

## **Treatment of URTIs**







Define the upper respiratory tract infections (URTIs) and list sites of infection

Identify etiology, signs, and symptoms of URTIs



Outline pharmacological options for URTIs

Determine the antibiotic of choice for the different URTIs



Determine the anti-viral drugs for URTIs



<sup>></sup> Describe pharmacological mechanisms of action of URTI drugs.

## URTIS

**Upper respiratory tract infections (URTI) is** inflammation of the upper airways or Infections of airway above glottis or vocal cords.

**URTIs involve:** the nose, sinuses, ears, pharynx, larynx, & large airways.

**infections of the upper respiratory tract include:** Otitis media - Sinusitis - Pharyngitis - Rhinitis - Laryngitis - Epiglottitis -Tonsillitis - Common cold - Flu.

#### **Common symptoms of URTIs:**

Cough - Sore throat - Running nose - Nasal congestion - Headache - Low-grade fever - Facial pressure - Sneezing - Nasal discharge - Painful swallowing (odynophagia)

no signs of pneumonia, or with no history of chronic obstructive pulmonary disease, emphysema, asthma, or chronic bronchitis.

The onset of symptoms usually begins one to three days after exposure and lasts 7-10 days, and can persist up to 3 weeks

## **Etiology of URTIs**

<b>Viruses</b> Should NOT be treated with antibiotics	Bacteria	
The most common virus is <mark>rhinovirus</mark> .	<b>The most common is</b> Streptococcus pyogenes [Group A (GAS)] Haemophilus influenza Moraxella Catarrhalis	
Other viruses include: the influenza virus, adenovirus, enterovirus & respiratory syncytial virus.	Bacteria may cause roughly 15% of sudden onset pharyngitis	

## **Aims of Pharmacotherapy**



# **Drugs for URTIs**

Incubation period of a cold = 1 to 4 days before onset of symptoms & first 3 days of the cold.

Home remedies = rest, chicken soup, Vitamins

#### 4 groups of drugs used to manage symptoms:

- antihistamines (H-1 blocker)
- decongestants (sympathomimetic amines), Short duration 3-5 days
- antitussives to reduce dry cough
- expectorants for productive cough

#### Other medications, may include:

- NSAIDs, ibuprofen for body pain. (Analgesic)
- Acetaminophen (Tylenol) to reduce fever and body ache.
- Nasal ipratropium (topical) to diminish nasal secretions.

### Normal saline

Local steroids

## **Acute Sinusitis**





#### DEFINITION

Acute rhinosinusitis is inflammation of the nasal cavities & Paranasal sinuses of less than four weeks duration.

The inflammation can lead to increased mucus production & blocked sinuses, due to a difficulty draining.

#### SYMPTOMS

• Fever.

- Purulent nasal discharge.
- Facial pain.
- Headache.

#### TREATMENT

Based on this microbiology, the first-line treatment for Acute <u>B</u>acterial rhinosinusitis is: amoxicillin/clavulanate (Augmentin).

Clavulanate Is Beta-Lactamase inhibitor which increase the efficacy of Amoxicillin.

#### ETIOLOGY

### Viruses (most common cause, Up to 90-98% of the cases):

Rhinoviruses, Influenza viruses, Parainfluenza viruses

### Bacterial agents(develop in 0.5% to 2% of all URIs):

Str. pneumoniae, H. influenzae, M catarrhalis, Pseudomonas & other gram negative bacilli (Nosocomial sinusitis: hospital-acquired infection)

#### **Agents of chronic sinusitis:** Obligate Anaerobes.

Staphylococcus aureus.

## **Pharyngitis/Tonsillitis**



#### DEFINITION

Pharyngitis is inflammation of the mucous membranes that line the pharynx, or back of the throat.

#### **SYMPTOMS**

- A sore or scratchy throat
- Inflammation
- Fever
- Headache
- Difficulty swallowing

#### ETIOLOGY

#### **Bacterial agents:**

Group A Streptococcus (GAS) (Str. pyogenes)

