COVID-19 ECHO

WELCOME BACK Q&A

JANUARY 6, 2021

WHITNEY ESSEX, APRN

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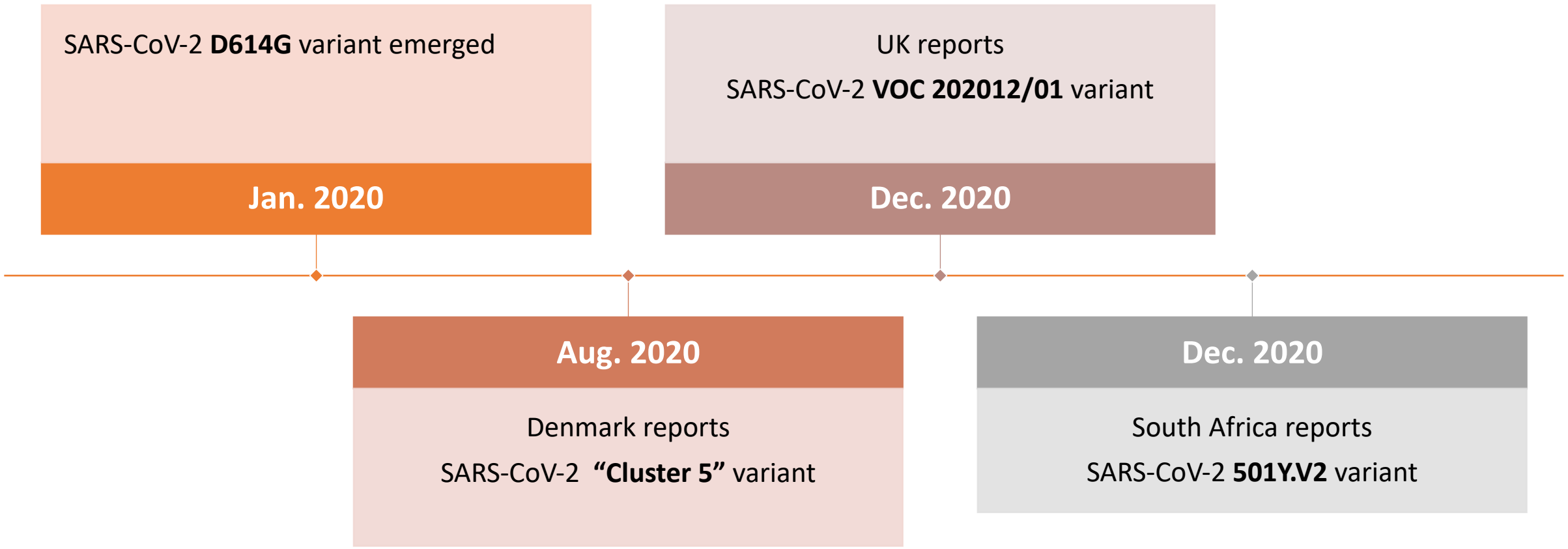
Outline

UPDATE ON MUTANT VARIANTS

UPDATE ON IMMUNITY AFTER INFECTION

Q & A

SARS-CoV-2 Variants



https://www.who.int/csr/don/31-december-2020-sars-cov2-variants/en/

SARS-CoV-2 Mutations

- SARS-CoV-2 mutates regularly, acquiring about one new mutation in its genome every two weeks.
- Many mutations are silent because they produce a three-letter codon that translates to the same amino acid (i.e., they are “synonymous”).
- Other mutations may change the codon in a way that leads to an amino acid change (i.e., they are “non-synonymous”), but this amino acid substitution does not impact the protein’s function.

