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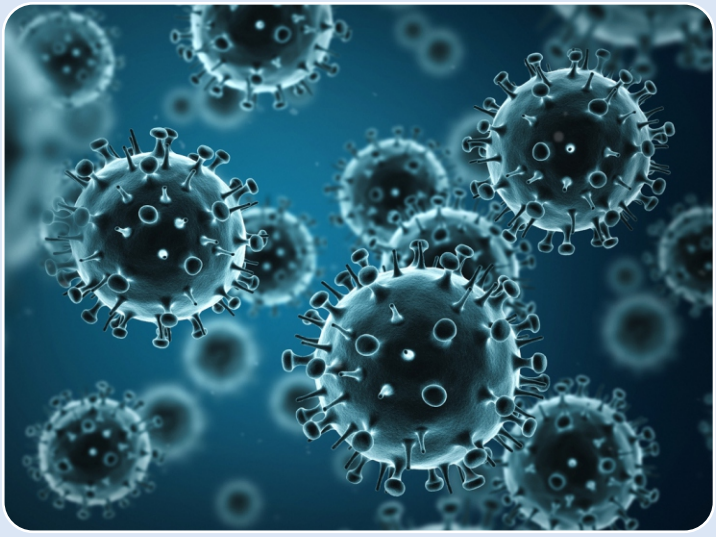
Medical Bulletin

EXCEL Division of Blue Cross Laboratories

Influenza

Influenza (flu) is a contagious respiratory illness caused by influenza viruses. The influenza viruses are classified into types A, B and C on the basis of their nucleoproteins. Only types A and B cause human disease.



SEASONAL INFLUENZA IN INDIA

As of February 2019, India has recorded a total of 6,701 H1N1 cases and 226 deaths across the country, according to National Centre for Disease Control (NCDC).

- ✓ The maximum number of cases have been reported from Rajasthan (2,363) followed by Delhi (1,011) & Gujarat (898).
- ✓ Rajasthan reported the highest number of deaths (85), followed by Gujarat (43) and Punjab (30).

MUTATION OF VIRUSES IS THE MAIN CAUSE OF CONCERN

Influenza viruses are constantly changing and are highly unstable, capable of causing pandemics. They can change in two different ways:

- ✓ **Antigenic Drift**

These are small changes in the genes of influenza viruses that happen over time as the virus replicates. However, these small genetic changes can accumulate over time and result in viruses that are antigenically different. When this happens, the body's immune system may not recognize those viruses.

- ✓ **Antigenic Shift**

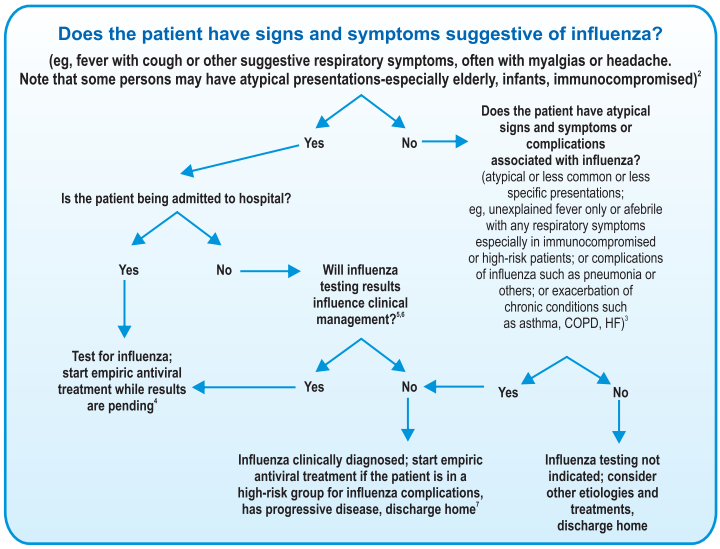
Antigenic shift is an abrupt, major change in the influenza A viruses, resulting in new hemagglutinin and/or new hemagglutinin and neuraminidase proteins in influenza viruses that infect humans. Shift results in a new influenza A subtype and most people do not have immunity to the new virus.

