

# **Emerging Infections Newsletter for Clinicians**

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## The Tripledemic

- Although JN.1 remains dominant, several new offshoots are showing up.
- Test positivity for SARS-CoV-2 within Sutter is at the lowest level since we started weekly reporting April 2023.
- The CDC decreased the required isolation for COVID in non-healthcare settings.
- Circulating influenza continues to transition from predominantly A H1N1 to all three strains (A H1N1, A H3N2 and B). The flu season will continue a little longer because of this.
- RSV season is almost below the 3% threshold that defines the outbreak.
- Common cold viruses are being increasingly identified in California.
- This is wonderful news. However, in healthcare and public health, we have to prepare for the next season.
  - <u>Among deaths from COVID-19</u> occurring from Jan.–Sept. 2023, 88% were among people ≥65 year. The additional monovalent COVID vaccine was recently recommended by the CDC for all persons ≥ 65 years old and at least 4 months from their last dose to address waning immunity. New safer, more effective treatments are being investigated.
  - Influenza vaccine for the 2024-25 Northern Hemisphere season was just announced by the WHO. The strain selected for A H3N2 is being changed. The vaccine is going back to trivalent since the B Yamagata appears to be extinct. Influenza resistance to available treatments continues to be monitored. Although levels of resistance remain low, the therapeutic options require early initiation to be effective and home testing, similar to what is available for COVID, might become available. New medications are being tested.
  - RSV season has also been a little less predictable. Because of that and the extended duration of effectiveness being demonstrated by the vaccine, immunization of persons 60 years and older should be considered year-round, especially in persons at increased risk of severe disease. It will not be surprising to see these recommendations extend to persons 50-59 years old.

## <u>COVID-19</u>

- JN.1 remains the most dominant strain in the world, but it is likely past the peak. Several new subvariants including JN.1.13 and JN.1.18 are being identified more frequently. The impact of these new subvariants is still being evaluated.
- <u>Hospitalizations</u> in the United States are a surrogate for the virulence of the circulating strain. The graph below has been modified to make it easier to see trends from the last 18 months. As before, the blue vertical bars represent the number of hospitalizations per week and the orange run line demonstrates the percentage of patients being diagnosed with COVID in emergency departments.
- Looking at the trend of the blue bars, the recent drop in hospitalization rates remains similar to one year ago. However, there remains a very significant difference in the number of patients hospitalized due to circulating variants this year versus last year.
- The week of Feb. 24, 2024 resulted in 17,310 hospitalizations (red arrow) compared to 24,080 during the week ending Feb. 25, 2023 (purple arrow). Hospitalizations are 28% less year over year. Over 6,700 less people in the hospital during this week in 2024 compared to 2023. Emergency room positivity rates were about the same during that 1-year comparison.



COVID-19 New Hospital Admissions and Percentage of Emergency Department (ED) Visits Diagnosed as COVID-19, by Week, in The United States, Reported to CDC

• The CDC tracks hospital admissions per 100,000 county population. Less than 10/100,000 is considered a low number of new hospital admissions. National rates have continued to decline and are down to 5.72/100,000. The table below shows the most recent weekly hospitalizations. The number dropped another 10.3%.



 <u>National genomic sequencing</u> was updated on March 1. Although JN.1 is still overwhelmingly dominant at 92%, that is down from 96% 2 weeks ago. New subvariants of JN.1 are now being displayed. These include JN.1.13 and JN.1.18.

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1	Unicron JN.1	92.3%	90.5-93.8%	
	JN.1.18	1.8%	1.1-2.9%	

- Surveillance of international air travelers is conducted at several major U.S. airports as an early warning system and to fill gaps in worldwide genomic surveillance. It covers flights from more than 135 countries.
  - Traveler-based genomic surveillance positivity rates are on the graph below. Positivity rates for the latest week reported (ending Feb. 15) dropped to 15.3%. This is the lowest positivity rate since the week ending Nov. 1, 2023. Remember that international testing data is at least 2 weeks from collection until reported on the graph.
  - Notably, JN.1 identification has decreased from 94% to 88% (data not shown).



