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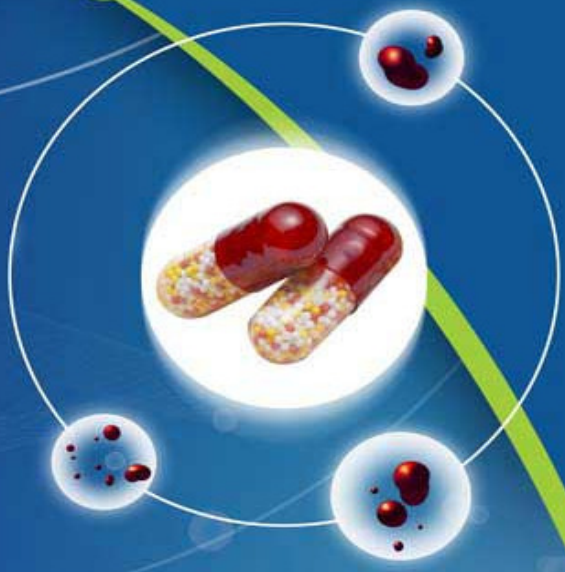

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Review Article

A REVIEW ON THE PERSPECTIVE OF PEPTIC, MOUTH AND CORNEAL ULCER AND THEIR TREATMENT FACTS

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ABSTRACT

The stomach is a bag of muscle that crushes and mixes food with the digestive "juices" - hydrochloric acid and pepsin. An ulcer is the result of an imbalance between aggressive and defensive factors. On one hand, too much acid and pepsin can damage the stomach lining and cause ulcers. The primary cause of ulcers is the bacterium called Helicobacter pylori (H. pylori). H. pylorus is a spiral-shaped bacterium found in the stomach. Although H. pylori is the primary cause of ulcers, there are other factors that play a role in ulcer development. NSAIDs such as aspirin, ibuprofen, naproxen, interfere with the stomach's ability to produce mucus and bicarbonate (a chemical produced in the stomach that neutralizes and breaks down the hydrochloric acid and pepsin into substances less harmful). Peptic ulcers are generally caused by an acid resistant bacterium called Helicobacter pylori (H. pylori) which infect the stomach. H pylorus is Gram negative spiral shaped bacteria. In human it colonizes in stomach and the likelihood of infections increases with age. The sensitivity and specificity of Biopsy urease test which detect H. pylori urease enzyme activity are above 90%. Urea breath test is based on urease production by H. pylori. The carbon 13 (Non radio active isotope) and carbon 14 (Radio active isotope) tests require that the patient ingest labeled urea, which is broken down in the stomach to ammonia and labeled bicarbonate.

***Keywords**: Ulcer, Hydrochloric acid, Helicobacter pylori (H. pylori), NSAIDs (Non-steroidal Anti-inflammatory Drugs).*

INTRODUCTION

There are six and a half billion human stomachs on this little planet of ours, and over half of them are home to a microbe called Helicobacter pylori. Scientists have known about the bacteria since the late 1800s, but it wasn't until the 1980s that Australian doctors noticed that *H. pylorus was* in the stomachs of just about everyone with an ulcer. A swig of antibiotics turned out to be a great way to make ulcers disappear. Scientists have since demonstrated that H. pylorus strikes up an uneasy truce with its human hosts.

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In most cases, H. pylori live amicably in our stomachs. When the truce is broken, the microbe triggers a cascade of reactions that leave a stomach cratered. (The co-discovers of the H. pylori-ulcer link shared a Nobel Prize in 2005, which I wrote about here.) Further research by Achtman and others indicated that other ethnic groups also carried their own strains of H. pylori. A debate then emerged about how germ and host got associated in this way. H. pylorus is not like the flu, which can move between continents in a matter of days. Scientists don't know much about how it gets from stomach to stomach, but it seems to move mostly within families. So it would make sense that H. pylori's genealogy tracked the genealogy of its hosts. On the other hand, some critics have argued, H.