MANAGEMENT OF INFLUENZA VIRUS

Symptomatic treatment:

These patients usually may present with fever, cough & cold, headache or body myalgia. These symptoms should be treated with medications like anti-pyretic, anti-histaminic, cough & cold preparations, decongestants & NSAIDs for pain relief.

Investigational Flow:



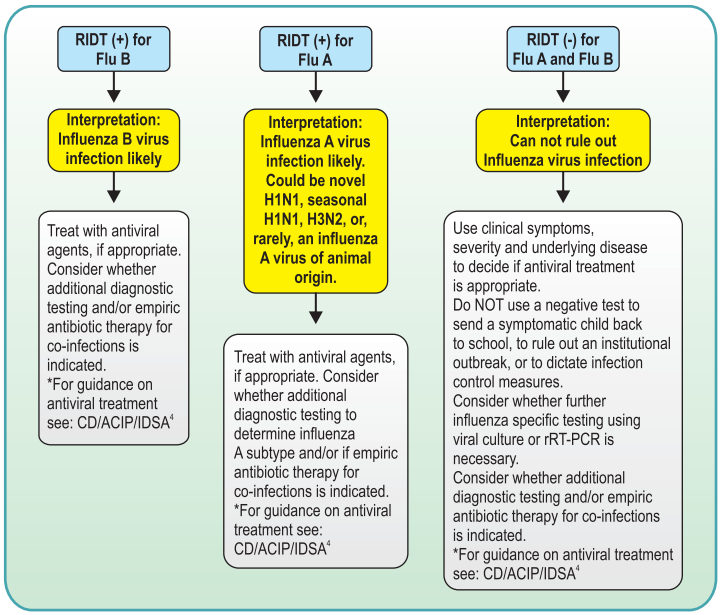
The management of influenza in populations is highly important & the foremost test that can be done is the Rapid Influenza Diagnostic Test (RIDT), which detect viral nucleoprotein antigen.

Rapid Influenza Diagnostic Tests

The commercially available RIDTs can either:

- ✓ Detect and distinguish between influenza A and B viruses.
- ✓ Detect both influenza A and B but not distinguish between influenza A and B viruses.
- ✓ Detect only influenza A viruses.

Algorithm to assist in the interpretation of RIDT results during period when influenza viruses are circulating in the community.



Currently, FDA approved RIDTs, can neither distinguish between influenza A virus subtypes nor provide any information about antiviral drug susceptibility.

However, based on the test results, the interpretation and management guidelines and algorithms have been established for medical practitioners to effectively manage the influenza virus.

Clinicians should start antiviral treatment as soon as possible for adults and children with documented or suspected influenza, irrespective of influenza vaccination history, who meet the following criteria:

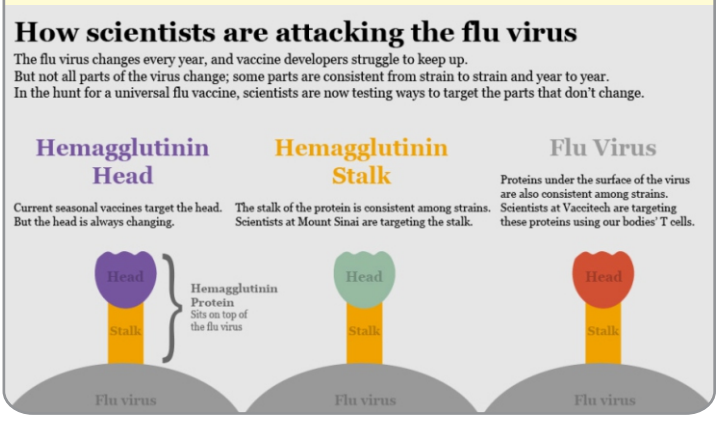
- ✓ Persons of any age who are hospitalized with influenza, regardless of illness duration prior to hospitalization (A-II).
- ✓ Outpatients of any age with severe or progressive illness, regardless of illness duration (A-III).
- ✓ Outpatients who are at high risk of complications from influenza, including those with chronic medical conditions and immuno-compromised patients (A-II).
- ✓ Children younger than 2 years and adults ≥65 years (A-III).
- ✓ Pregnant women & those within 2 weeks postpartum (A-III).