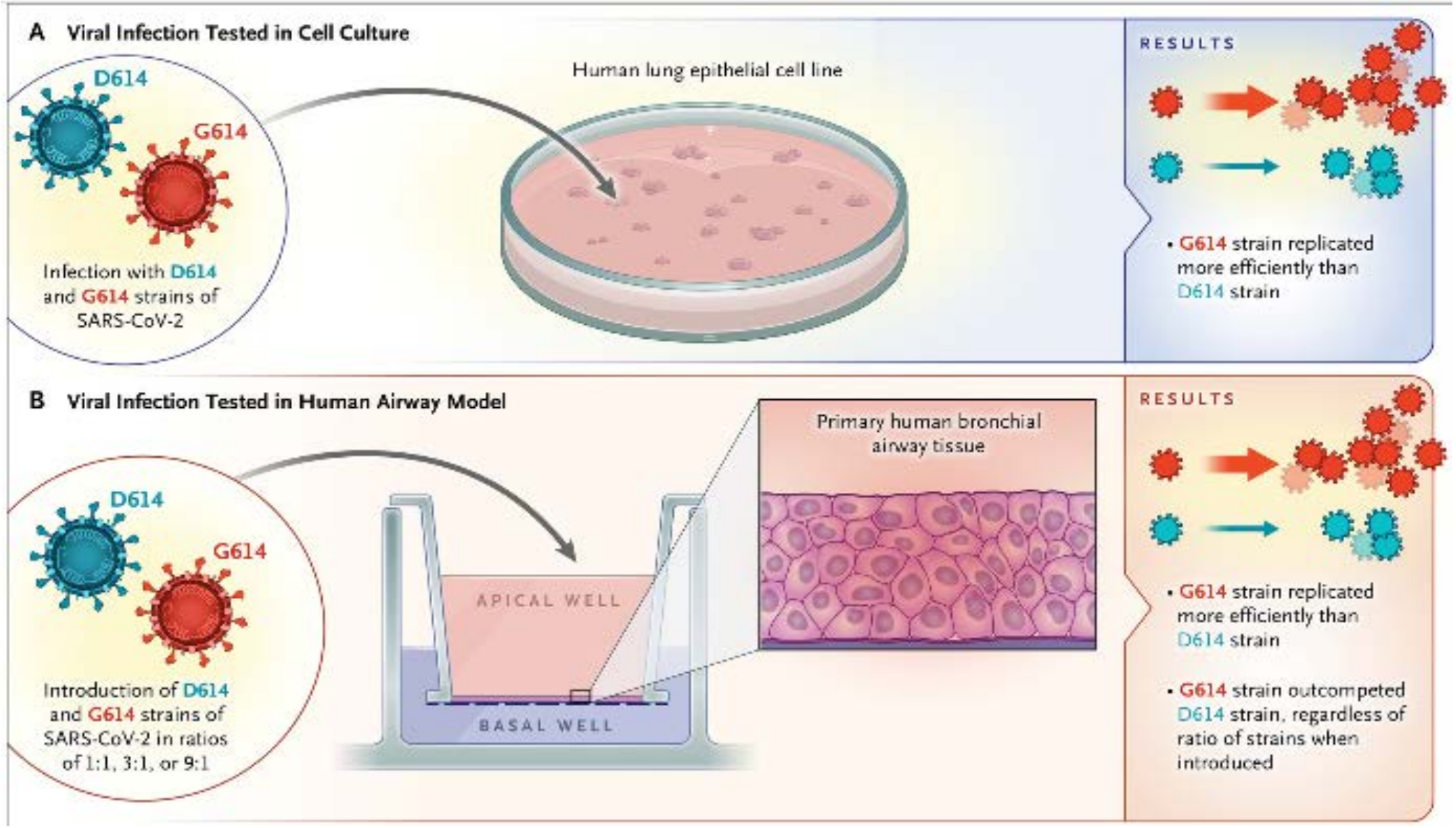
https://www.who.int/csr/don/31-december-2020-sars-cov2-variants/en/

D614G identified in January 2020

- This variant of SARS-CoV-2 had a **D614G** substitution (Aspartic acid for Glycine) in the gene encoding the spike protein
- By June 2020, this variant became the dominant strain circulating globally
- Studies in human respiratory cells and in animal models demonstrated that the strain has **increased infectivity and transmission**
- **It does not cause more severe illness** or alter the effectiveness of existing laboratory diagnostics, therapeutics, vaccines, or public health preventive measures.