pylori might be a recent arrival in our stomachs. If it jumped from animals to humans on several occasions in different parts of the world, it might have produced the same patterns seen by Achtman and others. In this week's Nature, Achtman and his colleagues report the latest data on humans and their ulcer bugs. They argue that our histories are even more intimately wrapped together than previously thought. They found that the bacteria fell into five major populations. The scientists then made a careful study of where the people who carried strains from those five branches live, and used that information to determine where each branch originated. The deepest branch of the H. pylori tree originated in East Africa (Two younger branches are closely related to one another–one originating in West Africa (Ancestral Africa1, fig. f) and another in North Africa. Another branch originated in India and is closely related to a branch found in East Asia and the New World This pattern, Achtman and his colleagues argue, bears a striking resemblance to the expansion of our own species over the past 100,000 years. A number of studies on human DNA (such as this one) indicate that Homo sapiens expanded from a small base in East Africa. At first they moved out through Africa, but then after about 60,000 years ago some populations pushed out into the Near East and then into Europe and Asia, and finally into the New World. The human genetic diversity found in Africa is greater than in the rest of the world, because humans have deeper roots there. Very small populations moved into other continents, and as a result, their genetic diversity is lower. In fact, the further away you go from Africa, the lower the genetic diversity gets. (Some scientists disagree, it should be pointed out.) Like humans, H. pylori have the greatest genetic diversity in Africa, and the further from Africa you go, the less diverse it gets. Achtman and his colleagues built statistical models to figure out how best to explain the patterns they've found in H. pylori DNA. They conclude that early humans already carried H. pylori in their stomachs. (How bad their ulcers were the scientists don't say.) When people began expanding from East Africa, they took H. pylori with them, and ultimately they carried the bacteria across the world. The major branches of H. pylori that Achtman and his colleagues identified emerged during later population booms. The scientists can even detect the arrival of different strains of H. pylori in Europe as successive waves of human immigrants moved into the continent. Because H. pylori are so unadventurous when it comes to infecting new hosts, it has become a chronicler of our past [1]. H. pylori even have something to say about the ever-controversial matter of race. When scientists were first gathering up information on H. pylori, the geographical differences seemed stark. The bacteria in Europe were distinct from the ones in Asia or Africa. Scientists studying human DNA had much the same experience. They found that by examining certain genetic markers they could accurately predict which continent a person came from. But other scientists challenged these results. They argued that the data in the early studies were far from a representative sample of the world's human genetic diversity. These scientists put together their own collection of human DNA and concluded that the clusters blurred smoothly into each other.

ULCER

An ulcer is a sore on the skin or a mucous membrane, accompanied by the disintegration of tissue. Ulcers can result in complete loss of the epidermis and often portions of the dermis and even subcutaneous fat. Ulcers are most common on the skin of the lower extremities and in the gastrointestinal tract. An ulcer that appears on the skin is often visible as an inflamed tissue with an area of reddened skin. A skin ulcer is often visible in the event of exposure to heat or cold, irritation, or a problem with blood circulation [2]. They can also be caused due to a lack of mobility, which causes prolonged pressure on the tissues. This stress in the blood circulation is transformed to a skin ulcer, commonly known as bedsores or decubitus ulcers. Ulcers often become infected, and pus forms. Ulcers are crater-like sores (generally 1/4

inch to 3/4 inch in diameter, but sometimes 1 to 2 inches in diameter) which form in the lining of the stomach (called gastric ulcers), just below the stomach at the beginning of the small intestine in the duodenum (called duodenal ulcers) or less commonly in the esophagus (called esophageal ulcers) [3].

Causes and Risk Factors of Ulcer

- The primary cause of ulcers is the bacterium called *Helicobacter pylori (H. pylori). H. pylori* are a spiral-shaped bacterium found in the stomach. Unlike other bacterium, *H. pylori* is able to twist through the layer of mucous that protects the stomach cavity and attach to cells on the surface of the stomach wall, where it produces urease, an enzyme that generates ammonia.
- Urease generates substances that neutralize the stomach's acid and allows *H. pylori* to thrive. *H. pylori* weakens the stomach's defenses by thinning the mucous coating of the stomach, making it more susceptible to the damaging effects of acid and pepsin; inflaming the area; poisoning nearby cells and producing more stomach acid.
- Although *H. pylori* are the primary cause of ulcers, there are other factors that play a role in ulcer development. These factors are the use of nonsteroidal anti-inflammatory drugs (NSAIDs), a person's lifestyle and the stomach's inability to defend itself against digestive fluids, hydrochloric acid and pepsin.
- NSAIDs such as aspirin, ibuprofen (Motrin, Advil, Nuprin), naproxen (Naprosyn, Anaprox), or piroxicam (Feldene) interfere with the stomach's ability to produce mucus and bicarbonate (a chemical produced in the stomach that neutralizes and breaks down the hydrochloric acid and pepsin into substances less harmful).
- NSAIDs also affect blood flow to the stomach, hinder cell repair and cause the stomach's defense mechanisms to fail.
- Lifestyle factors such as smoking, drinking caffeine, consuming alcohol and stress are also associated with ulcers.
- Smoking slows the healing of ulcers and makes them likely to recur.
- Caffeine stimulates acid secretion in the stomach, thus aggravating the pain of an existing ulcer.
- Studies on alcohol consumption and ulcers have been less conclusive, although alcoholic cirrhosis has been linked to an increased risk of ulcers, and heavy drinking has been shown to delay the healing of ulcers.

