به‌نام خدای بخشاینده مهربان

In the name of Allah, the Beneficent, the Merciful.

انواع انفلوانزا

- ویروس انفلوانزا از خانواده orthomyxoviruses می باشد و دارای ۳ genera or **types** زیر می باشد
  - A
  - B
  - C

- بیماری اپیدمیک توسط ویروس انفلوانزا types A and B ایجاد می شود
- آنتی ژن های انفلوانزا types A and Bدر واکسن انفلوانزا موجود است

- **Type C** influenza viruses cause **sporadic** mild influenza-like illness in children, and type C antigens are not included in influenza vaccines

- Influenza A viruses are subclassified into **subtypes** by 2 surface antigens,
  - hemagglutinin (HA)
  - neuraminidase (NA)
- Examples of these virus subtypes include H1N1 and H3N2 influenza A viruses.

Antigenic drift

- A minor antigenic variation within the same influenza A or B subtypes is termed *antigenic drift*.

- *دریفت آنتی ژنی به صورت مداوم اتفاق می افتد و باعث ایجاد* ***new strains*** *of influenza A and B می شود که اپیدمی های فصلی را ایجاد می کند*

Antigenic shifts

- تغییرات عمده و بزرگ در ویروس انفلوانزای A می باشد که منجر به ایجاد **ساب تایپ** جدید می شود
- Antigenic shift occurs only with influenza A viruses and can lead to a 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.

- Antigenic shift has produced 4 influenza pandemics in the 20th and 21st centuries.

- پاندمی انفلوانزای نوع A (H1N1)در سال ۲۰۰۹ هم زمان دارای دو ویژگی ویرولانس بالا و فقدان ایمنی نسبت آن بوده که باعث افزایش ۴ برابر مرگ و میر کودکان نسبت به قبل بوده است

- As with previous antigenic shifts, the 2009 pandemic influenza A (H1N1) viral strain subsequently has replaced the previously circulating seasonal influenza A (H1N1) strain in the ensuing influenza seasons.

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

swine influenza

- عفونت انسان با انفلوانزای خوکی به صورت یک بیماری شبه انفلوانزای تیپیک بروز می کند

- تشخیص آن با کشف ویروس انفلوانزا با منشا خوکی swine origin به صورت گذشته نگر طی تایپینگ ویروس های انفلوانزای انسانی در routine surveillance تعیین می شود

avian influenza

- ویروسهایی که در آزمایش‌ها جداسازی می‌شوند از گونهٔ Aاین ویروس و از زیررده‌های H5و H7اند.

- Human infections with **avian** influenza viruses are uncommon but may result in a spectrum of disease from
  - mild respiratory symptoms and conjunctivitis
  - severe lower respiratory tract disease,
  - acute respiratory distress syndrome (ARDS),
  - 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

- As of 2017, Asian H7N9 is ranked as the influenza virus with the highest potential pandemic risk.
- **No efficient or sustained human-to-human** transmission has been detected, but when human infections occur, they are associated with severe illness and high mortality.
- Infection with a novel influenza A virus is a nationally notifiable disease and should be reported

Influenza Pandemics

- *Influenza pandemics 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

EPIDEMIOLOGY

- The **incubation period**

usually is 1 to 4 days, with a mean of 2 days

- Influenza is spread person to person, primarily through
- **large-particle** respiratory droplet transmission (eg, coughing or sneezing near a susceptible person),
- which requires close contact between the person who is the source and person who is the recipient,
- because droplets generally only travel short distances

- Another indirect mode of transmission comes from **hand transfer** of influenza virus from droplet-contaminated surfaces to mucosal surfaces of the face (**autoinoculation**).
- **Airborne transmission** via smallparticle aerosols in the vicinity of the infectious individual also may occur

- During community outbreaks of influenza, the highest incidence occurs among **school-aged children.**

- 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

- prevalence of each type and subtype can vary among communities and within a single community over the course of an influenza season
- In temperate climates, seasonal epidemics usually occur **during WINTER months**
- Peak influenza activity 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 may produce **bimodal peaks** in activity

- Influenza is highly contagious, especially among semienclosed institutionalized populations; other ongoing closed-group gatherings, such as
  - schools and preschool
  - child care classrooms
  - travelers who have returned from areas where influenza viruses may be circulating, including
  - participants in organized tour groups,international mass gatherings
  - summer camps
  - cruise or military ship passengers

- 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 degreeof 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.

