

DIAGNOSTICS

INFLUENZA DIAGNOSTICS REFERENCE TABLE

APEX Name	Assay Type	Viruses	Sensitivity	Specificity	Sample	COVID on same swab?	Turn around time
POCT FLU A and B RNA, QUAL RAPID ¹	Molecular	Influenza A/B	95%	>95%	Nasal swab	No	15-20 min Available in Parnassus and Mission Bay ED
Influenza A/B/RSV PCR	Molecular	Influenza A/B RSV	>95%	>95%	NP/MNT +/- OP swab recommended (AN +/- OP accepted ²)	Yes	4-8 h (STAT ³) 12-24h (Routine)
Respiratory Viral Panel PCR (RVP)	Molecular	Influenza A/B RSV Parainfluenza Metapneumovirus Rhinovirus Adenovirus	>95%	>95%	NP/MNT +/- OP swab (AN +/- OP accepted ²) or lower tract sample (BAL, ET aspirate)	Yes	4-8 h (STAT ³) 24-72hh (Routine)

¹Note: the POCT test is a rapid molecular test that is 95% sensitive (this is different than prior POCT antigen tests).

² Anterior nares (AN) swab is approximately 10-15% less sensitive than NP/MNT swabs for respiratory virus testing.

³ STAT testing should be prioritized for new hospital admissions only when the results will change acute patient management.

WHICH PATIENTS SHOULD BE TESTED FOR INFLUENZA DURING INFLUENZA SEASON?

Inpatients/ER pending admission

- All patients on admission with:
 - Acute respiratory illness including pneumonia, with or without fever
 - Acute worsening of chronic cardiopulmonary disease (COPD, asthma, CAD, CHF)
 - Fever alone if immunocompromised or high risk
- All hospitalized patients who develop acute onset of respiratory symptoms without a clear alternative diagnosis

Outpatients/ER anticipated discharge

- High risk patients with influenza-like illness, pneumonia, or nonspecific respiratory illness, with or without fever
- Non-high risk patients presenting with a complication of influenza (e.g., pneumonia)
- Consider in other patients with influenza-like illness, pneumonia, or nonspecific respiratory illness if it will change management

*Test only if results will change management including decisions around antivirals, antibiotics, further diagnostic testing, or infection control.

Influenza Signs and Symptoms (usually abrupt onset)

- Respiratory symptoms: dyspnea, cough, chest pain

- Systemic signs and symptoms: chills, malaise, fatigue, myalgia **with or without fever**
- ENT symptoms: headache, sore throat, hoarseness (nasal congestion, rhinorrhea more common in children)
- GI symptoms: abdominal pain, vomiting (diarrhea more common in children)

Patients at High Risk of Complications

- Adults ≥ 65 years or children <5 years (especially <2 years)
- Chronic pulmonary, CV, renal, hepatic, heme, neuro/neurodevelopmental, metabolic disorders (incl. diabetes)
- Immunocompromised
- Pregnant or postpartum (within 2 weeks after delivery)
- Children <18 years receiving aspirin or salicylate containing medications (risk of Reye syndrome if get flu)
- American Indians/Alaska Natives
- Extreme obesity (BMI ≥ 40)
- Residents of chronic care facilities

WHICH TEST SHOULD I ORDER IN SYMPTOMATIC PATIENTS?

See the section above for guidance on indications for influenza testing. For the 2021-22 season, all patients who require influenza testing should also be tested for COVID.

Outside of Flu Season

Inpatients/ER pending admission

- Critically ill or immunocompromised: COVID + RVP
- All other patients: COVID only

Outpatients/ER anticipated discharge

- COVID only
- Consider RVP in immunocompromised

During Flu Season

Inpatients/ER pending admission

- Critically ill or immunocompromised: COVID + RVP
- All other patients: COVID + Influenza A/B/RSV PCR

Outpatients/ER anticipated discharge

- COVID + influenza (POCT or influenza/RSV PCR depending on setting)
- Consider RVP instead of flu testing in immunocompromised

Important Notes on Testing

- The start of flu season will be indicated by UCSF Health with an institution-wide email based on internal influenza testing and SFPD influenza surveillance. The onset of the influenza season varies but is usually in late December/early January in Northern California; the end of the season also varies.
- To maximize detection, respiratory specimens should be collected as close to illness onset as possible, preferably <4 days after symptom onset (but can and should be done later if patients do not present early)
- **In critically ill patients, send upper and lower respiratory tract samples for RVP to improve sensitivity for diagnosis of respiratory viral infection.**
- Co-infection with influenza and SARS-CoV-2 is uncommon but can occur. A positive influenza test does not preclude SARS-CoV-2 infection, and vice versa.

