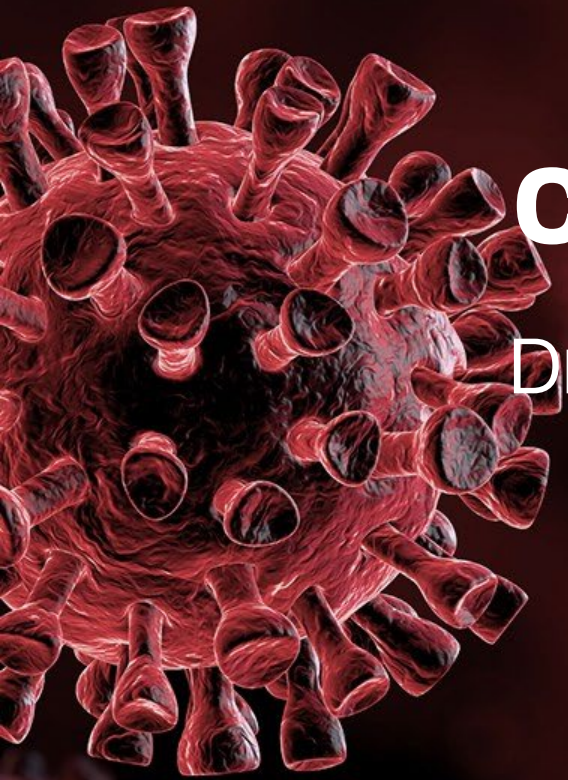
NORTHEAST
BUSINESS GROUP ON HEALTH



COVID-19 Update

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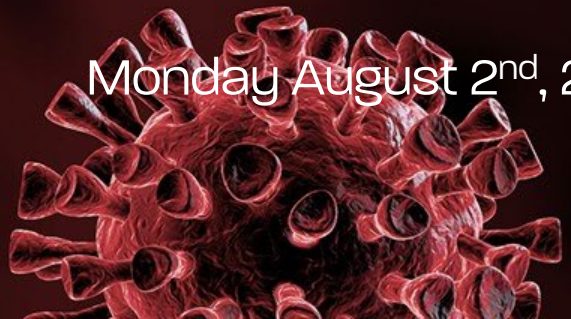
Monday August 2nd, 2021



