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N/réf : LK/MS/PV

Geneva Centre for
Emerging Viral Diseases

Division of Infectious
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Medicine

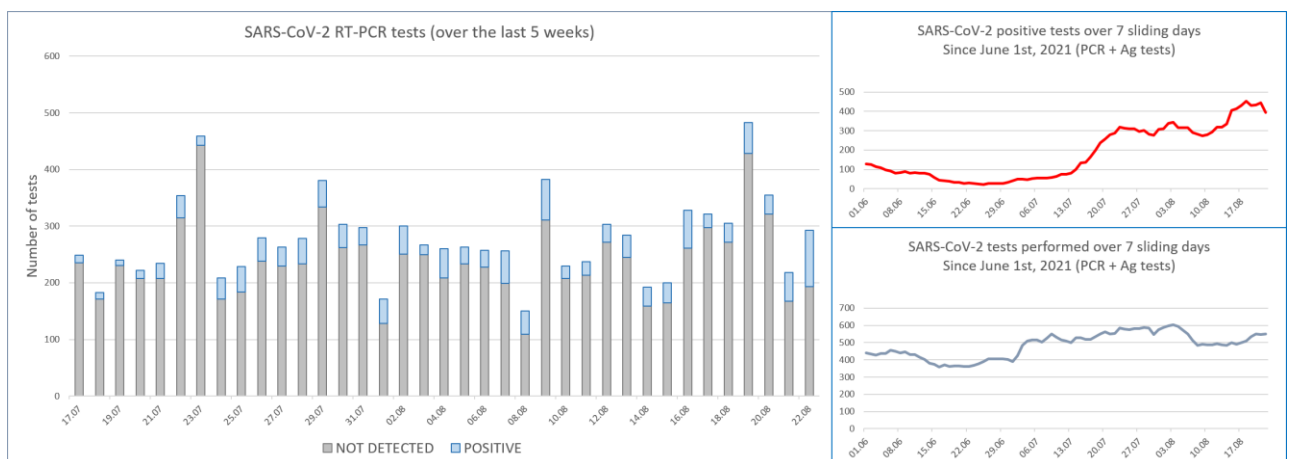
Diagnostic Department

SARS-CoV-2 genomic and variants surveillance in Geneva: weekly update
**With a focus on variants identified in hospitalized patients and post-
vaccination infections**

**The laboratory of virology of the Geneva University Hospitals as a sentinel site for the
Geneva area**

The number of tests (PCR and antigen tests) performed at the laboratory of virology of Geneva University Hospitals represents around 30% of the total number of tests performed in the canton of Geneva during week 32 and 33 (7331/25118). Roughly 40% of the positive specimens collected in the Geneva area were processed at HUG (N=801/1953) during weeks 32 and 33. Tests performed at our outpatient testing center (located in the Hospital but open to anyone from the community) are either PCR-based or antigen-based. Most symptomatic patients are screened by RT-PCR and all positive antigen-based tests are confirmed by PCR, allowing screening for variants.

