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Objectives

1. Remembering

Students will be able to ${\bf recall}$ the common symptoms, causes, and typical duration of coughs and colds.

2. Understanding

Students will be able to **explain** the differences between the symptoms of a cold, flu, and COVID-19.

3. Applying

Students will be able to **apply** their knowledge to recommend appropriate OTC treatments for managing cough and cold symptoms.

4. Analyzing

Students will be able to **analyze** patient case studies to determine the necessity for further medical intervention or referral.

5. Evaluating

Students will be able to **evaluate** the appropriateness of antibiotic use in patients presenting with coughs and colds, considering the risks of overprescription.

6. Creating

Students will be able to **create** effective patient education plans that promote self-management and proper use of OTC medications, while also considering potential drug interactions and contraindications.





Respiratory Tract infections

- Respiratory tract infection comprise largely of a mixture of viral infections and to less extend bacteria, fungi, and, less commonly, parasites.
- The symptoms colds, flu and SARS-CoV-2 (COVID19) infections are similar.
- All patients meeting certain diagnostic criteria should consider **staying at home** during the pandemic.



Respiratory Tract infections

- It is commonly **self-limiting**.
- OTC medicines used for symptomatic relief.
- Some OTC remedies may interact with prescribed therapy, occasionally with serious consequences. Therefore, careful attention to be given to taking a <u>Medication History</u> and providing <u>Patient Education</u>.
- NSAID (Naproxen) + ACEI or ARBs------Reduce the antihypertensive effects, renal dysfunctions, may increase BP
 Naproxen + Amilorid ...increase BP, Hyperkalaemia, nephrotoxicity

Vaproxen

1-Common Colds and Flu

- Two most common upper respiratory tract conditions –
- The common cold and influenza exhibit **similar symptoms** and are often confused by patients.



1-Common Colds and Flu

<u>Aetiology</u>

- Virus **invades** the nasal and bronchial **epithelia**, **attaching** to specific **receptors** and causing **damage** to the **ciliated** cells.
- This results in the **release** of **inflammatory** mediators, and inflammation of the tissues lining the nose.
- **Permeability** of capillary cell walls **increases**, resulting in **oedema**, which is experienced by the patient as **nasal congestion and sneezing**.
- Fluid might drip down the back of the throat, spreading the virus to the throat and upper chest, causing cough and sore throat.
- Colds are most contagious during the first 1 to 2 days of symptoms.



Airway epithelial cells

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CE2 TMPRSS2

Significance Of Questions And Answers

I- Age

- The age will influence decision for referral and/or choice of treatment.
- Infants and Children are more susceptible to complications (bronchiolitis, pneumonia and croup)
- **Elderly** with comorbidities (e.g. diabetes), at risk of developing complications (e.g pneumonia), serious illness and death.





III- Symptoms of common cold

1. Runny/blocked nose

- Most patients will experience a runny nose (i.e. **rhinorrhoea**).
- **Rhinorrhoea** is initially a **clear watery fluid**, which later becomes a **thicker** and more **tenacious**, often **coloured**, mucus.
- Nasal congestion occurs because of dilatation of blood vessels, which leads to swelling of the lining surfaces of the nose and can cause discomfort. This swelling narrows the nasal passages that are further blocked by increased mucus production.

III- Symptoms of common cold

2. Sneezing/coughing

- Sneezing occurs because the nasal passages are irritated and congested.
- A **cough** may be present either because the **pharynx** is irritated (producing a dry, tickly cough) or as a result of irritation of the **bronchus** due to postnasal drip.







III- Symptoms of common cold

3. Aches and pains/headache

- **Headaches** may be experienced because of inflammation and congestion of the nasal passages and sinuses.
- A fever may also cause headache.
- A persistent or worsening frontal headache (pain above or below the eyes) may be due to sinusitis.
- People often report **muscular and joint aches** and these are more likely to occur with **flu and COVID-19** than with the common cold.



III- Symptoms of common cold

4. High temperature

- In general, a high temperature (e.g. exceeding 38°C)
 will not be present.
- The **presence of fever** may be an indication that the patient has **flu or COVID-19** rather than a cold.



