Hoovashafi

# CLINICAL MANIFESTATIONS:

sudden onset of
fever, often accompanied by chills or rigors,
headache,
malaise,
diffuse myalgia,
nonproductive cough.

Subsequently, respiratory tract signs, including sore throat, nasal congestion, rhinitis, and cough, become more prominent.

Conjunctival injection, abdominal pain, nausea, vomiting, and diarrhea less commonly

## influenza can appear as an :

upper respiratory tract infection

as a febrile illness with few respiratory tract symptoms.

an important cause of odds media

Acute myositis>>>>> tenderness and refusal to walk.

In infants >>>>>>> sepsis-like picture.

occasionally can cause croup, bronchiolitis, or pneumonia.

recover fully after 3 to 7 day

Neurologic complications >>>>>> range from febrile seizures to severe encephalopathy
encephalitis with status epilepticus,
neurologic sequelae
death.

## Guillain barre >>>>>>>>>> rare

Reye syndrome >>>>>> very rare >>>>> aspirin therapy during the illness.

Death from influenza-associated myocarditis has been reported.

Invasive secondary infections or coinfections :

group A streptococcus,
Staphylococcus aureus (including MRSA),
Streptococcus pneumoniae,
other bacterial pathogens in severe disease and death.

# ETIOLOGY:

orthomyxoviruses of 3 genera or types (A, B, and C).

Epidemic disease is caused by A and B,

both A and B virus antigens are included in influenza vaccines.

Type C cause sporadic mild influenza-like illness in children .

antigens are not included in influenza vaccines.

seasons with influenza A (H3N2) as the predominant circulating strain have had 2.7 times higher average mortality rates than other seasons.

The 2009 influenza A (H1N1) pandemic combined both exceptional pediatric virulence and lack of immunity, which resulted in nearly 4 times as many pediatric deaths as usually recorded.

Influenza A viruses are subclassified into subtypes by 2 surface antigens, hemagglutinin (HA) and neuraminidase (NA).
Examples >>>>>>> H1N1 and H3N2 viruses.

Specific antibodies to these various antigens, especially to hemagglutinin, are important determinants of immunity.

Minor antigenic variation within the same influenza B type or influenza A subtypes is called antigenic drift.

Antigenic drift occurs continuously and results in new strains of influenza A and B viruses, leading to seasonal epidemics

Antigenic shifts are major changes in influenza A viruses that result in new subtypes that contain a new HA alone or with a new NA.

Antigenic shift occurs only with influenza A viruses and can lead a to pandemic if the new strain can infect humans and be transmitted efficiently from person to person in a sustained manner in the setting of little or no preexisting immunity.

Humans of all ages occasionally are infected with influenza A viruses of swine or avian origin.

Human infections with swine viruses have manifested as typical influenza like illness, and confirmation of infection caused by an influenza virus of swine origin has been discovered retrospectively during routine typing of human influenza isolates.

human infections with avian influenza viruses are uncommon but may result in a spectrum of disease including mild respiratory symptoms and conjunctivitis to severe lower respiratory tract disease, acute respiratory distress syndrome (ARDS), and death.

Most notable among avian influenza viruses are A (H5N1) and A (H7N9), both of which have been associated with severe disease and high case-fatality rates.

Influenza A (H5N1) viruses emerged as human infections in 1997 and have since caused human disease in Asia, Africa, Europe, and the Middle East, areas where these viruses are present in domestic or wild birds.

Influenza A (H7N9) infections were first detected in 2013 and have been associated with sporadic disease in China.

# EPIDEMIOLOGY:

spread from person to person, primarily by respiratory tract droplets created by coughing or sneezing.

Contact with respiratory tract droplet contaminated surfaces followed by autoinoculation is another mode of transmission.

Secondary spread to adults and other children within a family is common.

Incidence and disease severity depend, in part, on immunity developed as a result of previous experience (by natural disease) or recent influenza immunization with the circulating strain or a related strain.

Influenza A viruses, including 2 subtypes (H1N1 and H3N2 ), and influenza B viruses circulate worldwide

In temperate climates, seasonal epidemics usually occur during winter months.