- Influenza and its complications have been reported to result in a **10% to 30% increase** in the number of courses of antimicrobial agents prescribed to children during the influenza season

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

- Rates vary among studies (190–480 per 100 000 population)

- It is clear, however, that children **younger than 24 months** consistently are at a substantially higher risk of hospitalization than older children

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

- Antecedent influenza infection sometimes is associated with development of pneumococcal or staphylococcal **pneumonia** in children.

CLINICAL MANIFESTATIONS

- Typically begins with **SUDDEN ONSET** of **FEVER**
- Often accompanied by
  - Chills or rigors
  - Headache
  - Malaise
  - Diffuse myalgia
  - Nonproductive cough

- Subsequently,these **respiratory tract signs and symptoms** become more prominent, including :
  - Sore throat
  - Nasal congestion
  - Rhinitis
  - Cough

- less commonly are associated with influenza illness
  - Conjunctival injection
  - Nausea
  - Vomiting
  - Diarrhea

- In some children, influenza can appear as an **upper respiratory tract illness** or as a **febrile illness with few** respiratory tract symptoms

- When influenza viruses are circulating in a community, the diagnosis of influenza should be considered in all children and adults (including health care personnel) with
  - acute onset of respiratory symptoms
  - regardless of degree of symptoms
  - whether or not there is fever
  - regardless of influenza vaccination status.

- Influenza is an important cause of

OTITIS MEDIA

- **ACUTE MYOSITIS** secondary to influenza can present with calf tenderness and refusal to walk

- In infants, influenza can produce a nonspecific sepsis-like illness picture

- in infants and young children, influenza occasionally causes
  - Croup
  - Pertussis like-illness
  - Bronchiolitis
  - Pneumonia.

- Although the large majority of children with influenza **recover fully after 3 to 7 days**
- Previously healthy children can have severe symptoms and complications

Neurologic complications

- Range from

FEBRILE SEIZURES to
SEVERE ENCEPHALOPATHY and
ENCEPHALITIS with STATUS EPILEPTICUS,
resulting in NEUROLOGIC SEQUELAE or DEATH.

- Reye syndrome
  - Now is a very rare condition, has been associated with influenza infection and the use of aspirin therapy during the illness
- Myocarditis
  - Death from influenza-associated myocarditis has been reported

- Invasive **SECONDARY INFECTIONS** or **COINFECTIONS** with
  - Group A streptococcus
  - *Staphylococcus aureus (including [MRSA]),*
  - *Streptococcus pneumoniae,*
  - *Other bacterial pathogens*
- *can result in severe disease and death*

DIAGNOSTIC TESTS

DIAGNOSTIC TESTS

- تست های بررسی انفلونزا هنگامی باید انجام شود که احتمال تاثیر بر روی مدیریت بالینی بیماری وجود داشته باشد

  - تصمیم برای شروع داروی آنتی ویرال
  - پی گیری سایر تست های تشخیصی
  - تصمیم برای شروع آنتی بیوتیک
  - معیار های کنترل عفونت و پیشگیری

- تصمیم برای انجام تست های انفلوانزا به موارد زیر بستگی دارد

- Level of suspicion for influenza
- local influenza activity
- sensitivity and specificity of commercially available influenza tests
  - rapid influenza molecular assays,
    - (RT-PCR) assays,
    - multiplex RT-PCR assays,
  - immunofluorescence assays
    - (direct fluorescent antibody [DFA]
    - indirect fluorescent antibody [IFA] staining),
  - rapid influenza diagnostic tests(RIDTs).

- تست انتخابی برای بررسی انفلوانزا بستگی به شرایط بالینی بیمار دارد

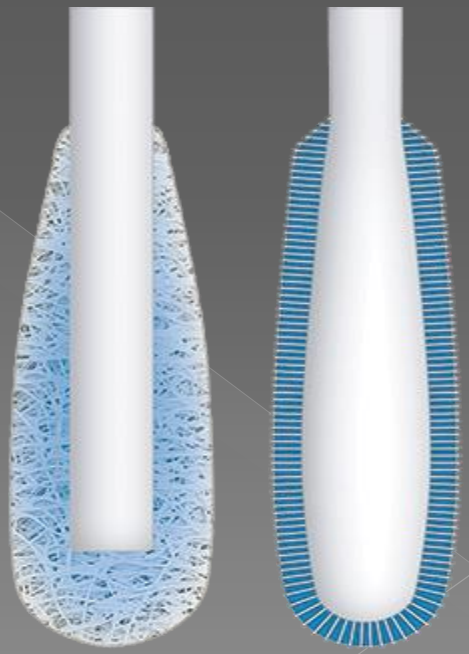
- برای تشخیص انفلوانزا در بیماران سرپایی نمونه توسط سوآپ دستگاه تنفسی فوقانی (نازال و یا نازوفارنژیال) هر چه سریعتر بعد از شروع بیماری (ترجیحا طی ۴ روز اول) باید جمع آوری شود

