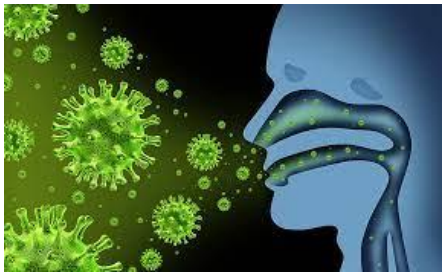


Sent on behalf of William Isenberg, M.D., Ph.D., Chief Medical & Quality Officer, Sutter Health, and Jeffrey Silvers, M.D., Medical Director of Pharmacy and Infection Control, Sutter Health

Emerging Infections Newsletter for Clinicians

May 24, 2023

Written by Dr. Silvers with contributions from Dr. Joan Etzell (Lab), Lisa Rieg (Pharmacy), and Gordon Sproul (Pharmacy). Please use Google Chrome for the best experience.

Topics

1. Eye Drops, Extensively Drug-Resistant Pseudomonas Aeruginosa (EDRPA) and Four Deaths
    a. Available without a prescription doesn't mean no risk
2. COVID-19
    a. IDSA updates treatment guideline
    b. Fall vaccine might be a monovalent XBB vaccine
    c. U.S. sequence data
3. Influenza
    a. WHO update
4. RSV
    a. First vaccine close to approval to be administered during pregnancy to protect infants
5. Mpox
    a. Outbreak update
    b. Jynneos vaccine
    c. Tecovirimat
        i. Low barrier to resistance
        ii. When to use
    d. Vaccinate
6. Sexually Transmitted Infections (STI)
    a. Updated collection and testing changes for some STI
7. Share the newsletter

Contaminated Eye Drops

- Feb. 2, the FDA warned consumers and healthcare practitioners to immediately discontinue purchase and usage of unexpired EzriCare Artificial Tears and Delsam Pharma's Artificial Tears due to potential bacterial contamination.
    - These are preservative-free products.
- Feb. 21, this was expanded to include Delsam Pharma's Artificial Eye Ointment.
- The organism identified is an extensively drug-resistant Pseudomonas aeruginosa.

- Most P. aeruginosa carbapenem-resistance is mediated by chromosomal substitutions resulting in porin changes and overexpression of the efflux pump. Genes for carbapenemases are less common.
- This P. aeruginosa actually produces two different carbapenemases from different Ambler Classes.
  - These include VIM metallo-β-lactamase (Ambler Class B) and GES β-lactamase (Ambler Class A).
  - Carbapenemases from different Ambler classes limit treatment options even more.
- The isolates are resistant to cefepime, ceftazidime, piperacillin-tazobactam (Zosyn™), aztreonam, carbapenems, ceftazidime-avibactam (Avycaz™), ceftolozane-tazobactam (Zerbaxa™), fluoroquinolones, polymyxins, amikacin, gentamicin and tobramycin.

- As of May 15, 81 patients in 18 states, including California, have been identified.
- In addition to eye cultures, isolates have been identified in sputum, bronchial washes, tracheal aspirates, blood, urine, ear and other non-sterile sites.
- Reported outcomes within 30 days of isolation of the organisms have included 18 patients with vision loss including four that required enucleation and four deaths.
- Most patients reported use of artificial tears with the brands mentioned above.
- Some cases have been identified secondary to nosocomial transmission in long-term care facilities.
- Bacteriophage treatment may be available through UCSD or Yale University.

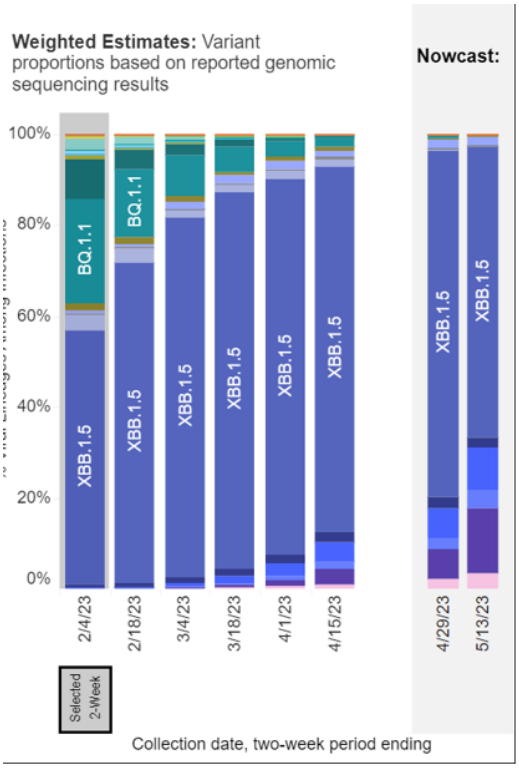
- **Take-Home on Extensively Drug-Resistant Pseudmonas aeruginosa**
  - Over-the-counter (OTC) medications have potential risks.
  - Preservative-free eye drops do not protect against bacterial contamination.
  - This eyedrop contamination is resulting in severe morbidity with vision loss, hospitalizations and death.
  - Cases are now being reported from long-term care facilities and there is a risk of this becoming endemic in some facilities.
  - Treatment options are exceptionally limited.
  - Carbapenemase-producing, carbapenem-resistant P. aeruginosa infections are relatively infrequent still. Of the five gene sequences identified on the Xpert Carba-R, only the VIM will test positive in this organism.
  - Immediately notify your local health department if you isolate an essentially pain-resistant Pseudomonas (including new antibiotics except possibly cefiderocol) with VIM being positive on the Xpert Carba-R.
  - Continue to ask patients about potentially contaminated OTC eye drops.

