



UPPER RESPIRATORY TRACT INFECTIONS¹⁻⁴

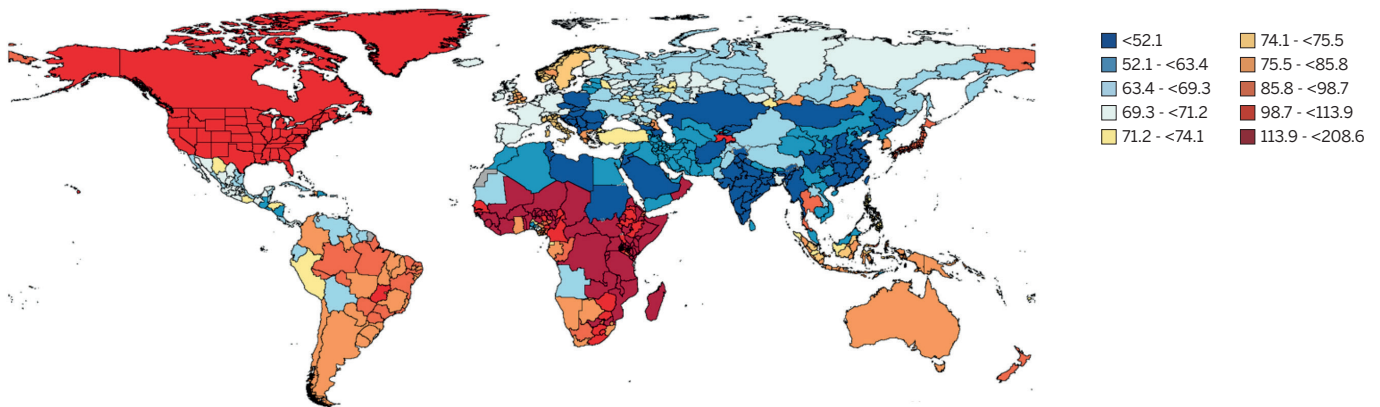
Upper respiratory tract infections (URTIs) are the most frequent type of illness in humans with incident cases numbering in the billions each year. While generally mild, URTIs frequently lead patients to seek help from healthcare professionals and can at times be severe or give rise to other more serious infections or medical complications.

THE GLOBAL BURDEN OF UPPER RESPIRATORY TRACT INFECTIONS^{1,2}

- While URTIs are generally self-limited, their frequency creates a substantial burden to health and well-being.
- **17.2 billion cases per year (42.82% of all disease).**
- Contributes to 9,460 deaths per year.
- 6.39 million disability-adjusted life years (DALY).
- **Average of 2.25 episodes per individual/year.**
- Children < 5 years old have the highest incidence rates.
- Children < 5 years old and the elderly have the highest associated mortality.

URTI rates worldwide expressed as Disability-Adjusted Life Years (DALY) per 100,000, 2021²

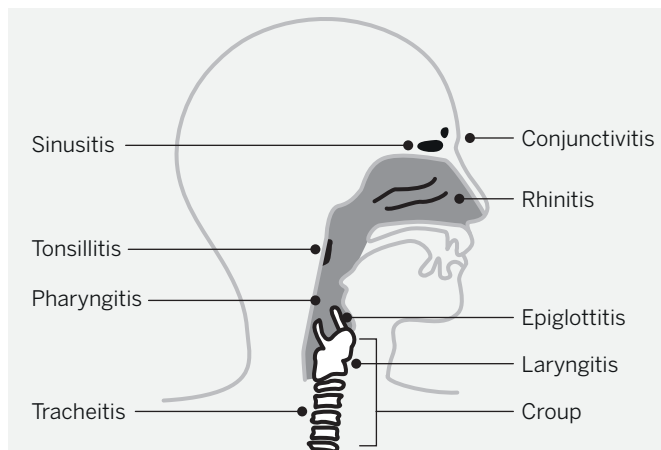
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INFECTIOUS AGENTS ASSOCIATED WITH STRUCTURES OF THE UPPER RESPIRATORY TRACT³⁻⁵

Structures that are part of the upper respiratory tract are found in the **head and neck** and include: nasal passages, paranasal sinuses, nasopharynx, oropharynx, middle ear, eyes, epiglottis, larynx, and the trachea. Inflammation in the upper respiratory tract may be caused by several **bacterial and viral pathogens**. Upper Respiratory Tract Infection (URTI) is sometimes equated with the common cold, but other localized syndromes of infection (e.g. pharyngitis) are also included in the category of upper respiratory tract infections.