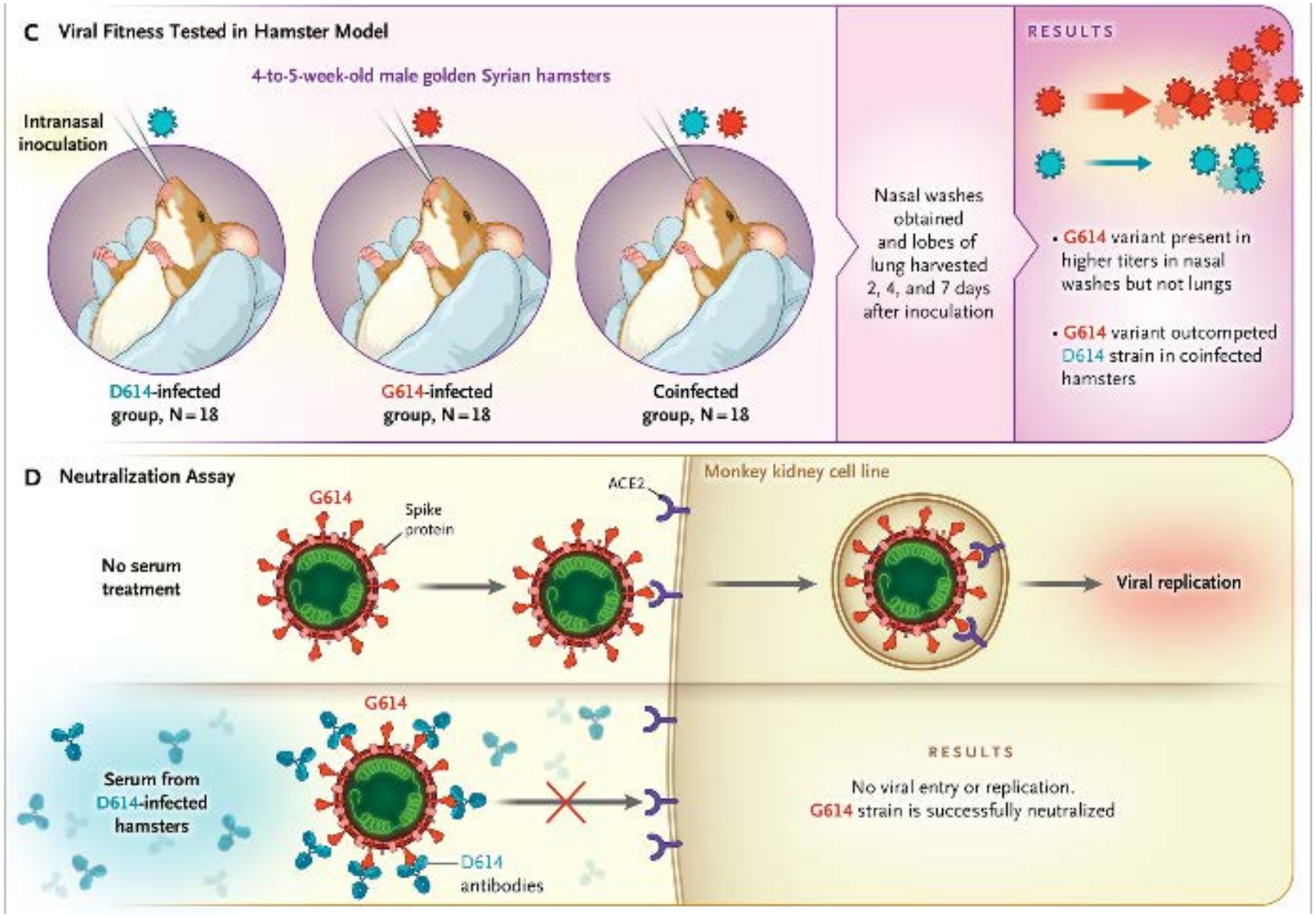
https://www.who.int/csr/don/31-december-2020-sars-cov2-variants/en/

Emergence of a Highly Fit SARS-CoV-2 Variant



December 16, 2020, at NEJM.org.

