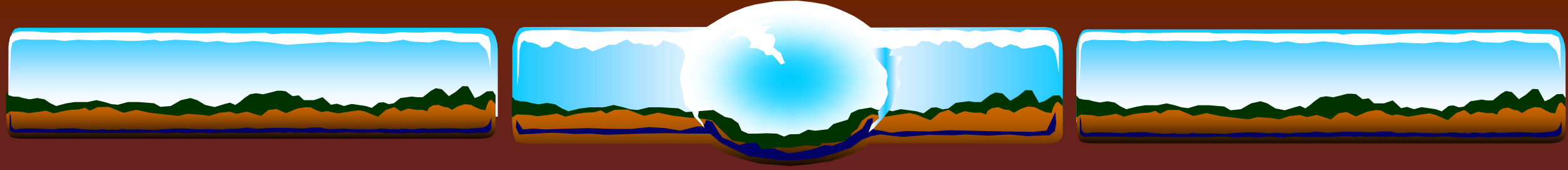
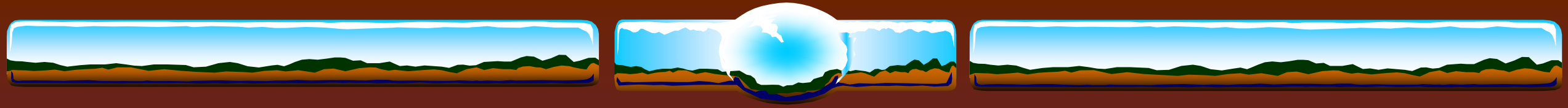


COVID-19 Clinical Update

Jonathan Vilasier Iralu, MD, FACP, FIDSA

Indian Health Service Chief Clinical Consultant
for Infectious Diseases



Disclosures

Virology
SARS-CoV-2 Variants

- DG614 variant arose late January/early February 2020
  - Increased infectivity and transmissibility, no change in severity, diagnostics, therapeutic response
- "Cluster 5" arose August/September 2020 in Danish mink and 12 people
  - Possible reduced virus neutralization in humans noted
- SARS-CoV-2 VOC 201212/01: reported in England December 14
  - 23 nucleotide substitutions
  - Now present in the USA and labeled B.1.1.7 variant

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

Virology

Estimated transmissibility and severity of novel VOC 202012/01 in England

- Novel SARS-CoV-2 variant emerged SE England November 2020
- Two strain mathematical model for admission, beds, death
  - 56% more transmissible than other variants
  - No evidence for greater or lesser severity
  - Hospitalizations and death projected to reach higher levels in 2021
  - November lockdown unlikely to get Ro < 1 unless schools are shut
  - Recommend greatly accelerated roll out of vaccine

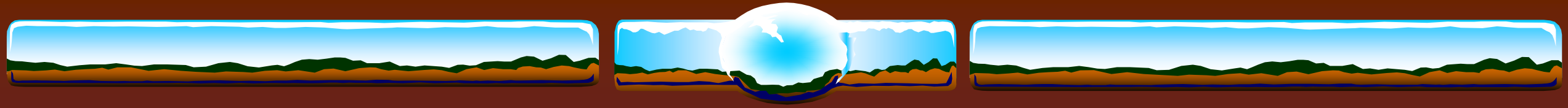
Davies et al, 12/26/2020: https://www.medrxiv.org/content/10.1101/2020.12.24.20248822v1

CDC report on B.1.1.7 Lineage

Galloway et al, MMWR, Jan 15, 2021

- 3 new variants:
  - B.1.1.7 from Britain: S-Gene Target Failure with TaqPath assay
  - B.1.351 S Africa → not detected in USA 1/12/21
  - B1.1.28 (P.1 variant) 4 travelers from Brazil → not detected in USA 1/12/2
- All have the S protein ACE-2 receptor binding mutation, N501Y
- Current B.1.1.7 US prevalence is thought to be <0.5%
- This variant will become dominant variant in March 2021 in the US
- SPHERES consortium at CDC now tracking variants

http://dx.doi.org/10.15585/mmwr.mm7003e2



Testing

- FDA Issues Alert Regarding SARS-CoV-2 Viral Mutation to HCPs and Clinical Laboratory Staff. https://www.fda.gov/news-events/press-announcements/fda-issues-alert-regarding-sars-cov-2-viral-mutation-health-care-providers-and-clinical-laboratory
  - Monitoring the effect of the B.1.1.7 variant on molecular diagnostics for false negatives
  - The FDA believes the risk of impact on molecular diagnostic tests is low
  - Possibly impacted are the MesaBiotech Accula, TaqPath, and Linea tests
  - “We believe the data suggests that the currently authorized COVID-18 vaccines may still be effective against this strain.”
- Cepheid and Abbott have put out statements that this variant is detectable by their tests.