Main infections of the upper respiratory tract



Main infectious agents of the upper respiratory tract^{4,5}

SITE	INFECTIOUS AGENTS
Nasopharynx	HRV, CoV, EV, RSV, PIV, Infl A, B
Oropharynx	GAS, <i>C. diphtheriae</i> , <i>C. pneumoniae</i> , <i>M. pneumoniae</i> , EBV, AdV, HRV, CoV, EV, RSV, PIV, Infl A, B, entero, hMPV, HSV, CMV
Middle ear and paranasal sinuses	<i>S. pneumoniae</i> , <i>H. influenzae</i> , <i>S. aureus</i> , <i>M. catarrhalis</i> , GAS, HRV, CoV, EV
Eye	<i>H. influenzae</i> , <i>S. pneumoniae</i> , <i>S. aureus</i> , <i>Moraxella</i> sp., AdV
Epiglottitis	<i>H. influenzae</i>
Larynx-trachea	<i>S. aureus</i> , AdV, HRV, CoV, EV, RSV, PIV, Infl A, B, hMPV

AdV: adenovirus; CMV: cytomegalovirus; CoV: coronavirus; EBV: Epstein Barr virus; EV: enterovirus; GAS: group A Streptococcus; hMPV: human metapneumovirus; HRV: human rhinovirus; HSV: herpes simplex virus; Infl A: influenza virus; PIV: parainfluenza virus; RSV: respiratory syncytial virus.

MOST COMMON UPPER RESPIRATORY TRACT INFECTIONS^{3,5-7}

Viral rhinosinusitis/nasopharyngitis (common cold) vs influenza

- Occur at any age but most common in children < 5 years old
- Erythema and edema of nasal mucosa, profuse nasal discharge/ sneezing, cough, sore throat, conjunctivitis
- Fever (more common in children or when caused by influenza)
- **Antibiotics are ineffective**, symptom-based supportive care is recommended
- Antivirals, such as oseltamivir, may be helpful when infection is caused by influenza
- Symptom resolution in 7-10 days

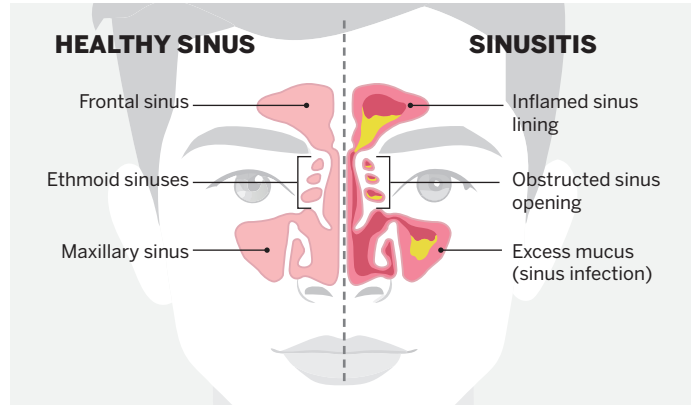
Is it a cold or flu?⁶

Source: CDC <https://www.cdc.gov/flu/symptoms/coldflu.htm>

SIGNS AND SYMPTOMS	COLD	FLU
Symptom onset	Gradual	Abrupt
Fever	Rare	Usual
Aches	Slight	Usual
Chills	Uncommon	Fairly common
Fatigue, weakness	Sometimes	Usual
Sneezing	Common	Sometimes
Chest discomfort, cough	Mild to moderate	Common
Stuffy nose	Common	Sometimes
Sore throat	Common	Sometimes
Headache	Rare	Common