Although emotional stress is no longer thought to be a cause of ulcers, people with ulcers often report that emotional stress increases ulcer pain. However, physical stress increases the risk of *developing* gastric ulcers.

PEPTIC ULCER

A peptic ulcer is a defect in the lining of the stomach or the first part of the small intestine, an area called the duodenum. A peptic ulcer in the stomach is called a gastric ulcer. An ulcer in the duodenum is called a duodenal ulcer. Peptic ulcers are generally caused by an acid resistant bacterium called Helicobacter pylori (H pylori) which infect the stomach. H pylori are Gram negative spiral shaped bacteria. In human it colonizes in stomach and the likelihood of infections increases with age. Peptic ulcer describes a condition in which there is a discontinuity in the entire thickness of the gastric mucosa that persist as a result of acid and pepsin in the gastric juice. **[11]** The word peptic refers to the pepsin i.e., stomach enzyme, which helps in breakdown of proteins.

Epidemiology

H. pylori infection is commonly seen in adult population. H pylori infections occur in 10% of children annually between the ages of 2 and 8 years. It is clear from the surveys conducted that the majority of person in the world are infected with H pylori [4].

Prevalence of H pylori infection correlates with socio-economic status rather than race with a

prevalence of 80% in developing countries compared to prevalence of 20-90% in developed countries. Peptic ulcer is common among older age individual and females. **[9]** H pylori infection was diagnosed in 82% of all peptic ulcer patients and also seen in 75% of Non steroidal anti-inflammatory drugs (NSAID) users. 5-10% of the adult population have peptic ulcer in life time.

Etiology

Although H. pylori is the major cause for peptic ulcers, other factors which cause peptic ulcer include:

- Non steroidal anti inflammatory drugs, Aspirin
- Zollinger Ellison Syndrome (Gastreinoma)
- Severe stress (e.g.: Trauma, Burns)
- Alcohol, smoking
- Bile reflux
- Pancreatic enzyme reflux
- Radiation
- Staphylococcus aureus exotoxin
- Bacterial or viral infection

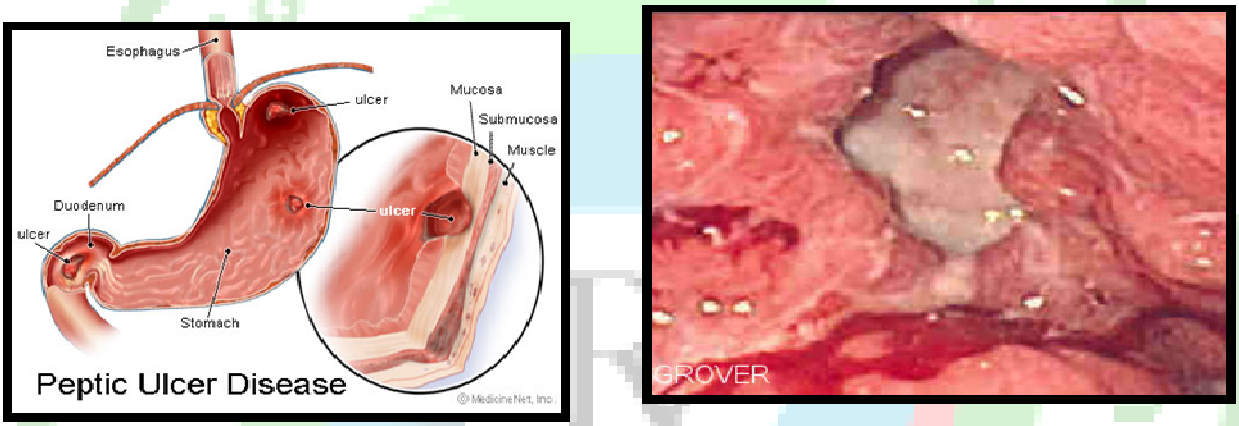

Fig 1: Peptic ulcer

Test for H Pylori

The diagnosis of H pylori can be made using invasive or non invasive tests. The invasive method requires upper GI endoscopy with a mucosal biopsy taken for histology, culture or detection of urease activity. The non invasive tests for H pylori do not require endoscopy or a mucosal biopsy and include the urea breath test and antibody detection test. These are less expensive than endoscopic tests. Various tests for detection of H pylori is given in table below.

