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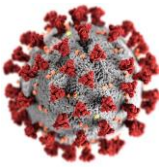
COVID-19 Variants

SARS-CoV-2, the virus causing the disease COVID-19, remains a focus of research and analysis. Emerging strains may present future public health and health care challenges.

Changes in SARS-CoV-2



SARS-CoV-2
www.cdc.gov

Since 2020 when COVID-19 was first recognized, the causal virus SARS-CoV-2 has evolved considerably. Frequent mutation and rapid evolution are hallmarks of single-stranded RNA viruses. Epidemiologists use these changes to track infectious disease dynamics at highly localized scales (such as setting-specific outbreaks) or at broad geographic scales (such as exploring global patterns of disease circulation).

SARS-CoV-2 evolves mainly through clonal evolution, a process in which a mutation in a parental strain is inherited by a child strain, and additional mutations accrue on top of the mutational backdrop of the earlier strain. Related viruses will have mutations in common, and the similarity of their genome sequences is a proxy for how closely they are related. “Clades” or “lineages” are terms describing a group sharing one or more mutations. Lineages are then defined by which mutation(s) is shared between all strains in the lineage. Talking about viral sequences in terms of lineages can be a helpful communication aid since it abstracts the actual nucleotide sequence to a shorthand label that can easily be tracked alongside epidemiological data.

The lineage of a SARS-CoV-2 virus is determined through whole genome sequencing of the virus from diagnostic specimens. The newly-generated sequence is compared with other sequences from around the world to determine shared mutations and therefore the lineage of the new sequence. If the particular constellation of mutations in a new sequence has not been observed previously, a new lineage can be proposed to define the new genotype. Over the course of the pandemic there have been numerous different lineages defined, some of which have spread widely and become dominant while most have faded and been replaced by other strains.

Washington State Department of HEALTH

Scott Lindquist, MD, MPH
State Epidemiologist,
Communicable Disease

Marcia J. Goldoft, MD
Scientific Editor

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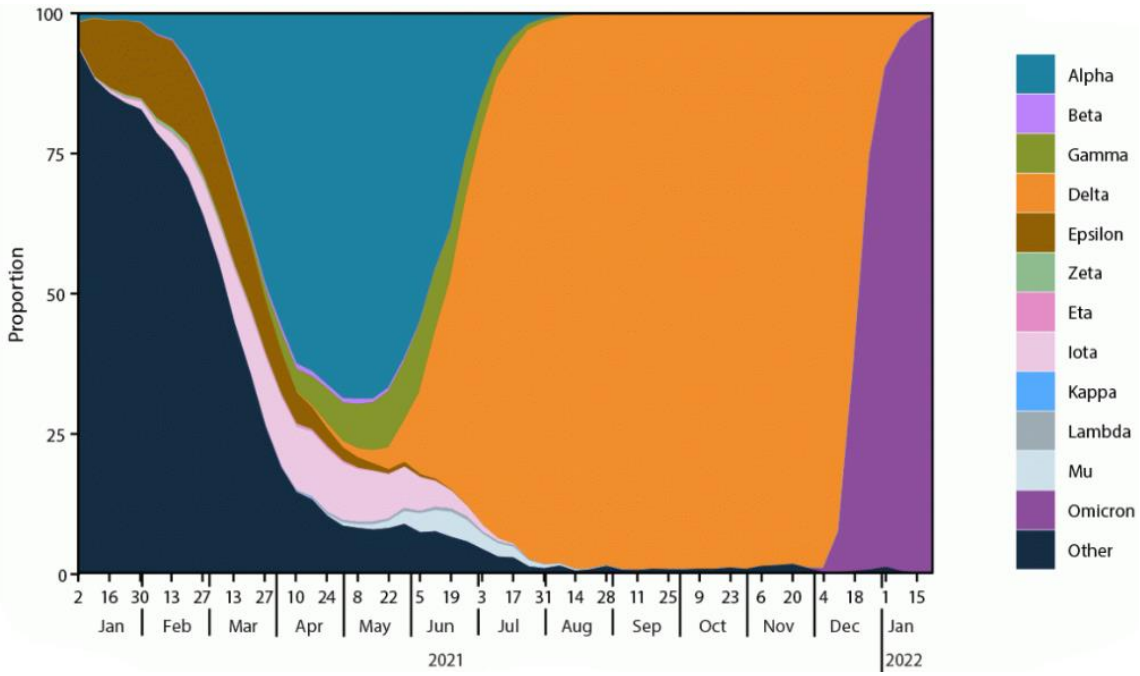
There are various systems for naming SARS-CoV-2 lineages. Providing the highest level of granularity, and leading to the greatest number of distinct lineages, is the Pango lineage system. The Pango system was proposed early in the SARS-CoV-2 pandemic and was one of the first widely adopted, standardized nomenclature systems. Pango lineage names follow a nested format of <letter>.<number> (e.g. B.1), and indicate relationships between lineages with a nested pattern in the nomenclature system itself. For example, B.1.1 would be a lineage of viruses sharing additional mutations on top of the B.1 genome backdrop. The WHO system for designating lineages based on the Greek alphabet was widely used between January 2021 (when Alpha was dominant) until November 2021 (when Omicron emerged). The high genetic diversity of Omicron-lineage viruses has prompted a return to general use of Pango lineage nomenclature (e.g. BA.1, BA.4, XBB.1.5).