- optimal respiratory tract swab specimen بستگی به این دارد که کدام تست مورد نظر باشد

- Nasopharyngeal swab specimens
  - بالا ترین میزان yield از نمونه ها ی دستگاه تنفسی فوقانی برای کشف ویروس انفلوانزا را دارا می باشد
- Midturbinate nasal swab specimens
  - این روش نیز قابل قبول می باشد

- combined nasal and throat swab specimens
- باعث افزایش میزان کشف ویروس انفلوانزا نسبت به نمونه گیری از یک سایت به تنهایی می شود (مخصوصا نسبت به نمونه سواپ throat به تنهایی)
- یک انتخاب مناسب برای جایگزینی روش nasopharyngeal swab specimens

- Using flocked swabs likely improves influenza virus detection over nonflocked swabs.



- در بیماران بستری که بیماری شدید راه هوایی تحتانی ندارند نمونه
- nasopharyngeal
- nasal
- combined nasal-throat

swab specimens should be collected

- در بیماران نارسایی تنفسی که تحت ونتیلاسیون مکانیکی هستند و تست انفلوانزا منفی از نمونه راه هوایی فوقانی دارند روش های زیر سودمند است
- endotracheal aspirate
- bronchoalveolar lavage (BAL) fluid

Nonrespiratory specimens such as

- blood
- plasma
- serum
- cerebrospinal fluid
- urine, and stool

should not be collected or tested for seasonal influenza viruses

Specimens should be obtained, if possible, during the

- **first 4 days of illness**

because the quantity of virus shed decreases rapidly as illness progresses beyond that point.

Results of influenza testing should be properly interpreted in the context of

- clinical findings
- local community influenza activity

- Molecular tests have the best performance characteristics
- RIDTs are significantly less sensitive than other methods and, therefore, produce more false-negative results
- rapid diagnostic antigen tests cannot distinguish between influenza subtypes, a feature that can be critical during seasons with strains that differ in antiviral susceptibility and/or relative virulence

- **False-positive results** are more likely to occur during periods of low influenza activity;
- **false-negative results** are more likely to occur during periods of peak influenza activity

rapid diagnostic test

rapid diagnostic test

- تصمیم گیری برای درمان و کنترل عفونت را می توان بر اساس نتایج مثبت rapid diagnostic test انجام داد
- Positive results are helpful, because they may reduce additional testing to identify the cause of the child's influenza-like illness
- **Treatment should not be withheld in high-risk patients awaiting test results.**

antigen-based testing

- Point-of-care testing in **outpatient** settings
- **inexpensive** kits

- use colorimetric changes upon antibody recognition of virus in nasal swab material to rapidly demonstrate the presence of antigen.

- Some tests can distinguish type A from type B influenza
- **none can currently subtype** influenza A strains or distinguish specific strains within an influenza A subtype or between the two major influenza B lineages

- low sensitivity but reasonable specificity compared to PCR
  - positive result is useful for directing care
  - negative result does not rule out influenza

- Rapid antigen testing is also commonly employed **in hospitals** as a point-of-care diagnostic in acute care settings such as emergency rooms,
- but typically with a more sensitive and specific test as a backup, performed in a central laboratory

fluorescent antibody test

- the presence of virus is determined by microscopy to detect fluorescence of dyes bound to those antibodies which recognize the virus
- This method is more sensitive and specific than rapid antigen tests
- may take **several hours** to achieve a result and requires **special training and experience**

PCR-based testing

- Rapid and sensitive
  - particularly real-time PCR assays.

- These assays have the advantages of **quick** turnaround times, improved sensitivity and specificity compared to all other methods, and can be designed to differentiate viruses by **type**, **subtype**, and even **strain**.