Clinicians can consider antiviral treatment for adults and children who are not at high risk of influenza complications, with documented or suspected influenza, irrespective of influenza vaccination history, who are either:

- ✓ Outpatients with illness onset ≤2 days before presentation (C-I).
- ✓ Symptomatic outpatients who are household contacts of persons who are at high risk of developing complications from influenza, particularly those who are severely immuno-compromised (C-III).
- ✓ Symptomatic healthcare providers who care for patients who are at high risk of developing complications from influenza, particularly those who are severely immuno-compromised (C-III).

UNIVERSAL FLU VACCINE

- ✓ The traditional yearly vaccine targets the head portion of the protein, hemagglutinin, which is generally more prone to mutations.
- ✓ The Universal Flu Vaccine, has been researched to target the hemagglutinin stalk, which is far more resistant to mutations.
- ✓ This may be the answer to the drawbacks of the yearly flu vaccine.



Ref:www.cdc.gov/flu/about/viruses/change.htm;www.scientificamerican.com/article/new-finding- advances-the-search-for-a-universal-flu-vaccine/; Mehrbod P et al. Biomed Res Int 2014; 2014: 872370; IDSA Influenza Clinical Guidelines 2018.

PAIN.. A NEGLECTED PROBLEM?

Pain is the most common reason for patients to seek medical advice globally and despite its ubiquity; pain is grossly under-treated and greatly neglected by health systems across the world. The World Health Organization estimates that 80% patients with severe pain never receive any adequate treatment.

International Association for the Study of Pain (IASP) defines CP as pain without apparent biological value that has persisted beyond the normal tissue healing time (usually taken to be 3 months).

Along with the world, CP is a hugely growing problem in **India and has become a chronic burden in our country with a prevalence rate of 19.3%, which translates into 180-200 million adults having CP.**

In India, it becomes complex due to underreporting, under treatment, and low priority in our country. The reasons for underreporting and tolerating pain is mainly because, either the patients do not want to report pain to the busy physician or the fear of the side effects from the pain medications.

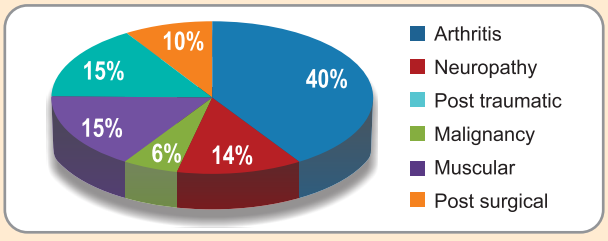
To address the issue of CP in our country and to improve awareness, one needs to get a better understanding of the factors that influence pain, it's etiology, what is the actual impact CP, and how patients deal with the problem of CP.

ETIOLOGY OF PAIN

Understanding the source or the cause of pain is the primary step in understanding how to treat it. The causes vary with age, gender and medical condition.

In India, it has been observed that the most significant cause for CP is arthritis followed by muscular pain.

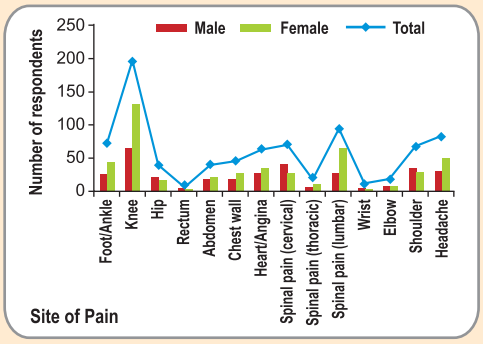
According to the World Health Organization (WHO), one in six people and one in three families suffer from arthritis in India, which is about 15% to 17% of the Indian population.