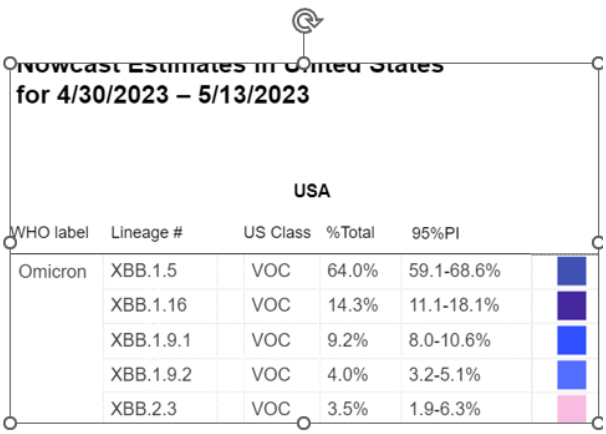
COVID-19

- Nirmatrelvir/ritonavir (Paxlovid™)
  - IDSA updated their COVID treatment guideline on May 15. Paxlovid™ is suggested for patients with mild-to-moderate COVID, who are at high risk of progression to severe disease.
  - Lancet March 2023 published a large study on effectiveness of Paxlovid™ in preventing hospitalization and deaths when prescribed within 5 days of symptom onset.
    - 5,472 participants: Paxlovid™ 84,657 participants: No Paxlovid™
    - 80% effectiveness if dispensed within 5 days of symptom onset
    - 90% effectiveness if dispensed at time of diagnosis and within 5 days of symptom onset
- WHO COVID Vaccine Composition
  - The WHO vaccine advisory group released a statement on May 18. This report provides a nice summary of the information used to develop their recommendations.

- The COVID-19 vaccine task force is recommending that the next iteration should be a monovalent vaccine based on the XBB.1, such as XBB.1.5.
- This is reasonable since neither the original Wuhan-related strain or Omicron-related strains are circulating to any significant extent.
- There is also concern about "immune imprinting" resulting from continuing with the same previously utilized strains.
- Also known as the "original antigenic sin", this concept says that our adaptive immune system develops a response to an organism with the first exposure to disease or vaccine.
- If the organism evolves, exposure to that evolved organism may elicit a blunted immune response. The immune response after repeat vaccinations with identical immunogenic antigens may be less robust. The best immune response will be when the antigens in the vaccine are significantly different from those provided in prior vaccinations.

- U.S. Sequence Data
  - No new significant isolates being reported.
  - Genomic sequencing data, below, shows the percentage of isolates due to a particular sequence but does not correspond with virulence or activity levels in any community.





Nowcast Estimates in United States
for 4/30/2023 – 5/13/2023

USA

WHO label	Lineage #	US Class	%Total	95%PI
Omicron	XBB.1.5	VOC	64.0%	59.1-68.6%
	XBB.1.16	VOC	14.3%	11.1-18.1%
	XBB.1.9.1	VOC	9.2%	8.0-10.6%
	XBB.1.9.2	VOC	4.0%	3.2-5.1%
	XBB.2.3	VOC	3.5%	1.9-6.3%

- **Take-Home on COVID**
  - Circulating strains of COVID appear relatively stable at this time.
  - Persons at high risk of developing severe disease should continue to be evaluated for treatment. Paxlovid remains the most highly recommended option, with 80-90% effectiveness in preventing hospitalization and/or death within 30 days.
  - A new COVID vaccine for primary and booster dosing is anticipated in September. If the CDC follows the WHO guidance, it will likely be a monovalent vaccine against the recombinant XBB

- **Related Links**
  - CDC Caring for Patients

- CDC Data Tracker
- CDC Latest Updates
- CDC Vaccine Information
- CDPH Tracking and Vaccination Updates
- Sutter Health for Clinicians
- Sutter Health for Patients
- WHO Table of Contents

Influenza

- WHO report of circulating levels of influenza
  - The WHO sends a report every 2 weeks that breaks down influenza activity throughout the world. No significant outbreaks are being identified in either hemisphere at this time.
  - We remain at inter-seasonal influenza levels.

