

## Respiratory Pathogen Testing Considerations for Patients Presenting to Children's Hospital Colorado During the 2020-2021 Influenza Season

*This algorithm is intended for use in the Emergency Departments, Urgent Cares and inpatient units within the Children's Hospital Colorado system, and serves as an institutional complement to existing recommendations from the Centers for Disease Control, Infectious Diseases Society of America and the American Academy of Pediatrics. This guidance may also be relevant for providers in ambulatory settings. The contents were developed via a multidisciplinary collaboration between the Sections of Emergency Medicine, Epidemiology, Hospital Medicine, Microbiology and Infectious Diseases. These guidelines will apply during the influenza season, but testing for influenza will be available from November 17, 2020 for patients with compatible illness. The start of the influenza season varies from year to year, and providers in the CHCO system will be notified of the official start of the season by the CHCO Epidemiology/Microbiology Departments.*

### **Goals for testing during the respiratory season**

- 1) Provide guidance to promote the judicious use of testing for influenza and SARS-CoV-2 testing at CHCO
- 2) Optimize outcomes through initiation of antiviral medication as early as possible for relevant high-risk groups in accordance with national recommendations
- 3) Minimize unnecessary testing and treatment, and associated side effects, costs, and impact on antimicrobial resistance
- 4) Minimize duplicative testing within our system
- 5) Enhance clinical management for patients and decrease transmission risks to team members
- 6) Support public health efforts to identify patients with SARS-CoV-2 to inform isolation and quarantine measures

### **Important Updates to Testing**

There will be three types of respiratory tests available for the upcoming respiratory season at the CHCO microbiology lab. All tests are run 24 hours a day, 7 days a week during influenza season. These tests will be available at all CHCO locations.

**SARS-CoV-2 PCR:** tests for SARS-CoV-2 ONLY. There will be no expedited SARS-CoV-2 test during the respiratory season. See [COVID-19 policy](#) for more details.

**SARS-CoV-2/Influenza/RSV PCR:** We are switching from an influenza only PCR test to a combined rapid test on November 17, 2020 which tests for influenza A, influenza B, RSV as well as SARS-CoV-2. Note this rapid test is NOT the same as the older rapid influenza or RSV detection test (RIDT) and has higher sensitivity and specificity than rapid antigen/immunoassay tests.

**Respiratory pathogen panel PCR (RPP 2.1):** The respiratory pathogen panel is an updated version of the panel that includes SARS-CoV-2.

The RPP also tests for adenovirus, coronaviruses HKU1, NL63, 229E and OC43, human metapneumovirus, rhinovirus/enterovirus, influenza A, A/H1-2009, A/H3, B, parainfluenza virus 1, 2, 3, and 4, *Bordetella pertussis* and *parapertussis*, *Chlamydomphila pneumoniae* and *Mycoplasma pneumoniae*.

## Respiratory Pathogen Testing Considerations for Patients Presenting to Children's Hospital Colorado During the 2020-2021 Influenza Season

Information regarding cost and turnaround time for each test is shown in Table 1.

### **Clinical considerations**

- Testing for influenza should be considered in situations when it will impact clinical care (e.g. help with decisions about starting an antiviral, avoid antibiotic use or other diagnostic evaluation) and in general does not need to be ordered for children who are being discharged home without risk factors outlined in Table 2.
- Influenza and COVID-19 have overlapping signs and symptoms with other respiratory pathogens, and it may not be possible to differentiate them based on clinical features alone.
- Classic influenza symptoms usually seen with older children include: high fever, dry cough, chills, sweats, myalgia, photophobia, headache, which may be symptoms of SARS-CoV-2.
- Loss of taste or smell with or without respiratory symptoms are more common in children with SARS-CoV-2, but have been reported to occur in children with influenza.
- The pre-test probability for either influenza or SARS-CoV-2 is higher if there is exposure to a confirmed case.

### **Influenza treatment**

Antiviral treatment is effective in reducing severity from influenza and illness duration, and is recommended as soon as possible for any patient with suspected or confirmed influenza who:

1. is hospitalized
2. has severe, complicated, or progressive illness; or
3. is at higher risk for influenza complications (Table 2)

Note, for these scenarios, treatment is beneficial even if started after 48 hours of illness.

For other scenarios in ambulatory/outpatient settings, it is most effective if started within 48 hours.

