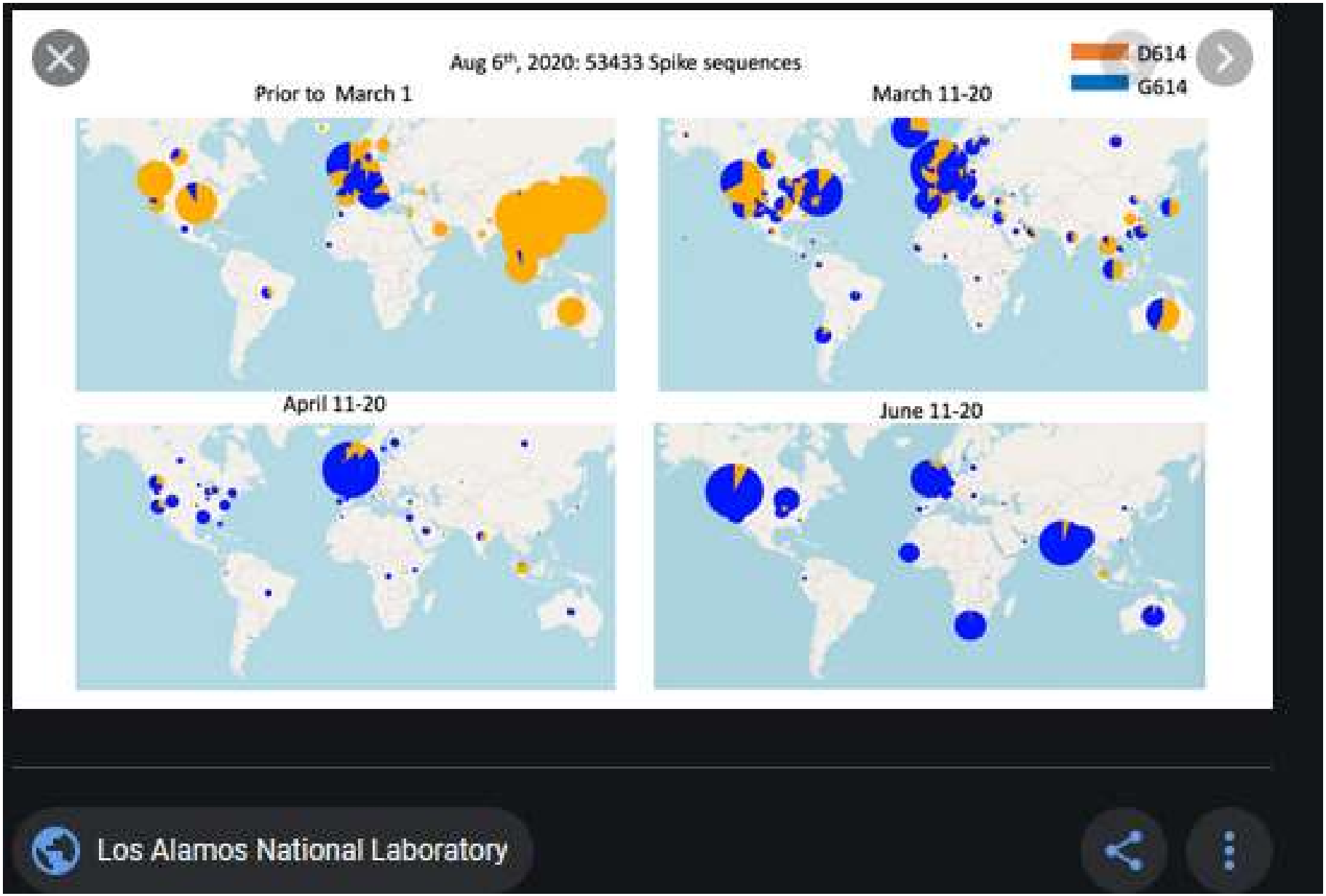
Virus with D614G change in Spike out-competes original strain, but may not make patients sicker