• The map below shows <u>national</u> molecular test positivity rates by region (updated Feb. 23). Region 4 is the last part of the country that is not green (<10%). Yellow means a positivity rate of 10-14.9%. Region 4 rates increased a little in the last week, going from 10.8% to 11.7%.



• SARS-Co-V-2 wastewater levels are shown on the two <u>CDC</u> maps below. The top map was reported Jan. 22 and the bottom March 1. Similar to hospitalizations and testing positivity, wastewater levels have progressively decreased since JN.1 became the dominant strain. Grey represents insufficient data.



• Updated Sutter testing data below show a continued decline in positivity rates in both the ambulatory and acute ED settings. Acute is down to 6.1% and ambulatory is 7.2%. These are the lowest numbers since tracking was started April 2023.





 COVID test positivity rates in persons greater than 60 years old are being pulled out to analyze. Rates in this elevated risk age group remain higher than the total cohort of all ages.



#### CDC relaxed public isolation guidance

- As anticipated, the <u>CDC</u> released new respiratory virus guidance on March 1 that encompasses COVID. This excellent report outlines and discusses the evidence that underlies the new recommendations.
- COVID persists year-round with some peaks and valleys, but hospitalizations, deaths and other complications of severe disease are less common. Immunity from prior infection and/or vaccines, masking, improved social behaviors (such as covering the cough and hand hygiene), plus available treatments have lessened the severity and impact of circulating strains.
- Similar to what was released by CDPH in January, this guidance does not apply to healthcare settings.
- Persons with respiratory virus symptoms, including COVID, should isolate until at least 24 hours after fevers have resolved without fever reducing medications, and the overall symptoms are improving.

#### **COVID-19 Take-Home:**

- JN.1 dominance has probably peaked. Vigilance remains necessary as the new strains start to appear.
- Hospitalizations and emergency room visits are much lower now compared to the identical week 1 year ago. This has to do with immunity, vaccines, available treatments and some changes in social behavior.
- All persons aged ≥ 6 months should stay up to date with COVID-19 vaccinations, including receiving an XBB monovalent vaccine this year.
- Persons 65 years and older are recommended to obtain another dose of the recent monovalent vaccine at least 4 months from the first dose of that vaccine.

#### **Related Links**

- <u>CDC Caring for Patients</u>
- <u>CDC Data Tracker</u>
- CDC Latest Updates
- <u>CDC Vaccine Information</u>
- CDPH Tracking and Vaccination Updates
- <u>Sutter Health for Clinicians</u>
- <u>Sutter Health for Patients</u>
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### <u>RSV</u>

 <u>CDPH</u> reports RSV data weekly during the season. The CDPH graph below demonstrates the current California RSV season (blue arrow) compared to other seasons since 2018. RSV rates are still elevated, but they are progressively decreasing and are down to 3.5% during calendar week 8 of 2024. The <u>CDC</u> in April 2023 published a report on the seasonality of RSV over 7 years. They used ≥3% as the threshold for an RSV outbreak.



Figure 12. Percentage of RSV Detections at Clinical Sentinel Laboratories, 2018-2024 Season to Date

 RSV identification rates continue to decrease. They are down to 2.6% in Sutter emergency departments but higher at 3.9% in ambulatory. See two graphs below. The emergency departments are testing more than twice the number of patients compared to the ambulatory setting and the average throughout Sutter is right at the 3.0% breakpoint.

• RSV was detected in the ambulatory settings starting the middle of August. The curve in the acute settings was not as broad.