First-line treatment for influenza is with a 5-day course of oseltamivir (trade name Tamiflu®). Dosing information is shown in Table 3. Baloxavir (trade name Xofluzax™) was approved for use in 2018 in children 12 years and older. In contrast to other influenza medications which are neuraminidase inhibitors, Baloxavir is an endonuclease inhibitor. Baloxavir can be given as a single dose, but is not on formulary at CHCO. Inhaled zanamivir (trade name Relenza®) is also approved for use (but is not on formulary at CHCO) and IV peramavir is available for those who are unable to take oseltamivir enterally, and is not more efficacious than oseltamivir.

### **Information regarding SARS-CoV-2 testing**

- At the present time, testing all symptomatic individuals with compatible illness for SARS-CoV-2 is optimal for isolation practices, contact tracing, quarantine recommendations, and school and daycare considerations. Best practices for the diagnosis of COVID-19 may evolve over time. Updated information regarding our testing platforms, PPE requirements, and other considerations for patients with SARS-CoV-2 is available in our [COVID-19 policy](#), and [COVID-19 Resource Center](#).

Respiratory Pathogen Testing Considerations for Patients Presenting to Children's Hospital  
Colorado During the 2020-2021 Influenza Season

**Information regarding RPP testing**

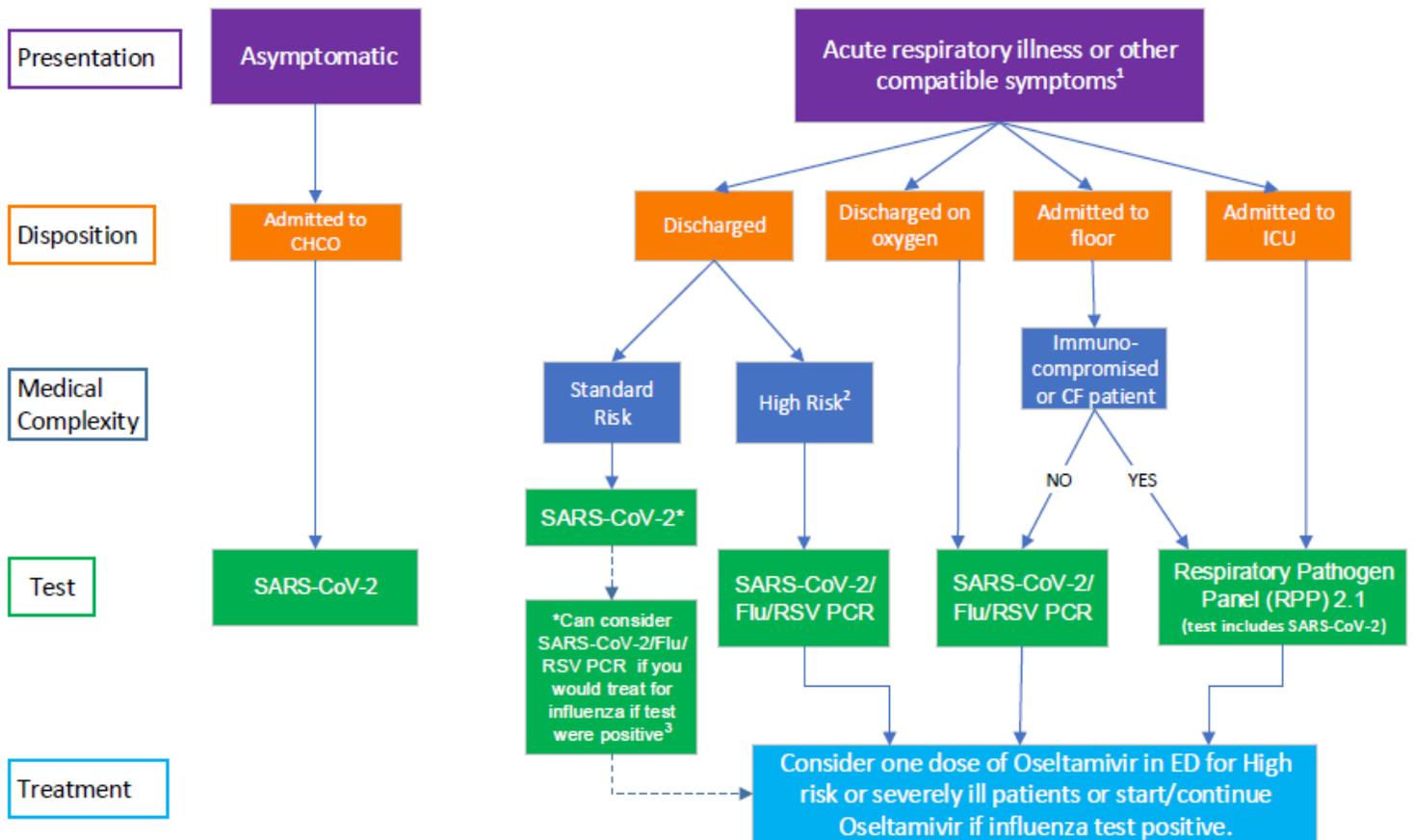
- We generally discourage the routine use of respiratory pathogen panel testing for respiratory conditions given that it is an expensive test and may not change clinical outcomes. Respiratory pathogen testing should be reserved for critically-ill patients, immunocompromised patients, or patients admitted with cystic fibrosis exacerbations. Other scenarios in which it may be beneficial include: part of a fever of unknown origin workup, fever in a returning traveler, or scenarios in which it will help avoid other diagnostic evaluations.
- A summary of respiratory test considerations during the influenza season in children with respiratory symptoms is outlined below (Figure 1).