Corynebacterium diphtheriae Neisseria gonorrhoeae



#### Viruses: Without pus

Epstein-Barr virus, Adenovirus, Influenza A&B, Coxsackie A, Parainfluenzae

#### TREATMENI

#### ORAL:

PENICILLIN V , AMOXICILLIN **PARENTERAL**: Benzathine PENICILLIN

#### ALLERGY TO PENICILLIN

DRAL Dr.: No Need for Doses				
Penicillin V	250	250 mg qid ,10 days		
Amoxicillin	50 n	50 mg/kg/day ,10 days		
PARENTERAL				
Benzathine penicillin Adults		Adults:<27kg:600 000 U single dose, IM		
	>27 kg:1.200 000 U single dose, IN			
ALLERGY TO	PENICI	LIN		
Erythromycin estolate		20-40 mg/kg/day, 2x1 or 3x1, 10 days		
Erythromycin ethylsuccinate		te 40 mg/kg/day, 2x1 or 3x1, 10 days		
Azithromycin		12 mg/kg once daily for 5 days		

Erythromycin estolate/ethylsuccinate, Azithromycin(Macrolides Antibiotic)

• A 10-day course of <u>penicillin</u> V or <u>amoxicillin</u> is the first-line therapy for group A betahemolytic streptococcal pharyngitis (GABHS). (Str. pyogenes)

Analgesic(pain relieve) or antipyretic(reduce fever) medications should also be considered.

## Acute Otitis Media (AOM)



is Inflammation of the middle ear. AOM is uncommon in adults, mainly in children.

- Fever.
- Ear pain
- Previous history of cold symptoms
  - (runny nose, nasal congestion or cough)

#### For Adult:

#### First line:

Amoxicillin/Clavulanate (Augmentin)

#### Penicillin allergy:

Cefdinir - Cefpodoxime (3rd gen. cephalosporin) Doxycycline (Tetracycline Antibiotic) Azithromycin (Macrolide Antibiotic)

#### For Children:

#### First line:

Amoxicillin

#### Penicillin allergy:

Cefdinir - Cefpodoxime (3rd gen. cephalosporin)

#### Second Line:

Amoxicillin/Clavulanate (Augmentin)

#### Acute Otitis Media AOM:

Str. pneumoniae 30% H. influenzae 20% M. Catarrhalis 15% Str. pyogenes 3% Dr. St. aureus 2% No Need for Percentage

#### **Chronic Otitis Media:**

Pseudomonas aeruginosa St. aureus anaerobic bacteria Viral (alone or with bacteria)

#### Appropriate Antibiotic Dosing for Outpatient Treatment of Upper Respiratory Tract Infections Children

#### Infection Adults

First-line treatment Amoxicillin/clavulanate, 875 mg orally twice per day or 500 mg orally every eight hours for five to 10 days\* or 600 mg orally per day for five to

Penicillin allergy:

five to 10 days\*

10 days\* Cefpodoxime, 200 mg orally twice per

#### First-line treatment Amoxicillin, 80 to 90 mg per kg per day orally divided e

#### Penicillin allergy.

Cefdinir, 14 mg per kg per day orally divided Cefdinir, 300 mg orally twice per day for five to 10 dayst

Second-line treatment (fo within the past 30 days, with concurrent purulent conjunctiviti

amoxicillin, or with no improvement after 48 to 72 hours of initia Amoxicillin/clavulanate, 90 mg per kg per day of amoxicillin v

#### orally on day 1 then 250 mg orally per day on days 2 to 5 Dr.: No Need for Doses

Doxycycline, 100 mg twice per day for

## Laryngitis



#### DEFINITION

Acute laryngitis is an inflammation of the larynx & vocal cords that clinically presents as a **horse voice** typically associated with other symptoms of URI.

#### TREATMENT

 The treatment of acute laryngitis with antibiotics is usually unnecessary because the infectious source is viral, & is self-limited

• Antibiotics in the treatment of laryngitis should be **avoided**.

• Rx. Corticosteroids (prednisone or Prednisolone) reduce inflammation of vocal cords.





#### **OVERVIEW**

• Edema & inflammation of epiglottis & soft tissue above vocal cords. Epiglottitis is a rare, life-threatening condition resulting from inflammatory edema of the epiglottis & surrounding supraglottic tissues, often due to infection.

- Age: children 2–6 years
- Symptoms: Fever, Difficulty in swallowing, Inspiratory stridor.

## Epiglottitis

ETIOLOGY

• **H influenzae type b (Hib)** is <u>no longer</u> the most common cause of epiglottitis since the vaccine was developed in 1985, & Hib now affects adults more than children.

Str. pneumoniae, group A beta-hemolytic streptococcus & St. aureus are among the pathogens responsible for epiglottitis.