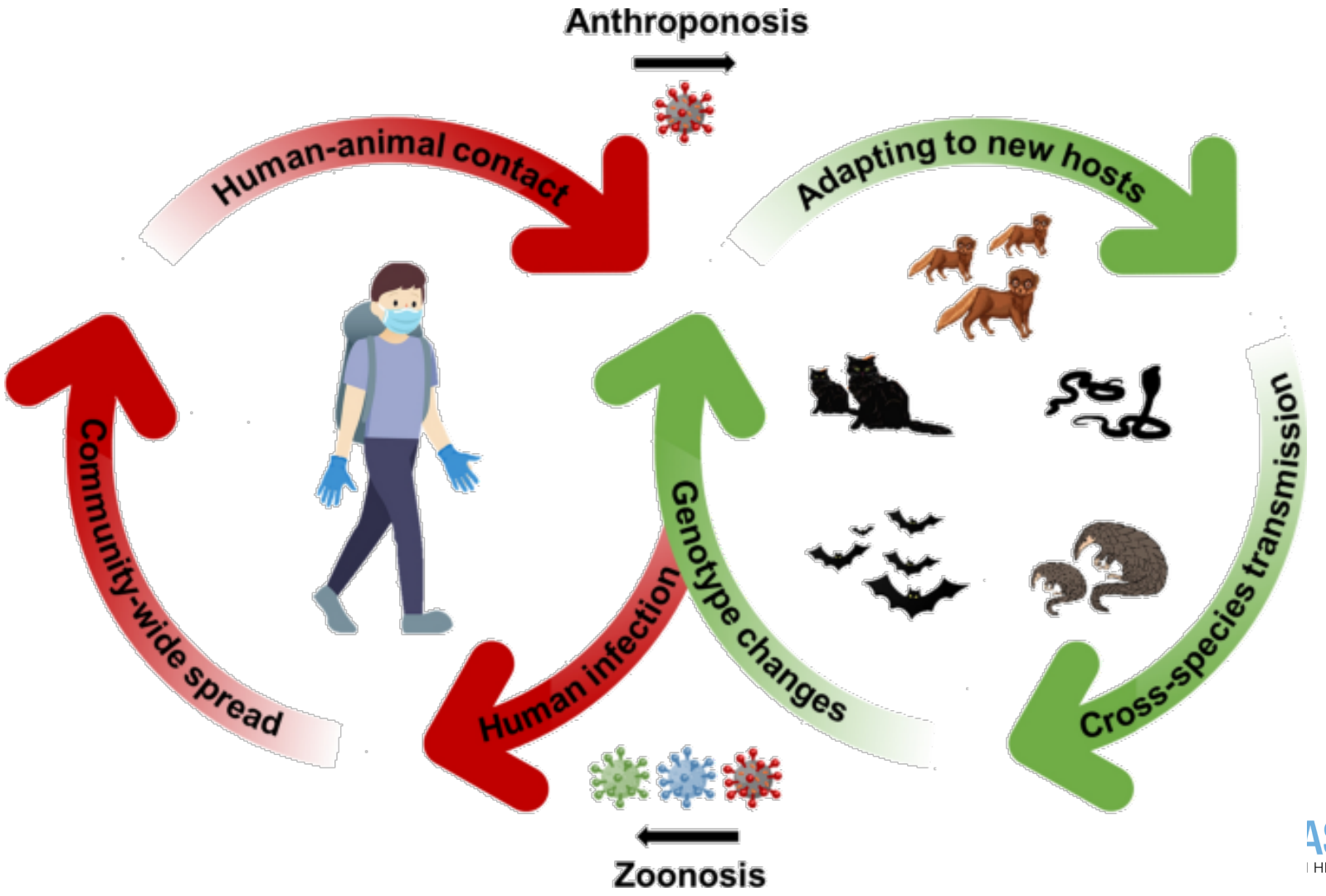
Scientific Advisory Group for Emergencies[1]

- The eradication of SARS-CoV-2 is unlikely
- Probable there will always be variants
- The number of variants will depend on control measures

1. https://www.gov.uk/government/organisations/scientific-advisory-group-for-emergencies

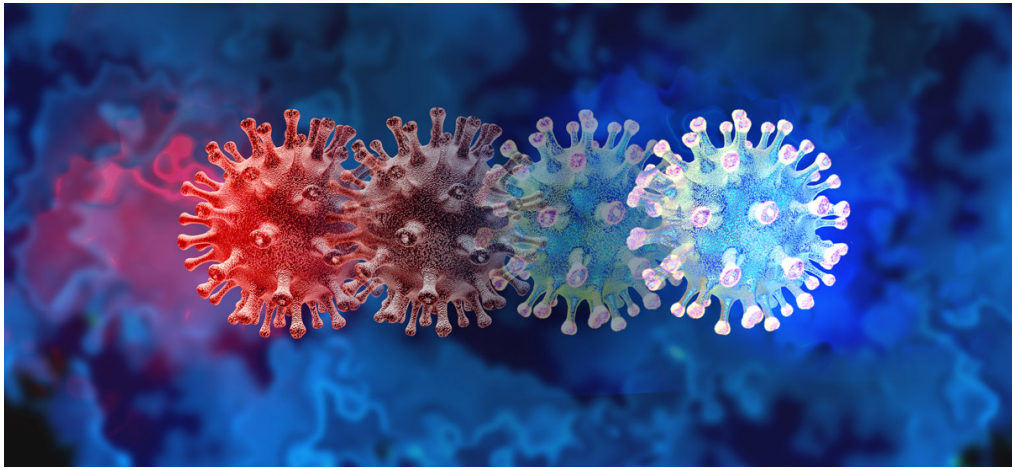
How does genetic change occur in SARS-COV-2?