**Information regarding drive-thru testing**

Due to shortages in testing supply availability, we will not be offering flu/SARS-CoV-2/RSV drive-thru testing. We will continue to provide SARS CoV-2 testing, and RPP testing while available, but RPP testing should only be limited to the clinical scenarios outlined above. Children who are not considered high risk and who do not have severe illness (ie. outpatients), do not generally require influenza testing as they will not benefit or only have modest benefits from treatment if within 48 hours of symptom onset.

Respiratory Pathogen Testing Considerations for Patients Presenting to Children’s Hospital Colorado During the 2020-2021 Influenza Season

**Figure 1. Respiratory Pathogen Testing Considerations for Children presenting to Children’s Hospital Colorado during influenza season**



<sup>1</sup> Symptoms include fever, cough, nasal congestion or rhinorrhea, sore throat, shortness of breath, fatigue, headache, myalgia, poor feeding/poor appetite, loss of taste or smell. Note: children with COVID-19 and influenza may present with nausea, vomiting or diarrhea.

<sup>2</sup> Children considered high risk are listed in Table 2.

<sup>3</sup> Consider SARS-CoV-2/Flu/RSV for patients in whom testing for influenza would change management, e.g. presenting within 48 hours of illness onset whereby oseltamivir therapy would be beneficial or results of testing would influence antibiotic prescribing, ancillary testing or child care/school-related decisions.

Abbreviations: ICU-intensive care units(including PICU, CICU & NICU), CF- cystic fibrosis exacerbation, PCR- polymerase chain reaction.

Updated 10/28/20

Respiratory Pathogen Testing Considerations for Patients Presenting to Children’s Hospital Colorado  
During the 2020-2021 Influenza Season

**Table 1. Respiratory testing information**

	SARS-CoV-2 PCR	SARS-CoV-2/Flu/RSV PCR	Respiratory pathogen panel
<b>Tests for</b>	SARS-CoV-2 only	SARS-CoV-2, influenza A, B and RSV	adenovirus, coronaviruses HKU1, NL63, 229E and OC43, human metapneumovirus, rhinovirus/enterovirus, influenza A, A/H1-2009, A/H3, B, parainfluenza virus 1, 2, 3, and 4, <i>Bordetella pertussis</i> and <i>parapertussis</i> , <i>Chlamydomphila pneumoniae</i> and <i>Mycoplasma pneumoniae</i> .
<b>Charge*</b>	\$200	\$270	\$534
<b>Procedure code</b>	LAB 9100	LAB 9373	LAB 5595
<b>Turnaround time for inpatients and ED patients</b>	12 hours (from arrival in the Microbiology Laboratory at Anschutz campus)		
<b>Turnaround time for outpatients (drive-thru testing site)</b>	24-72 hours (from arrival in the Microbiology Laboratory at Anschutz campus)		
<b>Drive-thru options</b>	Available	Not available	Available while supplies last
<b>Other considerations</b>	Expedited testing will no longer be available	Will only report flu A or B, does not provide subtype information	Panel includes SARS-CoV-2
*Pricing effective November 1. Please note that under federal mandate patients will NOT be billed for SARS-CoV-2 testing. However, depending on insurance coverage patients may still be billed for testing for other respiratory pathogens (including influenza).			