RECOMMENDED TREATMENT

Life style changes

Doctors used to recommend eating bland foods with milk and only small amount of food with each meal. People who find that certain foods cause irritation should discuss the problem with their physicians. Smoking has been shown to delay ulcer healing and has been linked to ulcer recurrence. Therefore people with ulcer should not smoke.

Various tests for detection of *H. pylori*

Tests	Description	Advantages	Disadvantages
Antibody detection (Laboratory based)	Detects antibodies to H pylori in serum	• Endoscopy not required • Inexpensive • Most accurate	• Low specificity
Antibody detection	Qualitative detection of IgG antibody to H pylori in whole blood	• Quick • Inexpensive	• May yield invalid results
Urea breath test	H pylori urease breaks down ingested labeled (urea, patients exhales labeled CO_2)	• Endoscopy not required • Less expensive	• Results are not immediate
Histology	Microbial examination	• High specificity and sensitivity	• Require endoscopy • Expensive
Culture	Culture of biopsy	• Used to test for antibiotic resistance • High specificity	• Require endoscopy • Patient discomfort • Expensive
Biopsy urease	Urease of H pylori generates ammonia which causes a colour change	• High specificity and sensitivity	• Require endoscopy • expensive

Medications

Several types of medication are given for the treatment of stomach and duodenal ulcer. Which includes?

- H_2 blockers to reduce the amount of acid in the stomach by blocking histamine, which is a powerful stimulant of acid secretion.
- Acid pump inhibitors which completely block stomach acid production by stopping the stomachs acid pump the final step of acid secretion.
- Mucosal protective agents to shield the stomach are mucous lining from the damage of acid and they do not inhibit the release of acid [9].

When treating H pylori, these medications are often used in combination with antibiotics.

Surgery

In most cases, antiulcer medicines heal ulcers quickly and effectively, and eradication of Helicobacter pylori prevents most ulcers from recurring. However, people who do not respond to medication or who develop complications may require surgery. At present, laparoscopic surgery is performed to treat ulcers and include-

- **Vagotomy:** A procedure that involves cutting parts of the vagus nerve (a nerve that transmits message from the brain to the stomach) to interrupt messages sent through it and thereby, reducing the acid secretion.
- **Antrectomy:** An operation to remove the lower part of the stomach (antrum), which produces a hormone that stimulates the stomach to secrete digestive juices. Sometimes a surgeon may also remove an adjacent part of the stomach that secretes pepsin and acid. The vagotomy is usually done in conjunction with an antrectomy.
- **Pyloroplasty:** A surgical procedure that may be performed along with a vagotomy, in which the opening in to the duodenum and small intestine (pylorus) are enlarged, enabling contents to pass more freely from the stomach. In the future laparoscopic methods may become the standard surgical treatment.

MOUTH ULCER

A mouth or oral is an open sore in the mouth, or rarely a break in the mucous membrane or the epithelium on the lips or surrounding the mouth. The types of mouth ulcers are diverse, with a multitude of associated causes including: physical abrasion, acidic fruit, infection, other medical conditions, medications, and cancerous and nonspecific processes. Once formed, the ulcer may be maintained by inflammation and/or secondary infection. Two common types are aphthous ulcers ("canker sores") and cold sores (fever blisters, oral herpes). Cold sores around the lip are caused by viruses [6].