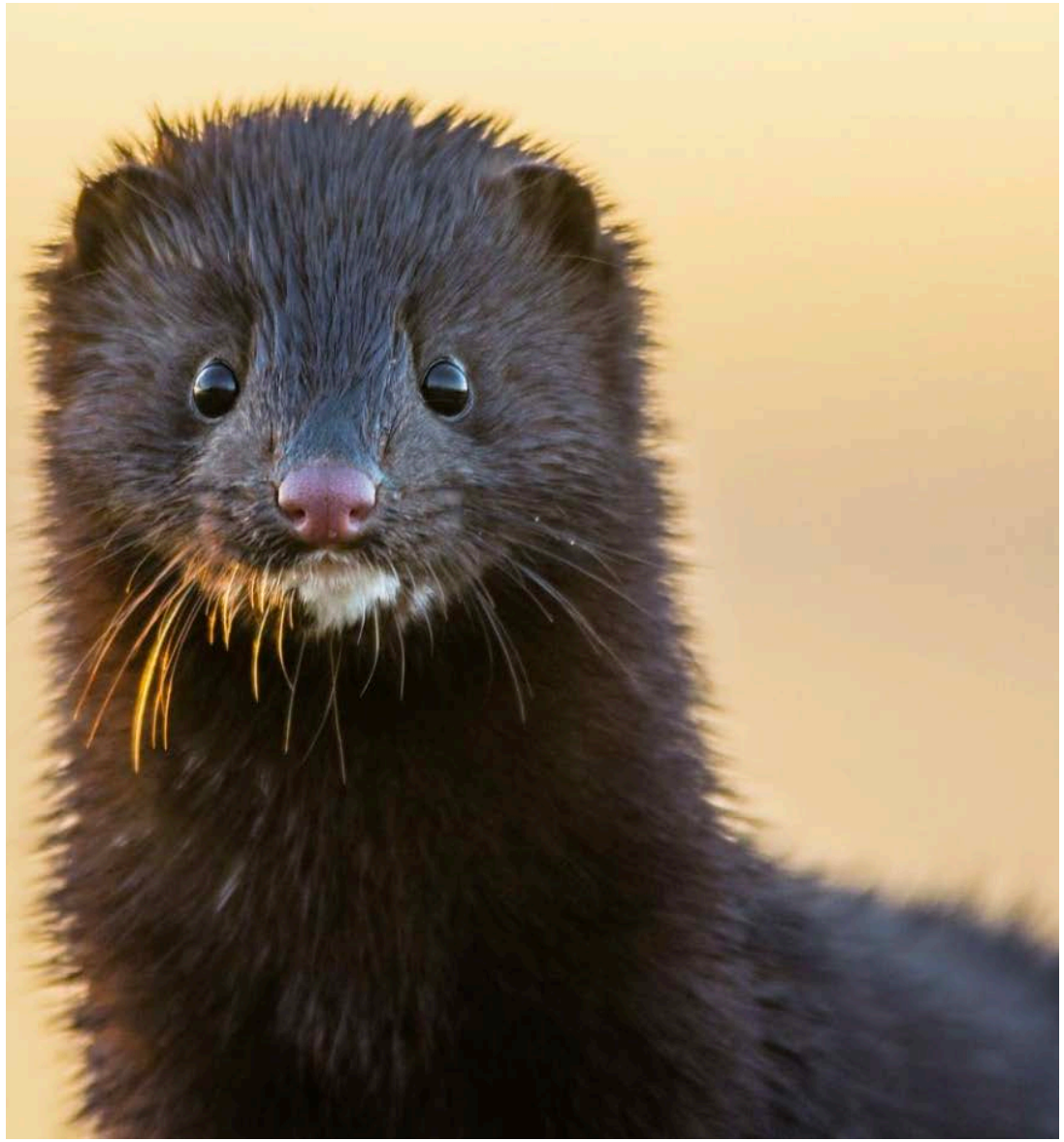
Emergence of a Highly Fit SARS-CoV-2 Variant



December 16, 2020, at NEJM.org.