**Table 2. Risk factors associated with complications or more severe disease from influenza**

- Children aged <2 years
- Individuals <19 years receiving long-term aspirin
- Adults aged >65 years
- Persons of all ages with chronic pulmonary (including asthma), cardiovascular, renal, hepatic, metabolic (including diabetes) hematologic, neurologic and neurodevelopment conditions (including seizure disorders, developmental delay, muscular dystrophy, or spinal cord injury)
- Persons with immunosuppression
- Pregnant or recently post-partum women
- American Indians/Alaska Natives
- Persons who are morbidly obese (BMI >40)

**Recommendations for the care of Patients with SARS-CoV-2**

The care of patients with SARS-CoV-2 including testing and treatment considerations is available on the [COVID-19 Resource Center](#).

**Recommendations for ED Care of Patients in whom Influenza is High on Differential Diagnosis**

**Consider Influenza testing and treatment for the following patients:**

Presentation consistent with influenza (e.g. high fever, cough, myalgias, fatigue) **AND** either one of the following:

1. Severe illness (hospitalized or requiring oxygen)
2. Risk factors outlined in Table 2

***Any patient requiring hospitalization from ED /Urgent care or patients being observed for home oxygen during influenza season:***

**Testing and treatment:**

*Scenario 1.* Influenza/RSV/ SARS-CoV-2 PCR; one-time dose of oseltamivir given in ED; consider one-time dose of oseltamivir given in ED for high-risk or severely ill patients

*Scenario 2.* Respiratory pathogen panel if admitted to ICU, or for a CCBD patient or patient with a CF exacerbation; one-time dose of oseltamivir given in ED for high-risk or severely ill patients

*Scenario 3.* SARS-CoV-2 PCR if asymptomatic

**Follow up:** Communicate with admitting team to continue or start oseltamivir course if patient is admitted and positive. Prescribe 5-day course of oseltamivir for those being discharged on oxygen with positive influenza results. Culture call back will follow up on positive influenza results and SARS-CoV-2 results if patient is discharged before results are available. See culture call back process below for details.

***Any patient with risk factors for more severe outcomes (see Table 2) who are being discharged home from the ED/Urgent care:***

**Testing and Treatment:**

Send SARS-CoV-2/Flu/RSV PCR test and consider one-time dose of oseltamivir given in ED. Document in EHR that patient will require oseltamivir (or baloxavir) if influenza test is positive.

**Follow up:** Culture call back will follow up on positive influenza results and SARS-CoV-2 results if patient is discharged before results are available. See culture call back process below for details.

***STANDARD RISK Patient who will be discharged home and presents within 48 hours of illness onset, and provider deems that results would influence clinical decision making***

*Treating with oseltamivir in this situation is not mandatory and can occur at the discretion of the treating provider. Consider treatment if clinically worsening.*

***Testing and Treatment Options:***

***Scenario 1.*** SARS-CoV-2 PCR (preferred)

***Scenario 2. Consider*** test for SARS-CoV-2/Flu/RSV PCR only if you will treat for influenza if test is positive. Provide family with prescription and instructions to fill if they receive a call that influenza test is positive. Document in EHR that patient will require treatment (oseltamivir or baloxavir) if influenza test is positive. Note that CDC and FDA recommend that for standard risk patient's treatment should be started within 48 hours of symptoms onset as clinical benefit is greatest when antiviral treatment is started as close to illness onset as possible.

***The Culture Call Back Team will be responsible for calling results of testing for the following scenarios:***

**SARS-CoV-2:**

- Negative - No call
- Positive - Call and route to PCP

**Influenza A/B:**

- Negative - No call
- Positive - Call and instruct family to fill prescription (or prescribe if not already given). If there are family members with risk factors (see Table 2), provide information that these family members need to be followed up by their PCP (treatment and prophylaxis of family members is not part of CCB procedure)

**RSV:**

- Negative - No call
- Positive - No call and forward results to PCP given there is likely to be a follow up appointment.

**Respiratory pathogen Panel:**

Call if positive for any of the following pathogens: SARS-CoV-2, influenza A, influenza B, *Bordetella pertussis* or *parapertussis*, *Chlamydomphila pneumoniae*, or *Mycoplasma pneumoniae*

***Recommendations for Ambulatory/Outpatient Office Care of Patients in whom Influenza is High on Differential Diagnosis***

**Testing and Treatment:**

Scenario 1: no risk factors as outlined in Table 2: SARS-CoV-2 PCR

Scenario 2: a) risk factors present, or  
b) worsening/progressive illness, or  
c) within 48 hours of illness onset and considering treatment

Send SARS-CoV-2 PCR and influenza test and prescribe oseltamivir or baloxavir if test is positive.