RSV

- On May 18, the FDA Vaccines and Related Biologic Products Advisory Committee recommended approval of the RSV Vaccine (Abrysvo) in pregnancy based on available efficacy and safety data.
- The recommendation is based on the multi-season, international, phase III MATISSE trial published in NEJM April 20.
  - Over 7,400 participants, assigned 1:1 vaccine versus placebo
  - No safety signals in maternal participants or infants/toddlers observed up to 24 months
  - Adverse events reported within 1 month of injection or birth similar in vaccine versus placebo
  - Major results in table below
    - A non-statistically significant, numerical increase in pre-mature births was noted.
    - Vaccine efficacy for infants was 82% at 90 days and 69% at 180 days after birth.

Group	Cases of Medically Attended Severe Resp. Illness		Pre-Mature Birth	
	90 Days	180 Days	28-<34 weeks	34-<37 weeks
Vaccine (3,570 infants)	6	19	20/3,568 (0.6%)	180/3,558 (5.0%)
Placebo (3,558 infants)	33	62	11/3,568 (0.3%)	157/3,558 (4.4%)
Vaccine Efficacy	82%	69%		

MPOX

- Jynneos
- CDC MMWR: Effectiveness of Jynneos in Preventing Mpox (May 19, 2023)
  - Multijurisdictional case control study conducted between August 2022 – March 2023.
  - First publication to assess real-world vaccine effectiveness (VE) by subcutaneous versus intradermal route as well as in immunocompromised persons.
  - Key results:
    - Among 917 participants included, 206 (23%) were fully vaccinated, 295 (32%) were partially vaccinated, and 416 (45%) were unvaccinated.
    - Adjusted VE was 75% after 1 dose and 86% after 2 doses of Jynneos.
    - Among fully vaccinated participants, adjusted VE was 89% for subcutaneous, 80% for intradermal, and 87% for heterologous administration.
    - Among immunocompromised persons, adjusted VE was 51% for partial vaccination and 70% for complete vaccination.
- Tecovirimat (TPOXX)
  - The safety and efficacy of tecovirimat is uncertain. Consequently, this medication remains under emergency use authorization (EUA).
  - The STOMP (Study of Tecovirimat for Human Mpox Virus) trial is enrolling patients remotely across the United States. Adults and children of any age with Mpox are eligible to enroll.
  - Tecovirimat is believed to have a low barrier to the virus developing resistance (FDA).
    - The NEJM, March 30, published a fatal case of Mpox with documented resistance to tecovirimat.
  - To minimize the risk of the development and spread of resistance, patients should be considered for tecovirimat when they meet the guidance provided by the CDC.
- Cepheid has EUA approval for point of care testing
  - Cepheid Xpert Mpox was approved Feb.10. It detects both non-variola orthopox and Mpox clade II.
- Alameda County Public Health Department published a health advisory on Mpox.
- None of the recently identified cases in fully vaccinated persons required hospitalization.
- Contagion should be assumed until all scabs have fallen off and new skin has formed.

- **Mpox Take Home**
  - Jynneos Mpox VE estimates are consistent with previous studies and strengthen the evidence to support use of Jynneos to protect against Mpox.
  - Jynneos administered subcutaneously or intradermally provides comparable protection.
  - Immunocompromised persons may mount a less effective immune response after vaccination though a two-dose series is still recommended for optimal protection.
  - Continue to vaccinate high-risk persons against Mpox.
  - Tecovirimat should be ordered, when appropriate, for patients with Mpox. Follow CDC guidance.
  - Test fully vaccinated persons with appropriate lesions for Mpox.
  - Be alert to possibly seeing more cases this summer.
  - CDC link for more information about MPOX.

Sexually Transmitted Infections (STI) – Collection/Testing Changes

- Sutter Shared Laboratory is changing molecular Chlamydia/Gonorrhea and HPV testing from the Hologic platform to Roche. Effective May 31, this change is happening for all Sutter Health in-patient and out-patient sites that send specimens to the Sutter Health Shared Laboratory. Learn more here.

Share the Newsletter

Anyone who would like to be added to the Emerging Infections newsletter should send a request to bryan.gardner@sutterhealth.org

This communication is intended for clinicians caring for Sutter patients. If you have questions, please reach out to us at clinicians@sutterhealth.org.