- Replication error –
  - CoVs are RNA virus and subject to replication errors (1 mutation is introduced about every 33-330 replications)
  - In an infected person the peak number of virus genomes exceeds 100 million genomes; therefore, the virus has the potential to mutate every nucleotide of its genome hundreds of times per infected person, therefore variant generation is common
- Recombination –
  - Process by which viruses swap genetic material between genomes, producing new combinations of genetic sequences
  - New sequence can be acquired from the same type of coronavirus or a different source of RNA altogether - between other animal coronaviruses (reverse zoonoses) and/or host RNA


Anthroponosis
Human-animal contact
Adapting to new hosts
Community-wide spread
Human infection
Genotype changes
Cross-species transmission
Zoonosis

Selection Pressure

- Genetic change accumulates at random
- Environmental factors known as selection pressures will influence whether that genetic change increases or decreases viral fitness
- Types of selection pressure:
  - Vaccines
  - Treatments
  - T-Cell response
  - Masks and physical distancing
  - Increasing immunity in the population



Scenario 1 – variant that causes severe disease

A variant that causes severe disease in a greater proportion of the population than has occurred to date:

- This could be caused by:
  - Point mutations or recombination with other host or viral genes. There is precedent for Coronaviruses to acquire additional genes or sequences from the host, from themselves or from other viruses.
  - By recombination between two VOC or VUIs
- Likelihood of genotypic change in internal viral genes: Likely
- Likelihood of increased severity: Realistic possibility
- Impact: High

Scenario 1 – What we can do

- Consider vaccine booster doses to maintain protection against severe disease.
- Reduce transmission of SARS-CoV-2 (to reduce risk of point mutations, recombination).
- Minimize introduction of new variants from other parts of the world (to reduce risk of recombination between variants).
- Targeted surveillance for reverse zoonoses, and if necessary, consider animal vaccination, slaughter, or isolation policies.
- Continue to monitor disease severity associated with variants
- Continue to develop improved prophylactic and therapeutic drugs for SARSCoV-2 and disease symptoms
- Consider stockpiling prophylactic and therapeutic drugs for SARS-CoV-2.

Scenario 2 – Variant that evades current vaccines

A variant that evades current vaccines. This could be caused by:

- Antigenic ‘shift’: Natural recombination events that insert a different spike gene sequence (or partial sequence) from human CoVs
  - Likelihood: Realistic possibility
  - Impact: High
- A longer-term version of shift whereby SARS-CoV-2 undergoes a reverse zoonotic event into an animal reservoir(s) and then back to humans.
  - Likelihood: Realistic possibility
  - Impact: Medium
- Antigenic drift: A gradual or punctuated accumulation of antigenic variation that eventually leads to current vaccine failure. Worst case is that this drift combines with significant antigenic sin
  - Likelihood: Almost certain
  - Impact: Medium

Scenario 2 – What we can do

- Monitor antigenic variants and update candidate vaccines to cover antigenic escape variants.
- Conduct clinical trials of re-vaccination with antigenically distant vaccines
- Consider clinical trials of multi-valent vaccines.
- Re-vaccinate vulnerable age groups at regular periods with updated vaccines to the dominant antigenic drift variants
- Reduce transmission of SARS-CoV-2 (to reduce risk of point mutations, recombination).
- Minimize introduction of new variants from other countries (to reduce risk of recombination between variants).
- Monitor for reverse zoonoses and if necessary, consider animal vaccination, slaughter, or isolation policies.
- Continue to develop improved prophylactic and therapeutic drugs for SARS-CoV-2.
- Stockpile prophylactic and therapeutic drugs for SARS-CoV-2