SITE OF PAIN

While describing pain understanding the type of pain is necessary, whether it is chronic or acute, which are the most common sites that are affected by chronic pain and who are most likely to be affected.

An Indian study revealed that the highest prevalence of CP was knee pain followed by low back pain.



GENDER

There is a stronger gender predisposition observed in India, the prevalence rate in females was 25.2%, which was significantly higher compared to 12.3% in males, which is similar to global surveys.

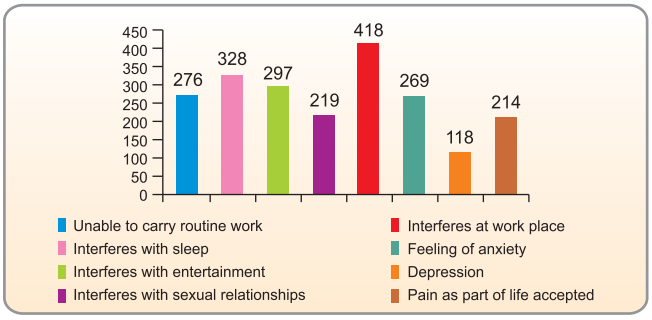
AGE

A strong relationship has been noted between increasing age and CP prevalence. In India, the prevalence rate of CP was observed to be higher in patients aged over 60 years as compared to younger group.

Age groups	Total (*n*=836)	Male (*n*=245)	Female (*n*=591)
18-40	243	68	175
40-60	274	80	194
90-80	319	97	222

The most frequent site of pain was the knee (23.6%), followed by low back indicating degenerative diseases due to wear and tear in elderly population.

IMPACT OF PAIN



CP can cause of simplest of issues or can impact daily life drastically where day to day activities are affected.

In India, it was seen that 33% were not able to do their routine work, 25.5% had accepted pain as part of their lives and nearly 14.1% of respondents were diagnosed with depression because of their pain.

TREATMENT

CP is a neglected and undertreated issue, Patients with CP consult physicians, specialists and quite often resort to self-medication.

In India, OTC drugs like paracetamol are easily available. Alternative therapies like acupuncture, Ayurveda and Homeopathy, though being very popular in India, were seen to be used by a few due to inefficacy.

CONCLUSION

To conclude, it is important to note that pain is not a negligible problem but a burden to our society. It should be treated as any other lifestyle disease. In order to increase the awareness in patients, the physicians and primary health care providers need to get aware first and understand it, address it and appropriately treat it.

Ref: Indian Journal of palliative Care 2018; 24(4): 472-477; Indian Journal of Pain 2016; 30(2): 111-115.

High Dose PPI with H2 Blocker for Long Term Remission of Symptoms in Cervical Inlet Patch

Presence of ectopic gastric mucosa in the cervical oesophagous is known as cervical inlet patch, also called heterotrophic gastric mucosa of the proximal oesophagus (HGMPE) .They are often found incidentally at upper GI endoscopy and have prevalence of 0.18% to 14%. Patients present with nonspecific oropharyngeal symptoms like odynophagia, globus sensation, dysphagia, throat irritation, cough, etc., related to acid secretion from the patch. PPI has been advised in symptomatic patients for acid suppression where remarkable improvement in symptoms with just 8 weeks of treatment without recurrence or any other complications have been observed.