Influenza Diagnostic Test	Method	Availability	Typical Processing Time	Sensitivity	Distinguishes Influenza A Virus Subtypes
Rapid influenza diagnostic tests[a]	Antigen detection	Wide	<15 min	10%–70%	No
Rapid influenza molecular assays[b]	RNA detection	Wide	<20 min	86%–100%	No
Nucleic acid amplification tests (including RT-PCR)	RNA detection	Limited	1–8 h	86%–100%	Yes
Direct and indirect Immunofluorescence assays	Antigen detection	Wide	1–4 h	70%–100%	No
Rapid cell culture (shell vials and cell mixtures)	Virus isolation	Limited	1–3 days	100%	Yes
Viral cell culture	Virus isolation	Limited	3–10 days	100%	Yes

TREATMENT

- 2 classes of antiviral medications currently are approved for treatment or prophylaxis of influenza infections:
  - **neuraminidase inhibitors**
    - oral oseltamivir,
    - inhaled zanamivir
    - intravenous peramivir
  - **adamantanes**
    - amantadine
    - rimantadine

- Oseltamivir
  - antiviral drug of choice
- Zanamivir
  - acceptable alternative but is more difficult to administer, especially in young children
- Peramivir
  - approved in 2017 for use in children **2 years and older**
  - has been approved for use in adults 18 years and older since 2014

- (FDA) has approved **oseltamivir** for children as young **as 2 weeks** of age

- Given preliminary pharmacokinetic data and limited safety data, oseltamivir can be used to treat influenza in both **term and preterm infants from birth**, because benefits of therapy are likely to outweigh possible risks of treatment.

- Widespread resistance to adamantanes has been documented
- influenza B viruses intrinsically are not susceptible to adamantanes

- Resistance to oseltamivir has been documented to be approximately 1% at most for any of the tested influenza viral samples during the past few years.

- Treatment for influenza virus infection should be offered as early as possible, without waiting for confirmatory influenza testing, to
  - any hospitalized child presumed clinically to have influenza disease
  - with serious, complicated, or progressive illness attributable to influenza,
- irrespective of influenza vaccination status or whether illness began greater than 48 hours before admission.

- Treatment also should be offered to influenza-infected children **at high risk** of complications from influenza, regardless of severity of illness.

- Treatment may be considered for any otherwise healthy child clinically presumed to have influenza disease

- The greatest effect on outcome will occur if treatment can be initiated **within 48 hours of illness onset**, but treatment still should be considered if it is later in the course of progressive, symptomatic illness

- Antiviral treatment also should be considered for children clinically presumed to have influenza disease and whose **siblings or household** contacts either are younger than 6 months or have 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

duration of treatment

- oseltamivir and zanamivir is **5 days**
- intravenous peramivir is **1 dose** administered over 15 to 30 minutes

Table 3.34. Antiviral Drugs for Influenza[a]

Drug (Trade Name)	Virus	Administration	Treatment Indications	Chemoprophylaxis Indications	Adverse Effects
Oseltamivir (Tamiflu)	A and B	Oral	Birth or older[b]	3 mo or older	Nausea, vomiting
Zanamivir (Relenza)	A and B	Inhalation	7 y or older	5 y or older	Bronchospasm
Peramivir (Rapivab)	A and B[c]	Intravenous	2 y or older	N/A	Diarrhea; some reports of skin reactions
Amantadine[d] (Symmetrel)	A	Oral	1 y or older	1 y or older	Central nervous system, anxiety, gastrointestinal
Rimantadine[d] (Flumadine)	A	Oral	13 y or older	1 y or older	Central nervous system, anxiety, gastrointestinal

۴. به تدریج حامل را به بطری اضافه می‌نماییم.

۵. در بطری را بسته و به مدت ۳۰ ثانیه تکان می‌دهیم تا پودر کاملا محلول شود.

۶. بر روی برچسب دارو ذکر شود " قبل از هر بار مصرف به‌خوبی هم زده شود ".

سوسپانسیون به مدت ۳۵ روز در یخچال و ۵ روز در دمای اتاق قابل نگهداری است. نباید به وسیله پیمانه سوسپانسیون کارخانه تجویز شود.