SARS-CoV-2 “Cluster 5” Identified in Denmark in August 2020

- This variant has new mutations.
- Linked to infection among farmed mink and subsequently transmitted to humans
- May result in reduced virus neutralization in humans
    - Which could potentially decrease the duration of immune protection following natural infection or vaccination.
- Only 12 human cases identified until September 2020, and it does not appear to have spread.



https://www.who.int/csr/don/31-december-2020-sars-cov2-variants/en/

SARS-COV-2 501Y.V2 Variant Reported in South Africa in December 2020

- This mutation is also present in the UK SARS-CoV-2 VOC 202012/01 variant, but phylogenetic analysis has shown that they are different virus variants
- This variant has largely replaced other SARS-CoV-2 viruses circulating in the Eastern Cape, Western Cape, and KwaZulu-Natal provinces
- This Variant is associated with a higher viral load
  - Suggesting potential for increased transmissibility
- There is no clear evidence of the new variant being associated with more severe disease or worse outcomes
- As of 30 December, the 501Y.V2 variant from South Africa has been reported from four other countries to date.

https://www.who.int/csr/don/31-december-2020-sars-cov2-variants/en/

SARS-CoV-2 VOC 202012/01 reported in the UK in December 2020

- **VOC 202012/01** (Variant of Concern, year 2020, month 12, variant 01), AKA "**B.1.1.7**."
- This variant has a mutation in the receptor binding domain (RBD) of the spike protein at position 50, where amino acid asparagine (N) has been replaced with tyrosine (Y).
  - The shorthand for this mutation is N501Y (also noted as S:N501Y to specify it is in the spike protein).
  - This variant carries many other mutations, including a double deletion (positions 69 and 70).
- This variant with N501Y suggests they **may bind more tightly** to the human angiotensin-converting enzyme 2 (ACE2) receptor.
  - It is unknown whether that tighter binding, if true, translates into any significant epidemiological or clinical differences
- How and where SARS-CoV-2 VOC 202012/01 originated is unclear.
  - By chance alone?
  - Better fit to spread in humans. ?

https://www.who.int/csr/don/31-december-2020-sars-cov2-variants/en/

SARS-CoV-2 VOC 202012/01 reported in the UK in December 2020

- SARS-CoV-2 VOC 202012/01 appeared in South East England but is now identified across the UK and represents 60% of variants in London
- Preliminary studies suggest that **it has increased transmissibility.**
- There is **no change in disease severity** or occurrence of
- Some mutations may affect the results of some PCR assays with an S gene target.
  - Most PCR assays in use worldwide will use multiple targets
  - No significant impact in antigen-based lateral flow performance has been seen
- As of 30 December, this variant has been reported in 31 other countries

https://www.who.int/csr/don/31-december-2020-sars-cov2-variants/en/

ABBOTT

- As the mutation has been recently identified, this viral strain is not yet available and therefore, Abbott has not been able to perform testing to confirm detection.
- ID NOW COVID-19 detects the RNA dependent RNA polymerase (RdRp) gene rather than the gene for the spike protein.
- This newly described variant harbors amino acid mutations in the spike protein of SARS-CoV-2.
- The detection region in the ID NOW COVID-19 assay is located in the RdRp gene, so it will be unaffected by any mutations outside of that region/gene.
- **The BinaxNOW COVID-19 Ag Card detects the nucleocapsid protein rather than the spike protein** and therefore is not expected to be affected by a mutation in the spike protein. Abbott will continue to monitor the global situation on VUI 202012/01 and on SARS-CoV

What are the potential consequences of these mutations?

- ***Ability to spread more quickly in humans.***
  - D614G, has this property to spread more quickly.
- ***Ability to cause either milder or more severe disease in humans.***
  - There is no evidence that VOC 202012/01 produces more severe illness than other SARS-CoV-2
- ***Ability to evade detection by specific diagnostic tests.***
  - Most commercial polymerase chain reaction (PCR) tests have multiple targets to detect the virus, such that even if a mutation impacts one of the targets, the other PCR targets will still work.
- ***Decreased susceptibility to therapeutic agents such as monoclonal antibodies.***
- ***Ability to evade vaccine-induced immunity***
  - FDA-authorized vaccines are “polyclonal,” producing antibodies that target several parts of the spike protein..

Implications of the Emerging SARS-CoV-2 Variant VOC 202012/01
https://www.cdc.gov/coronavirus/2019-ncov/more/scientific-brief-emerging-variant.html

What are the potential consequences of these mutations?