18

July 1, 2020

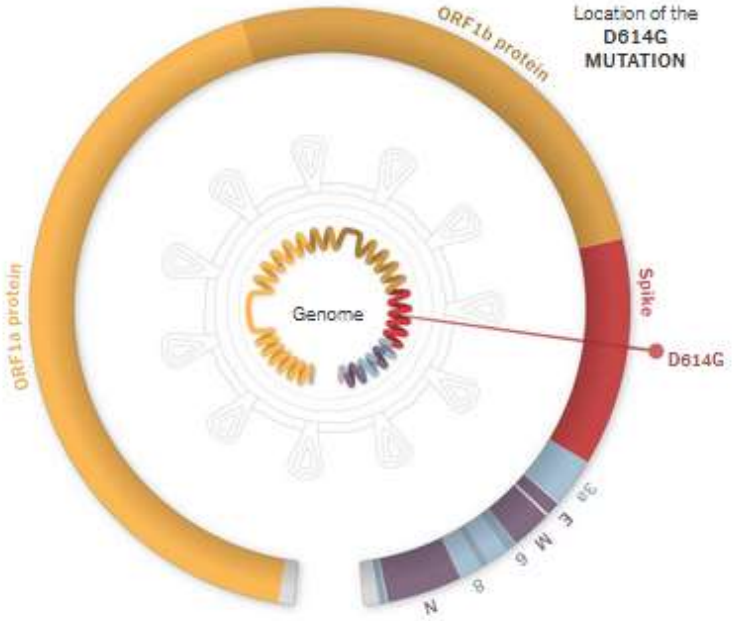


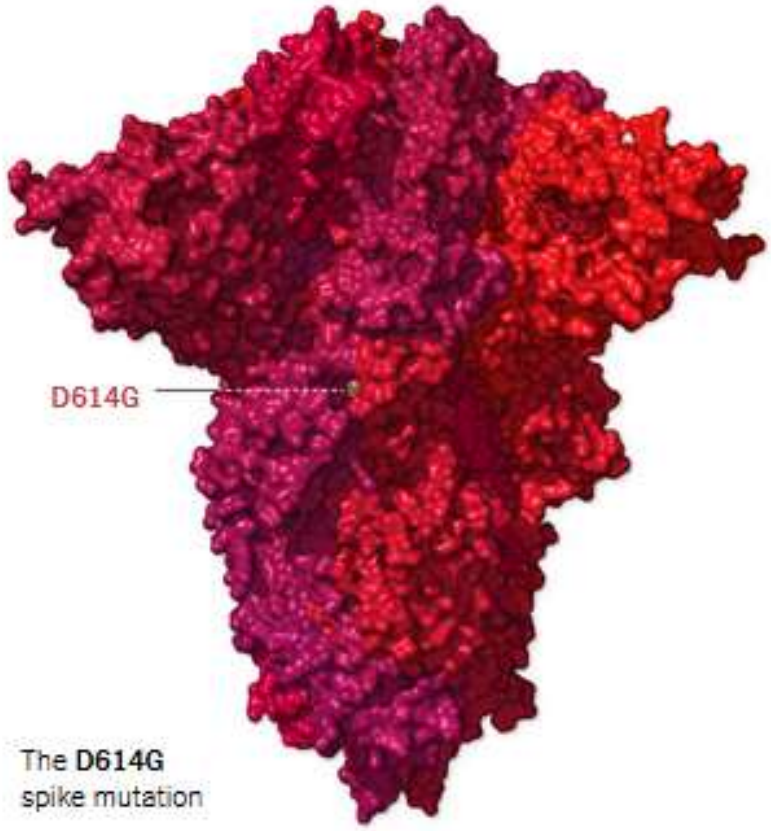
This chart tells the essential story of how the pandemic has shifted over time from orange (the original D type of the virus) to blue (the now-widespread G form, D614G).


Aug 6th, 2020: 53433 Spike sequences
D614
G614
Prior to March 1
March 11-20
April 11-20
June 11-20
Los Alamos National Laboratory