Peak influenza activity in the United States can occur anytime from November to May but most commonly occurs between January and March.

Community outbreaks can last 4 to 8 weeks or longer.

Circulation of 2 or 3 influenza virus strains in a community may be associated with a prolonged influenza season of 3 months or more and bimodal peaks in activity.

Influenza is highly contagious.

Patients may be infectious 24 hours before onset of symptoms.

Viral shedding in nasal secretions usually peaks during the first 3 days of illness and ceases within 7 days but can be prolonged in young children and immunodeficient patients for 10 days or even longer.

Viral shedding is correlated directly with degree of fever.

Incidence of influenza in healthy children generally is 10% to 40% each year, but illness rates as low as 3% also have been reported, depending on the circulating strain.

bacterial coinfections with a variety of pathogens, including MRSA, have been reported.

Hospitalization rates among children younger than 2 years are similar to hospitalization rates among people 65 years and older

children younger than 24 months consistently are at higher risk of hospitalization.

influenza infection sometimes is associated with development of pneumococcal or staphylococcal pneumonia in children( MRSA has been reported).

Rates of hospitalization and morbidity attributable to complications, such as bronchitis and pneumonia, are even greater in children with high-risk conditions, including asthma, diabetes mellitus, hemodynamically significant cardiac disease, immunosuppression, and neurologic and neurodevelopmental disorders.

Influenza virus infection in neonates also has been associated with considerable morbidity, including a sepsis-like syndrome, apnea, and lower respiratory tract disease.

Fatal outcomes, including sudden death, have been reported in both chronically ill and previously healthy children.
During the entire influenza A (H1N1) pandemic period lasting from April 2009 to August 2010, a total of 344 laboratory-confirmed, influenza-associated pediatric deaths were reported.

Both influenza A and B viruses have been associated with deaths in children, most of which have occurred in children younger than 5 years.

Almost half of children who die do not have a high-risk condition as defined

The incubation period usually is 1 to 4 days, with a mean of 2 days. Influenza Pandemics.

Pandemics, therefore, can lead to substantially increased morbidity and mortality rates compared with seasonal influenza.

During the 20th century, there were 3 influenza pandemics, in 1918 (H1N1), 1957 (H2N2), and 1968 (H3N2).

The pandemic in 1918 killed at least 20 million people in the United States and perhaps as many as 50 million people worldwide.

The 2009 influenza A (H1N1) pandemic was the first in the 21st century, lasting from April 2009 to August 2010; there were 18 449 deaths among laboratory-confirmed influenza cases.

DIAGNOSTIC TESTS:

viral culture, RT-PCR,
rapid influenza molecular assays,
or rapid diagnostic tests  if possible,

during the first 72 hours of illness, because the quantity of virus shed decreases rapidly as illness progresses beyond that point.

Specimens of nasopharyngeal secretions obtained by swab, aspirate, or wash should be placed in appropriate transport media for culture.

influenza virus usually can be isolated within 2 to 6 days.

Rapid diagnostic tests reported sensitivity (44%-97°/o) and specificity (76%-100%) compared with viral culture, RT-PCR, and rapid influenza molecular assays are variable and differ by test and specimen type.

Additionally, many rapid diagnostic antigen tests cannot distinguish between influenza subtypes

# TREATMENT:

2 classes of antiviral medications currently are approved for treatment or prophylaxis of influenza infections:

neuraminidase inhibitors (oseltamivir and zanamivir) and adamantanes (amantadine and rimantadine).

Oseltamivir, an oral drug, remains the antiviral drug of choice.

Zanamivir, an inhaled drug, is an acceptable alternative but is more difficult to administer; especially to young children.

oseltamivir can be used to treat influenza in both term and preterm infants .

Widespread resistance to adamantanes has been documented among H3N2 and H1N1 influenza viruses since 2005 (influenza B viruses intrinsically are not susceptible to adamantanes).

Since January 2006, neuraminidase inhibitors (oseltamivir, zanamivir) have been the only recommended influenza antiviral drugs against influenza viruses.

