



COVID-19: KEEPING UP WITH A MOVING TARGET

January 6, 2021 UPDATE



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Paul G. Auwaerter, MD, MBA, FIDSA	Scientific Advisor: DiaSorin, Shionogi Inc. JNJ: Ownership equity

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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Learning Objectives

- Discuss changes in SARS-CoV-2 since the Wuhan strain was identified
- Discuss implications of newer variants on vaccine development





Thank You

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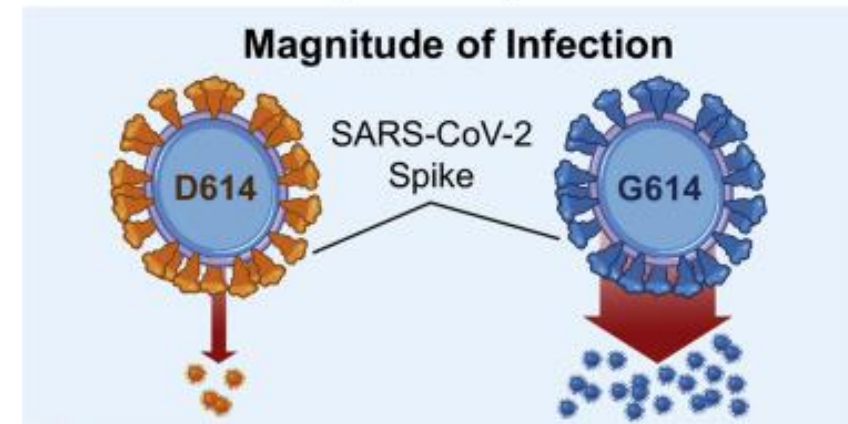
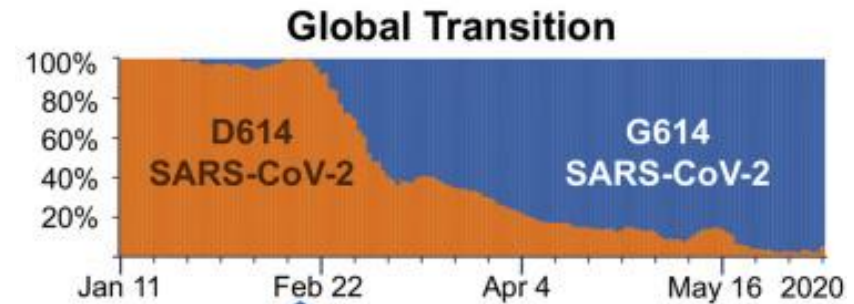


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Viruses Change, including SARS-CoV-2

- Original Wuhan strain, L (Dec 2019)
- Multiple variants (six by spring 2020)
- D614G substitution variant (S-protein)
 - First seen Jan-Feb 2020
 - Has overwhelmed Wuhan strain
 - Jun 2020 = dominant global strain
 - No apparent change in virulence
 - More transmissible?
 - Lower CT values = higher respiratory viral loads



Grubaugh Cell 182(4) Aug 2020



UK Actions: Variant SARS-CoV-2

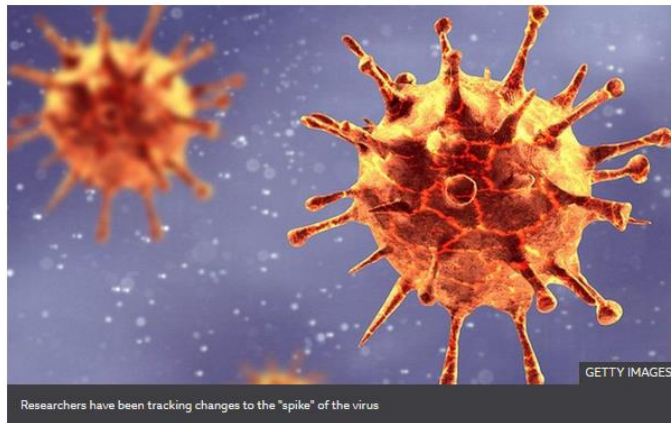
- Transmissibility enhanced by R 0.4-0.7 (Imperial College)
- Current R estimated in UK 1.1-1.3
- Spread despite severe November restrictions