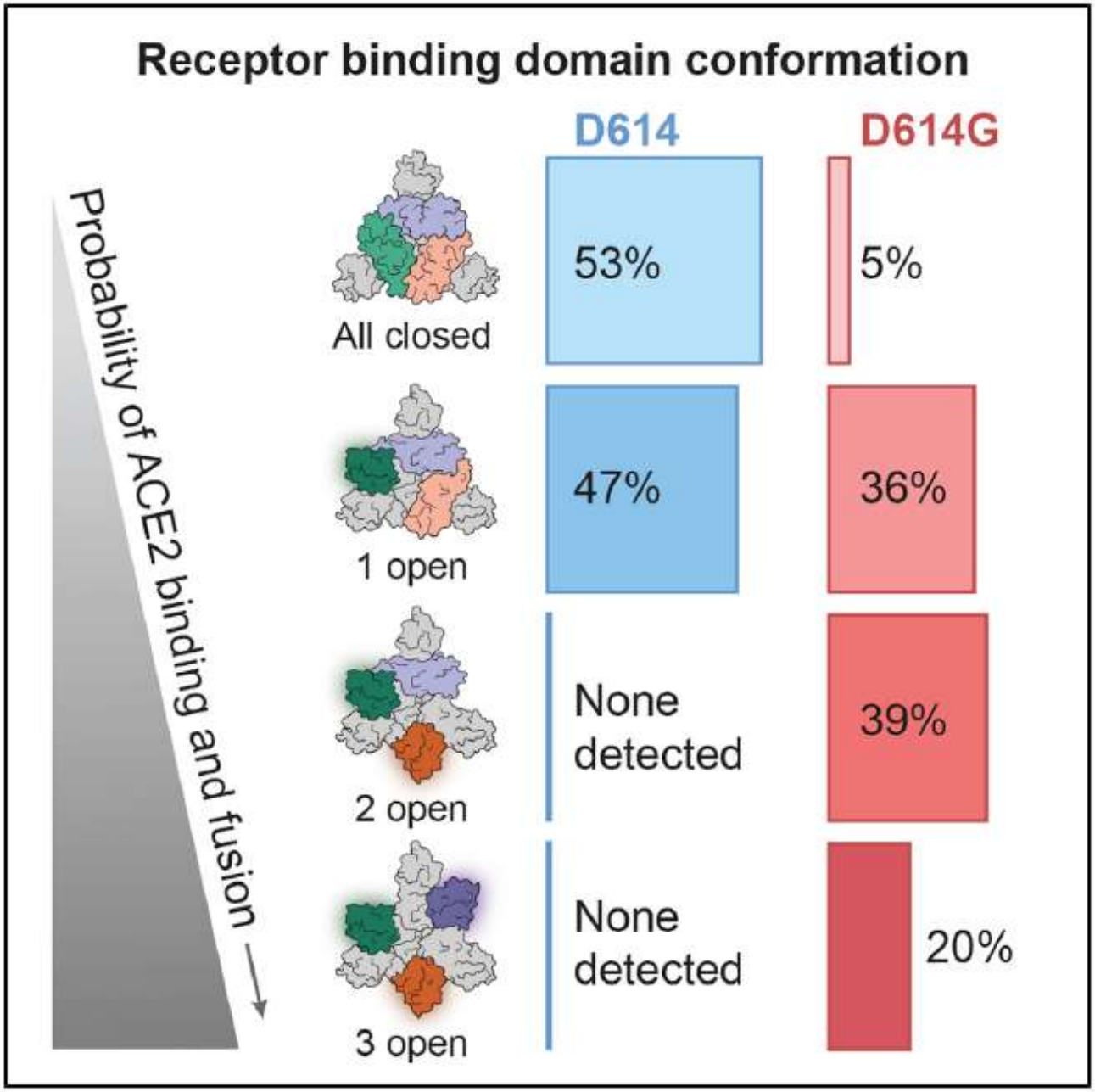
The D614G Spike Mutation

The D614G mutation emerged in eastern China early in the pandemic and then quickly spread around the world, displacing other coronaviruses that did not have the mutation.