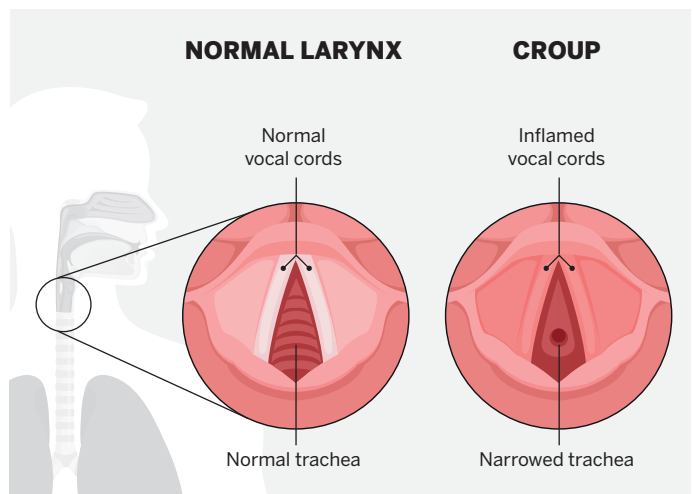
Acute bacterial rhinosinusitis⁸⁻¹⁰

- Fever, localized sinus pain and pressure, purulent nasal discharge
- Abrupt worsening after initial improvement of cold symptoms
- Persistent symptoms of nasal congestion, rhinorrhea, or cough >10 days duration without improvement
- **May be treated with antibiotics** for faster recovery and to avoid complications such as vision problems, meningitis, or chronic sinus infection
- Guidelines give recommendations on choice of antibiotics for empiric treatment



Laryngotracheitis (croup in children)^{11,12}

- Difficult or painful swallowing
- Sensation of lump in the throat
- Stridor, hoarseness or loss of voice, or barking-like cough (children)
- **Antibiotics are ineffective** (viral cause)



Group A streptococcal pharyngitis/tonsillitis¹³⁻¹⁷

Inflammation of the mucous membranes of the oropharynx and/or tonsils caused by infection from *Streptococcus pyogenes* (also known as Group A *Streptococcus*)

- Most common in patients between 5 and 15 years old
- Acute symptoms begin 2-5 days post-exposure
- Generally does not include cough, coryza, or conjunctivitis
- Symptoms resolution in 3-5 days without antibiotics or 1-3 days with antibiotics
- Always susceptible to penicillin
- If left untreated, may lead to Acute Rheumatic Fever (ARF) and Rheumatic Heart Disease (RHD)
- Guidelines regarding when to test or treat empirically differ by geographic location¹⁷

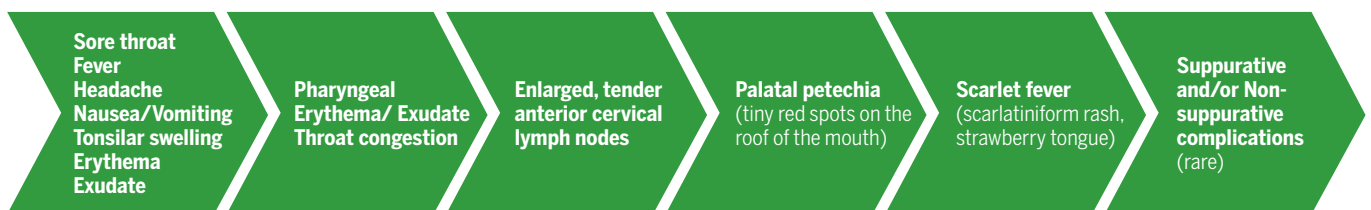
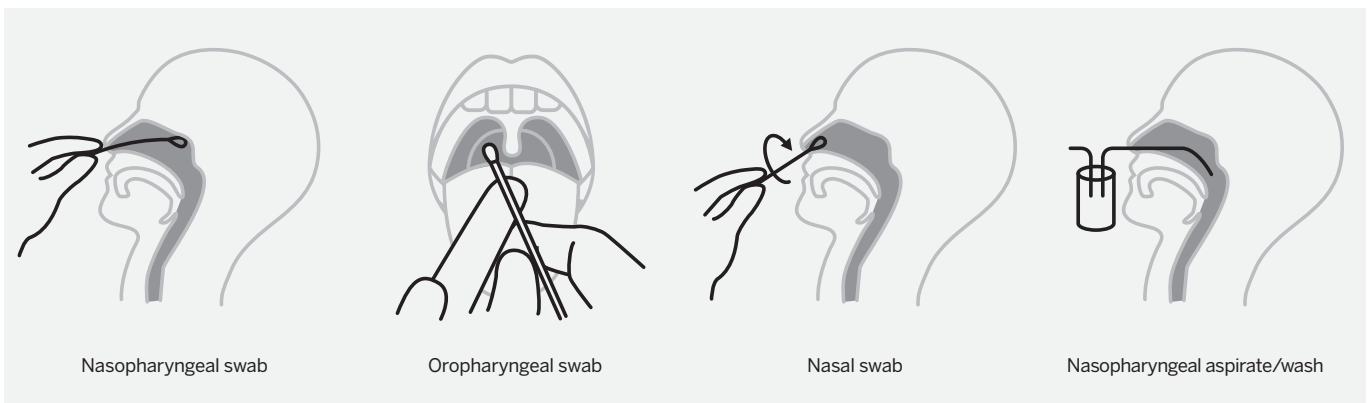