Middle ear

Eardrum

Eustachian tube

قحة Sore

Fluid buildup

Outer ear

III- Symptoms of common cold

5. Earache/otalgia

- Nasal mucus and congestion blocks the eustachian tube leads to **earache** is a common, especially in children
- The patient may feel uncomfortable and deaf.
- It often resolves **spontaneously**, but decongestants and inhalations can be helpful.
- The situation worsens the ear becomes acutely painful (**otalgia**).
- This ear pain is common in young children and usually the **best treatment is pain-relief medicine**. A secondary infection with inflammation may follow and when this occurs, this is called **acute otitis media** (AOM).

III- Symptoms of common cold

5. Earache/otalgia

- Evidence from clinical trials shows that without antibiotic treatment, symptoms will improve within 24 h in 60% of children and will settle spontaneously within 3 days in 80% of children.
- Antibiotics have been shown to increase the risk of vomiting, diarrhoea and rashes.
- Antibiotics are most useful in children **under 2 years of age** who have pain in both ears or a painful ear with discharge from that ear (i.e. otorrhoea);
- In summary, a painful ear can initially be managed by the pharmacist. There is evidence that *paracetamol* and *ibuprofen* are effective treatments for both otalgia and AOM. However, if pain persists or is associated with an unwell child (e.g. high fever, very restless or listless, and vomiting), then refer to the GP practice.

III- Symptoms of common cold

6. Facial pain/frontal headache

- Facial pain or frontal headache may signify **sinusitis**.
- During a cold, their lining surfaces become **inflamed** and **swollen**, producing mucus. The secretions drain into the nasal cavity. If the **drainage passage becomes blocked**, fluid builds up in the sinus, which causes pain from pressure and is called **acute sinusitis**. It can become secondarily (bacterially) infected, but this is rare.
- A systematic review indicated only a small benefit from antibiotics even in **acute sinusitis** that had lasted for longer than 7 days.

III- Symptoms of common cold

6. Facial pain/frontal headache

- However, antibiotics may be recommended
- \checkmark if the symptoms persist for > 10 days or
- ✓ Symptoms are severe with fever (> 38° C),
- \checkmark Severe local pain and discoloured or purulent nasal discharge, or
- ✓ if a marked deterioration in sinusitis symptoms develops following a recent cold that had started to settle (so-called 'double sickening').
- These may be reasons to direct patients for further assessment.

III- Symptoms of common cold

6. Facial pain/frontal headache

- Treatment Options include:
- ✓ *Paracetamol* or *ibuprofen* to reduce pain;
- ✓ An intranasal **decongestant** (for a maximum of 1 week, in adults only)
- ✓ Steam **inhalation** or nasal **irrigation** with saline are advised for painful sinuses.
- ✓ **Sitting in the bathroom** with a running hot shower is a safer option.
- ✓ **Drinking adequate fluids** and **rest** will generally help.

III- Symptoms of common cold

7. Sore throat

- The patient often feels their **throat** is **dry and sore** during a cold and this may sometimes be **the first sign that a cold is imminent.**
- A sore throat can be a prominent feature in colds and flu, and it is often treated **erroneously** as a **throat infection**.
- Sore throat can also be a feature of COVID-19



SNEEZING

ACRIMATION

III- Symptoms of common cold

8. Summer colds

- The **main symptoms** of summer colds are :
- ✓ Nasal Congestion,
- ✓ **Sneezing** And
- ✓ Irritant Watery Eyes
- Similar symptoms are commonly caused by allergic rhinitis.

Differentiating between colds and influenza

Influenza (flu) is generally considered to be likely, if:

- 1. **Temperature** is 38°C or higher (37.5°C in the elderly).
- 2. A minimum of **one respiratory symptom**, such as cough, sore throat, nasal congestion or rhinorrhoea, is present.
- 3. A minimum of **one constitutional symptom**, such as headache, malaise, myalgia, sweats/chills or prostration, is present.

Symptoms of Influenza

Infection with the influenza virus usually

- 1. Starts abruptly with sweats and chills, muscular aches and pains in the limbs,
- 2. Dry sore throat, cough and high temperature.
- 3. Someone with flu may be **bedbound**.
- 4. There is often a period of generalised weakness and malaise and this may last a week or more.
- 5. A dry cough may also persist for some time.

Influenza complications

• Flu can cause secondary lung infections, such as **pneumonia**.