Jonathan Corum and Carl Zimmer New York Times Feb. 11, 2021

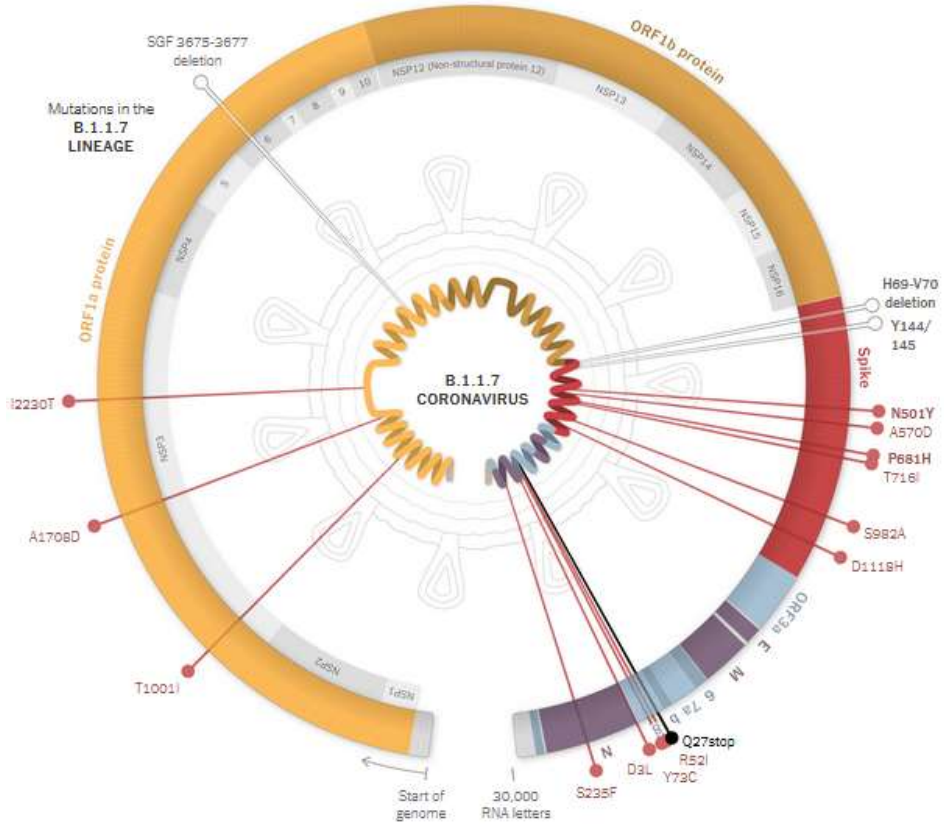


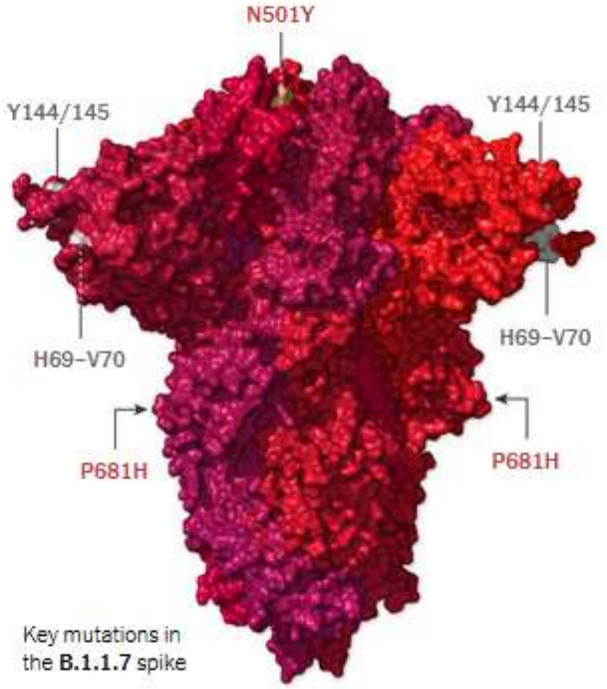
Yurkovetskiy, L. et al. Cell 183, P739-751, October 29, 2020

B.1.1.7

— **P681H**, which may help infected cells create new spike proteins more efficiently.

— The **H69–V70** and **Y144/145** deletions, which alter the shape of the spike and may help it evade some antibodies.





