Early intervention in acute upper respiratory tract infections

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Foreword

Upper respiratory tract infections (URTIs) are one of the most common diagnoses in the primary care setting across the world,[1] with more than 18.8 billion cases[2] occurring worldwide every year. Most adults will have 2–4 episodes of acute URTI each year, while children have an average of 6–10 episodes.[3-6]

Most URTIs are of short duration and with mild symptoms, but some can lead to serious complications such as pneumonia, rhinosinusitis, otitis media, and exacerbation of asthma and COPD among high-risk individuals. It not only affects an individual's health, but also his/her social life, sleep, school, and/or work performance representing an important burden to society. However, for most URTIs neither cure nor wide-scale prevention through immunisation is yet available – so appropriate treatment requires early intervention. During the pandemic of an acute URTI, early intervention is even more important to prevent viral transmission and infection in susceptible or at-risk populations.

The consensus collated in this paper is an important step to help everyone better understand the impact of URTI and the definition, benefits, and impact of early intervention. This would go a long way towards its advocacy among healthcare professionals as well as the public.

What is early intervention

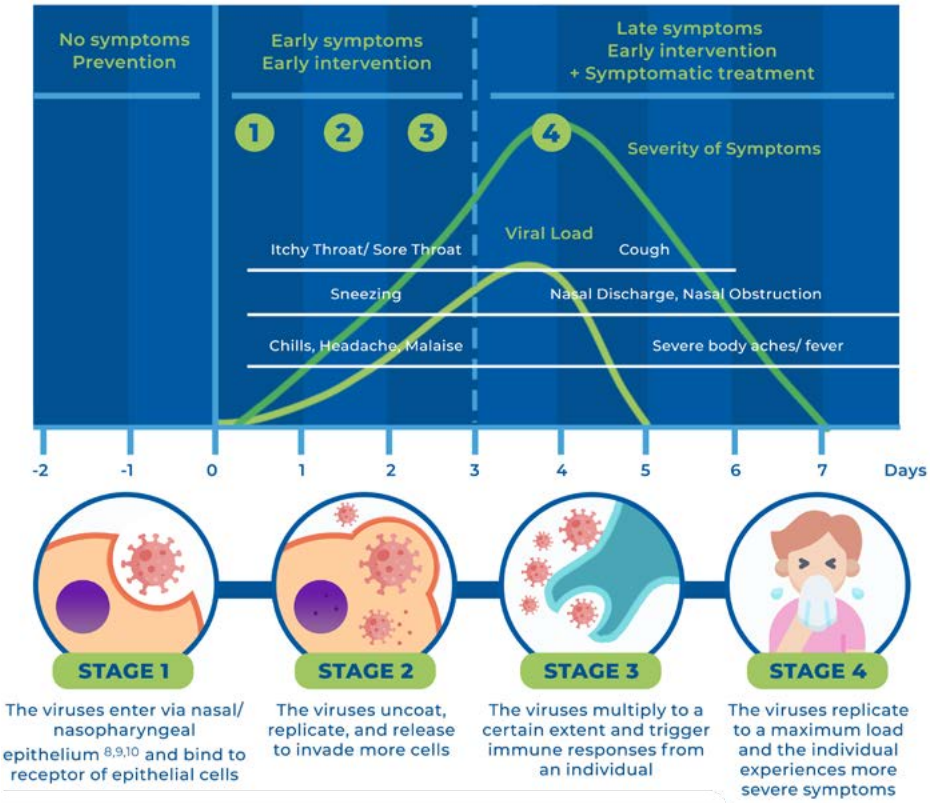
Before defining early intervention, it is critical to understand the life cycle of an acute URTI.

URTIs are mostly caused by viruses and there are over 200 types of respiratory viruses that cause URTIs.[1,3] The development of viral URTIs is largely similar and constitutes four stages. However, there are some variations in duration and symptom manifestation at each stage across different types of URTI viruses.

How does an acute URTI develop?

Early symptoms of acute URTI include sniffling, sneezing, and throat irritation, with occasional chills, headache, and malaise. They can appear anytime within the first 36–48 hours of infection.

Late symptoms include nasal discharge/obstruction, throat pain from inflamed tonsils/adenoids and cough. Chills, headache and



malaise may also occur. These tend to develop over several days and last 1 week or more.

When to intervene?

Stage 1: In absence of symptoms (before)

Those frequently exposed to infected individuals should intervene even in the absence of symptoms when they feel they are at risk of catching an URTI. Intervention at this stage can create a hostile environment for viruses to bind and replicate.

Stage 1, 2 and 3: As early as possible (36 hours)

It is best to intervene as early as possible upon 1st symptom appearance to reduce the chance of developing a full-blown acute URTI. It is easier to slow down or even halt viral replication at the early stages of infection.

- Within 36 hours of 1st symptom appearance.
- Common early symptoms include sniffling, sneezing and throat irritation, with occasional chills, headache and malaises.

Stage 4: After symptoms progress (48 hours)

Intervention may not be as effective in preventing the development of a full-blown URTI or the progression of symptoms once they become disturbing, as viruses have already replicated to a large amount. However, intervening at this stage can still slow down viral replication and minimise spreading to other people.

- ~48 hours to one week of 1st symptom appearance.
- Late symptoms include nasal discharge/obstruction, throat pain from inflamed tonsils/adenoids, and cough. Chills, headache and malaise may also occur at this stage.

"The earlier the better when it comes to early intervention of any infection ... it is like putting a fire out."
R Eccles

"Where there is exposure to the virus; the exposed person may start [using early intervention] as a preventive measure."
A Chua

"Once the viruses replicated in huge numbers and go down to the throat, it will be a bit late ... However, we should intervene at any time to stop viral replication."
DY Wang

Benefits of early intervention

As there is no cure or prevention for acute URTIs, it is important to intervene as early as possible to disrupt the viral replication cycle. There are several benefits of timely and appropriate early intervention in acute URTI.