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DIAGNOSTIC APPROACH^{4,6,8,12,15,17}

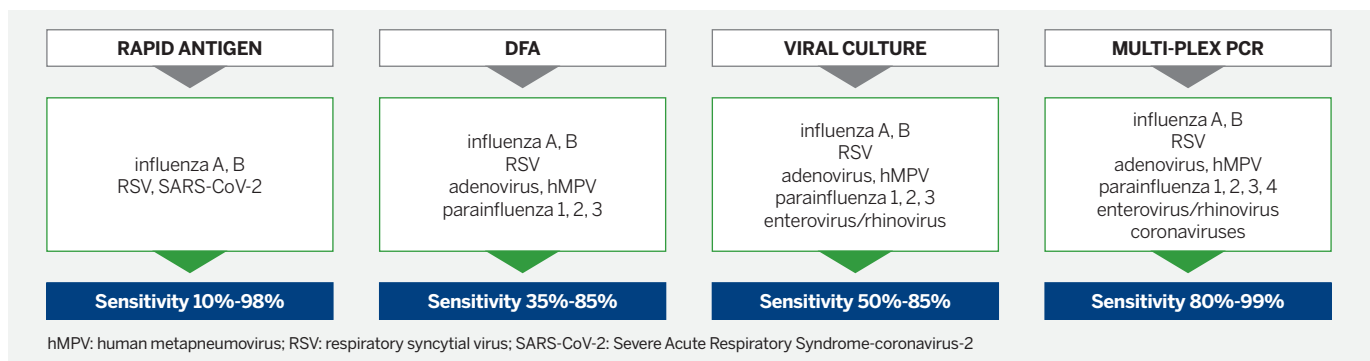
- A rapid biological diagnosis of the etiology of URTIs has been limited historically to only a few specific pathogens in most cases. These pathogens are: **Influenza A and B, RSV, SARS-CoV-2, and Group A Streptococcus.**
- **Specimens** used to evaluate the biological diagnosis include: nasopharyngeal, oropharyngeal, nasal, and oral swabs, and nasopharyngeal aspirates/washes.



LABORATORY CONFIRMATION 4,6,8,12,15,17,18

- URTI samples are most often evaluated with **rapid antigen tests**, **direct fluorescent antibody tests (DFA)**, or **bacterial and/or viral cultures**. Sensitivities of these testing methods vary widely, especially in the detection of viral pathogens (see below).
- Blood tests and radiographic imaging are rarely done in the evaluation of URTIs.
- **Molecular diagnostics** such as **multi-plex PCR** are emerging as new and powerful diagnostic tools. The molecular syndromic testing approach enables rapid accurate identification of multiple target pathogens. This may aid in more effective antimicrobial stewardship and more rapid optimal treatment.

Varying Sensitivities of Viral Testing Methods¹⁸



TREATMENT AND PREVENTION STRATEGIES 4,6,8,12,15,17

Many URTIs are treated empirically with antibiotics when believed to be **bacterial** (e.g. acute sinusitis and otitis media) or with supportive care when likely **viral** (e.g. common colds).

- **Bacterial URTIs** such as **Group A Streptococcal pharyngitis** should be treated with an appropriate antibiotic to prevent complications and improve patient outcomes.
- **Certain viral URTIs** such as **influenza** or **SARS-CoV-2** may be treated with specific anti-viral medication to help prevent severe illness and shorten the overall course of the illness.
- **Temporary isolation**, social distancing or other hygienic measures such as wearing a mask may help to decrease transmission of the infecting pathogens.
- **Vaccines** that are available for specific URTI-causing pathogens, such as **SARS-CoV-2** or **influenza**, help to decrease both infection rates and the severity of associated disease but do not prevent all cases of infection.
- **Guidelines** for treatment and prevention vary depending on the pathogen and geographic region.

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