تهیه سوسپانسیون اسلتامیویر ۶ mg/ml

وزن بدن	حجم توتال برای هر بیمار[1]	تعداد کپسول‌های ۷۵mg مورد نیاز[2]	حجم آب مورد نیاز	حجم حامل مورد نیاز[2و3]	دوز درمانی (بر اساس وزن)[4]	دوز پروفیلاکسی (بر اساس وزن)[4]
≤۱۵kg	۷۵ml	۶	۵ ml	۶۹ ml	۵ ml (۳۰mg) دو بار در روز برای ۵ روز)	۵ ml (۳۰mg) روزانه برای ۱۰ روز
۱۶-۲۳ kg	۱۰۰ml	۸	۷ml	۹۱ml	۷/۵ ml (۴۵mg) دو بار در روز برای ۵ روز)	۷/۵ ml (۴۵mg) روزانه برای ۱۰ روز
۲۴-۴۰ kg	۱۲۵ml	۱۰	۸ml	۱۱۵ml	۱۰ ml (۶۰mg) دو بار در روز برای ۵ روز)	۱۰ ml (۶۰mg) روزانه برای ۱۰ روز
≥۴۱Kg	۱۵۰ml	۱۲	۱۰ml	۱۳۷ml	۱۲/۵ ml (۷۵mg) دو بار در روز برای ۵ روز)	۱۲/۵ ml (۷۵mg) روزانه برای ۱۰ روز

۱. کل دوره درمانی

۲. بر اساس کل حجم مورد نیاز برای هر بیمار

۳. حامل‌های قابل قبول شامل شربت گیلاس یا شربت ساده است. (براساس شرایط و جهت راحتی بیمار می توان از کنسانتره آب میوه های موجود در بازار با طعمهای مختلف بعنوان حامل استفاده نمود).

۴. در صورت استفاده ازسوسپانسیون ۶mg/ml

- 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.
- 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 some 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.

Chemoprophylaxis

- *Chemoprophylaxis should not be considered a substitute for* immunization.
- **Oseltamivir** and **zanamivir** are important adjuncts to influenza immunization for control and prevention of influenza disease.
- Neither **oseltamivir** or **zanamivir** are a contraindication to immunization with IIV, and neither interferes with the immune response to IIV.
- Chemoprophylaxis is <u>not</u> recommended for infants <u>younger than 3 months</u>

Indications for Chemoprophylaxis

- • 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** wit seasonal influenza **vaccine** strains, on the basis of current data from the CDC and local health departments.

- given for **10 days** (following known exposure)
- for **up to 6 wk** (preexposure during community outbreak);

Generic (Trade Name)	Indication	Route	Age	Usually Recommended Dosage
Zanamivir (Relenza)	Influenza A and B: treatment (see Influenza, p 476)	Inhalation	≥7 y (treatment)	10 mg (one 5-mg blister per inhalation), twice daily for 5 days; first 2 doses can be separated by as little as 2 h; only use diskhaler device
	Influenza A and B: prophylaxis	Inhalation	≥5 y (prophylaxis)	10 mg, once daily for as long as 28 days (community outbreaks) or 10 days (household setting)
Peramivir[b] (Rapivab)	Influenza A and B	IV	≥2 y	2–12 y: 12 mg/kg, once (maximum dose: 600 mg) ≥13 y: 600 mg, once
Oseltamivir[b,j] (Tamiflu)	Influenza A and B: treatment (see Influenza, p 476)	Oral (suspension)	Birth to <9 mo[k]	3 mg/kg twice daily for 5 days[k]
		Oral (suspension)	9–11 mo	3.5 mg/kg twice daily for 5 days
		Oral (suspension and tablets)	1–12 y	≤15 kg: 30 mg, twice daily; 15.1–23 kg: 45 mg, twice daily; 23.1–40 kg: 60 mg, twice daily; >40 kg: 75 mg, twice daily for 5 days
		Oral (tablets)	≥13 y	75 mg, twice daily for 5 days

Influenza A and B: prophylaxis	Oral	3 mo–12 y	Same as the above treatment doses for patients 3 mo–12 y of age, except dose given once rather than twice daily, and given for 10 days rather than 5 (following known exposure) or for up to 6 wk (preexposure during community outbreak); not routinely recommended for infants <3 mo given lack of efficacy data
	Oral	≥13 y	75 mg, once daily for 10 days (following known exposure) or for up to 6 wk (preexposure during community outbreak)

ISOLATION OF THE HOSPITALIZED PATIENT

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

INFLUENZA VACCINE

- The influenza virus strains selected for inclusion in the seasonal vaccine may change yearly in anticipation of the predominant influenza strains expected to circulate in the United States in the upcoming influenza season
- AAP recommends annual use of inactivated influenza vaccines (IIVs) in all people 6 months and older