Reduce chances of developing a full blown acute URTI	Early intervention can slow down and potentially halt viral replication. This may potentially allow the immune system to catch up and eliminate the viruses.
Decrease severity of acute URTI symptoms	Even if a full-blown acute URTI is unavoidable, early intervention can result in shorter or less severe symptoms as it reduces viral load in the infected person.
Reduce viral transmission	Early intervention can reduce breadth of viral transmission by preventing virus particles from reaching their host cells and creating a hostile environment for replication.

High risk groups for acute URTI

URTI is a multi-symptom illness, with symptom profiles varying across individuals in terms of severity, duration, and types.[11,12] However, some people are at higher risk of having a URTI, spreading URTI viruses, or developing more serious URTI complications.[13]

Pre-existing respiratory conditions or smokers

- 80–85% of asthma exacerbations among school-age children are associated with URTI.[11,12]
- URTI is associated with over 50% of COPD exacerbations.[14] The presence of URTI leads to more severe exacerbations, longer recovery times, and can lead to hospitalisation.[14]
- Smoking is a known risk factor for URTI, both for the people who smoke and those around them.

"Patients with asthma or COPD are at high risk ... you will need to intervene as fast as possible to avoid complications."
N Schellack

Children

Children can have 2–4 more URTI episodes than adults per year.[1] While URTI symptoms only persist in 20% of adults at day 10.73% of children still experience symptoms.[15]

"Children often come home from school or daycare with all types of infections and spread them around to the rest of the family."
J Bell

Elderly

Upper and lower respiratory tract infections are the leading causes of death and disability due to infection in the elderly. Compared to the general population, hospitalisation rate for URTI-related pneumonia is 12 times higher for those aged over 75 years.[16]

Immunocompromised individuals

Those with cystic fibrosis, HIV, use of corticosteroids, transplantation, and post-splenectomy are at high risk of developing severe URTI complications such as pneumonia.[13]

Those with frequent contact with infected individuals or high-risk groups

As URTI can easily spread from an infected individual to people around them by contact and airborne transmission,[17] family members of an infected person, healthcare professionals, and adults having frequent contact with infected children can also be at high risk of developing acute URTI.

"As an example – in a household of five, if everyone uses early intervention when one family member caught URTI, four cases can be prevented."
S Salvi

Which early interventions?

Most URTI guideline recommendations focus on treatments that alleviate symptoms such as pain, fever, or inflammation. However, four characteristics[18] of an ideal early intervention include:

- Quick onset of action to tackle rapid viral replication
- Safe to use across the general population
- Effective against a wide variety of pathogens
- Low risk of resistance development against the intervention

Experts also recommend several early interventions, such as mucoadhesive gel nasal sprays and neuraminidase inhibitors. Mucoadhesive gel nasal sprays, in particular, have been gaining more attention from experts in recent years.

What is mucoadhesive gel intranasal spray?

Mucoadhesive gel intranasal spray is a medical device that contains ingredients such as Carbopol, Carrageenan and Hydroxypropyl Methylcellulose (HPMC), and have known physical actions against virus particles in the nose.

The intranasal spray should be used at the first symptom of an emerging acute URTI or upon exposure to URTI viruses.

Mechanism of action

The intranasal spray acts at the back of the nose directly where acute URTI viruses start to bind and replicate. Mucoadhesive gel intranasal sprays can work in the following ways:

1. Trap

Trap the inhaled URTI viruses and cover receptor surface, preventing viruses from reaching their complementary receptors.

2. Slow down

In a formulation with lower pH of 3.5–4.0, it can create a hostile environment for URTI viruses and slow down viral replication.

3. Washout

Have a nasal washout effect to flush out viruses either through nose blowing or swallowing.

Scientific evidence

Several human clinical studies[19-21] indicate that the mucoadhesive gel intranasal spray is effective in reducing URTI duration and symptom severity, and is safe to use.

Forward-looking action

As the most frequently observed infectious disease, acute URTI warrants more attention and proactive management to reduce its burden. We suggest that every individual presenting to a pharmacy/clinic with suspected URTI symptoms, or has comorbid conditions such as a history of asthma/COPD, or has frequent contact with infected individuals should receive a "value brief" on the benefits of early intervention for acute URTI to help pre-empt current and future URTIs.

Effective early intervention

- Reduces chances of the user developing a full-blown acute URTI
- Results in shorter or less severe acute URTI symptoms
- May reduce viral transmission, protecting people around an infected person from contracting a URTI
- Slows down the viral infection rate and may allow the immune system to catch up and eliminate the virus
- Reduces viral replication by preventing virus particles from reaching their host cells and create a hostile environment for replication

When it comes to selecting an appropriate early intervention for acute URTI, mucoadhesive gel intranasal spray fits the requirements as it is effective and well tolerated with a rapid onset of action. Consumer education should focus on when, why and how to use the intranasal spray to effectively fight against acute URTI.

Early intervention guide

WHEN	WHY	HOW
As early as possible upon symptom appearance	Reduce the chance of developing a full blown acute URTI	Apply intervention directly into each nostril

When symptoms are prominent	Decrease duration or severity of symptoms, and minimise viral transmission	Use in combination with symptomatic treatments Administer for at least 2–4 days, and beyond should there be progression of symptoms
In absence of symptoms when being exposed to an infected individual	Prevent virus particles from binding and reduce the chance of developing an URTI	Continue to use until symptoms subside

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