High-risk groups	 Young babies with undeveloped immunity. Elderly and frail individuals with impaired immune responses. People with pre-existing conditions, such as heart disease, asthma, or COPD. Individuals with kidney disease, weak immune systems, or diabetes.
Signs of pneumonia	 Severe or productive cough. Persistent high fever. Pleuritic chest pain. Delirium.
• Antibiotics may be antibiotic resistance	e needed but should be reserved for confirmed cases to avoid e.

IV- Previous History	
People with COPD (chronic br	onchitis or emphysema) may need referral.
COPD considered in patients over 35 years old	 long-term smokers Shortness of breath during exercise. Persistent cough. Regular sputum production. Frequent winter bronchitis or wheeze.
Warning signs of COPD exacerbation	 Worsening cough. Purulent sputum. Increased shortness of breath.
COPD patients should ideally receivDoctors may increase bronchodilato	ve an annual flu vaccination. or doses, prescribe oral steroids, and antibiotics during exacerbations.

• Certain OTC medications should be avoided by those with heart disease, hypertension, and diabetes.

IV- Previous History

- Asthma
- Exacerbations of asthma can be triggered by **respiratory viral infections**.
- Most people with asthma learn to start or increase their usual medication to prevent such an occurrence. However, if these measures fail, referral is needed.

V- Present Medication

- The pharmacist must ascertain if any medicines are being taken by the patient. It is important to remember that **interactions** might occur with some of OTC medicines.
- If medication has already been tried for relief of respiratory virus symptoms with no improvement, and if the remedies tried were appropriate and used for a sufficient amount of time, referral for primary care assessment might occasionally be needed. However, in most cases of colds and flu, treatment with OTC medicines will be appropriate.

	Common cold (infectious rhinitis)	Influenza
Symptoms	 Onset is gradual, with Initially a discomfort in the eyes, nose and throat Mild fever in children, but it is uncommon in adults Symptoms are mild to moderate. There is sneezing and nasal discharge (rhinorrhoea), usually followed by congestion. There may be sore throat and cough due to irritation for the basis of the solution. 	 Onset is rapid. Initially shivering, headache, myalgia, vertigo and back pain. There is always fever Severe symptoms last up to 4–5 days. Dry cough, nasal congestion and sore throat Anorexia, depression, nausea and vomiting
	 Recovery is within 4–10 days 	• Recovery is complete in 7–10 days , but lassitude, fatigue and depression can persist for several weeks
	 Complications – laryngitis, sinusitis and otitis media 	 Secondary bacterial complications may lead to pneumonia

	Compariso	n
	Common cold (infectious rhinitis)	Influenza
Causes	 A viral infection of the nose, nasopharynx and upper respiratory tract. > 100 causative viruses, of which rhinoviruses (40%) and coronaviruses (10%) are the most common. Immunity to each is specific with little cross-protection; a vaccine is therefore impossible. 	 An acute infection of the respiratory tract It is caused by three types of myxovirus (Influenza A, B, C). A vaccine is available, which is reformulated each year to keep up with antigenic shift in the viruses.
Transmission	 Nasopharyngeal droplets, released by sneezing and coughing 	• Droplet inhalation; it is highly contagious
Epidemiology	 Adults suffer 2–4 colds per year Children up to 12 per year Incidence is mainly in autumn and winter 	 Up to 15% of the population may develop influenza in any one year It occurs in epidemics every 3 years; and pandemics every 10 years It normally occurs in the winter months

Symptoms and circumstances for <u>Referral</u>

- 1. In the very young and very old patients
- 2. In those with **heart or lung disease**, e.g. COPD, kidney disease, diabetes and a compromised immune system
- **3. Persistent or Night cough, or wheezing** in children (asthma)
- 4. Dyspnoea in elderly (cardiac failure)
- 5. Severe pain on coughing (pulmonary embolism)
- 6. Suspected **adverse drug reactions**, e.g. dry cough (ACEI), sore throat a sign of drug-induced blood dyscrasias

- 7. Yellow/green/brown sputum (bacterial infection)
- 8. **Blood sputum** (tuberculosis, carcinoma)
- 9. Fever > 48 hours
- **10.Sore throat** >1 week's duration, and/or persistent hoarseness, and/or dysphagia
- **11.Dysphagia**, and/or rash, and/or neck stiffness (meningitis)
- **12.Earache**. Pain usually means bacterial infection of middle ear (otitis media).
- 13. Patients developed **delirium**

Prevention of colds and flu

A Flu Pandemic

- A flu pandemic is an epidemic of an influenza virus that spreads on a worldwide scale and infects a large proportion of the population.
- There were three flu pandemics in the last century, occurring in 1918, 1957 and 1968.