- Among these possibilities, the ability to evade vaccine-induced immunity, would likely be the most concerning because once a large proportion of the population is vaccinated, there will be immune pressure that could favor and accelerate emergence of such variants by selecting for “escape mutants.”

- There is no evidence that this is occurring, and most experts believe escape mutants are unlikely to emerge because of the nature of the virus.

Implications of the Emerging SARS-CoV-2 Variant VOC 202012/01
https://www.cdc.gov/coronavirus/2019-ncov/more/scientific-brief-emerging-variant.html

What is CDC doing to track emerging variants of SARS-CoV-2?

- In November 2020, CDC officially launched the **National SARS-CoV-2 Strain Surveillance (NS3) program** to increase the number and representativeness of viruses undergoing characterization.
- When fully implemented in January 2021, **each state will send CDC at least 10 samples biweekly** for sequencing and further characterization. In addition, CDC's COVID-19 response is actively seeking samples of interest, such as samples associated with animal infection and, in the future, samples from vaccine-breakthrough infections.
- **Data from these efforts are continuously analyzed at CDC, and genomic data are rapidly uploaded to public databases** for use by researchers, public health agencies, and industry. To coordinate US sequencing efforts outside of CDC, since early in the pandemic, CDC has led a national coalition of laboratories sequencing SARS-CoV-2 (SPHERES).
- The SPHERES coalition consists of more than 160 institutions, including academic centers, industry, non-governmental organizations, and public health agencies. Of the approximately 275,000 full-genome sequences currently in public databases, 51,000 are from the United States. (The UK currently has the most sequences, with 125,000).

Outline

UPDATE ON MUTANT VARIANTS

UPDATE ON IMMUNITY AFTER INFECTION

FREQUENT ASKED QUESTIONS IN 2021

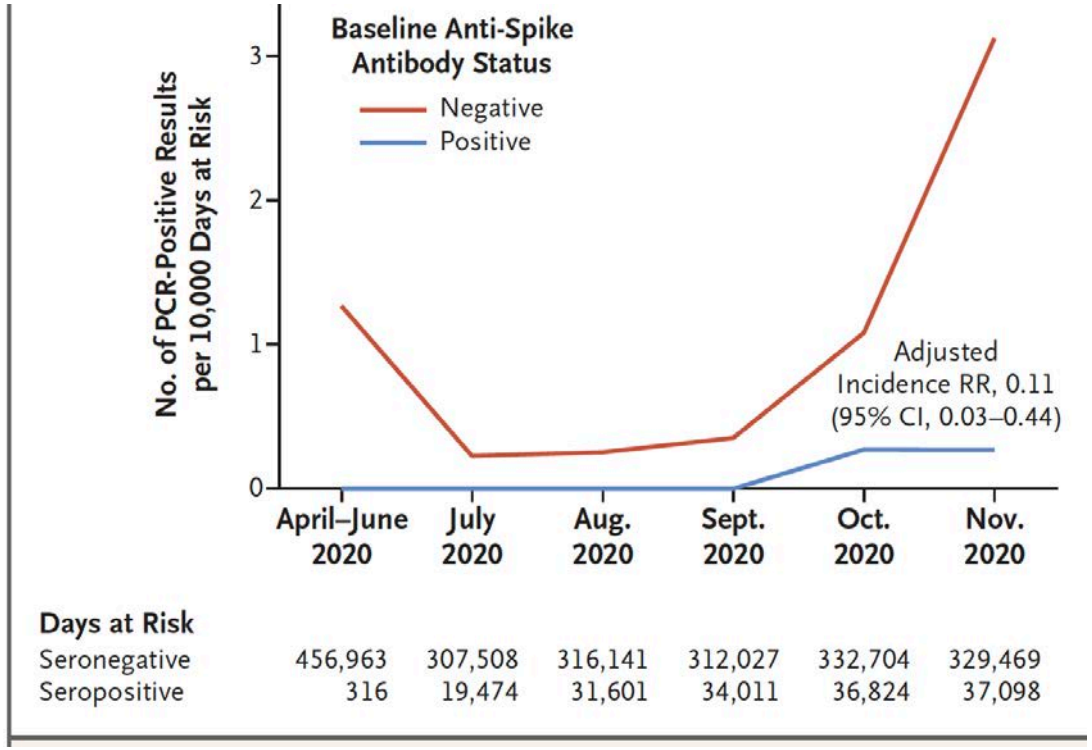
Antibody Status and Incidence of SARS-CoV-2 Infection in Health Care Workers

