syndrome has been reported following influenza infection and, uncommonly, after influenza vaccination (see "Prophylaxis," below).

Toxic shock syndrome associated with *S. aureus* or group A streptococcal infection following acute influenza infection has been described (Chaps. 172 and 173).

Reye's syndrome is a serious complication in children that is associated with influenza B and—to a lesser extent—influenza A virus infection as well as with varicella-zoster virus and other viral infections. An epidemiologic association between Reye's syndrome and aspirin therapy for the antecedent viral infection has been noted; the syndrome's incidence has decreased markedly with widespread warnings regarding aspirin use by children with acute viral respiratory infections.

In addition to complications involving the specific organ systems described above, influenza outbreaks include cases in which elderly and other high-risk individuals develop influenza and subsequently experience a gradual deterioration of underlying cardiovascular, pulmonary, or renal function—changes that occasionally are irreversible and lead to death. These deaths contribute to the overall excess mortality associated with influenza outbreaks.

LABORATORY FINDINGS AND DIAGNOSIS

During acute influenza, virus may be detected in throat swabs, nasopharyngeal swabs or washes, or sputum. Reverse-transcriptase polymerase chain reaction (RT-PCR) is the most sensitive and specific technique for detection of influenza viruses. RT-PCR can differentiate among influenza subtypes and is used for detection of avian influenza viruses. Rapid influenza diagnostic tests (RIDTs) detect influenza virus antigens by immunologic or enzymatic techniques. RIDTs yield results quickly, and some tests can distinguish between influenza A and B viruses. Although relatively specific, RIDTs vary in sensitivity with the technique and the virus to be detected.

Influenza virus may be isolated from tissue culture or chick embryos, but these labor-intensive procedures generally are no longer used for diagnostic purposes. Serologic methods for diagnosis require comparison of antibody titers in sera obtained during the acute illness with those in sera obtained 10–14 days after the onset of illness and are useful primarily in retrospect and for epidemiologic studies.

Other laboratory tests generally are not helpful in the specific diagnosis of influenza virus infection. Leukocyte counts are variable, frequently being low early in illness and normal or slightly elevated later. Severe leukopenia has been described in overwhelming viral or bacterial infection, whereas leukocytosis with >15,000 cells/μL raises the suspicion of secondary bacterial infection.

DIFFERENTIAL DIAGNOSIS

During a community-wide outbreak, a clinical diagnosis of influenza can be made with a high degree of certainty in patients who present to a physician's office with the typical febrile respiratory illness described above. In the absence of an outbreak (i.e., in sporadic or isolated cases), influenza may be difficult to differentiate on clinical grounds alone from an acute respiratory illness caused by any of a variety of respiratory viruses or by *Mycoplasma pneumoniae*. Severe streptococcal pharyngitis or early bacterial pneumonia may mimic acute influenza, although bacterial pneumonias generally do not run a self-limited course. Purulent sputum in which a bacterial pathogen can be detected by Gram's staining is an important diagnostic feature in bacterial pneumonia.

TREATMENT INFLUENZA

(See also Chap. 215e) Specific antiviral therapy is available for influenza (Table 224-3): the neuraminidase inhibitors zanamivir and oseltamivir for both influenza A and influenza B and the adamantane agents amantadine and rimantadine for influenza A. The epidemiologic patterns of resistance to the influenza antiviral drugs are crucial elements in the selection of treatment. Up-to-date information on patterns of resistance to influenza antiviral drugs is available through *www.cdc.gov/flu*.

A 5-day course of oseltamivir or zanamivir reduces the duration of signs and symptoms of uncomplicated influenza by 1–1.5 days if treatment is started within 2 days of the onset of illness and may be effective if started up to 5 days after onset of symptoms. Zanamivir is administered via an oral inhalation device and may exacerbate bronchospasm in asthmatic patients. Oseltamivir has been associated with nausea and vomiting, whose frequency can be reduced by administration of the drug with food. Oseltamivir has also been associated with neuropsychiatric side effects in children. Peramivir, an investigational neuraminidase inhibitor that can be administered intravenously, is being evaluated in clinical trials, as is an intravenous form of zanamivir.

Amantadine and rimantadine are active only against influenza A, and widespread resistance exists among influenza A/H1N1 and A/H3N2 viruses that are circulating currently; thus, the use of these drugs is not recommended unless influenza isolates are known to be sensitive. Amantadine or rimantadine treatment of illness caused by sensitive strains of influenza A virus reduces the duration of symptoms of uncomplicated influenza by ~50% if begun within 48 h after onset of illness—an effect similar to that of the neuraminidase inhibitors. Of amantadine recipients, 5–10% experience mild

TABLE 224-3 ANTIVIRAL MEDICATIONS FOR TREATMENT AND PROPHYLAXIS OF INFLUENZA

	Age Group (Years)		
Antiviral Drug	**Children (≤12)**	**13–64**	**≥65**
Oseltamivir			
Treatment, influenza A and B	Age 1–12, dose varies by weight[a]	75 mg PO bid	75 mg PO bid
Prophylaxis, influenza A and B	Age 1–12, dose varies by weight[b]	75 mg PO qd	75 mg PO qd
Zanamivir			
Treatment, influenza A and B	Age 7–12, 10 mg bid by inhalation	10 mg bid by inhalation	10 mg bid by inhalation
Prophylaxis, influenza A and B	Age 5–12, 10 mg qd by inhalation	10 mg qd by inhalation	10 mg qd by inhalation
Amantadine[c]			
Treatment, influenza A	Age 1–9, 5 mg/kg in 2 divided doses, up to 150 mg/d	Age ≥10, 100 mg PO bid	≤100 mg/d
Prophylaxis, influenza A	Age 1–9, 5 mg/kg in 2 divided doses, up to 150 mg/d	Age ≥10, 100 mg PO bid	≤100 mg/d
Rimantadine[c]			
Treatment, influenza A	Not approved	100 mg PO bid	100–200 mg/d
Prophylaxis, influenza A	Age 1–9, 5 mg/kg in 2 divided doses, up to 150 mg/d	Age ≥10, 100 mg PO bid	100–200 mg/d

[a]<15 kg: 30 mg bid; >15–23 kg: 45 mg bid; >23–40 kg: 60 mg bid; >40 kg: 75 mg bid. For children <1 year of age, see *www.cdc.gov/h1n1flu/recommendations.htm*. [b]<15 kg: 30 mg qd; >15–23 kg: 45 mg qd; >23–40 kg: 60 mg qd; >40 kg: 75 mg qd. For children <1 year of age, see *www.cdc.gov/h1n1flu/recommendations.htm*. [c]Amantadine and rimantadine are not currently recommended (2013–2014) because of widespread resistance in influenza A viruses. Their use may be reconsidered if viral susceptibility is reestablished.