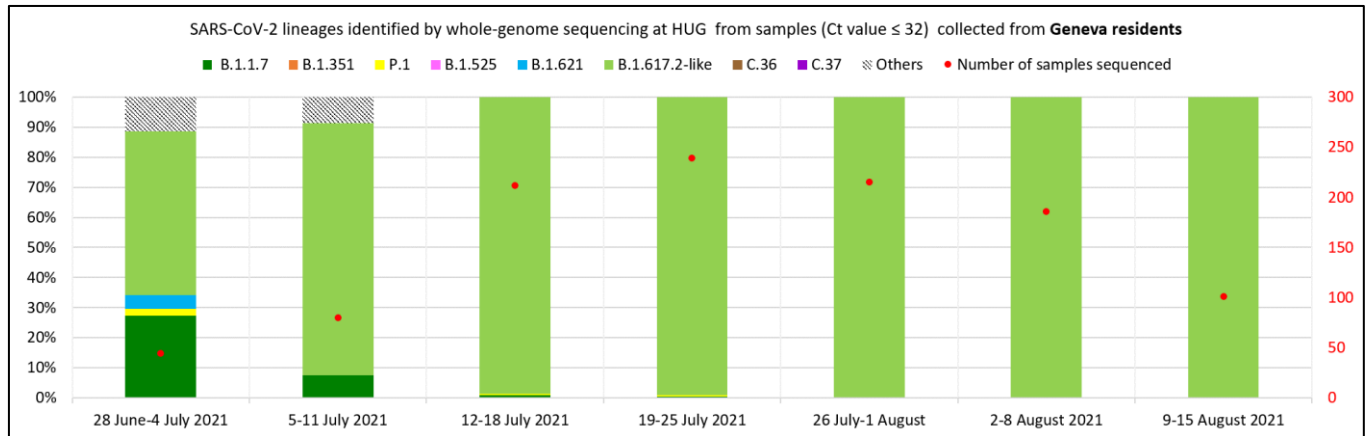
WGS is carried out in close collaboration with the Health 2030 Genome Center in Geneva and Philippe Le Mercier from the Swiss Institute of Bioinformatics. Since March 1, 2021, the sequencing has been done within the Swiss national SARS-CoV-2 genomic and variants surveillance program. All specimens with a Ct value ≤32 are sequenced. In some instances, sequencing can be done on specimens sent by other laboratories in Switzerland. Phylogenetic analysis data are produced by Nextstrain, in collaboration with Richard Neher's group at the University of Basel. The number of positive tests in the canton and the total number of tests done during the surveilled week come from the website of the Direction Générale de la Santé in Geneva (available at <https://infocovid.smc.unige.ch/>), accessed August 23, at 10:00 am.



The number of weekly positive cases diagnosed at HUG, as well as the mean positivity rate sharply increased over week 32 and 33 (mean positivity rate of 11%, compared to 8.5% the weeks before).

The mean positivity rate was on average 40% over the last week at the dedicated outpatient department (secteur E' – testing only symptomatic patients) for the 4th week in a row. It peaked above 50% twice during 2 consecutive days over week 32.

SARS-CoV-2 lineages identified by whole-genome sequencing at HUG from samples (Ct value ≤32) collected from Geneva residents

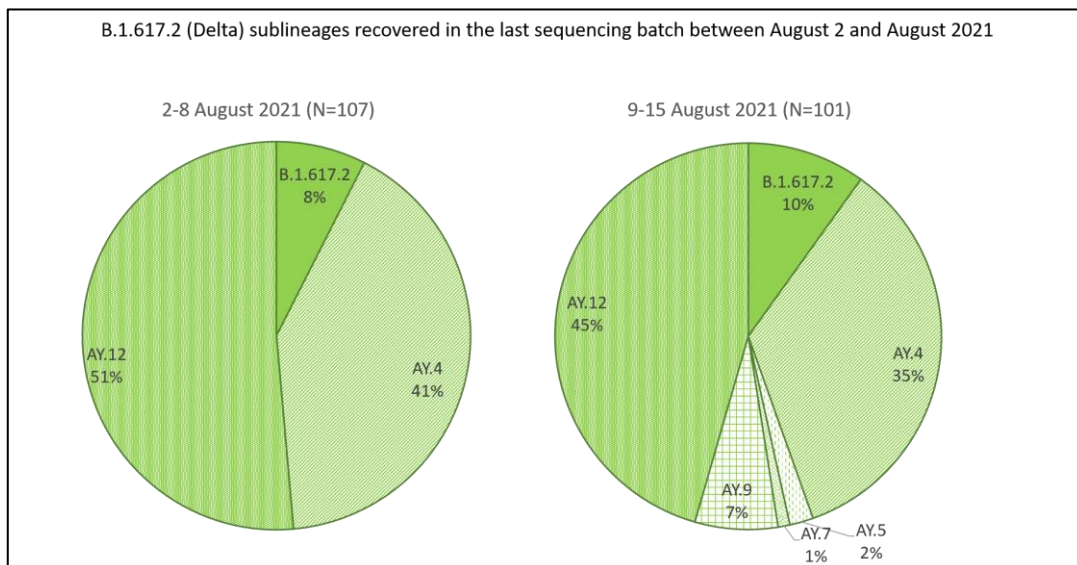


Results of WGS of 1077 sequences submitted to GISAID between June 21 and August 8, 2021.