## Table 3.33. Antiviral Drugs for Influenza'

| Drug (Trade Name) | Virus | Administration | Treatment Indications | Chemoprophylaxis Indications | Adverse Effects |
|---|---|---|---|---|---|
| Oseltamivir (Tamiflu) | A and B | Oral | Birth or older" | 3 mo or older | Nausea, vomiting |
| Zanamivir (Relenza) | A and B | Inhalation | 7 y or older | 5 y or older | Bronchospasm |
| Amantadinec (Symmetrel) | A | Oral | 1 y or older | 1 y or older | Central nervous system, anxiety, gastrointestinal |
| Rimantadinec (Flumadine) | A | Oral | 13 y or older | 1 y or older | Central nervous system, anxiety, gastrointestinal |

'For current recommendations about treatment and chemoprophylaxis of influenza, consulting specific drug information, see

Therapy for influenza virus infection should be offered to any hospitalized child who has severe, complicated, or progressive respiratory illness that may be influenza related, regardless of influenza-immunization status or whether onset of illness has been greater than 48 hours before admission.

Outpatient therapy should be offered for influenza infection of any severity in children at high risk of complications of influenza infection, such as children younger than 2 years.

The greatest impact on outcome will occur if treatment can be initiated within 48 hours of illness onset but treatment still should be considered if later in the course of illness, especially for hospitalized patients.

Antiviral treatment also should be considered for symptomatic siblings of children younger than 6 months or with underlying medical conditions that predispose them to complications of influenza.

Children with severe influenza should be evaluated carefully for possible coinfection with bacterial pathogens (eg, S aureus) that might require antimicrobial therapy.

If antiviral therapy is prescribed, treatment should be started as soon after illness onset as possible and should not be delayed while waiting for a definitive influenza test result, because early therapy provides the best outcomes.

The duration of treatment is 5 days for the neuraminidase inhibitors (oseltamivir and zanamivir).

Patients with any degree of renal insufficiency should be monitored for adverse events.

Only zanamivir, which is administered by inhalation, does not require adjustment for people with severe renal insufficiency.

The most common adverse effects of oseltamivir are nausea and vomiting.

Zanamivir use has been associated with bronchospasm in some people and is not recommended for use in patients with underlying airway disease.

Control of fever with acetaminophen or another appropriate nonsalicylate-containing antipyretic agent may be important in young children, because fever and other symptoms of influenza could exacerbate underlying chronic conditions.

Children and adolescents with influenza should not receive aspirin or any salicylate-containing products because of the potential risk of developing Reye syndrome.

## ISOLATION OF THE HOSPITALIZED PATIENT:

In addition to standard precautions, droplet precautions are recommended for children hospitalized with influenza or an influenza-like illness for the duration of illness.

Respiratory tract secretions should be considered infectious, and strict hand hygiene procedures should be used.

# CONTROL MEASURES:

Influenza Vaccine.
The influenza virus strains selected for inclusion in the seasonal vaccine may change yearly.

There are 2 forms of the vaccine:

inactivated influenza vaccine (IIV), administered intramuscularly or intra dermally,
live-attenuated influenza vaccine (LAIV), administered intra nasally.

In the past, IIV and LAW contained the same 3 virus strains (A [H3N2], A [H1N1], and B [1 of 2 lineages]), which were selected annually on the basis of influenza circulation in the southern hemisphere.

In the 2013-2014 season, quadri valent vaccines that contained both antigenically distinct lineages (ie, Victoria or Yamagata) of influenza B viruses, in addition to A(H3N2) and A(H1N1), were introduced.

The trivalent LAIV formulation has been replaced by a quadrivalent LAW formulation (LAIV4).