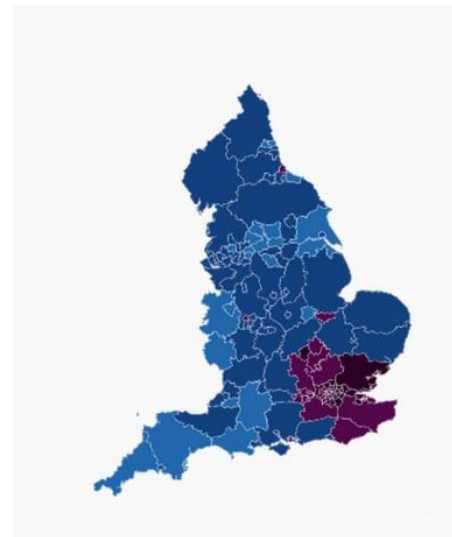
Covid-19: New variant 'raises R number by up to 0.7'

1 day ago

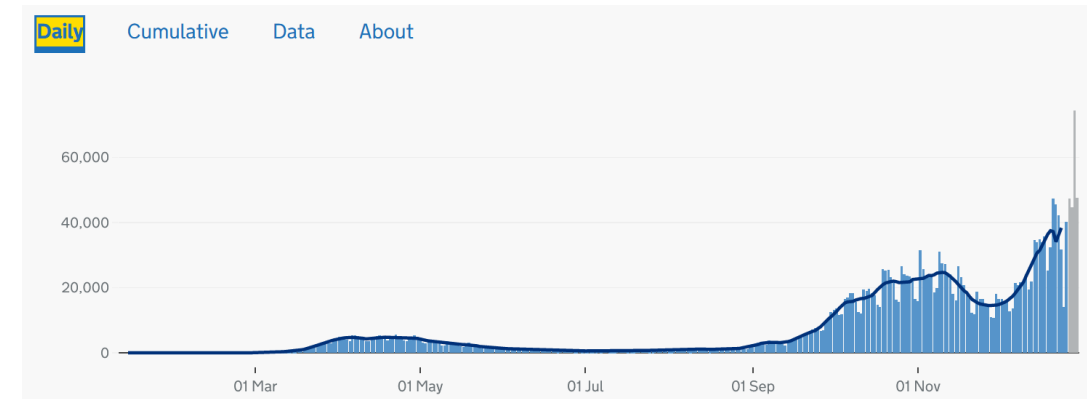
Coronavirus pandemic



The new variant of Covid-19 is "hugely" more transmissible than the virus's



Daily Positive Cases UK



<https://coronavirus.data.gov.uk/> accessed 1/3/21

BBC 1/1/21



UK Strain SARS-CoV-2, B.1.1.7 (aka by CDC: “SARS-CoV-2 VOC (variant of concern) 202012/01”)

- 23 mutations (!) accumulated since original Wuhan strain
 - Newly identified lineage B.1.1.7
 - Unprecedented 14 AA replacement.
 - Eight of these mutations occur in the spike protein --three are particularly worrisome including receptor binding domain change that could mean antigenic escape
 - **N501Y**, reportedly → increased binding affinity to human and murine ACE2 receptors
 - **69-70del**, linked to farmed minks
 - **P681H**, close to the furin cleavage site
 - Unique furin-like cleavage site in the spike protein (S) is absent in other lineage β -CoVs, such as SARS-CoV, possibly responsible for its high infectivity and transmissibility

ARTIC Network <https://virological.org/> (Dec 2020)
NERVTAG Mtg (12/18/20)



B.1.1.7

- First identified Sept 2020
- Why UK?—country has established genomic sequencing of virus
- B.1.1.7 detected in > 33 countries (Jan 2021)
 - In US, FL, GA, CO and CA including patients without travel history



*Kings Crossing, London
Third Lockdown in the UK*

Jason Alden/Bloomberg via Getty Images





Variant implications beyond increased transmission

- Growth rate is 71% faster
 - CT decline of ~ 2 compared to earlier strains → transmission ↑↑
 - Given high prevalence of infection, suggests selective advantage
- No clear change in disease severity
- Appears to be detected by routine testing
 - Commercial testing uses PCR primers with multiple targets
- May have decreased susceptibility to monoclonal antibody therapies
- Broad S-protein immune responses from current mRNA vaccines thought to be sufficient

NERVTAG Mtg (12/18/20)



South Africa (501Y.V2 --a.k.a. B.1.351)

- This variant has multiple mutations in the spike protein, including N501Y.
 - Unlike the UK variant, VOC 202012/01, this variant does not contain the deletion at 69/70.
- First identified October 2020
- Concern is that this has greater virulence
- Hospitals in South Africa hit with second wave COVID-19



Search

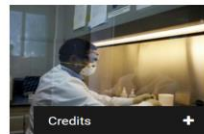
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WHO Africa / WHO urges greater surveillance as new COVID-19 variants emerge...