Prevention of colds and flu

Flu immunisation – adults

- Flu vaccinations are offered to individuals at high clinical risk, including those with:
- 1. Chronic respiratory (e.g., Asthma), heart, renal, neurological disease.
- 2. Diabetes mellitus or immunosuppression
- 3. Pregnant women.
- 4. Residents of long-stay care facilities.
- 5. Primary carers for older or disabled persons
- 6. Health or social care workers, including pharmacy staff.

Prevention of colds and flu

Flu immunisation – Children

- Flu immunisation for children is updated annually, similar to adults.
- 1. The nasal spray flu vaccine is provided for all children aged 2 to 15 years.
- 2. Children aged 16 or 17 years at **high clinical risk** should also receive the nasal spray instead of an injection.
- 3. Children aged 6 months to 2 years in high-risk groups will be offered a flu vaccine injection, as the nasal spray is not licensed for this age group.

Reducing transmission – hand hygiene and face masks

Good hygiene practice and social distancing, prevent transmission of respiratory viruses

- Viruses can survive for up to 72 h on hard surfaces and for several hours on the skin.
- Handwashing with soap and water for at least 20 s or Ethanol-based hand sanitisers
- People should be advised not to touch their eyes, nose or mouth
- Use tissues to cover their mouth and nose when coughing or sneezing,
- Wearing of a face mask
- Keeping a **distance** (2 metres or more).
- Ventilation (opening windows, doors and air vents)

OTC cough and cold remedies **are not recommended** for children **under the age of 6** years:

1- Antitussives: Dextromethorphan (for children > 12 years only) and pholoodine

2- Expectorants: Guaifenesin and Ipecacuanha

3- Nasal decongestants: Ephedrine, oxymetazoline, phenylephrine, pseudoephedrine and xylometazoline

4- Antihistamines: chlorphenamine, diphenhydramine, promethazine and triprolidine

Children aged between 6 and 12 years can use these preparations, not > 5 days.

Simple cough remedies (glycerine, honey or lemon) are used in children.

Remember that all aspirin-containing products are contraindicated in all children under the age of 16 years.

Management

- Antibacterial are not appropriate as infections are viral.
- Patients with suspected bacterial secondary infection should be referred to a doctor.
- Antivirals: zanamivir, oseltamivir and amantidine may be used as prophylaxis and treatment, it may reduce the severity and duration of symptoms, but are not a cure.
- Once the pharmacist has recommended symptomatic treatment, the patient should be advised to consult doctor in 1-3 weeks if the symptoms does not improved.

Nonpharmacological therapy measures: Although evidence of efficacy is lacking, include:

- 1. Fluid intake
- 2. Rest
- **3.** Nutritious diet and tea with lemon and honey, chicken soup are soothing.
- 4. Saline nasal sprays or drops moisten irritated mucosal membranes and loosen encrusted mucus;
- 5. Salt gargles may ease sore throats.
- **6. Medical devices**, (Breathe Right nasal strips).
- 7. Humidification with steamy showers, vaporizers (Vicks (camphor 6.2%), or humidifiers. Aromatic oil (camphor, menthol, and eucalyptus) products such as Theraflu Vapor Patch (ages ≥ 12 years) and Vicks VapoRub (ages ≥ 2 years) ease nasal congestion and improve sleep by producing a soothing sensation.

Management

Nonpharmacological therapy measures for infants : Although evidence of efficacy is **lacking**, include:

- Upright positioning to enhance nasal drainage.
- Because children typically cannot blow their own noses until about 4 years of age, carefully clearing the nasal passageways with a **bulb syringe** to remove mucus accumulation which interferes with sleeping or eating.





1. Decongestants (Sympathomimetics)

- Decongestants specifically treat sinus and nasal congestion.
- Decongestants are adrenergic agonists (sympathomimetics). Stimulation
 α adrenergic receptors constricts blood vessels, thereby decreasing sinusoid vessel engorgement and mucosal edema.
- The nasal membranes are effectively shrunk; therefore, **drainage** of mucus and **circulation** of air is improved, and the **nasal stuffiness** is relieved.
- These medicines can be given **orally** or applied **topically**. **Tablets** and **syrups** are available, as are **nasal sprays** and **drops**.