#### **RSV Take-Home:**

- The RSV season is very close to the end in California.
- This 2023-24 season saw ambulatory positivity rates exceed 3% in the middle of August, but ED acute rates did not cross that threshold until the middle of October.
- With appropriate use of nirsevimab and the RSV vaccines for persons ≥ 60 years and during pregnancy, we can dramatically alter the threat of RSV.
- Based on new data submitted to the FDA, at least 1 RSV vaccine may also be approved for persons 50-59 years old who are at increased risk of severe RSV disease before the 2024 season starts.

#### <u>Influenza</u>

- The biweekly <u>WHO</u> influenza update was released on March 4. It includes data up to Feb. 18. Overall influenza activity In the Northern Hemisphere is decreasing. Southern Hemisphere influenza remains at inter-seasonal levels.
- The weekly <u>CDC</u> Influenza Surveillance Report was released on Feb. 23.

- Influenza B continues to be identified in a larger percentage of isolates, now up to 39% in clinical labs compared to 21% reported by the <u>CDC</u> in their Jan. 19 report.
- AH3N2 continues towards overtaking A H1N1. A H3N2 now represents 49% of subtyped influenza A isolates.
- Influenza-like illness (ILI), the surrogate for influenza used by the <u>CDC</u>, is represented by the two maps below. This shows the difference over the last 2 reported weeks. The first has data for the week ending Feb. 17 and the second has data ending Feb. 24.
- Notice the color difference between the states on the two maps. This shows variation between states and regions. California has moved from minimal to moderate between the 2 weeks. Some of these dramatic changes may be due to variations between when data is sent to the CDC. There are still substantial parts of the country where ILI is still quite high. Remember that this does not measure influenza but measures fever plus either sore throat or cough.



2023-24 Influenza Season Week 8 ending Feb 24, 2024



• The <u>CDPH</u> map below of influenza (last updated through Feb. 24) shows that influenza rates remain low everywhere. The state influenza positivity rate decreased from 6.8% to 5.7% over the last 2 weeks.



Influenza Activity Levels<sup>+</sup>

CDPH Influenza Activity Levels:

Minimal: The percentage of positive specimens is <2%</li>
Low: The percentage of positive specimens is 2 - <10%</li>
Moderate: The percentage of positive specimens is 10 - <20%</li>

The <u>CDPH graph</u> below demonstrates that present influenza activity continues to drop (blue arrow).





- The graphs below show Sutter emergency department and ambulatory influenza positivity rates. In the acute setting (emergency departments), positivity rates decreased to 5.0% in the last week. Although the ambulatory setting rates are improving, they are still 8.2%.
- Ambulatory testing is a little higher than state rates. These are clearly different patient populations. Within Sutter, weekly acute testing is performed almost three times as often as ambulatory.







#### Influenza resistance to neuraminidases

The CDC monitors for influenza virus resistance to neuraminidase inhibitors (oseltamivir, peramivir and zanamivir) as well as baloxavir (the only PA Cap-dependent endonuclease inhibitor). Very small amounts of decreased susceptibility are being identified. See table below. Out of the 2 A H1N1 isolates identified with reduced susceptibility, one had highly reduced inhibition to both oseltamivir and peramivir.

Antivirals	# positive/# tested. %			
	A H1N1	A H3N2	В	
Oseltamivir	2/2229 (0.8%)	All sensitive	All sensitive	
Peramivir	1/2229 (0.4%)			
Zanamivir	All sensitive			
Baloxavir	All sensitive	1/972 (0.2%)		

#### 2024-25 Northern Hemisphere flu vaccine

- Influenza vaccines are reverting back to trivalent. The wild-type B Yamagata lineage has not been confirmed in the world since April 2020. <u>Eurosuveillance</u> Sept. 2022 published a letter suggesting that influenza B Yamagata may have become extinct.
- The very small number of flu B Yamagata found later in 2020 may have resulted after administration of the live attenuated vaccine. In addition, the table below, from that same article, shows that B Yamagata was already on the decline in 2019 (red arrow) before COVID.

