Novel influenza A virus infection

2024 Case Definition

CSTE Position Statement(s)

2024 Position Statement (24-ID-09)

Clinical Criteria

In the absence of a more likely alternative diagnosis or cause, an acute illness compatible with novel influenza virus infection is characterized by either:

- One or more of the following symptoms:
    - Cough, sore throat, fever (measured or subjective), shortness of breath or difficulty breathing, conjunctivitis (red eye, discharge from eye),

  OR
- Two or more of the following symptoms:
    - Headache, myalgia, arthralgia, fatigue, rhinorrhea or nasal congestion, diarrhea, vomiting.

Laboratory Criteria

Confirmatory Laboratory Evidence

Category 1 (novel influenza virus detection):

- Positive confirmatory molecular test result (e.g., reverse transcriptase polymerase chain reaction [rT-PCR]) for novel influenza subtype,
  OR
- Genetic sequence indicative of novel influenza A strain.

Category 2 (viable virus):

- Isolation of a novel influenza virus from a clinical specimen.*

Category 3 (evidence of infection):

- Significant IgG antibody rise to novel influenza A (i.e., at least a 4-fold rise in a quantitative titer or seroconversion) in paired acute and convalescent serum IgG in the absence of another explanation (such as vaccination).

Presumptive Laboratory Evidence

Category 1:

- Presumptive positive for novel influenza virus on tests specifically designed to detect novel influenza viruses, such as H5 or H7.

Category 2:

- Viral testing results indicative of variant influenza virus, such as H1v or H3v, as determined in consultation with subject matter experts at CDC.**

** Isolation of a novel virus should not be performed outside of CDC.*
*** See Appendix A below.*

Epidemiologic Linkage Criteria

- Close contact with a confirmed human case of novel A virus infection,
  OR
- Shared a common exposure (such as an agricultural fair or live animal market) with a confirmed novel influenza A case,
  OR
- Direct or indirect contact (such as touching an animal, their environment, or their raw or unprocessed animal products) with animals with confirmed influenza A,

OR
- Inadequate use or breach of PPE and exposed to novel influenza A virus in a laboratory.

Case Classification

Confirmed

- Meets clinical criteria **AND** confirmatory laboratory evidence category 1,
  OR
- Meets confirmatory laboratory evidence category 2,
  OR
- Meets confirmatory laboratory evidence category 3.

Probable

- Meets confirmatory laboratory evidence category 1,
  OR
- Meets clinical criteria **AND** presumptive laboratory evidence category 1,
  OR
- Meets clinical criteria **AND** epidemiological linkage criteria **AND** presumptive laboratory evidence category 2.

Note: A probable case classification should not undermine the diagnosis of novel influenza A under CLIA guidelines, and the patient should be provided the same care and investigation as a confirmed case.

Suspect

- A case that meets the clinical criteria **AND** epidemiologic linkage criteria **AND** laboratory testing results are positive for influenza A virus but no laboratory evidence is available that would rule out novel influenza A.

Criteria to Distinguish a New Case from an Existing Case

A person should be enumerated as a new case of a novel influenza A virus infection if:

- The virus is distinguishable from the individual's previous novel influenza A virus infection,
  OR
- The virus is indistinguishable from the individual's previous novel influenza A virus infection, AND
  - The person has recovered fully or returned to baseline health,
    OR
  - It has been >30 days since symptom onset date (if available) or first positive specimen collection date.

Note: For severely immunocompromised individuals, judgment should be used to determine if a repeat positive test is likely to result from long-term shedding and, therefore, not be enumerated as a new case. CDC defines severe immunocompromise as certain conditions, such as being on chemotherapy for cancer, untreated human immunodeficiency virus (HIV) infection with CD4 T lymphocyte count <200, combined primary immunodeficiency disorder, and receipt of prednisone >20mg/day for more than 14 days.

Comment(s)

Beginning on September 29, 2024, a new Council of State and Territorial Epidemiologists (CSTE) case definition for novel influenza A virus infection was implemented, making both confirmed and probable cases nationally notifiable.

Appendix A: Non-Standard Results with the Influenza A Subtyping Kit (After Re-Testing)*

InfA (M)	H3 (HA)	pdm InfA (NP)	pdmH1 (HA)	RP (human)	Result Interpretation
+	+	+	-	±	Influenza A detected; Presumptive positive for Influenza A(H3N2) variant virus Inconclusive – possible swine origin H3**
+	-	+	- If the pdmH1 target is weak + and large gaps between CT—consult CDC**	±	Inconclusive – may be indicative of swine origin H1 (pre-2009 human or Asian avian lineage)**

*CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel (CDC Flu rRT-PCR Dx Panel) Influenza A Subtyping Kit (VER 2), Instructions for Use, Package Insert

**Text not included in CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel (CDC Flu rRT-PCR Dx Panel) Influenza A Subtyping Kit (VER 2), Instructions for Use, Package Insert

Influenza A/H5 Subtyping Kit Specimen Results Interpretation**

InfA	H5a	H5b	RP	Result Interpretation
+	+	+	±	Influenza A Detected; Presumptive positive for Influenza A(H5) virus

**CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel (CDC Flu rRT-PCR Dx Panel) Influenza A/H5 Subtyping Kit (VER 3), Instructions for Use, Package Insert

Influenza A/H7 (Eurasian Lineage) Subtyping Kit Specimen Results Interpretation***

InfA	EuH7	RP	Result Interpretation
+	+	±	Influenza A Detected; Subtype: Eurasian H7 detected; Presumptive positive for influenza A(H7) virus

***CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel – Influenza A(H7) [Eurasian Lineage] Assay, Instructions for Use, Package Insert