Jonathan Corum and Carl Zimmer New York Times Feb. 11, 2021

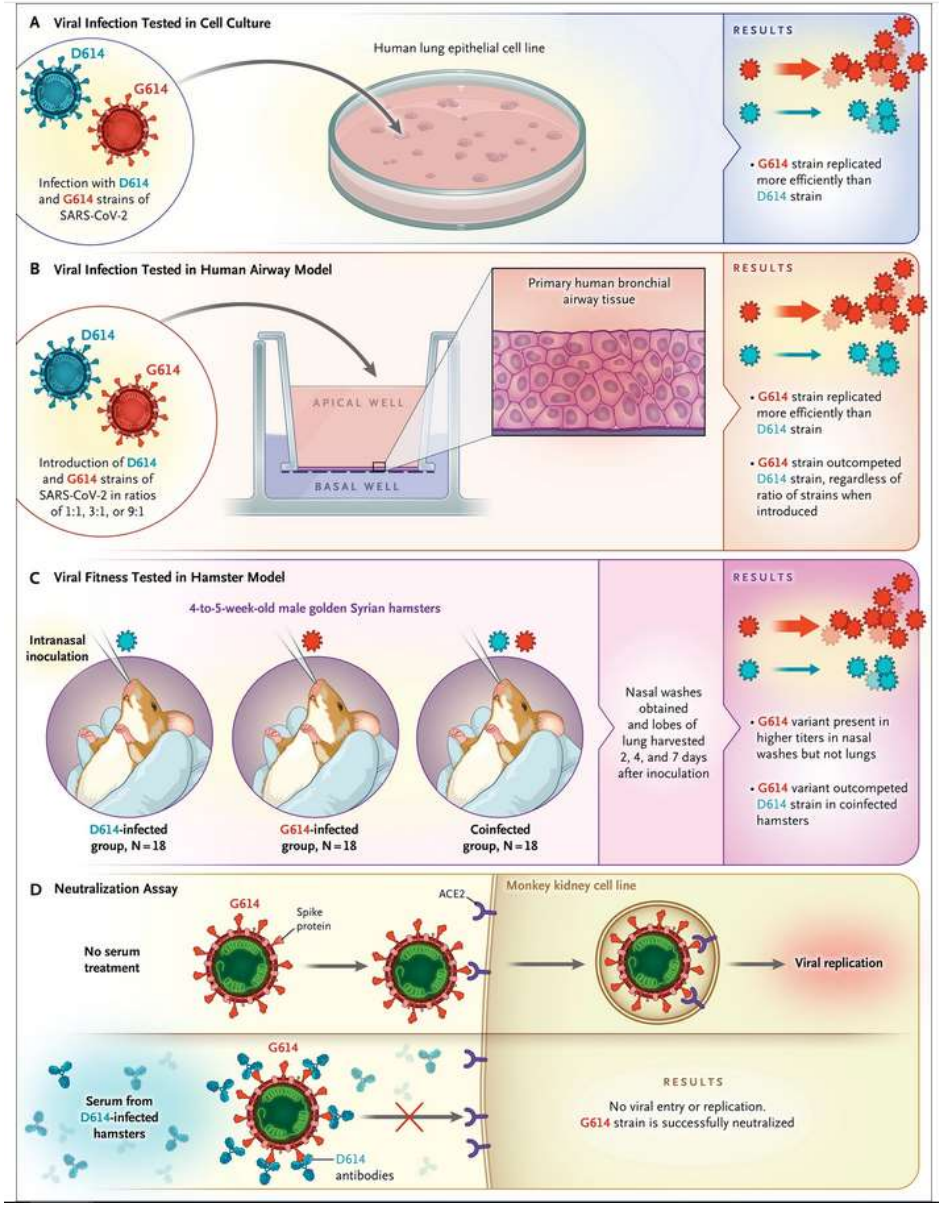


Figure 1. Increased Infectivity of SARS-CoV-2 Bearing the Spike Protein D614G Substitution.

A study recently reported by Plante et al.[5] showed that a variant of SARS-CoV-2 carrying the spike protein D614G substitution results in increased virus infectivity and yield in human lung epithelial cells (Panel A), in primary human airway tissue (Panel B), and in the upper airway of hamsters (Panel C). These data suggest that the D614G mutation results in enhanced transmissibility. In addition, serum samples from D614-virus–infected hamsters can efficiently neutralize the G614 virus from infecting cells (Panel D), which suggests that SARS-CoV-2 vaccines, all of which are based on the D614 variant of the spike protein, will protect against G614 variants of the virus.