Influenza B/Yamagata virus haemagglutinin segment sequences by year of specimen collection, GISAID database, 1 January 2017-29 August 2022 (n = 12,559)

Year	B/Yamagata	Number of countries	Countries (number of sequences)	
2017	4,888	121	Too many to list	
2018	6,564	133	Too many to list	
2019	988	74	Too many to list	
2020	119	14	United States (75), France (10), Tunisia (8), Norway (6), Russia (5), Chile (4), Trinidad and Tobago (3), Australia (2), Germany (1), Honduras (1), Jamaica (1), Japan (1), South Korea (1), Spain (1)	
2021	0	0	NA	
2022	0	0	NA	

- For the last 3 years, discussions have been held by the WHO, CDC and European CDC about eliminating B. Yamagata from the annual influenza vaccinations.
- The <u>WHO</u> on Feb. 23 voted on the recommendation for the 2024-25 Northern Hemisphere flu vaccine. It will be trivalent. A H1N1 and B Victoria are unchanged but A H3N2 has an updated strain in all vaccines. The A H1N1 and A H3N2 lineages are slightly different in the egg-based vaccines versus the cell culture or recombinant vaccines. This is required because of immunogenicity differences in the production methodologies. Influenza B Victoria strains are all identical.
- The <u>NEJM</u> Feb. 28 published a historical and explanatory perspective on this change. This
  article importantly pointed out that if B Yamagata does return, it likely will be antigenically
  dissimilar to the 2013 strain used until this time. Converting to only a single influenza B
  strain also raises the possibility of including two A H3N2 strains in future vaccines. This,
  however, would require multiple additional studies before that suggestion could be
  implemented.

#### Take-Home Influenza:

 Influenza B now represents almost 40% of all influenza isolates. Out of the 60% influenza A, A H3N2 is now being found almost as much as A H1N1. ILI and positivity rates remain significantly elevated in parts of the country, especially east of the Mississippi. Because of the transition from predominantly A H1N1 to all three types of influenza circulating, the season is anticipated to continue at elevated levels.

- The influenza vaccine is a good match to circulating strains. Vaccination of everyone 6 months and older should continue to be recommended.
- The influenza vaccine for the 2024-25 season will be a trivalent vaccine.

## **Other Respiratory Viruses**

- As we develop new diagnostic tools, we need to continue to consider lab stewardship. Multiplex molecular infectious disease panels are quick and can reliably help determine the etiology of a number of different infections in groups of patients. They are expensive for the patient and a large use of valuable resources. Before ordering the test, the stewardship question should always be considered. What will be the action from test results?
- <u>CDPH</u> tracks respiratory viruses beyond SARS-CoV-2, influenza and RSV. They started reporting again last October. SARS-CoV-2 (yellow run line), included in the graph below, has reached a low-level plateau.
- Enterovirus/Rhinovirus (green arrow) remains the one most commonly identified as a percentage of positive tests. Over 20% of tests have been positive for the last 4 weeks. The common human Coronavirus (orange arrow) is also being reported more frequently than SARS-CoV-2 (yellow arrow).



- Over 30% of these panels are demonstrating a "common cold" pathogen. Are changes made based on these results?
- The <u>CDC</u> writes "*it is rarely possible to determine the type of virus without testing, and often times testing does not change clinical management.*"

#### Take-Home Other Respiratory Viruses:

- "Common cold" respiratory viruses now comprise 30% of isolates. COVID, RSV and influenza are decreasing.
- Testing patients with symptoms of a common cold can be an unnecessary, expensive use of laboratory resources.
- Use of a narrower panel that includes SARS-CoV-2, influenza and RSV (based on age) is much more cost-effective. Broader panels frequently identify additional viruses that neither affect treatment nor prognosis.

#### Frequency of Newsletter

Now that we are at the end of the tripledemic for this season, the newsletter is going to be decreased from weekly to every other week.