# Table 3.34. Schedule for Inactivated Influenza Vaccine (IIV) Dosage by Agea

| Age | Dose, mLb | No. of Doses | Routec |
|---|---|---|---|
| 6 through 35 mo | 0.25 | 1-2[d] | Intramuscular |
| 3 through 8 y | 0.5 | 1–2[d] | Intramuscular |
| 9 y or older | 0.5 | 1 | Intramuscular |
| 18 y or older (Intradermal) | 0.1 | 1 | Intradermal |
| 18 y or older (Non-egg-based) | 0.5 | 1 | Intramuscular |

Manufacturers include Sanofi Pasteur (Fluzone and Fluzone Quadrivalent, split-virus vaccines licensed for people 6 months or

# Table 3.35. Schedule for Live-Attenuated Influenza Vaccine (LAIV)a

| Age | Dose, mLb | No. of Doses | Route |
|---|---|---|---|
| 2 through 8 y | 0.2 | 1 2c | Intranasal |
| 9 y through 49 y | 0.2 | 1 | Intranasal |

aManufacturer: MedImmune Vaccines, Inc (FluMist Quadrivalent).

bFrom: American Academy of Pediatrics, Committee on Infectious Diseases. Recommendations for prevention and control of influenza in children, 2014-2015. *Pediatrics*. 2014;134(5):e1503—e1519. Dosage is the one recommended in recent years. Physicians should refer to the product circular each year to ensure that the appropriate dosage is given.

cTwo doses administered at least 4 weeks apart are recommended for children younger than 9 years who are receiving LAIV for

IIVs now are available in both trivalent (IIV3) and quadrivalent (IIV4) formulations.

IIVs contain no live virus.

IIVs are administered via intramuscular (IM) or intradermal (ID) injection.

IIV4 is likely to offer broader protection than IIV3, especially if the circulating B strain is not included in the IIV3.

An ID formulation of IIV3 is licensed for use in people 18 through 64 years of age administration.

There is no preference for IM or ID immunization with IIV3 in people 18 years or older.

IIV4 is not currently available as an ID formulation.

# immunogenicity in Children.

Children 9 years and older require only 1 dose of influenza vaccine annually, regardless of their influenza immunization history.

Children 6 months through 8 years of age who previously have not been immunized against influenza require 2 doses of IW or LAW administered at least 4 weeks apart to produce a satisfactory.

# antibody response:

Significant protection against disease is achieved 1 to 2 weeks after the second dose.

In subsequent years, children 6 months through 8 years of age may require 1 or 2 doses, depending on the child's age at the time of the first administered dose, his or her vaccine history, and the makeup of the current year's vaccine.

A dosing algorithm for children 6 months through 8 years of age is prepared each year and can be found in the annual policy statement on influenza from the American Academy of Pediatrics (AAP) published in September in Pediatrics and available at Red Book Online .

For children requiring 2 doses, vaccination should not be delayed to obtain a specific product for either dose.

Any available, age-appropriate trivalent or quadrivalent vaccine can be used;

IIV and LAIV are considered interchangeable.

A child who receives only 1 of the 2 doses as a quadrivalent formulation is likely to be less primed against the additional B virus.

# Vaccine Efficacy and Effectiveness:

The efficacy (ie, prevention of illness among vaccine recipients in controlled trials) and effectiveness (ie, prevention of illness in populations receiving vaccine) of influenza vaccines depend primarily on the age and immune competence of vaccine recipients, the degree of similarity between the viruses in the vaccine and those in circulation, and the outcome being measured.

Protection against virologically confirmed influenza illness after immunization with IIV in healthy children older than 2 years ranges from 50% to 95% depending on the closeness of vaccine strain match to the circulating wild strain.

Efficacy of LAIV was 86% to 96% against virologically confirmed influenza A (H3N2) virus infection in a large clinical pediatric trial during 1 year.

Efficacy of IIV in children 6 through 23 months of age appears to be lower than in older children, although data are limited.

The effectiveness of influenza immunization on acute respiratory tract illness is less evident in pediatric than in adult populations because of the frequency of upper respiratory tract infections and influenza-like illness caused by other viral agents in young children.

Antibody titers for all seasonal influenza vaccines wane up to 50% of their original levels 6 to 12 months after immunization.

An annual dose is critical to maintain protection in all populations.

## Co administration With Other Vaccines.

IIV can be administered simultaneously with other live and inactivated vaccines.

inactivated or live vaccines can be administered simultaneously with LAIV.

