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GW Covid-19 Intelligence Unit-Brief Report Delta Variant of SARS-CoV2

George Washington University

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GW COVID-19 Intelligence Unit – Brief Report
Delta Variant of SARS-CoV2

Authors' Summary: *The current situation is challenging due to the rise of a highly transmittable SARS-CoV2 variant, which seems to generate higher viral loads faster in the course of the disease, in parallel with evidence of waning effectiveness of vaccines in preventing infection and transmission over time (though they remain highly effective at preventing severe illness in the immunocompetent). The percentage of population which needs to be vaccinated in order to aspire to herd immunity is now even higher, while vaccine hesitancy and delayed access persist. Overload of critical care, pediatric, and total hospital resources and staffing is causing dramatic shortages across large areas of the country, threatening availability and quality of medical care for other conditions as well. Vaccination is more than ever a shared social responsibility, necessary not only to protect the vulnerable but also to reduce uncontrolled spread of the virus and the emergence of new immunity-evading variants.*

Regional Updates

- The US CDC reports over 38.7 million cumulative COVID-19 cases and over 634,000 deaths.
- As per DC district government data, the daily case rate, positivity rate and the rate of transmission (effective R_0) have trended upwards since mid-July, holding at over 20 cases daily in later August.
- In Virginia and nationally, Delta now contributes to more than 90% of incident COVID cases.
- In DC, test positivity rate is now over 5% and daily case rate exceeds 15 (evidence of substantial community spread). Hospitalization rate for COVID-19 patients in DC has been slow to increase and remains <5% at this time (sufficient hospital capacity) but is rising here, as in VA and MD.
- DC has a relatively high vaccination rates (>66% at least partially vaccinated, >56% fully vaccinated). However, substantial disparities remain by ward and neighborhood. Vaccination coverage of patients aged 65+ ranges 63-88% across DC wards.
- DC Health is administering COVID-19 vaccines to homebound patients.
- DC Health and Mayor Bowser have announced that all health professionals in DC will be required to be vaccinated against COVID-19 by September 30th, and all DC government employees by September 19th.
- DC requires masks to be worn in public indoor settings regardless of vaccination status.

Brief background about Delta variant

- Delta variant of SARS-CoV2, or B.1.617.2 lineage, has been characterized as a variant of concern (VOC) by the WHO owing to its greater transmissibility, possible association with greater severity of disease, and potential reduction in efficacy of preventive measures.
- Since the first reported case of Delta in October 2020 in India, it spread to more than 60 countries within few months and is the major reason for prolongation of the pandemic as it first peaked during May in India, followed by Israel and UK in June; Australia in July, closely followed in August by other European countries and the USA.
- Due to its high transmissibility as well as erosion of public health measures and waning immune protection from prior infection or early immunization, Delta VOC has largely displaced others to become the dominant strain globally.

Genetics of Delta variant

- The alarming features of delta variant come from its characteristic mutations in spike protein and thereby affecting the action of receptor binding domain.

- D614G mutation increases the density of spike protein on the surface of virions and makes it easier for the virus to enter cells.
- A preprint suggests P681R mutation enhances cell entry and viral replication by improving the efficiency of spike protein cleavage at the furin site, potentially explaining higher viral loads and faster progression.
- L452R mutation in the receptor-binding domain (RBD) reduces antibody-mediated neutralization of the virus and may enhances viral evasion of cellular immunity.
- Together, these mutations increase Delta's ability to attach to host receptors, enter and infect host cells, replicate rapidly once inside, and achieve higher viral load in airways, contributing to higher transmissibility. There is some debate about whether this results in more severe clinical illness.

Transmissibility of Delta variant

- A study of Delta outbreak in a gymnastics facility in Oklahoma showed particularly high secondary attack rate especially among unvaccinated contacts.
- GISAID analysis of global SARS-CoV sequence data showed a 55% increase in R_0 of Delta variant compared to Alpha (B.1.1.7) VOC and 97% increase compared to non-VOC.
- The increased transmissibility is attributed to increased viral load / shedding in the respiratory tract, which is estimated to be >1,000 times greater as compared to the original strain. Average duration from exposure to detection of virus by PCR is estimated at 4 days compared to 6 days.
- In a large outbreak in Provincetown, MA, transmission of Delta VOC occurred in spite of high baseline vaccination rates and viral loads were similar between vaccinated vs. unvaccinated.
- A preprint describing Delta virus kinetics showed similar initial viral loads in unvaccinated and breakthrough infections with Delta, however VL cleared significantly faster in the vaccinated.