Scenario 3 -Emergence of a drug resistant variant

- Emergence of new variants following the administration of directly acting antiviral therapies - drugs that target the:
  - viral 3C protease, and polymerase – impact viral replication
  - monoclonal antibodies that target the spike glycoprotein
  - Likelihood: Likely - unless the drugs are used correctly
  - Impact: medium unless a scenario arises where drugs are needed more widely
- What we can do:
  - Only use antiviral combination therapy, using ≥2 drugs with different targets or mechanism of action.
  - Preserve antiviral use for an emergency in which a SARS-CoV-2 variant is more severe, and a matched vaccine is unavailable and takes time to develop.
  - Use antivirals cautiously in immunocompromised people in whom long term evolution can happen –
    - monitor for treatment failure and resistance,
    - minimize risk of onwards transmission of resistant variants using appropriate PPE.

Scenario 4 -SARS-CoV-2 evolves to become less virulent

- Variants arising with increased transmissibility but decreased pathogenesis/virulence as the virus adapts to the human host becoming an endemic infection.
- Coupled with the likelihood of eventual high populations immunity the infection produces less disease.
- The virus will become like other human CoV that causes common colds, but with much less severe disease predominantly in the old or clinically vulnerable.
- Likelihood: Unlikely in the short term, realistic possibility in the long term
- Impact: Low

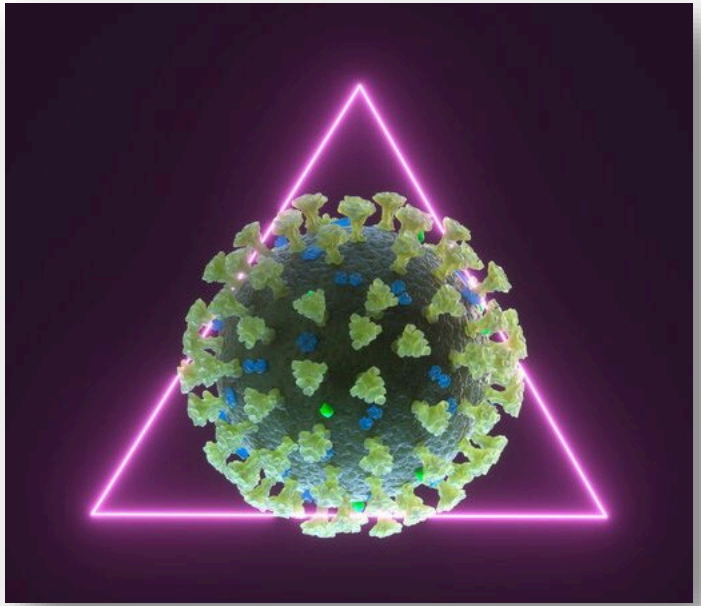
General Measures to Reduce Risks from Variants

- Research focused on vaccines that also induce high and durable levels of mucosal immunity - reduce infection of and transmission from vaccinated individuals
- Global vaccination
- Global genomic surveillance of SARS-CoV-2 to monitor for variants
- Rapid laboratory phenotypic evaluation of variants at scale + clinical observations
- Studies and AI that predict future variants
- Sharing of viral sequences, clinical, biological materials, and virus isolates
- Use antivirals cautiously


DELTA VARIANT

What we know about the Delta variant

- It is very infectious
- Vaccinated people can get infections and can spread the virus to others just as readily as unvaccinated people
- High viral loads – 1000 x higher
- Shorter incubation period
- Has more spike proteins



Implications for Employers

- Mask policies
- Approach to vaccination status
- Testing strategies
- Who is high risk
- Timing of return to work

Questions

Upcoming NEBGH virtual events:

- **Aug. 9 –** Special Edition Dr. Mark – Delta Variant
- **Aug. 10 –** Heads Up, Employers! Mental Health Parity is on the Front Burner
- **Nov. 18 –** Annual Membership Meeting