- **METHODS**
  - Investigation of the incidence of SARS-CoV-2 infection confirmed by PCR in seropositive and seronegative health care workers at Oxford University Hospitals in the United Kingdom.
  - Baseline antibody status was determined by anti-spike (primary analysis) and anti-nucleocapsid IgG assays, and staff members were followed for up to 31 weeks.

- **RESULTS**
  - A total of 12,541 health care workers participated and had anti-spike IgG measured;
  - 11,364 were followed up after negative antibody results and 1265 after positive results,
  - A total of 223 anti-spike–seronegative health care workers had a positive PCR test, 100 during screening while they were asymptomatic and 123 while symptomatic
  - A total of 2 anti-spike–seropositive health care workers had a positive PCR test, and both workers were asymptomatic (P = 0.002).
  - Rate ratios were similar when the anti-nucleocapsid IgG assay was used alone or in combination with the anti-spike IgG assay to determine baseline status.

- **CONCLUSIONS**
  - The presence of anti-spike or anti-nucleocapsid IgG antibodies was associated with a substantially reduced risk of SARS-CoV-2 reinfection in the ensuing 6 months

Antibody Status and Incidence of SARS-CoV-2 Infection in Health Care Workers



Observed Incidence of SARS-CoV-2–Positive PCR Results According to Baseline Anti-Spike IgG Antibody Status

- The incidence of polymerase-chain-reaction (PCR) tests that were positive for SARS-CoV-2 infection during the period from April through November 2020 is shown per 10,000 days at risk among health care workers according to their antibody status at baseline.
- In seronegative health care workers, 1775 PCR tests (8.7 per 10,000 days at risk) were undertaken in symptomatic persons and 28,878 (141 per 10,000 days at risk) in asymptomatic persons;
- In seropositive health care workers, 126 (8.0 per 10,000 days at risk) were undertaken in symptomatic persons and 1704 (108 per 10,000 days at risk) in asymptomatic persons. RR denotes rate ratio.

December 23, 2020, at NEJM.org. DOI: 10.1056/NEJMoa2034545

Scenario

- I got my first COVID-19 vaccine and then tested positive for COVID-19 prior to my second vaccine.
  - When should I get the second vaccine?
  - Should we test a person for COVID-19 prior to administering the vaccine?

Scenario

- I have a patient that is wondering how long he has to stay at home. He had COVID-19, mild symptoms like head congestion, weakness, lightheaded. Six days after he was diagnosed, his wife was diagnosed.
  - So, does he stay home for 10 days or 10 days after wife diagnosed?
- One month later, he is exposed at work and sent home to quarantine.
  - Should he be quarantined? Should he be tested for antibodies?

Scenario

- A patient received bamlanivimab for treatment of mild to moderate COVID-19.
  - When should he/she/they start the COVID-19 vaccine series?

Scenario

- Several of my colleagues are prescribing PO steroids for patients diagnosed with COVID-19.
  - When is that appropriate?
  - Should I be offering steroids to patients with COVID-19?