All new retrieved sequences collected from Geneva residents are Delta or one of its sublineages for the third week in a row.

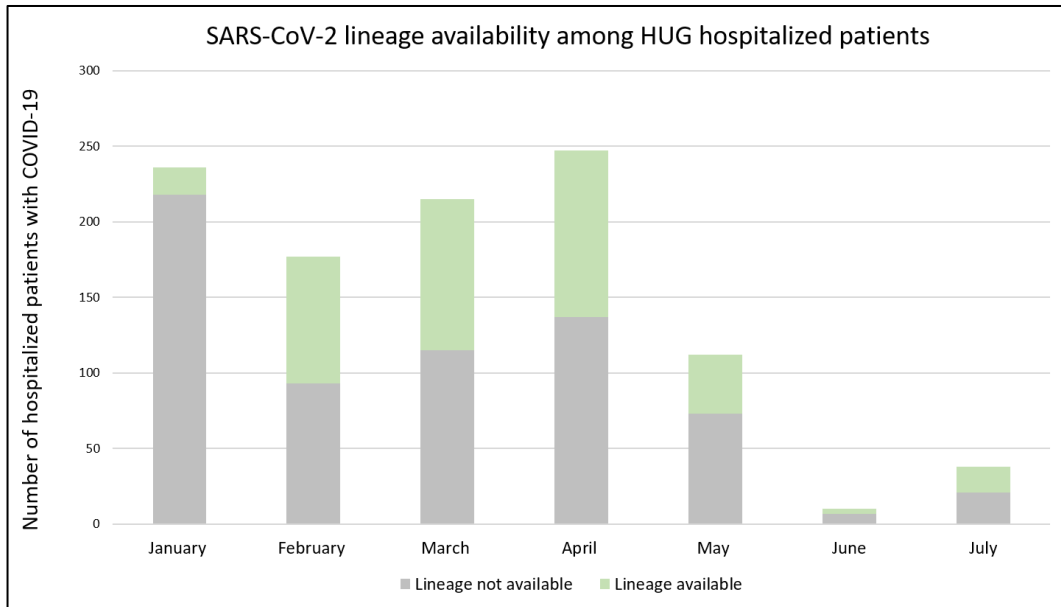
A variety of Delta sublineages has started to be observed among the last sequenced batch and are depicted below. No special issue regarding immune escape, clinical severity or diagnostics between Delta and its various sublineages has yet been identified, but only scarce data are yet available and more information will follow.

Note that AY.1, a Delta sub-lineage which caused a large cluster in early June in the Geneva area, has not been detected since the end of June. *In vitro* experimental data confirmed that the presence of the additional 417N mutation in this variant did not increase its ability to escape previous immunity (post-vaccination or natural immunity), compared to Delta. However, this mutation may have an impact in decreasing neutralization capacity of one monoclonal antibody authorized for SARS-CoV-2 treatment in Switzerland (casirivimab, included in the REGN-CoV-2), without any *in vitro* impact on the effect of the combination of the REGN-COV-2 cocktail imdevimab + casirivimab.