- IIVs contain no live virus.
  - subvirion vaccines, prepared by disrupting the lipid-containing membrane of the virus, or
  - purified surface-antigen vaccines
- The intramuscular (IM) IIV is licensed for administration to those **6 months and older** and is available in both trivalent (IIV3) and quadrivalent (IIV4)

- An intradermalID) formulation of IIV4 is licensed for use in people 18 through 64 years of age
- no preference for IM or ID immunization with IIV4 in people 18 years or older
- A high-dose inactivated influenza vaccine is available for adults 65 years and older

- Intranasal quadrivalent live attenuated influenza vaccine (**LAIV4**) **not be used in any setting**
- although it is still licensed by the FDA for healthy people **2 through 49 years** of age

- Two types of IIVs manufactured using **egg-free technologies** are available
  - Cell culture-based inactivated influenza vaccine (**ccIIV4**)
    - 4 years or older
    - IM injection
  - recombinant influenza vaccine (**RIV3 and RIV4**)
    - 18 years or older
    - IM injection.

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** 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

Vaccine Effectiveness

- 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

- Effectiveness of IIV in children **6 through 23 months** of age appears to be lower than in older children

- Antibody titers for all seasonal influenza vaccines wane up to 50% of their original levels **6 to 12 months after immunization**, necessitating annual influenza vaccination to maintain protection in all populations

Coadministration With Other Vaccines

- *IIV can be administered simultaneously with other live* and inactivated vaccines

Recommendations for Influenza Immunization

- All people **6 months and older should receive** influenza vaccine annually.
- Influenza vaccine should be administered **as soon as available** each year, preferably **before the start of influenza season**, at the time specified in the annual recommendations of the ACIP

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 CF .
- 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 or salicylate-containing medication, including juvenile idiopathic arthritis or Kawasaki disease, that may place a child atincreased risk of Reye syndrome if infected with influenza.
- Chronic renal dysfunction.
- Chronic metabolic disease, including DM .
- 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.
- Pregnancy

Special Considerations

- In children receiving immunosuppressive **chemotherapy**

The optimal time

  - more than **3 weeks after** chemotherapy has been discontinued,
  - when the peripheral granulocyte and lymphocyte counts are **greater than 1000**

- Prolonged administration of **high doses of corticosteroids** (prednisone of either 2 mg/kg or greater or a total of 20 mg/day or greater or an equivalent)
  - immunization can be deferred
  - provided deferral does not compromise the likelihood of immunization befor the start of influenza season

Close Contacts of High-Risk Patients

- 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

- • 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, is in the postpartum period, or is breastfeeding during the influenza season.
- • Close contacts of immunosuppressed people.
- • Children and adolescents of American Indian or Alaska Nativ heritage.
- • Children who are members of households with high-risk adults, any children 6 through 59 months of age, and children with HIV infection.

Health Care Personnel

- 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

Reactions, Adverse Effects, and Contraindications

- Special precautions for egg-allergic recipients of IIV are not warranted
- Standard immunization practice should include the ability to respond to rare acute hypersensitivity reactions

- The risk of influenza vaccine-associated GBS was higher among people 25 years or older than among people younger than 25 years
- If there is an association between seasonal influenza vaccine and GBS, the risk is rare, at no more than 1 to 2 cases per million doses
- Whether influenza immunization specifically might increase the risk of recurrence of GBS is unknown

- Immunization of children who have asthma or cystic fibrosis
  - not increase adverse events or exacerbations.
- IIV immunization for individuals with HIV infection is considered safe.

- IIVs contain only inactivated subvirion or surface antigen particles and, therefore, **cannot produce active influenza**

- The **most common** adverse events after IIV3 administration are **local injection site pain and tenderness**
- **Fever** may occur within 24 hours after immunization in approximately **10% to 35%** of children **younger than 2 years**
  - but **rarely in older children and adults**

- Mild systemic symptoms , may occur after administration of IIV3.
  - Nausea
  - Lethargy
  - headache
  - muscle aches
  - chills

- most common injection site adverse reactions associated with IIV4
  - pain,
  - redness
  - swelling.
- The most common systemic adverse events are
  - drowsiness
  - irritability
  - loss of appetite
  - fatigue
  - muscle aches
  - headache
  - arthralgia
  - gastrointestinal tract symptoms
- comparable frequency with trivalent vaccines.