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#### TREATMENT ----

- Maintenance of airway
- Treatment includes:

broad-spectrum IV antibiotics such as third-generation cephalosporins (ceftriaxone, cefotaxime, cefixime) or ampicillin/sulbactam\* (Unasyn) may also require methicillin-resistant *S. aureus (MRSA) such as Vancomycin* or other bacterial or fungal coverage.
Empiric drugs: (Drug For emergency conditions)

Ceftriaxone (3rd gen. cephalosporin)

Vancomycin (Glycopeptides Antibiotic)

Amoxicillin-clavulanate, 2nd or 3rd generation cephalosporin

\*Sulbactam Is Beta-Lactamase inhibitor

## **Epiglottitis**

#### PREVENTION

- HiB vaccination.
- H influenzae type b (Hib) Vaccine for infant & children.
- Hib vaccine can prevent H influenzae type b (Hib) disease.



## **Antibiotics in URTIs**

Will Discuss in details Next Lecture (LRTIs)

### **Classification of Antibiotic**

Mechanism of action	Class
Inhibits Cell Wall Synthesis	Cephalosporins Penicillins Carbapenems Glycopeptides
Inhibits Protein Synthesis	Macrolides Aminoglycosides Lincosamides Tetracyclines MALT =protein
Inhibits <b>Fo</b> late Metabolism	Sul <b>FO</b> namides
Inhibits DNA Replication	Fluoro <b>QUIN</b> olones

## Examples for antibiotic drugs (drug of choice; DOC) from each class and names of susceptible bacteria



See github.com/betherist/entibleoptem for details. For educational purposes only. TMPSXX = Trimethoppim-sultamethoaszole, MRSA = Methicillin-resistant Staphylococcus aureus, MSSA = Methicillin-sensitive Staphylococcus aureus, ESCAPPM = Enterobacter spp., Cembacter freundi, Aeromonas spp., Proteus spp., Providencis spp. and Morganella morgani.

Cell Wall Synthesis	Folate synthesis	Nucleic Acid Synthesis
Beta Lactams Penicillins Cephalosporins Carbapenems Monobactams	Trimethoprim	DNA Gyrase Quinolones RNA Polymerase Rifampin
Vancomycin Bacitracin	505 305	505 subunit Macrolides Clindamycin Linezolid Chloramphenicol
Cell Membrane Polymyxins ©2011 TheMedSchool.com	30S subunit Tetracyclines Aminoglycosides	Streptogramins Protein Synthesis

Class	Examples	How They Work	
Penicillins	penicillin, amoxicillin	Penicillins kill bacteria by preventing formation of the bacterial cell wall.	
Macrolides	azithromycin, erythromycin	Macrolides prevent bacteria from multiplying by keeping bacteria from making proteins.	
Cephalosporins	cephalexin, cefdinir	Cephalosporins kill bacteria by preventing formation of the bacterial cell wall.	
Fluoroquinolones	ciprofloxacin, levofloxacin	Fluoroquinolones kill bacteria by keeping bacteria from making DNA.	
Beta-lactams with increased activity	amoxicillin/clavulanate, ceftazidime/avibactam	Beta-lactams with increased activity are combinations that consist of two different drugs: a penicilin or cephalospoin and a beta-factamase inhibitor. The penicilin or cephalospoin kills bacteria by preventing formation of the bacterial cell wail. The beta-lactamase inhibitor has little antibitotic activity on its own. Its job is to protect the penicilini or cephalosporin from being destroyed by an enzyme some bacteria produce. This protection increases the activity of the penicilin or cephalosporin.	
Tetracyclines	tetracycline, doxycycline	Tetracyclines prevent bacteria from multiplying by keeping bacteria from making proteins.	
Trimethoprim- sulfamethoxazole	trimethoprim- sulfamethoxazole	Trimethoprim and sulfamethoxazole work together to inhibit the ability of bacteria to make folic acid, which is necessary to make DNA and proteins. This prevents bacteria from multiplying.	



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## **Therapy for URTI**



For elderly and children younger than 4 years of ages: be caution with Cough and cold drugs, may cause excessive **drowsiness**. Antibiotics are sometimes used for URTIs if the cause of infection **bacteria**. Such as in bacterial sinusitis, strep throat, epiglottitis.

The use of antibiotics is associated with bacterial resistance and secondary infections.