After administration of a live vaccine, at least 4 weeks should pass before another live vaccine is administered.

## Recommendations for Influenza Immunization:

All people 6 months and older should receive influenza vaccine annually.

begin in September or as soon as.

LAIV should be considered for healthy children 2 through 8 years of age who have no contraindications or precautions to the intranasal vaccine.

If LAIV is not readily available, IIV should be used; vaccination should not be delayed to obtain LAW.

Particular focus should be on the administration of IIV for all children and adolescents with underlying medical conditions associated with an elevated risk of complications from influenza, including the following:

- Asthma or other chronic pulmonary diseases, such as cystic fibrosis
- Hemodynamically significant cardiac disease
- Immunosuppressive disorders or therapy
- Human immunodeficiency virus (HIV) infection
- Sickle cell anemia and other hemoglobinopathies
- Diseases that necessitate long-term aspirin therapy, including juvenile idiopathic arthritis or Kawasaki disease
- Chronic renal dysfunction
- Chronic metabolic disease, including diabetes mellitus
- Any condition that can compromise respiratory function or handling of secretions or can increase the risk of aspiration, such as neurodevelopmental disorders, spinal cord injuries, seizure disorders, or neuromuscular abnormalities.

# LAIV Indications.

LAIV is indicated for healthy, non pregnant people 2 through 49 years of age.

IIV is preferred for close contacts of severely immunosuppressed people.

People should not receive LAIV :

if they received other live vaccines within the last 4 weeks,
have a moderate to severe febrile illness,
are receiving salicylates,
have a known or suspected immune deficiency disease or are receiving immunosuppressive or immunomodulatory therapies,
are pregnant or considering pregnancy,
have the diagnosis of asthma,
have a history of egg allergy,
increase the risk for aspiration .

IIV is preferred over LAIV for children with chronic underlying medical conditions,
including metabolic disease, diabetes mellitus, other chronic disorders of the pulmonary or cardiovascular systems, renal dysfunction, or hemoglobinopathies.

The safety of LAIV in these populations has not been established.

# FIG 3.8. PRECAUTIONS FOR ADMINISTERING IIV TO PRESUMED EGG-ALLERGIC CHILDREN.'

## Approach to Children With Presumed Egg Allergy

**History of an allergic reaction to eggs?**

**NO** → Administer influenza vaccine per usual protocol

**YES**

**Was the allergic reaction severe?**

**NO** → **Administer influenzavaccine with preconditions***

**(eg, hives)**

**YES**

**Anaphylaxis or Severe Reaction**

- *Cardiovascular changes (eg, low BP)
- *Gastrointestinal (eg, vomiting)
- *Respiratory (eg, wheezing, throat swelling)
- *Episode required epinephrine

**Allergy consultation**
**(Alternatively, R;V3 may *be* given if 18-49 years old)**

'Necessary steps for administering influenza vaccine to any child with presumed egg allergy

- in-office observation fur 30 minutes
- Appropriate resuscitative equipment available

a American Academy of Pediatrics, Committee on Infectious Diseases. Recommendations for prevention and control of influ-

LAIV is not recommended for children whose parent or guardian answers yes to this question or for children who have had a wheezing episode or asthma diagnosis noted in his or her medical record within the past 12 months.

Precaution also should be taken when considering LAIV administration to people with minor acute illness, such as a mild upper respiratory tract infection, with or without fever.

LAIV should not be administered if nasal congestion will impede delivery of the vaccine to the nasopharyngeal mucosa until the congestion-inducing illness is resolved.

Children taking an influenza antiviral medication should not receive LAIV until 48 hours after stopping the influenza antiviral therapy.

If a child recently received LAIV but has an influenza illness for which antiviral agents are appropriate, the antiviral agents should be given.

Re immunization may be indicated because of the potential effects of antiviral medications on LAIV replication and immunogenicity.

The preference of IIV over LAIV for such people is because of the theoretical risk of transmission of LAIV vaccine strain to an immunocompromised contact of an LAIV-immunized child.

people recently immunized with LAIV should restrict contact with severely immunocompromised patients for 7 days after immunization, even though there have been no reports of LAIV transmission between these 2 groups.