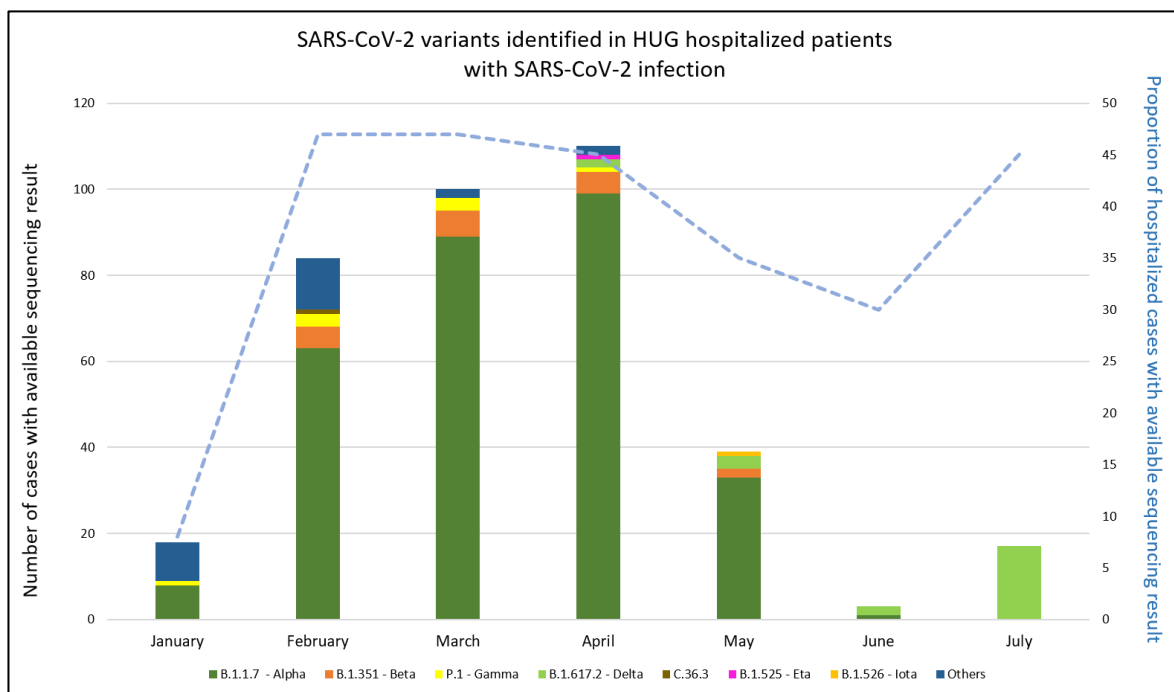


SARS-CoV-2 lineages identified by whole-genome sequencing in patients hospitalized at HUG from samples with Ct value ≤ 32 over the first 7 months of 2021

Both the number of hospitalizations and the sequencing results come from the FOPH CH-SUR database. (Acknowledgements A Iten)



Since February, 2021, a SARS-CoV-2 lineage has been obtained for between 30% and 45% of hospitalized patients with COVID-19 at HUG.



As expected, the most common identified variant in patients hospitalized each month follows the circulation of the variants in the community: Alpha was retrieved in 75% of hospitalized cases in February. This proportion increased over time to reach around 90% in March and April 2021 and started to decrease in May, when Alpha was progressively replaced by Delta.

Of note, Beta was identified in around 5% of the cases between February and April, 2021. A further in-depth analysis is required to assess risk factors for infection with the different variants.

Post-vaccination infections in the canton of Geneva

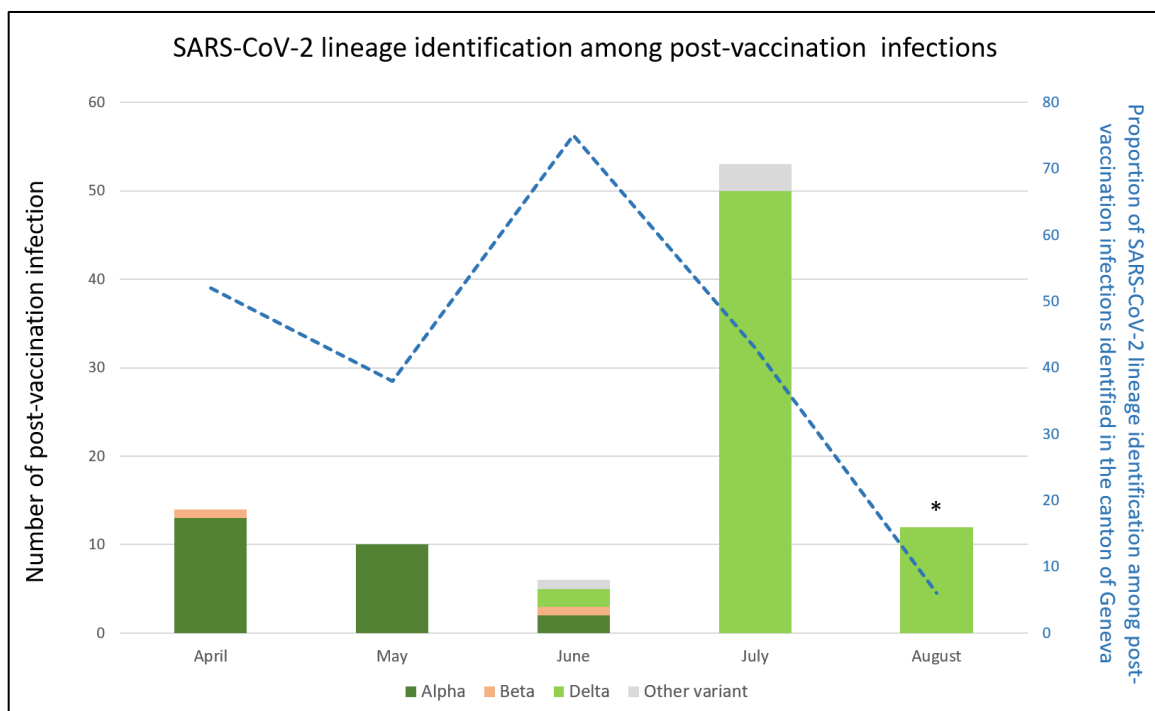
Post-vaccination infection is defined here as a positive SARS-CoV-2 test occurring more than 14 days after the second vaccine dose. This surveillance is done in collaboration with the Direction Générale de la Santé (DGS) of Geneva. Data are collected by the DGS of Geneva during contact tracing calls after having obtained informed consent from SARS-CoV-2 positive patients. The list of patients with post-vaccination infections is sent weekly to HUG virology laboratory, which makes an effort to retrieve initial diagnostic samples in order to ensure sequencing, as recommended by FOPH.