## **Antibiotics adverse effects:**

### Antibiotic resistance

usually mild (e.g., diarrhea, rash)

could be sever EX: -stevens johnson syndrome ( severe skin reaction), clostroides difficile colitis

life threatening such as anaphylaxis or sudden cardiac death



## **Common cold**

IS A **VIRAL INFECTION** OF URT. E.G. **RHINOVIRUSES (FREQUENT PATHOGEN)**, CORONAVIRUS, INFLUENZAS, PARAINFLUENZA VIRUSES, ADENO, ENTEROVIRUSES.

USUALLY LAST WITHIN 7 DAYS.

### Common cold signs and symptoms

fatigue, fever, feeling cold

nose burning, obstruction and rhinorrhea and nasal secretions(usually clear and watery)

redness and swelling of nasal mucus membranes, sneezing and watery eyes.

Treatment:

- Specific antiviral and antibiotic therapy has no role in the treatment of common cold.
- Prevention: face mask and handwashing

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Complications:

- Otitis media (AOM), esp. in children
  - Sinusitis
- Exacerbation of asthma.



# Management of common cold



Treatments with established effectiveness for those symptoms in adults are limited to over-the-counter (OTC) ( الويه ما تحتاج وصفه (طبه):

-analgesics -antihistamine/decongestant combinations.

The American Academy of Pediatrics Choosing Wisely recommendation states that cough and cold medicines should be avoided for respiratory illness in children younger than four years Antibiotics are ineffective for the treatment of the common cold in adults and children and should not be prescribed based on consistent findings of no benefit and increased adverse effects and resistance.



## Influenza(flu)



influenza start In

33:53 to 47:26



till the end





	Types of influenza viru	Fluenza Ises: A, B, C, and D:	
1	Influenza <b>A</b> and <b>B</b> viruses cause seasonal ep (known as flu season) almos	pidemics of disease in people t every winter	
2 Influenza C virus infections generally cause mild illness and are not thought to cause human epidemics.			
3 Influenza <b>D</b> viruses primarily affect <b>cattle</b> with spillover to other animals but are not known to infect people to cause illness.			
Influenz o	a <b>A</b> viruses are divided into subtypes based on two proteins on the surface of the virus: hemagglutinin (H) and neuraminidase (N)( for release).	Nucleoprotein (RNA) Virus Anatomy	

• There are **18** different **hemagglutinin** subtypes and **11** different **neuraminidase** subtypes (H1 through H18 and N1 through N11, respectively).

بالنسبه لإختلاف الارقام بين الفارما والمايكرو ، دكتورة المايكرو قالت نعتمد الفارما





## viral replication

 FOUR INFLUENZA ANTIVIRAL MEDICATIONS APPROVED BY THE U.S. FOOD AND DRUG ADMINISTRATION (FDA).

1. Drugs are chemically related antiviral medications known as **neuraminidase inhibitors** that **block the viral neuraminidase enzyme & have activity against both influenza A and B viruses**:



Antiviral drug

Amantadine.

Rimantadine

Relenza and

Tamiflu

Target

Haemagglutinin

protein

Neuraminidase

inhibitors

2. Baloxavir is a cap-dependent endonuclease inhibitor that interferes with viral RNA transcription & blocks virus replication

3- M2 proton channel antagonists (like amantadine) are not recommended for antiviral treatment or chemoprophylaxis because of high levels of resistance to circulating influenza A viruses.

> For more information , and if you want to see the MOA clearly <u>Click here</u>

> > Page no. 531

Extra note from the doctor

#### Mechanism of Action

Virus

Influenza A

Influenza A

&B

Amantadine and rimantadine share two concentration-dependent mechanisms of anti-influera action. Low concentrations inhibit the ion channel function of the M2 protein of influenza A viruses, which affects two different stages in virus replication.<sup>193</sup> The primary effect involves inhibition of viral uncoating or disassembly of the virion during endocytosis. For subtype H5 and H7 viruses, a late effect on hemagglutinin maturation and viral assembly is presunably mediated through altered pH regulation of the trans-Golgi network. Amantadine and rimantadine block proton permeation and prevent M2-mediated changes in pH. This action probably accounts for inhibition of the acid-mediated dissociation of the matrix protein from the ribonucleoprotein complex within endosomes early in replication and potentiation of acidle pH-induced alterations in the hemagglutinin during its transport late in infection.



### 1- Neuraminidase Inhibitors (NAIs)



NAIs are the largest group of drugs and are currently the most commonly prescribed and used drugs in the treatment of human influenza.