In the theoretical scenario in which symptomatic LAW infection develops in an immunocompromised host, oseltamivir or zanamivir could be prescribed because LAIV strains are susceptible to these antiviral medications.

Children with hemodynamically unstable cardiac disease constitute a large group potentially at high risk of complications of influenza.

The immune response to and safety of IIV in these children are comparable to immune response and safety in healthy children.

data from some studies suggest that influenza vaccination in pregnancy

may decrease the risk of preterm birth as well as giving birth to infants who

are small for gestational age.

Immunization of people who are in close contact with children with high-risk conditions or with any child younger than 60 months (5 years) is an important means of protection for these children.
In addition, immunization of pregnant women may benefit their unborn infants, because trans placentally acquired antibodies and human milk may protect infants from infection with influenza virus.

annual influenza immunization are recommended for the following people:

- Close contacts of infants younger than 6 months
- Household contacts and out-of-home care providers of children younger than 5 years and at-risk children of all ages
- Health care personnel (HCP) or health care volunteers
- Any woman who is pregnant or considering pregnancy (IIV only)
- Close contacts of immunosuppressed people
- Children and adolescents of American Indian or Alaska Native heritage
- Children who are members of households with high-risk adults , any children 6 through 59 months of age, and children with HIV infection

The AAP recommends a mandatory annual immunization program for HCP, because

they frequently come into contact with patients at high risk of influenza illness in their clinical

settings.‘

Influenza vaccination of HCP has been shown to reduce both morbidity and mortality among patients.

# Chemoprophylaxis :

Chemoprophylaxis should not be considered a substitute for immunization.

Influenza vaccine always should be offered if not contraindicated, even after influenza virus has begun circulating in the community.

Antiviral medications currently licensed are important adjuncts to influenza immunization for control and prevention of influenza disease.

Because of high rates of resistance of 2009 pandemic influenza A (H1N1), influenza A (H3N2), and influenza B strains to amantadine or rimantadine, only oseltamivir or zanamivir currently are recommended.

However, recommendations for use of these drugs for chemoprophylaxis may vary by location and season, depending on susceptibility patterns.

Pediatricians should inform recipients of antiviral chemoprophylaxis that the risk of influenza is lowered but still remains while taking medication, and susceptibility to influenza returns when medication is discontinued.

Oseltamivir use is not a contraindication to immunization with IIV (unlike LAIV).

chemoprophylaxis during an influenza outbreak, as defined by the CDC, is recommended:

- For children at high risk of complications from influenza for whom influenza vaccine is contraindicated
- For children at high risk during the 2 weeks after IIV immunization
- For family members or HCP who are unimmunized and are likely to have ongoing, close exposure to:
  - unimmunized children at high risk; or
  - unimmunized infants and toddlers who are younger than 24 months
- For control of influenza outbreaks for unimmunized staff and children in a closed institutional setting with children at high risk (eg, extended-care facilities)
- As a supplement to immunization among children at high risk, including children who are immunocompromised and may not respond to vaccine
- As postexposure prophylaxis for family members and close contacts of an infected person if those people are at high risk of complications from influenza

• For children at high risk and their family members and close contacts, as well as HCP, when circulating strains of influenza virus in the community are not matched with seasonal influenza vaccine strains, on the basis of current data from the CDC and local health departments These recommendations apply to routine circumstances, but it should be noted that guidance may change on the basis of updated recommendations from the CDC in concert with antiviral availability, local resources, clinical judgment, recommendations from local or public health authorities, risk of influenza complications, type and duration of exposure contact, and change in epidemiology or severity of influenza.

Chemoprophylaxis is not recommended for infants younger than 3 months, unless the situation is judged critical, because of limited safety and efficacy data in this age group.

Chemoprophylaxis does not interfere with the immune response to IIV; however, people immunized with LAW should not receive antiviral prophylaxis for 14 days after receipt of LAIV because of the potential effects of antiviral medications on LAIV replication and immunogenicity.

# Thanks for your attention