Clinical Features and Treatment of Delta variant

- The symptoms experienced by patients remain mostly the same, however with comparatively lower prevalence of shortness of breath and anosmia and more common headache and sore throat.
- A study from Scotland found Delta to be associated with 1.85 times higher rates of hospitalization especially in unvaccinated adults and those with pre-existing co-morbidities.
- Another study from Canada (currently in pre-print) has reported similar findings of increased oxygen requirements, ICU admissions and death for Delta cases.
- A study in Singapore reported that vaccinated individuals have significantly lower odds of severe oxygen requiring pneumonia [aOR 0.07; 95% CI 0.01 – 0.33; p-value = 0.001], in addition to faster clearance of viral load.
- NIH guidelines for treatment of COVID-19 caused by Delta VOC is not changed from non-VOC.
- *Authors' note: However, based on the above studies, clinicians may beware of faster progression to severe disease in Delta, especially in high-risk unvaccinated patients, and make management decisions accordingly.*
- An *in vitro* study showed cellular entry by Delta SARS-CoV2 to be efficiently inhibited by casirivimab (REGN10933 mAb) and imdevimab (REGN10987 mAb).
- The combination of casirivimab and imdevimab is now recommended for post-exposure prophylaxis (PEP) in patients who are severely immunocompromised or unvaccinated *and* at high risk of poor outcome after close contact with a COVID-positive person.
- While long-term data on outcomes after Delta infection will not be available for some months, complications are expected to be similar to those from non-VOC COVID-19, including acute (e.g. ARDS, cytokine storm, myocarditis, thrombosis) and post-acute (prolonged dyspnea, dysautonomia, neurocognitive impairment, fatigue, and more).Whether Long COVID can develop after breakthrough infection in a previously vaccinated person is a matter to be determined.
- Delta variant is also responsible for causing nearly 9,000 cases COVID-related-mucormycosis in India during its deadly wave. Mucormycosis is a necrotic fungal infection affecting nasal mucosa and para-nasal sinuses. Diabetes or COVID-related blood glucose derangement and prolonged

treatment with high-dose steroids are predisposing factors. Treatment may require aggressive ENT debridement, reconstructive surgery, and intravenous liposomal amphotericin initially, followed by a consolidation course of azole antifungals.

- The number of cases in children, especially unvaccinated children (<12 years old), is continuing to increase and now matches rates from winter 2020. Although overall rate of children needing hospitalization or intensive care is low at <2% of those infected, this amount is taxing pediatric healthcare resources in some areas that are already feeling the burden of an increased number of infants and children sick and hospitalized with RSV, other respiratory illnesses, and exacerbations of asthma that can happen during any respiratory virus infection.
- Pediatric fatalities from COVID-19 infections remain extremely uncommon at 0-0.03% of cases, but long-term developmental and neurologic effects of COVID-19 in children are unknown.