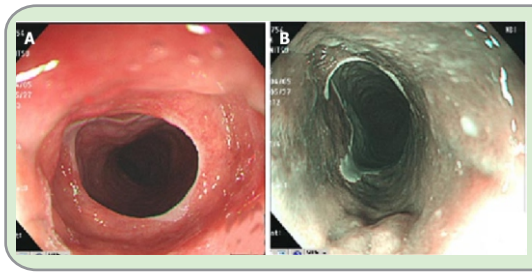
Table 1. Clinicopathological classification for heterotopic gastric mucosa of the proximal esophagus, *(BH von Rahden et al. 2004)*

Category	Description	Symptoms/findings
I	Asymptomatic	None
II	Symptomatic	Laryngopharyngeal reflux
III	Symptomatic with benign complications	Strictures/webs/fistula/ bleeding
IV	Intra-epithelial dysplasia	None/non-specific
V	Malignant transformation	Asymptomatic/dysphagia

Source: VH Chong, 2013.

Development of cervical inlet patch is unknown and is based on different theories. i) First it is widely considered as a congenital anomaly. Since during development of the oesophagus squamous lining replaces the columnar lining from the middle oesophagus extending in both direction which accounts for the post cricoid location of inlet patch. ii) Second is acquired theory due to chronic acid injury as seen in Barret's Oesophagus. iii) Third less common theory involves rupture of proximal Oesophagus retention cystic glands.

It is difficult to detect the heterotopic gastric mucosa during routine endoscopy & the final diagnosis of inlet patch is confirmed by biopsy.



Endoscopic images depicting the cervical inlet patches (A: circumferential patch, B: Small Inlet patch)

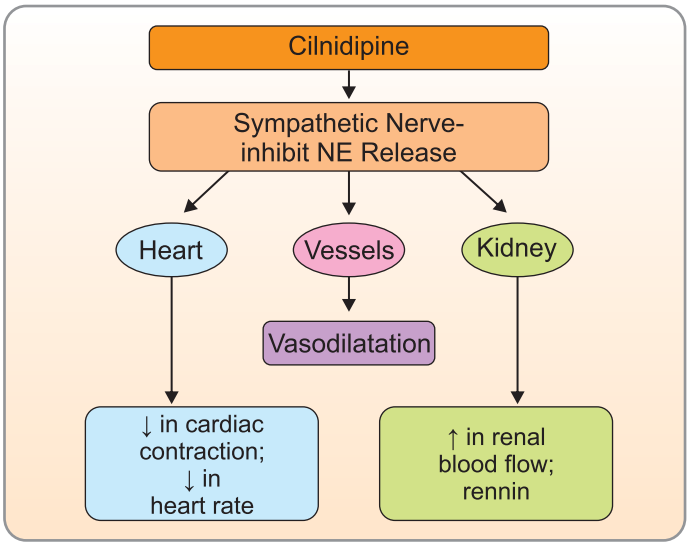
The clinical significance of IP is mainly acid related complications and rarely neoplastic transformations. It is reported that most of the symptoms are mild. Few have recurrent and chronic symptoms of laryngopharyngeal reflux thus frequent visit to ENT or Gastroenterologist. Presence of symptoms like odynophagia, globus, dysphagia, cough, etc., in heterotopic gastric mucosa can be treated with **high dose PPI and H2 blocker combination for 8 weeks** which gives long term relief.

Ref: J Gen Pract 2018,6:4; Frontline Gastroenterology 2017;0:1-7.

Cilnidipine: Next Generation Calcium Channel Blocker

Hypertension is one of the most common conditions seen in primary care and a major public health problem in India. It can lead to various complications if not detected early and treated appropriately. As per the latest Eighth Joint National Committee (JNC 8) the goal BP in patients age <60 years should be **140/90 mm Hg** and treatment can be started by selecting drugs from among 4 specific medication classes i.e. angiotensin converting enzyme inhibitor (ACEI) or angiotensin receptor blocker (ARB), calcium channel blocker (CCB) or diuretics.