Vaccine and N501Y mutant

- Neutralization of N501Y mutant SARS-Cov-2 by BNT162b2 vaccine elicited sera (Xie et al,1/7/2021): https://www.biorxiv.org/content/10.1101/2021.01.07.425740v1.full.pdf
  - Generated isogenic N501 (wild type) and Y501(the mutant) virus
  - Sera from 20 people who received the BioNTech/Pfizer vaccine were drawn 2 and 4 weeks after vaccination were tested on these 2 viruses
  - There was no no reduction in neutralization against the virus bearing the mutant Y501 spike

Virology
SARS-CoV-2 Variants

- 501Y.V2: Reported in South Africa December 18, 2020
  - Same mutation seen in English variant but is a different variant
  - This mutation is in the receptor domain:
    - Asparagine to Tyrosine at codon 501
  - Associated with higher viral load and potential for increased transmission
  - No sign of increased severity or worse outcomes
  - By 12/30,2020 it was reported in four other countries

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

New IDSA Testing Guidelines

- Recommend
  - NAAT test even if suspicion is low
  - NP, mid-turbinate, anterior nasal swab, saliva tests are preferred over OP
  - Patient or provider performed mid turbinate or anterior tests are OK
  - If NP NAAT negative in lower tract Dz, get a sputum, BAL, tracheal NAAT
  - Send only one test if clinical suspicion is low; repeat test if suspicion high
  - RT-PCR or Lab based NAAT are preferred over isothermal test (Abbott ID Now)

New IDSA Testing Guidelines

- Recommend
  - Test exposed individuals
  - Don’t test hospitalized people with no exposure in low prevalence areas
  - Do test hospitalized people with no exposure in HOT SPOTs
  - Do test hospitalized immunocompromised people with no exposure
  - Do test prior to transplantation, chemotherapy, immunosuppressive Rx
  - Do test prior to urgent surgery (within 72H)
  - Do not test before procedures like bronchoscopy if PPE available but do test if limited

https://www.idsociety.org/practice-guideline/covid-19-guideline-diagnostics/

New IDSA Treatment Guideline 12/23/2020

- Remdesivir/Baricitinib is recommended over Remdesivir alone if steroids are contraindicated
  - Based on Study ACTT-2, baricitinib and remdesivir arm had a lower risk of serious adverse events through day 28 (16% vs. 21%; RR 0.76; 95% CI 0.59,0.99)
  - Dosed Baricitinib at 4 mg per day for 14 days
  - List price is $2,378.40 for a 30-day supply of 2 mg pills

https://www.idsociety.org/practice-guideline/covid-19-guideline-treatment-and-management/

Treatment- Plasma for mild disease

Libster et al, NEJM. 1/6/2021

- Early High-Titer Plasma Therapy to Prevent Severe COVID-19 in Older Adults
  - 160 patients age 75 years and older or 65 and older with comorbidities were enrolled (DM,HTN,obesity, CKD,CVD,COPD) with positive PCR, symptoms but not severe Dz.
  - Randomized to high titer convalescent plasma (spike IgG titer 1:1000) vs normal saine with 72 hours of symptom onset administered over 1.5-2 hours
  - Severe COVID-19 developed in 16% of plasma vs 31% placebo (RR 0.52; P=0.03)
  - Modified Intention to Treat analysis excluding 6 patients who already showed a primary endpoint before infusion yielded a relative risk of 0.40 of progression to severe disease
  - Hospitalized donors had the highest titers

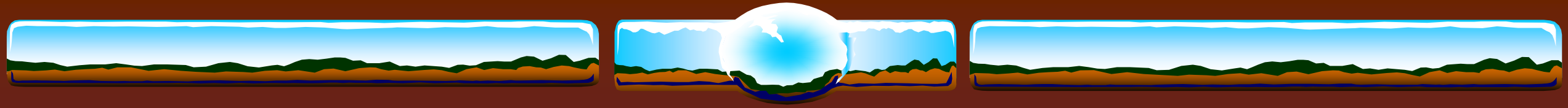
https://www.nejm.org/doi/full/10.1056/NEJMoa2033700

Treatment- Plasma for severe disease

Joyner et al, NEJM, January 13, 2021

- 3082 patients from a national database who received plasma were studied retrospectively
  - Primary outcome was death within 30 days
  - 22.3% of high titer patients died vs 27.4% medium titer vs 29.67% low titer
  - Lower risk of death significant for those not receiving mechanical ventilation (RR = 0.66, CI 0.48-0.91) vs RR 1.02 if ventilated mechanically
  - Conclusion: high titer plasma is beneficial when given early in COVID-19

https://www.nejm.org/doi/full/10.1056/NEJMoa2031893



More COVID-19 Training

- CDC: https://www.cdc.gov/coronavirus/2019-ncov/hcp/index.html
- ACP Physician Handbook: https://www.acponline.org/clinical-information/clinical-resources-products/coronavirus-disease-2019-covid-19-information-for-internists
- UW Protocols: https://covid-19.uwmedicine.org/Pages/default.aspx
  - UW IDEA Program: https://covid.idea.medicine.uw.edu/
  - NIH Guidelines: https://covid19treatmentguidelines.nih.gov/
- Brigham and Women's Hospital: covidprotocols.org