Delta VOC and Currently Available Vaccines

- In the HEROES-RECOVER cohort study of HCWs in 6 US states followed 12/2020-8/2021, overall vaccine efficacy was 80% (85% within 120 days of vaccination, vs. 73% at >150 days). Vaccine efficacy declined from 91% before Delta VOC became dominant to 66% since. These findings were based on positive test results only and did not account for the severity of cases.
- In a UK study of PCR testing results published in NEJM, a single dose of either Pfizer mRNA or AstraZeneca (AZ) adenovirus vaccine was 31% effective against infection with Delta VOC (c/f 49% effective against Alpha VOC). Two doses of Pfizer were 88% effective against infection with Delta, compared to 67% effectiveness after two doses of AZ. This study evaluated effectiveness against testing positive only, and did not evaluate risk of severe infection or death.
- Decrease in vaccine-elicited neutralizing antibody titers against Delta described in a preprint.
- A review by the Canadian COVID-END network shows reduced protection against infection with Delta (33 to 47%) after a single dose of mRNA vaccine. However, a single dose is 90% effective in protecting against hospitalization. Two doses of either mRNA vaccine confer strong protection against infection (79 to 90%) and hospitalization (96%) due to Delta.
- In trials in Brazil, South Africa, and the UK, two doses of AZ were 67% effective against Delta infection but 90% effective against hospitalization.
- Earlier in 2021, Phase 3 trial data of Janssen (J&J) vaccine in the US, Central and South America, and South Africa, showed 77% efficacy against severe-critical disease at ≥14 days post vaccination, improving to 85% at ≥28 days post-vaccination, including against variants circulating at the time.
- Measured ~2 months after vaccination, neutralizing antibody titers were significantly lower against B.1.351 and P.1 variants but cell-based processes including natural killer cell activation were largely preserved including against the variants. However, Delta VOC was not prevalent.
- Neutralizing antibody titers in patients recovering from natural infection who received vaccination with even one dose of mRNA vaccine were amplified almost 50-fold and enhanced immune protection against VOC.
- There is an on-going debate about the duration for which the vaccines remain protective. Pre-print data from Israel shows waning immunity after 5 months from Pfizer vaccination, more pronounced among older adults. Israel has been offering boosters to people aged 60s and higher.
- Moderna has promising preliminary data on booster shot using spike protein of two variants of concern B.1.351. and P.1.
- Whether "booster" vaccination will confer improved protection due to unique antibody response targeting the mutated areas on the spike protein, due to overall raised levels of antibodies, or due to boosting immune memory response by another mechanism, is yet to be determined.
- Further complicating the discussion is the question of whether neutralizing antibody titers are a reliable marker of real-world protection against disease including B- and T-cell response. However, at least preliminary studies link real-world outcomes to antibody levels.
- Studies show that a robust T-cell response in COVID-19 patients is important for recovery and also provides cross-protection against subsequent infection with different variants.

Healthcare Policy for Combating Delta variant

- WHO released a statement of concern that mass offering of boosters in high-vaccine-access countries will further negatively impact equitable distribution of vaccines to poorer nations. WHO prioritizes extending global coverage with primary series; it emphasized that the pandemic cannot be put to an end unless it is tackled by a global strategy.
- WHO's guidance on heterologous priming of COVID vaccines states that if a two-dose vaccine series is inadvertently administered with different vaccine products, there is no need to administer any additional dose. It also states that though certain "mix and match" schedules provide higher neutralizing antibody titers and greater T-cell response in comparison to homologous priming, more data about safety and efficacy is needed before planning broad use.
- Studies of waning immune protection and breakthrough infections after mass vaccination with Pfizer product in early 2021 in Israel shed light on the duration vaccine-acquired immunity and implications for the current Delta crisis. Israel's government has been providing booster shots starting with oldest age groups now progressively lowering the threshold to younger people.
- FDA and CDC have issued new recommendations to administer a 3rd dose of vaccine to moderately to severely immunocompromised people including those with primary immunodeficiency, organ or recent bone marrow transplant, active cancer treatment, advanced or untreated HIV, or active treatment with high-dose steroids or biologic immunosuppressants.
- On August 18th DHHS and CDC leaders issued a joint statement regarding vaccination "boosters" for the general population, anticipated to be authorized in mid-late September for people who are at least 8 months out from completing their initial vaccine series.
- Staffing shortages in hard-hit areas are threatening availability and safety of care for patients with COVID-19 as well as those requiring acute care for other conditions. Nursing staff burnout is particularly high. Non-emergent procedures have been postponed in many areas for weeks now.
- FEMA has issued an advisory for medical staffing during this emergency and federal agencies are additionally mobilizing in response to Hurricane Ida which threatens to compound the health care crisis on the Gulf Coast.
- Current supply-chain shortages, including test kits, tocilizumab, and oxygen, can be tracked at: https://www.cidrap.umn.edu/covid-19/supply-chain-issues. Twenty-four (60%) of 40 critical COVID-19 drugs are currently listed in shortage.

GW Update: Additional vaccine doses (Pfizer) are available to individuals who meet current FDA and CDC recommendations at the GW COVID-19 Vaccine Clinic at 2300 M Street NW. Additional planning for staff vaccination is in progress, pending further federal guidance. Emphasis remains on completing primary vaccination targets for the GW community. Vaccination is mandatory for studying and working on GWU campus, hospital, and the Medical Faculty Associates.

This edition of the COVID-19 Intelligence Report was produced by Drs. Dhruvil Prajapati and Hana Akselrod with support from the Himmelfarb Librarian team and the entire GW Intelligence Unit led by Dr. Lawrence Deyton and Dr. Hana Akselrod.

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