Note: Rapid influenza antigen testing is more reliable if sensitivity and specificity are > 80% and is during time of high influenza prevalence in the community. We do not recommend rapid SARS-CoV-2 antigen testing at this time given lower sensitivity and specificity.

Note: CDC and FDA recommend that for standard risk patient's treatment should be started within 48 hours of symptom onset as clinical benefit is greatest when antiviral treatment is started as close to illness onset as possible

**Table 3: Medications for the treatment of Influenza**

Drug	Dose (Treatment)	Duration (Treatment)	FDA Approval Age	Price*	Monitoring	Side effects and Considerations
<b>Oseltamivir (oral)</b>  <b>Only influenza medication on CHCO formulary</b>	<b>14 days – 3 months:</b> 3 mg/kg/dose twice a day <b>3-12 months:</b> 3 mg/kg/dose twice a day  <b>Children 1-12 years of age and weighing:</b> ≤ 15 kg: 30 mg/dose twice a day > 15-23 kg: 45 mg/dose twice a day >23-40 kg: 60 mg/dose twice a day >40 kg: 75 mg/dose twice a day  <b>Children &gt; 13 years of age and adults:</b> 75 mg/dose twice a day  Prophylaxis dosing – same dose as treatment except given once daily***	5 days	<b>Treatment:</b> 14 days and older <b>Prophylaxis:</b> 1 year and older	Capsule: \$154 Suspension: \$326	Renal function (Scr, BUN, urine output) Glucose in those with DM Behavioral changes	GI upset Insomnia Behavioral changes  Requires renal dose adjustment
<b>Zanamivir (inhaled)</b>	Two inhalations (10 mg) twice daily	5 days	<b>Treatment:</b> 7 years and older <b>Prophylaxis:</b> 5 years and older	\$71	Behavioral changes	Headache, Sore throat Behavioral changes  Not recommended in patients with underlying airway disease due to risk of bronchospasm. Contraindicated in those with milk-protein allergy
<b>Peramivir (IV)</b>	<b>Children 2-12 years:</b> 12 mg/kg once daily  <b>13 years and older:</b> 600 mg once daily	5-10 days (consult ID)	<b>Treatment:</b> 2 years and older	\$5500	Renal function (Scr, BUN, urine output) Behavioral changes Hypersensitivity reactions	Diarrhea Skin hypersensitivity reactions Behavioral changes  Available as an intravenous infusion only  Requires renal dose adjustment
<b>Baloxavir (oral)</b>	<b>Children 12 years of age and older weighing</b> 40 to < 80 kg: 40 mg as a single dose >80 kg: 80 mg as a single dose	1 day	<b>Treatment:</b> 12 years and older	\$90	Hypersensitivity reactions	Diarrhea  Avoid administration with dairy, calcium fortified drinks or polyvalent cations

\*Average Wholesale Price based a treatment course for a 40 kg child (exact pricing will vary depending on pharmacy)

## Respiratory Pathogen Testing Considerations for Patients Presenting to Children's Hospital Colorado During the 2020-2021 Influenza Season

\*\* Oral oseltamivir is approved by the FDA for treatment of acute uncomplicated influenza within 2 days of illness onset in people 14 days and older, and for chemoprophylaxis in people 1 year and older. Although not part of the FDA-approved indications, use of oral oseltamivir for treatment of influenza in infants less than 14 days old, and for chemoprophylaxis in infants 3 months to 1 year, is recommended by the CDC and the American Academy of Pediatrics.

\*\*\*We do not recommend widespread or routine use of antivirals for chemoprophylaxis. Chemoprophylaxis is not recommended if more than 48 hours have elapsed since the last exposure to an infected person. Persons receiving chemoprophylaxis should be encouraged to seek medical attention as soon as they develop a febrile respiratory illness that might indicate influenza. For effective prophylaxis, an antiviral medication must be taken each day for the duration of potential exposure to a person with influenza, and continued for 7 days after the last known exposure.

### References:

1. CDC website <https://www.cdc.gov/flu/professionals/diagnosis/index.htm>
2. Hanson et al. Molecular testing for acute respiratory tract infections: clinical and diagnostic recommendations from the IDSA's Diagnostics Committee; Clin Infect Dis. 2020 May
3. AAP, Committee on Infectious Diseases. Recommendations for Prevention and Control of Influenza in Children, 2020–2021 Pediatrics October 2020, 146 (4) e2020024588.