

Delta variant B.1.617.2 lineage and AY sublineages

Background

In Luxembourg, where about 52% of the positive samples are sequenced, 2850 Delta cases have been identified by the Microbiology Department at the Laboratoire national de santé, as of 13 September 2021. As shown in Table 1, the parental lineage B.1.617.2 remains predominant (72,1%), followed by AY.5 (12,4%) and AY.4 (5,2%), while the remaining sublineages account individually for less than 5% of all Delta cases in the country. The appearance of AY sublineages raised questions, as whether these are new variants and what their impact might be. This scientific briefing aims to address these and other concerns regarding the Delta variant and its sublineages.

Table 1. Number of Delta cases sequenced worldwide and in Luxembourg

Lineage	Worldwide		Luxembourg	
	N	%	N	%
B.1.617.2	442 771	43.01%	2054	72.07%
AY.4	344 492	33.46%	149	5.23%
AY.12	42 604	4.14%	100	3.51%
AY.25	41 464	4.03%	5	0.18%
AY.9	28 679	2.79%	97	3.40%
AY.3	25 917	2.52%	4	0.14%
AY.5	25 295	2.46%	354	12.42%
AY.6	10 899	1.06%	0	0.00%
AY.20	10 058	0.98%	3	0.11%
AY.7.1	10 026	0.97%	14	0.49%
AY.23	8188	0.80%	1	0.04%
AY.10	6245	0.61%	39	1.37%
Other AY	32 881	3.19%	30	1.05%
Total	1 029 519	100%	2850	100%

Sources: outbreak.info (worldwide, accessed 13 September 2021) and internal (Luxembourg, updated 13 September 2021).

History and geographical distribution of Delta variant

The Delta variant, as B.1.617.2, was first identified in 2020 in India. After observation of its spread in India, suggesting higher transmission and severity in comparison to previous variants, B.1.617.2 was designated firstly as variant of interest (VOI) on 4 April 2021 and finally as variant of concern (VOC) on 11 May 2021. Since then, the Delta variant has been detected in 170 countries across all continents¹.

During August 2021, the Phylogenetic Assignment of Named Global Outbreak Lineages (PANGOLIN) software used for assigning SARS-CoV-2 lineages underwent several updates to introduce new sublineages of the parental B.1.617.2 lineage: from AY.1 up to AY.25^{2,3}. Most of these sublineages are not new: although some have only been identified as of July 2021 (e.g. AY.17), the oldest ones can be traced back to 2020 (e.g. AY.12)⁴. However, many of them used to be classified as B.1.617.2, given the limited amount of differences in their genetic code⁵, and despite this new distinction, they remain part of the Delta variant group⁶.

The reason for the introduction of these sublineages is that they show distinct geographical distributions. The increased precision of assigning Delta variant by sublineages enables a more detailed tracking of the virus². This is especially relevant for places where the Delta variant is the dominant one, where distinguishing among different Delta variant subtypes may help identify clusters, trace their source and reveal the transmission chain.

According to sequences uploaded to the GISAID database, a global platform for sharing genomic data, at least 862 966 Delta cases have been found as of 6 September 2021 (Table 1)⁷. Although this figure is certainly underestimated, since a part of COVID-19 cases are not sequenced or even detected, the relative importance of the different variants and sublineages remains valid. The parental lineage B.1.617.2 is the most frequent one (50,9%), followed by its sublineages AY.4 (28,8%) and AY.12 (4,8%). The remaining sublineages account individually for less than 4% of all registered Delta cases worldwide.

Genotypic characteristics

The defining mutations of the Delta variant are T19R, L452R, T478K, P681R and D950N to the spike protein plus 7 additional mutations to other proteins (membrane, nucleocapsid, ORF3a and ORF7a)⁸. Specifically, P681R mutation is suspected to be responsible for the enhanced virus replication in Delta cases, compared to Alpha variant⁹. In addition to that, further mutations define each of the AY sublineages, as displayed in Figure 1.



Figure 1. Mutation prevalence to the spike (upper), ORF1a (lower-left) and ORF1b (lower-right) proteins in most frequent Delta lineages and other variants of concern. Adapted from outbreak.info (Lineage Comparison, accessed on 6 September 2021).

Phenotypic characteristics

Transmissibility, severity (virulence) and impact on immunity, diagnostic and treatments are the main factors analysed regarding variants of concern. Changes in clinical presentation or decreased effectiveness of public health and social measures are also relevant.

With respect to the Delta variant, the following findings determine its status as variant of concern:

- Transmissibility. It is known to be increased in comparison to previous variants (both non-VOC/VOI and Alpha variants), which causes Delta cases to infect more people on average (higher secondary attack rate)¹⁰⁻¹². This is partly due to a higher viral load and a shorter incubation period with delta Variant^{13,14}.
- Severity. Higher risk of hospitalisation has been observed among Delta cases, showing a directly proportional relation with age^{11,12,15}.
- Impact on immunity. There is still limited evidence in this regard, but a reduction of neutralising activity of 10-30% has already been reported both in vaccinated people^{11,12} and previously infected people¹², which increases the risk for breakthrough infections and reinfections. Nevertheless, it has been observed that vaccinated people retain high levels of protection against severe disease¹².

Regarding a potential impact on diagnostic techniques, no finding has been reported to date¹².

The evidence presented above has been analysed so far regardless of Delta sublineages, which have only recently been defined and can now be analysed separately. Nonetheless, given the broad correspondence between AY sublineages and B.1.617.2 parental lineage in mutations to the spike protein, a similar behaviour is to be expected.

In conclusion, the evidence available to date shows that Delta variant increases the risk of transmission and severe disease, but protection from vaccination remains high, especially against severe disease. Hence, vaccination of all population should be further encouraged and public health and social measures, including wearing masks in public indoor places, should be maintained.

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