Management

- 1. Decongestants (Sympathomimetics)
- There are three types of decongestants.
- **1. Direct acting** (e.g., phenylephrine, oxymetazoline, and tetrahydrozoline) bind directly to adrenergic receptors.
- 2. Indirect acting displace norepinephrine from storage vesicles in prejunctional nerve terminals and tachyphylaxis can develop as stored neurotransmitter is depleted.
- **3. Mixed decongestants** (e.g., ephedrine, pseudoephedrine) have both direct and indirect activity.

1. Decongestants (Sympathomimetics)

A- Systemic nonprescription decongestants include pseudoephedrine and phenylephrine, when taken orally,

- 1. Stimulate CNS and may cause insomnia
- 2. Stimulation of the heart and an increase in BP
- 3. Affect diabetic control because they can increase blood glucose levels.

Management

- **1. Decongestants (Sympathomimetics)**
- Systemic decongestants are rapidly metabolized by MAO in the gastrointestinal mucosa, liver, and other tissues.
- Pseudoephedrine is well absorbed after oral administration;
- Phenylephrine has a low oral bioavailability (about 38%).
- Both pseudoephedrine and phenylephrine have short halflives (pseudoephedrine, 6 hours; phenylephrine, 2.5 hours), and peak concentrations for both drugs occur at 0.52 hours after oral administration.

1. Decongestants (Sympathomimetics)

B. Topical, Intranasal nonprescription decongestants include:

I. The short acting ephedrine, naphazoline, phenylephrine,

II. The long acting xylometazoline (10 hours) and oxymetazoline (12 hours).



Management

Topical, Intranasal nonprescription decongestants

- **Topically applied nasal sprays/drops**, not to be used > 7 days. Why ?
- **Rebound congestion** (i.e. rhinitis medicamentosa) can occur with **topically applied** sympathomimetics, but **not** with orally given ones.
- Nasal sprays used for adults and children > 6 years because it has a faster onset of action and cover a large surface area.
- Nasal drops used for children aged < 6 years because their nostrils are not sufficiently wide to allow effective use of sprays. (But the drops cover a limited surface area and easily swallowed which increase the possibility of systemic effects.

1. Decongestants (Sympathomimetics)

- A combination topical product containing xylometazoline and ipratropium in a nasal spray for the symptomatic treatment of nasal congestion and rhinorrhoea (runny nose) in adults aged 18 years and above.
- Use should **not exceed 7 days**.
- Ipratropium is an **antimuscarinic/anticholinergic** drug that helps to reduce mucus secretion.

	Management			
Dosage of some topical nas	al decong	gestant	5	DANAPHA
Drug	Conc.	Age	Dose (Drop) in each nostril	Thuốc nhỏ mũi Naphazolin 0,05 % Danapha
Nauharaliu	0.05%	> 12	1-2, QID	HộP 50 Lộ X 10 ML
Napnazolin	0.025%	6-12	1-2, QID	Concepted America Trans
	0.05%	>12	2-3, BID	Anefrin
Oxymetazoline (Nazordine®)	0.025%	6-12	2-3, BID	Otrivin Nasal
	0.01%	>12	2-3, TID	Spray
Xylometazoline (Otrivine®)	0.05%	6-12	1-2, BID	Oxymetazoline HCI 0.05% Nasal Decongestant Soothing
				CLOSSS Truide nhò mùl ciám nghệt thứi ở NOVARTIS

Adverse effects of decongestants

- Cardiovascular stimulation (e.g., Elevated BP, tachycardia, palpitation, or arrhythmias)
- CNS stimulation (e.g., Restlessness, insomnia, anxiety, tremors, hallucinations).
- Children and older adults are more likely to experience adverse effects.
- Adverse effects are more common with **systemic decongestants** because topical decongestants are minimally absorbed.
- However, **accidental ingestion of decongestants** can cause nausea, vomiting, hypotension, hyperthermia, lethargy, and coma.
- Adverse effects specifically related to **topical decongestants** include burning, stinging, sneezing, or local dryness. It also cause Rhinitis medicamentosa (RM; i.e., rebound congestion).