Overview of IDSA COVID-19 Treatment Guidelines

Version 3.5.1 – December 2, 2020

		Setting and severity of illness			
		Ambulatory care: *mild-to-moderate disease*	***Hospitalized:*** *mild-to-moderate disease without need for suppl. oxygen*	***Hospitalized:*** *severe but non-critical disease (spO_2 <94% on room air)*	***Hospitalized:*** *critical disease (e.g., in ICU needing MV, or septic shock, ECMO)*
1	*Hydroxy-chloroquine (HCQ)**	NA	**Recommend against use** ⊕⊕⊕◯	**Recommend against use** ⊕⊕⊕◯	**Recommend against use** ⊕⊕⊕◯
2	*HCQ* + azithromycin*	NA	**Recommend against use** ⊕⊕◯◯	**Recommend against use** ⊕⊕◯◯	**Recommend against use** ⊕⊕◯◯
3	*Lopinavir + ritonavir*	NA	**Recommend against use** ⊕⊕⊕◯	**Recommend against use** ⊕⊕⊕◯	**Recommend against use** ⊕⊕⊕◯
4-6	*Corticosteroids*	NA	**Suggest against use** ⊕◯◯◯	**Suggest use** ⊕⊕⊕◯ R: If dexamethasone is unavailable, equivalent total daily doses of alternative glucocorticoids may be used.**	**Recommend use** ⊕⊕⊕◯ R: If dexamethasone is unavailable, equivalent total daily doses of alternative glucocorticoids may be used.**
7	*Tocilizumab*	NA	**Suggest against routine use** ⊕⊕◯◯	**Suggest against routine use** ⊕⊕◯◯	**Suggest against routine use** ⊕⊕◯◯
8	*Convalescent plasma*	NA	Recommended only in the context of a clinical trial (knowledge gap)	Recommended only in the context of a clinical trial (knowledge gap)	Recommended only in the context of a clinical trial (knowledge gap)
9-11	*Remdesivir*	NA	**Suggest against routine use** ⊕◯◯◯	**Suggest use** ⊕⊕◯◯ R: In patients on mechanical ventilation or ECMO, the duration of treatment is 10 days.	**Suggest use** ⊕⊕⊕◯ R: For consideration in contingency or crisis capacity settings (i.e., limited remdesivir supply): Remdesivir appears to demonstrate the most benefit in those with severe COVID-19 on supplemental oxygen rather than in patients on mechanical ventilation or ECMO.
12	*Famotidine*	NA	**Suggests against use except in a clinical trial** ⊕◯◯◯	**Suggests against use except in a clinical trial** ⊕◯◯◯	**Suggests against use except in a clinical trial** ⊕◯◯◯
13	*Bamlanivimab*	**Suggest against routine use** ⊕◯◯◯ R: In patients at increased risk*** bamlanivimab is a reasonable treatment option if, after informed decision-making, the patient puts a high value on the uncertain benefits and a low value on uncertain adverse events.	NA	NA	NA

NA: not applicable/not reviewed; **MV**: mechanical ventilation; **ECMO**: extracorporeal membrane oxygenation; **R**: remark; **AE**: adverse events

*Chloroquine is considered to be class equivalent to hydroxychloroquine.

**Dexamethasone 6 mg IV or PO for 10 days (or until discharge) or equivalent glucocorticoid dose may be substituted if dexamethasone unavailable. Equivalent total daily doses of alternative glucocorticoids to dexamethasone 6 mg daily are methylprednisolone 32 mg and prednisone 40 mg.

***Patients at increased risk, see EUA at https://www.fda.gov/media/143603/download

Certainty of evidence

⊕⊕⊕⊕ high

⊕⊕⊕◯ moderate

⊕⊕◯◯ low

⊕◯◯◯ very low

Scenario

- A patient comes in for treatment of COVID-19 with bamlanivimab and is found to have a pulse ox consistently 92%. This excludes them from receiving a monoclonal antibody, but they may not meet admission criteria for remdesivir, especially if their SPO2 is not consistently below 94%.
  - Any treatment recommendations for patients who have a O2 saturation of less than 94%? Seems like this is a grey area.

Scenario

- Some are saying that to get at least some protection to more people, only one of the two-part series of the COVID-19 vaccine should be given right now.
  - Thoughts?

Variant Virus

- How concerned should we be about the "new variant" of COVID-19?
- Do the tests we have pick it up?
- Will the treatments we have work the same?
- Will the illness look much different?

References

- https://www.idsociety.org/practice-guideline/covid-19-guideline-treatment-and-management/
- Antibody Status and Incidence of SARS-CoV-2 Infection in Health Care Workers, NEJM, December 16, 2020
- Implications of the Emerging SARS-CoV-2 Variant VOC 202012/01. CDC.gov

*All images are free stock images from bing.com photo gallery