Surveillance for SARS-CoV-2 Variants

Surveillance during 2021 demonstrated the arrival and disappearance of variants. In early May, the Alpha variant dominated but was rapidly replaced by Delta. In turn, Omicron displaced Delta with incredible rapidity, going from initial detection to dominance in roughly three weeks. Gamma and Iota each had a period of increase but then diminished while Kappa and Lambda did not achieve a high proportion of infections (Figure 1). The initial appearance of Omicron resulted in the highest number of COVID-19 hospital admissions during the entire pandemic.

Figure 1. National weekly proportion estimates of SARS-CoV-2 variants – United States, January, 2021-January 22, 2022

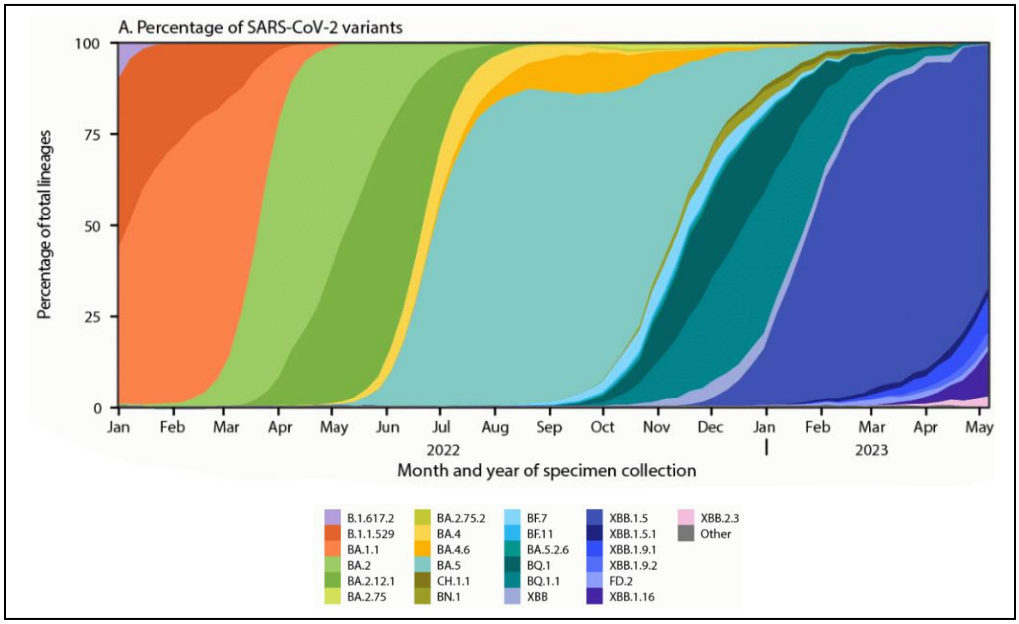


https://www.cdc.gov/mmwr/volumes/71/wr/mm7106a4.htm#F1_down

During 2022, surveillance identified numerous genetically diverse Omicron lineages that emerged and faded out sequentially, displaced by newer lineages. Many of the emerging variants appeared to increase due to slightly improved abilities to evade immunity derived from previous natural

infections or from vaccinations. The ability of virus to evade human immunity, resulting in individuals having repeat infections, will likely continue to shape lineage turnover dynamics. This dynamic occurs in other infections as well, most notably influenza A, and is the reason vaccines must be regularly updated for pathogens such as SARS-CoV-2 and influenza.