Management

Rebound congestion (i.e. Rhinitis Medicamentosa)

- Treatment of RM consists of:
- 1. Slowly withdrawing the topical decongestant (one nostril at a time);
- 2. Replacing **the decongestant with topical normal saline**, which soothes the irritated nasal mucosa
- 3. Using topical corticosteroids and systemic decongestants.
- Two to 6 weeks of withdrawal measures may be necessary before mucous membranes return to normal

Mana	gement	
Contraindication of decongestants		
• Decongestants are contraindicated		
• MAO inhibitors (MAOIs). (The sympathomimetics and MAOIs is potentia interaction can induce a hypertensive crist occurred)	e interaction between ally extremely serious. the is and several deaths have	MAOI Phenelzine (Nardil) Tranylcypromine (Parnate Isocarboxazid (Marplan) Selegiline (Emsam)
 These drugs should NOT be used in people with: 1. Glaucoma 2. BPH 3. DM 		
 Heart disease Hypertension Hyperthyroidism 		49

2- Antihistamines

- Antihistamine can reduce some of symptoms of a cold: runny nose (rhinorrhoea) and sneezing but are not so effective in reducing nasal congestion.
- There is no evidence that any antihistamine is preferable to another in the treatment of rhinorrhoea . although individual response to specific drugs varies widely.
- <u>Mechanism of actions :</u>
- Antihistamines compete with histamine at central and peripheral histamine1 (H1) receptor sites, preventing the histamine receptor interaction and subsequent mediator release.
- In addition, second generation antihistamines inhibit the release of mast cell mediators and may decrease cellular recruitment.

Classifications of Antihistamines

- Antihistamine can be classified into:
- **A-Sedating Antihistamine**:
- chlorphenamine (chlorpheniramine), dexchlorpheniramine , clemastine, triprolidine, promethazine and diphenhydramine.
- Side effects:
- Anticholinergic activity (dry mouth, blurred vision, constipation and urinary retention).
- **Drowsiness** (what to advice the patients?)
- These effects will be increased if the

patient is already taking another drug with anticholinergic effects (e.g. tricyclic antidepressants, neuroleptics)

• Accordingly they are **not recommended**: **Glaucoma**, or **prostate hy** in **elderly patients**.



Management

Classification of Antihistamines

B-Non-Sedating Antihistamine:

- Loratadine, acrivastine and cetirizine.
- Adult dose of loratadine: 10 mg once daily.
- Antimuscarinic adverse effects are not a significant problem with the non sedating antihistamines.
- Note: although the drowsiness is rare, but the warning that these drugs may affect driving and skilled tasks is still present.



Management		
Antihistamines	Dosing frequency	Cetirizine 10 mg Film-coated Tablets cetirizine dihydrochloride Oral use (30 film-coated tablets)
Cetirizine 10mg Loratadine 10mg Fexofenadine 180mg	Once daily (every 24 hours)	Clarityn (1) 20 mm
Brompheniramine Chlorpheniramine Dexchlorpheniramine Diphenhydramine Triprolidine	every 4-6 hours	Fexofenadine 180 mg Film-Coated Tablets
Clemastine	Bid	30 rim-Cooted Tablets 4771000-

3- Combination products

- **Sympathomimetics** (for congestion) + **antihistamine** (for rhinorrhoea and sneezing):
- The antihistamine is usually combined with sympathomimetics because :
- 1. Suppression of rhinorrhea can provokes congestion so the sympathomimetics will offset this effect.
- 2. Sympathomimetics may also help to counteract sedation caused by antihistamines (because the sympathomimetics cause CNS stimulation).

4- Analgesics, antipyretics:

- Paracetamol, aspirin and ibuprofen can be used to reduce fever, if present, and ease headache and muscle pains in influenza and general discomfort with colds.
- Aspirin is restricted in its use by its pronounced side-effect profile, and may not be **given to children under 16 years because of its association with Reye's syndrome**, a rare but occasionally fatal encephalopathy in children.

Management

5- Others

Inhalants:

• Preparations containing **volatile substances for inhalation**, either directly or via **steam**, produce a sensation of clearing the nasal passages and are used for the relief of cold symptoms. They have few, if any, contraindications.

Vitamin C in common cold:

- Vitamin C does not prevent colds and even high-dose vitamin C (over 1 g/day) produce minimum benefits.
- In case of vitamin **C effervescent tablets**, large quantities of **sodium bicarbonate** are required in this formulation, which could disturb the electrolyte balance of patients with **cardiovascular diseases**, especially those whose sodium intake is restricted