Among the 1029 and 1012 new COVID-19 cases reported by the Direction Générale de la Santé in Geneva respectively over week 32 and 33, 13% and 11% have been identified as post-vaccination infections for sequencing. For the third week in a row, post-vaccination infections are identified in 10 to 13% of the new COVID-19 cases. This number is expected given existing data regarding mRNA vaccine effectiveness against the Delta variant.

The epidemiology of the variants causing post-vaccination infections follows the local epidemiology of circulating SARS-CoV-2 variants.

During April and May 2020, Alpha was almost exclusively identified in post-vaccination infections. Among variants carrying the 484K mutation involved in vaccine immune escape, only Beta has been identified in post-vaccination infection in the canton of Geneva, although only very rarely.

Since June 2021, and the replacement of Alpha by Delta, Delta has been almost exclusively identified as causing post-vaccination infections.



*Incomplete data due to sequencing delay – only available for the first week of August.

A total of 419 post-vaccination infections have been identified in the Canton of Geneva among 4293 cases within the last 5 weeks. Over the same period of time, only 22 fully vaccinated patients have been hospitalized at HUG**. More than 40% of them only have mild disease and are hospitalized for another reason than severe COVID-19.

**Available data from the Geneva University Hospitals COVID-19 surveillance, available in detail in a separate report.

Conclusions

- The positivity rate among symptomatic outpatients tested at HUG remained high, around 40% on average over the last 3 weeks. This high positivity rate in this population is a signal that the virus is widely circulating in the community.
- WGS confirmed that it has almost exclusively been the B.1.617.2 (Delta) variant circulating in the Geneva area since mid-July. Of note, only Delta has been identified since the beginning of August.
- Most positive tests (88%) occurred in non-vaccinated individuals, and between 10 and 13% of SARS-CoV-2 cases were identified as breakthrough infections after vaccination during weeks 31 to 33 in the canton of Geneva. Those numbers are expected given existing data on mRNA vaccine effectiveness against infection by the Delta variant.
- The epidemiology of SARS-CoV-2 variants identified in post-vaccination infections has followed the local epidemiology of circulating SARS-CoV-2 variants since March 2021. Notably, the Beta variant carrying the 484K mutation involved in vaccine immune escape has only been very rarely identified.
- Similarly, since the beginning of the SARS-CoV-2 genomic surveillance program in January 2021, the most common identified variant in hospitalized patients has also followed the epidemiology of circulating variants in the community.
- The absolute number of hospitalized people at Geneva University Hospitals has continued to gradually increase since the beginning of July, 2021, reaching 54 as of August, 23, 2021. The vast majority are young (median age = 53) and not vaccinated.



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