Role of Cilnidipine in Management of Hypertension and Co-morbid Conditions:



Cilnidipine is a unique Ca^{2}+ channel blocker because of its inhibitory action on the sympathetic N-type Ca^{2}+ channels along with L-type Ca^{2}+ channels. Cilnidipine has been classified as a fourth-generation CCB based on its actions on sympathetic neuro-transmitter release. Cardio-protective, reno-protective & neuro-protective effects of cilnidipine have been reported in clinical animal studies.

Cilnidipine by attenuating norepinephrine release from sympathetic nerve endings leads to vasodilatation in vessels, decrease in heart rate and increase in renal blood flow.

Cardio-protective Action

Various studies have demonstrated once-daily administration of cilnidipine (5-20 mg) for 1-3 weeks decreased the 24-hour average BP significantly, without causing excessive drop in the BP or a reflex tachycardia.

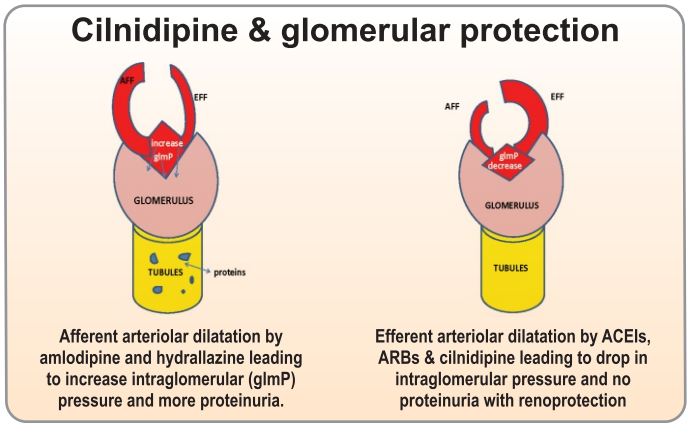
Effect on Left Ventricular Diastolic Dysfunction /Left Ventricular Hypertrophy (LVH)

Left ventricular (LV) diastolic dysfunction is related to increase in the cardiac sympathetic activity. Treatment with cilnidipine improved LV diastolic function by suppressing cardiac sympathetic over activity.

Effect on Morning Hypertension

An elevated morning BP has been associated with target organ damage. In ACHIEVE ONE trial Cilnidipine reduced both morning SBP and PR more markedly in patients with higher baseline morning SBP and PR.

Reno protective/ Antialbuminuric Effects



Podocyte permeability barrier restricts the passage of large molecules like albumin. Various glomerular diseases that induce proteinuria demonstrate significant structural damage to these podocytes which become the hallmark of proteinuria and serve as the diagnostic marker. Therefore podocyte protection action of cilnidipine may play an important role and offer reno protective action.

The protection is provided by efferent arteriolar vasodilation via attenuation of glomerular hypertension reducing glomerular pressure significantly.

Effect on Insulin Sensitivity

Cilnidipine improves insulin sensitivity, possibly due to its exerting a vasodilatory action without stimulating the sympathetic nervous activity. Hypertensive obese patients treated with 10 mg of cilnidipine showed improved insulin resistance.

Key Points (Cilnidipine)

- ✓ Additional to L-type Ca_{2}+ channel actions, exerts unique action on sympathetic N-type Ca_{2}+ channels as well,
- ✓ It attenuates norepinephrine release and leads to vasodilatation, decrease in heart rate and increase in renal blood flow,
- ✓ Causes less reflex tachycardia and pedal oedema,
- ✓ Better control of proteinuria, suppressing podocyte damage,
- ✓ It also helps increase the insulin sensitivity,
- ✓ CCB of choice in hypertensive patients with diabetes, chronic kidney disease and in patients developing pedal edema with other CCB.

Ref: Journal of the Association of Physicians of India ■ Vol. 64 ■ April 2016; Journal of General Practitioners; 2018, Vol.6: issue.4: 1000366 Journal of Geriatric Cardiology (2017) 14: 67-72.

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