Figure 2. National estimates of weekly proportion estimates of SARS-CoV-2 variants – United States, January 2, 2022-May 13, 2023

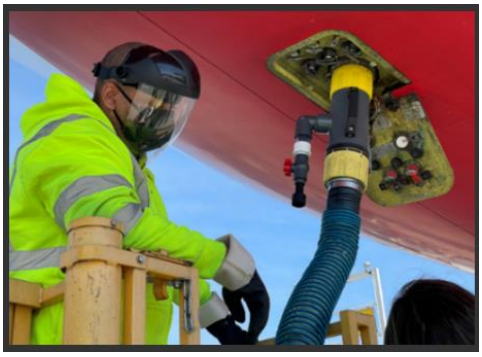


The Future of SARS-CoV-2

Variant naming systems provide a simple way to summarize which mutations are characteristic of a particular viral genotype. Special attention is needed when mutations confer a noticeable functional change to the virus, such as increasing the virus' inherent transmissibility; causing more severe disease; increasing the virus' ability to evade immunity generated from previous illness or vaccines, or decreasing the effectiveness of existing therapeutics and diagnostic tests. Agencies in the United States including Centers for Disease Control and Prevention, National Institutes of Health, Food and Drug administration, Biomedical Advanced Research and Development Authority (BARDA), and Department of Defense (DoD) identify certain SARS-CoV-2 strains as Variants of Concern based on genomic sequencing results combined with phenotypic data.

National viral surveillance is intended to collect, analyze, and share information about the genetic diversity of SARS-COV-2. Sources of viruses include clinical diagnostic laboratories, state and local health public health laboratories, universities, and published data from other countries. With greater availability of home testing as the pandemic progressed, fewer diagnostic specimens are available for sequencing. This trend means there is less data now for tracking variants through genomic surveillance than earlier in the pandemic, and the surveillance system will likely be slower to detect the presence of a new circulating variant. Emerging variants will also likely need to rise to a higher frequency to be detected. Viral genomic sequence data has significant utility beyond variant surveillance, and targeted sequencing efforts during outbreaks can continue to help detect, characterize, and mitigate transmission.

Another source of information about variants is surveillance through arriving air travelers to provide a more global perspective. The Traveler-Based Genomic Surveillance Program (TGS) takes respiratory samples from international travelers arriving at a number of major airports in the United States, including SeaTac Airport in Washington State. Travelers who volunteer to participate take a short survey and are swabbed, with specimens forwarded without identifiers for testing. These data provide information about what variants appear to circulate in areas the traveler recently visited, and can help resolve the dynamics of new variant introductions. In addition, at some sites airplane wastewater is being tested for SARS-CoV-2. The results of TGS activities can provide an early warning on a global basis of new SARS-CoV-2 variants that may emerge.



Collecting wastewater from an airplane for TGS
www.cdc.gov

Department of Health maintains a directory of testing sites as a resource for the public. Local health jurisdictions can also check the Department of Health variant surveillance update for the most recent data (see Resources below). Maintaining awareness of circulating SARS-CoV-2 variants can assist with planning and response to the ongoing COVID-19 outbreak.

Resources

Variant surveillance, CDC:
https://www.cdc.gov/coronavirus/2019-ncov/variants/cdc-role-surveillance.html

SARS-CoV-2 Variant Classifications and Definitions, CDC:
https://www.cdc.gov/coronavirus/2019-ncov/variants/variant-classifications.html

Genomic surveillance (figures):
https://www.cdc.gov/mmwr/volumes/71/wr/mm7106a4.htm
https://www.cdc.gov/mmwr/volumes/72/wr/mm7224a2.htm

Traveler-based surveillance: https://wwwnc.cdc.gov/travel/page/travel-genomic-surveillance

COVID-19 variant surveillance, Washington State Department of Health
COVID-19 testing: https://doh.wa.gov/emergencies/covid-19/testing-covid-19
Background on variants: https://doh.wa.gov/emergencies/covid-19/variants
Update: https://doh.wa.gov/sites/default/files/2022-02/420-316-SequencingAndVariantsReport.pdf

Detailed information about variant naming and surveillance

Proposal for nomenclature, *Nature* 2020: https://www.nature.com/articles/s41564-020-0770-5

Pango lineages: https://cov-lineages.org/

Scripps Research information on lineage-defining mutations and global prevalence of lineages:
https://outbreak.info/

University of Bern and Swiss Institute of Bioinformatics on variants: https://covariants.org/