WHO urges greater surveillance as new COVID-19 variants emerge

30 December 2020

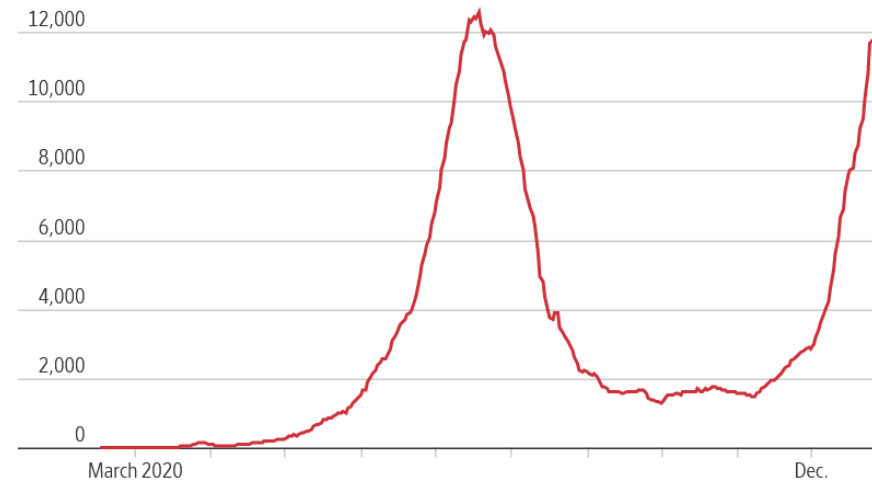
Brazzaville – With the recent emergence in the African region of new COVID-19 variants which seem to have higher transmissibility, the World Health Organization (WHO) calls on countries to boost genomic surveillance and analysis through the African genome sequencing laboratory network to detect any new mutations and strengthen the efforts to curb the pandemic.



Credits

Click image to enlarge

South Africa's daily confirmed Covid-19 cases, seven-day rolling average



Note: As of Dec. 29.

Source JHU



Nigeria (B.1.207)

- P681H S-protein change (near s1/s2 furin cleave site)
- Variant does not have any of the other 22 mutations
- Unclear when first emerged
 - Possibly August
- Nigeria is 1 of 12 centers in Africa sequencing virus
- Unclear if impact on transmission or virulence



The screenshot shows a news article from the Anadolu Agency (AA) celebrating its 100th anniversary (1920-2020). The article is titled "Nigeria hit by second wave of COVID-19" and reports that more than 76,000 cases have been diagnosed so far, with a death toll of 1,201. The author is Adam Abu-bashal, and the date is 18.12.2020. The main image shows a person in blue gloves holding a test tube labeled "Coronavirus". To the right, there is a sidebar with a "Coronavirus" section containing several related headlines: "Pandemic kills 25, sickens 1,064 in Palestine", "Iran says managed to contain 3rd wave of pandemic", "India conducts COVID-19 vaccination trial run", "Anadolu Agency's Morning Briefing - Jan. 2, 2021", and "Coronavirus cases rising in Arab countries". Below the main image, there are social media sharing icons (Facebook, Twitter, Email, Print) and a section titled "ABUJA, Nigeria" which states: "Nigeria has entered a second wave of coronavirus infections, an official announced Thursday. The number of COVID-19 cases detected in the country in the past two weeks indicates that a second wave of the outbreak has begun, said Boss Mustapha, Secretary to the Government of the Federation and chairman of the Presidential Task Force on COVID-19."





Conclusions

- Likely this B.1.1.7 variant will predominate worldwide
- More genetic sequencing of virus can help anticipate problems
- mRNA vaccines can be changed quickly dependent on new strains





To submit your own question, please email QA@dkbmed.com





Vitamin D is, once again, suggested by some to have a role in COVID severity. What do you think about this?





What is your opinion about the UK's vaccination program (eg, mix and match, one-dose)?





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