Mechanism of action: Interfere with **release of progeny** influenza virus from infected host cells, thus halting the spread of infection within the respiratory tract. These agents competitively & reversibly interact with the active enzyme site to inhibit viral neuraminidase activity. An enzyme essential for release of newly formed virus particles from infected cells. All of them are effective against most strains of influenza A and B and, unlike amantadine, are associated with low toxicity and are significantly less likely to promote the development of drug resistance. NAIs are also available for

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NAIs are also available for prophylaxis, and their use is especially recommended in people suffering from high-risk flu during influenza season.



### Flu Antiviral Drugs for flu illness season

they block the viral neuraminidase enzyme & have activity against both

drugs:	Adminstratio n	Dose	М.О.А	-
Oseltamivir phosphate (Tamiflu)	orally Termitic Service Termitic Service	five days	NeurAminidase Inhibitors (NAIs) (an enzyme essential for release of newly formed virus particles from infected cells and further spread of the infectious virus.)	
Zanamivir (Relenza)	Inhaled	five days		NeurAminidase Inhibitors (NAIs) also include laninamivir
Peramivir (Rapivab)	IV	one dose		
2- Baloxavir marboxil (Xofluxa) Trade Name not important -used in case of resistance to oseltamivir	Orally Menore under Seiner Propertiesen Menore Seiner Menore S	one dose	-(polymerase acidic endonuclease inhibitor)Baloxavir marboxil (after conversion to baloxavir acid) acts to block influenza virus replication by inhibiting the cap-dependent endonuclease activity of the PA protein.	Active baloxavir inhibits influenza virus replication by selective binding of the RNA- dependent influenza virus RNA polymerase complex. $\overbrace{\downarrow\downarrow\downarrow\downarrow}_{lag}$

### Cont...

drugs:	Contraindications	adverse effects	
Oseltamivir phosphate ( <mark>Tamiflu</mark> )	<ul> <li>Its is not recommended in infants younger than 1 year (because of fatalities in mice).</li> <li>Probenecid reduces renal clearance of oseltamivir by 50%. Serum concentrations of oseltamivir increase with declining renal function; therefore, dosage should be adjusted in patients with renal insufficiency</li> </ul>	Skin reaction, Headache and nausea, Vomiting, bronchitis, sore throat, nasopharyngitis, sinusitis, pain, and dizziness.	
Zanamivir (Relenza)	<ul> <li>allergy to milk protein</li> <li>patients with glucose-galactose malabsorption, hereditary galactose intolerance,</li> <li>Lapp lactase deficiency.</li> <li>Zanamivir should be <b>avoided</b> in those with <b>asthma or chronic obstructive</b> <b>pulmonary disease</b> because it may cause <b>bronchospasm</b>.</li> </ul>	<b>skin reaction</b> , such as rash, Diarrhea, hepatocellular injury, increased levels of transaminases (ALT and AST), neutropenia, and renal failure	
Peramivir (Rapivab)	-	Diarrhea, Neutropenia, nausea, vomiting, injection site rash, and increased AST and ALT.	
Baloxavir marboxil (Xofluxa)	-	Vomiting, diarrhoea	

### Drugs Used for Influenza Treatment and Prophylaxis

### **3- M2 proton channel antagonists**

amantidine, rimantidine

Amantadine was the **first** antiviral drug used in the treatment of influenza. It can **only** be used against **influenza A**.

#### This drug **inhibits viral replication** by **blocking the M2 proton channel specific to influenza A virus**.

Due to increased global **resistance**, amantadine has **not** been recommended for the treatment of influenza since 2006. However, influenza viruses are now largely resistant to M2 inhibitors  Currently, amantadine is mainly used in neurodegenerative diseases, such as Parkinson's disease, therapy after traumatic brain injury, and multiple sclerosis.

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### **CDC Antiviral treatment Recommendations**



### **CDC Antiviral treatment Recommendations**



### " study smarter , not harder "

### **Active recall**



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### summary





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A girl with 5 years old came to Emergency with ear pain and fever, what is the diagnosis /most common caustive /treatment?

> Diagnosis: Acute Otitis Medias Etiopocycus pneumonia Ureatment: treatment:

Enumerate two class of Antibiotics and give one example of each, and their mechanism of action

tetracycline
 tetracycline
 tetracycline
 example:tetracycline

MOA: inhibit cell wall synthesis example: penicillin, amoxicillin

• Penicilin



## **Team leaders**

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