TREATMENT

WHICH PATIENTS WITH INFLUENZA/SUSPECTED INFLUENZA SHOULD BE TREATED WITH ANTIVIRALS (DURING FLU SEASON)?

Inpatients/ER pending admission

- **All inpatients with influenza or suspected influenza, irrespective of time of symptom onset**
- This is because treatment is associated with lower mortality in inpatients, even if >48h of symptoms
- Treat as early as possible and do not delay therapy while awaiting lab confirmation

Outpatients/ER anticipated discharge

- High risk patients or patients with severe or progressive illness
 - Treat irrespective of time of symptom onset
 - Treat as early as possible and do not delay while awaiting lab confirmation
- Can consider treatment in:
 - Non-high-risk patients if ≤48h symptoms
 - Household contacts of high-risk patients
 - HCWs who take care of high-risk patients

Important Notes on Indications for Treatment

- Household contacts of HCWs who take care of high-risk patients should only be treated if they have a specific indication, not solely to prevent spread to the HCW.
- For young children, routine empiric influenza therapy in this age group is somewhat controversial. It is recommended to offer therapy to this group of patients, but individual treatment decisions may be considered via shared decision-making and incorporation of other clinical factors.

Drug options

Drug	Route	Adverse Effects	Comments
Oseltamivir	PO	Nausea/vomiting, rare neuropsychiatric effects.	Drug of choice for most patients, including hospitalized patients, immunocompromised patients, and patients who are pregnant or breastfeeding.
Zanamavir	Inhaled	Cannot use in intubated patients or those with respiratory disease (asthma/COPD) as it can cause cough, bronchospasm.	Consider if patient cannot take PO although requires patient participation with use
Peramivir	IV	GI side effects, neutropenia	Consider use in hospitalized patients with influenza in whom there is a concern for GI absorption that would limit the use of oral oseltamivir.
Baloxavir	PO	Diarrhea	Not routinely recommended given concerns about treatment emergent resistance. Can be considered for uncomplicated infection in immunocompetent outpatients. Not recommended for hospitalized patients, immunocompromised patients, or patients who are pregnant or breastfeeding given lack of data.

Important Notes on Antiviral Therapy

- Please see IDMP (idmp.ucsf.edu) for dosing recommendations for oseltamivir in children and adults

- If you are considering zanamavir, peramivir, or baloxavir, please consult ID
- For ICU patients, treatment courses may be extended based on severity of illness and repeat RVP testing of lower respiratory tract samples. Please consult ID for assistance in these cases.

Considerations Regarding Bacterial Superinfection in Patients with Confirmed Influenza

- Bacterial superinfection is more common at clinical presentation in influenza than in COVID (~10% of hospitalized patients with influenza vs. <1-3% of hospitalized patients with COVID)
- If patients with influenza are started on antibiotics for CAP, consider early discontinuation (at 48-72h) if patient is clinically stable and there is a low suspicion for bacterial pneumonia based on labs and radiologic features.

PROPHYLAXIS

- These guidelines do not address the use of antivirals for chemoprophylaxis.
- For detailed guidance on indications for and use of antivirals for chemoprophylaxis, please see the CDC Antiviral Guidelines (section on chemoprophylaxis) which can be found here:
<https://www.cdc.gov/flu/professionals/antivirals/summary-clinicians.htm>

REFERENCES

1. Uyeki et al, IDSA 2018 Update on Diagnosis, Treatment, Chemoprophylaxis, and Institutional Outbreak Management of Seasonal Influenza, CID 2019, 68:e1.
2. CDC, Seasonal Influenza Antiviral Drugs, <https://www.cdc.gov/flu/professionals/antivirals/index.htm>, accessed September 27, 2021.
3. Metlay et al, Joint ATS/IDSA Guidelines for the Diagnosis and Treatment of Adults with CAP, AJRCCM 2019, 200:e45.