Baric, R. December 31, 2020
N Engl J Med 2020; 383:2684-2686

UPDATE COVID-19: focus on VACCINES

Feb, 2021

Thomas M File Jr. MD, MSc, MACP, FIDSA, FCCP
Chair, Infectious Disease Division
Co-Director, Antimicrobial Stewardship Program;
Summa Health;
Professor of Internal Medicine, Chair ID Section,
Master Teacher NEOMED;
Immediate Past President Infectious Diseases Society of America

COVID-19

What have we Learned: selected thoughts

- Virology (SARS-CoV-2; evolution)
  - Endemic vs novel coronaviruses
  - Variants
- Transmission (-2 to day 5); droplets and aerosols
  - Contagion
  - Asymptomatic spreaders
  - Mitigation (Masks, etc.)
- Manifestations
  - Pathophysiology
  - Virologic vs immune/inflammatory
  - 'long-term' effects
- Therapeutics (evidence vs opinion)
  - Antivirals; monoclonal antibodies; anti-inflammatories
  - Evidence-based Guidelines (IDSA; NIH)
- Control (Vaccine)

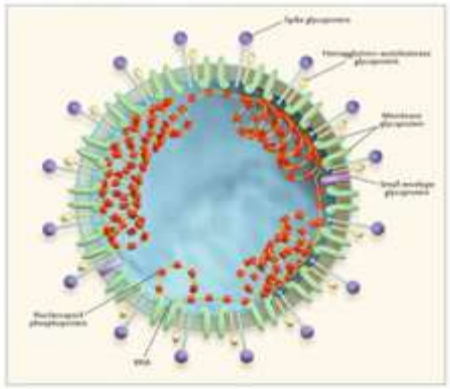
Summa Health

VACCINE STATUS

Vaccine projects Nov 2020

Preclinical	Phase I	Phase II	Phase III	Limited use	Approved
149	26	13	9	5	0

WHO: Vaccines landscape
https://www.who.int/publications/m/item/draft-landscape-of-covid-19-candidate-vaccines



	Moderna	Pfizer	AztraZeneca	J&J	Novavax
Target	Spike protein	Spike protein	Spike protein	Spike protein	Spike Protein
Technology	mRNA	mRNA	Adenovirus vector	Adenovirus vector	Spike Protein +Adjuvant
Doses/Storage	2/Freezer)	2/Ultra-cold	2/ Refrig	1/Refrig	2/Refrig
Efficacy-disease	94%	95%	76% overall (90% half dose; Minimal S Africa)	66% overall (72% US; 57% S Africa)	89% (60% HIV-neg; S Africa)
Efficacy-Death	100%	100%	100%	100%	100%

VIRAL MUTATIONS: D614G; B.1.1.7 (Spike Protein) mutation spreading- More transmissible, likely susceptible to vaccine AB

Dosing and administration

- Authorized age groups:
  - Pfizer-BioNTech: ≥ 16 years
  - Moderna: ≥ 18 years
- Administration: two-dose series administered intramuscularly
  - Pfizer-BioNTech: three weeks apart
  - Moderna: four weeks apart
- Persons should not be scheduled to receive the second dose earlier than the recommended intervals
  - However, doses administered earlier should not be repeated
- The second dose should be administered as close to the recommended interval as possible. However, if it is not feasible to adhere to the recommended interval, the second dose of Pfizer-BioNTech and Moderna COVID-19 vaccines may be scheduled for administration up to **6 weeks** (**42 days**) after the first dose.

https://www.cdc.gov/vaccines/covid-19/info-by-product/clinical-considerations.html

About these COVID-19 mRNA vaccines

- These mRNA vaccines are expected to produce side effects after vaccination, especially after the 2nd dose.
  - Side effects may include:
    - Fever
    - Headache
    - Muscle aches

- No significant safety concerns were identified in the clinical trials.
- At least 8 weeks of safety data were gathered in the trials. It is unusual for side effects to appear more than 8 weeks after vaccination.

Source: https://www.cdc.gov/vaccines/hcp/acip-recs/vacc-specific/covid-19/clinical-considerations.html

Reactogenicity reported to v-safe

Local and systemic reactions, day 0-7*,†	All vaccines %	Pfizer- BioNTech dose 1 %	Pfizer-BioNtech dose 2 %	Moderna dose 1 %
Pain	70.7	67.7	74.8	70.1
Fatigue	33.4	28.6	50.0	29.7
Headache	29.4	25.6	41.9	26.0
Myalgia	22.8	17.2	41.6	19.6
Chills	11.5	7.0	26.7	9.3
Fever	11.4	7.4	25.2	9.1
Swelling	11.0	6.8	26.7	13.4
Joint pain	10.4	7.1	21.2	8.6
Nausea	8.9	7.0	13.9	7.7

