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Clinical Review

CLINICAL MIMICS: AN EMERGENCY MEDICINE–FOCUSED REVIEW OF INFLUENZA MIMICS

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☐ **Abstract—Background: Influenza viruses are a significant cause of morbidity and mortality in the United States. Given the wide range of symptoms, emergency physicians must maintain a broad differential diagnosis in the evaluation and treatment of patients presenting with influenza-like illnesses. Objective: This review addresses objective and subjective symptoms commonly associated with influenza and discusses important mimics of influenza viruses, while offering a practical approach to their clinical evaluation and treatment. Discussion: Influenza-like symptoms are common in the emergency department (ED), and influenza accounts for > 200,000 hospitalizations annually. The three predominant types are A, B, and C, and these viruses are commonly transmitted through aerosolized viral particles with a wide range of symptoms. The most reliable means of identifying influenza in the ED is rapid antigen detection, although consideration of local prevalence is required. High-risk populations include children younger than 4 years, adults older than 50 years, adults with immunosuppression or chronic comorbidities, pregnancy, obesity, residents of long-term care facilities, and several others. The Centers for Disease Control and Prevention recommends treatment with neuraminidase inhibitors in these populations. However, up to 70% of patients with these symptoms may have a mimic. These mimics include infectious and noninfectious sources. The emergency physician must be aware of life-threatening mimics and assess for these conditions while beginning resuscitation and treatment. Conclusions: The wide range of symptoms associated with influenza overlap with several life-threatening conditions. Emergency physicians must be able to rapidly identify patients at risk for complications and those who require immediate resuscitation. Published by Elsevier Inc.**

☐ **Keywords—influenza; mimic; viral illness; upper respiratory infection; viral syndrome**

INTRODUCTION

Emergency physicians play a significant role in the evaluation, diagnosis, and treatment of viral respiratory illnesses. Fever, headache, cough, and complaints related to the throat are among the 10 most commonly cited reasons for patient presentation to United States (US) emergency departments (EDs) (1–3). From 2007 to 2009, approximately 1.3 million individuals experiencing the symptoms mentioned were assigned a formal diagnosis of influenza by an emergency physician (1–4). Each year, nearly 220,000 patients require hospitalization secondary to influenza; an infection with a mortality rate of 1.4 deaths per 100,000 laboratory-confirmed cases (5,6).

Influenza A, B, and C, named for their respective viral surface proteins, are single-stranded ribonucleic acid viruses belonging to the *Orthomyxoviridae* family (7–9).

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While all of the influenza viruses possess the capability for human infectivity, influenza types B and C are primarily responsible for the majority of illness observed in the human population (8,9). Of the influenza viruses, only influenza A (commonly affecting birds, horses, swine, and dogs) is characterized by subtype based on the composition and morphology of its envelope glycoproteins (7,8).

Influenza viruses are unique in their ability to generate antigenic variability. Minor (antigenic drift) and major (antigenic shift) genomic changes are responsible for several historical and recent influenza epidemics and pandemics (7–9). Given the socioeconomic cost associated with influenza infection (annual direct costs of care estimated as $4.6 billion, with approximately $7 billion lost to sick days/productivity), primary prevention remains a significant public health concern (10). Risk factors predisposing to a severe clinical course include extremes of age, numerous medical comorbidities, and pregnancy; therefore, the Centers for Disease Control and Prevention (CDC) has published recommendations for influenza vaccination, as detailed in Table 1 (11,12).

DISCUSSION

Influenza is a respiratory virus primarily transmitted by aerosolized viral particles. Infection by influenza A subtypes can occur through direct contact with an infected animal, exposure to contaminated environment, or ingestion of inadequately prepared food stuffs (7). Upon failure of host immunologic defenses (immunoglobulin A secretory antibody and mechanical respiratory mucociliary clearance), influenza viruses invade columnar respiratory epithelium, triggering a molecular cascade responsible for the inactivation of host-cell protein synthesis (9,13,14). Local destruction of respiratory epithelium, resulting in the release of pro-inflammatory cytokines, in addition to viral invasion of polymorphonuclear leukocytes, lymphocytes, and monocytes, are responsible for systemic symptoms (9,15). Table 2 discusses the affected systems in infection.

Signs of Influenza

Signs and symptoms of influenza commonly begin after a 1- to 2-day incubation period and are highly variable (7–10). The majority of adolescent and adult patients present with complaints of fever, headache, myalgias, malaise, anorexia, rhinorrhea, pharyngitis, cough, and chest discomfort (9,10). Abdominal pain, nausea, and emesis are also commonly reported among the pediatric population (15). At the extremes of age, influenza can manifest as malaise, lethargy, or altered mental status (9,13).

While symptoms of influenza may be caused by a number of respiratory viruses (respiratory syncytial virus, parainfluenza virus, adenovirus, rhinovirus, and coronavirus), in the setting of a local outbreak, the accuracy of clinical diagnoses in healthy adolescent and adult patients approximates 80%–90% (9,23,24). It is recommended that confirmatory testing be performed in all populations at high risk for complications secondary to infection (see Table 1) and in closed settings in which an influenza outbreak is suspected (e.g., long-term care facilities, inpatient treatment centers) (9,25).

Methods for influenza detection include antigen detection (rapid influenza diagnostic tests [RIDTs]), direct immunofluorescence, reverse transcription polymerase chain reaction (RT-PCR), viral culture, and serology (9,26). Ideally, samples should be obtained within 4–5 days after the onset of symptoms, before the decline in viral replication and shedding (9). Processing time varies according to laboratory and manufacturer. The majority of RIDTs provide results within approximately

Table 1. Centers for Disease Control and Prevention's Recommendations for Influenza Vaccination (11)

Populations at risk for influenza complications in whom vaccination should be prioritized

- Children ≥ 6 months of age to 4 years (59 months)
- Adults ≥ 50 years of age
- Individuals with chronic pulmonary, cardiovascular, renal, hepatic, neurologic, hematologic, or metabolic disorders (including diabetes mellitus)
- Individuals who are immunosuppressed
- Women who are or will be pregnant during influenza season and up to 2 weeks postpartum
- People ages 6 months to 18 years receiving long-term aspirin therapy and might be at risk for Reye syndrome after influenza infection
- Residents of nursing homes or long-term care facilities
- American Indians/Alaska Natives
- The super obese (body mass index > 40)
- Health care personnel
- Caregivers of children < 5 years and adults ≥ 50 years of age

Populations in whom caution must be utilized

Severe egg allergy: Should be vaccinated in a medical setting and supervised by a health care professional
History of Guillain-Barré syndrome associated with vaccination: physician discretion advised