* v-safe data lock point 1/14/2021, 5:00 AM ET
† Reported on at least one health check-in completed on days 0-7 after receipt of vaccine

Persons with a history of SARS-CoV-2 infection

- Data from clinical trials indicate that mRNA COVID-19 vaccines can **safely** be given to persons with evidence of prior SARS-CoV-2 infection
- Vaccination should be offered to persons regardless of history of prior symptomatic or asymptomatic SARS-CoV-2 infection
- Viral or serologic testing for acute or prior infection, respectively, is not recommended for the purpose of vaccine decision-making

https://www.cdc.gov/vaccines/covid-19/info-by-product/clinical-considerations.html

Pregnant women

- COVID-19 and pregnancy
  - Increased risk of severe illness (ICU admission, mechanical ventilation and death)
  - Might be an increased risk of adverse pregnancy outcomes, such as preterm birth
- There are limited data on the safety of COVID-19 vaccines in pregnant women
  - Limited animal developmental and reproductive toxicity (DART) data
  - Studies in humans are ongoing and more planned
- If a woman is part of a group (e.g., healthcare personnel) who is recommended to receive a COVID-19 vaccine and is pregnant, she may choose to be vaccinated.

https://www.cdc.gov/coronavirus/2019-ncov/need-extra-precautions/pregnancy-breastfeeding.html

Summary of v-safe data

	Pfizer-BioNTech	Moderna	All COVID-19 vaccines
People receiving 1 or more doses in the United States*	12,153,536	9,689,497	21,843,033
Registrants completing at least 1 v-safe health check-in†	997,042	1,083,174	2,080,216
Pregnancies reported to v-safe	8,633	6,498	15,131

* COVID Data Tracker data as of 1/24/2021
† v-safe data as of 1/20/2021, 5:00 AM ET

COVID-19 Vaccine: Other Considerations

- Effectiveness in populations
  - High in those with comorbid conditions
  - High in elderly
- Effectiveness for mutant variants
  - Mutations common in RNA viruses
    - B.1.1.7—studies indicate vaccine effective
    - S Africa—some reduced neuralization activity, but some effect
    - Increases importance of genetic sequencing
- Will I need to wear masks after being vaccinated?
  - Yes:
    - Until studies document prevention of infection and therefore transmission;
    - Not all will be protected
    - Concern of variants

Summa Health

COVID-19 Vaccine: Other Considerations

- Quarantine after vaccination (2/10/2021)
  - Unnecessary if:
    - Within 3 months of full immunization
    - Full immunization -2 weeks after 2nd dose mRNA
    - Asymptomatic
    - *Aligns with advice assoc with natural infection*
- Travel after vaccination
  - No change in CDC guidance *yet*
- Should I stop my regular medications
  - Currently no medications contraindicated for mRNA vaccines.
  - For patients who have received monoclonal antibodies for COVID-19, the recommendation is to wait 90 days for the dose of vaccine.
  - Certain medications may reduce the immune response (such as high dose steroids, cancer chemotherapy, and transplant therapy) but are not reasons to avoid the vaccine. If patients are on a tapering or transient dose of steroids, it is reasonable to wait until the steroid regimen has been discontinued.

Summa Health

COVID-19 Vaccine: Other Considerations

- Should I take ibuprofen or acetaminophen prior
  - Not recommended.
    - information on the impact of this on both the immune response to the vaccine and on post-vaccine symptoms is not currently available.
- Is it safe to take Ibuprofen or acetaminophen or similar medications after receiving the vaccine?
  - Yes; OK to take for side effects after receiving the vaccine.
  - Effects such as pain on the injection site, achiness, fatigue, arthralgia and/or fever, are expected, are transient but can be ameliorated by these medications.
  - recommended to administer at the onset of side effects.
  - **Acetaminophen (Tylenol) is recommended by the CDC, ACOG and AAP for women who are pregnant.**

Summa Health

Promoting Vaccine Uptake

- The greater % of population vaccinated; the greater protection of population
- Anti-vaxxers vs Vaccine Hesitancy
- Promoting Vaccinations
  - Communication; transparency
  - Address concerns
    - Vary among groups
  - Strong, clear recommendation by healthcare provider and key leaders