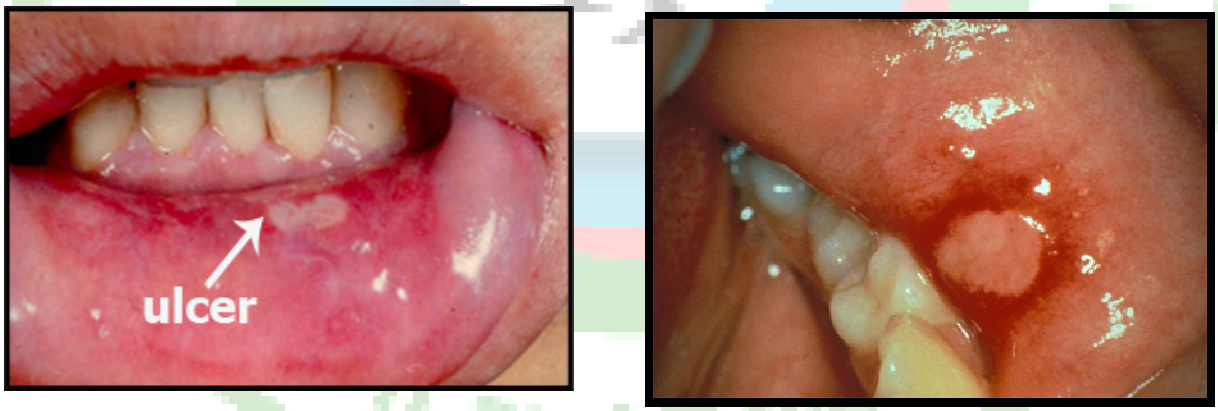

Fig 2: Mouth Ulcer

CAUSES

Trauma

Trauma to the mouth is a common cause of bacterial introduction. A sharp edge of a tooth, accidental biting (this can be particularly common with sharp canine teeth, or Wisdom teeth), sharp, abrasive, or excessively salty food, hot drinks, poorly fitting dentures, dental braces or trauma from a toothbrush may injure the mucosal lining of the mouth resulting in an ulcer. These ulcers usually heal at a moderate speed if the source of the injury is removed (for example, if poorly fitting dentures are removed

or replaced). These ulcers also commonly occur after dental work, when incidental abrasions to the soft tissues of the mouth are common. A dentist can apply a protective layer of petroleum jelly before carrying out dental work in order to minimize the number of incidental injuries to the soft mucosa tissues [7].

Chemical injuries

Chemicals such as aspirin or alcohol that are held or that come in contact with the oral mucosa may cause tissues to become necrotic and slough off creating an ulcerated surface. There is limited evidence to suggest that Sodium laurel sulfate (SLS), one of the main ingredients in most toothpaste, is associated with an increased incidence of oral ulcers.

Smoking cessation

It is fairly common for smokers to experience mouth ulcers within a week of cessation. The duration varies between individuals, and can range from a month to years. Oral nicotine supplements have shown some reduction in the occurrence.

Infection

Viral, fungal and bacterial processes can lead to oral ulceration. One way to contract pathogenic oral ulcerations is through the contact of chapped lips with unwashed hands. The reason for this is that bacteria sink into the minuscule, open cuts caused by the chapped lips.

Viral

The most common is *Herpes simplex* virus which causes recurrent herpetiform ulcerations preceded by usually painful multiple vesicles which burst. *Varicella Zoster* (chicken pox, shingles), *Coxsackie A virus* and its associated subtype presentations, are some of the other viral processes that can lead to oral ulceration. HIV creates immunodeficiency's which allow opportunistic infections or neoplasm's to proliferate.

Bacterial

Bacterial processes leading to ulceration can be caused by *Mycobacterium tuberculosis* (tuberculosis) and *Treponema pallidum* (syphilis).

Opportunistic activity by combinations of otherwise normal bacterial flora, such as aerobic streptococci, *Neisseria*, *Actinomyces*, spirochetes, and *Bacteroides* species can prolong the ulcerative process [8].

Fungal

Coccidioides immitis (valley fever), *Cryptococcus neoformans* (cryptococcosis), *Blastomyces dermatitidis* ("North American Blastomycosis") are some of the fungal processes causing oral ulceration.

Protozoans

Entamoeba histolytica, a parasitic protozoan, is sometimes known to cause mouth ulcers through formation of cysts.

Immune system

Many researchers view the causes of aphthous ulcers as a common end product of many different disease processes, each of which is mediated by the immune system. Aphthous ulcers are thought to form when the body becomes aware of and attacks chemicals which it does not recognize.

Immunodeficiency

Repeat episodes of mouth ulcers can be indicative of an immunodeficiency, signaling low levels of immunoglobulin in the oral mucous membranes. Chemotherapy, HIV, and mononucleosis are all causes of

immunodeficiency with which oral ulcers become a common manifestation.

Autoimmunity

Autoimmunity is also a cause of oral ulceration. Mucous membrane pemphigoid, an autoimmune reaction to the epithelial basement membrane, causes desquamation/ulceration of the oral mucosa.

Allergy

Contact with allergens, such as amalgam, can lead to ulcerations of the mucosa. Alternative materials may well bring about other types of allergy.

Dietary

Vitamin C deficiencies may lead to scurvy which impairs wound healing, which can contribute to ulcer formation. Similarly deficiencies in iron, vitamin B12, zinc have been linked to oral ulceration. Acidic food such as citrus fruit may cause mouth ulcers.

Treatment

Symptomatic treatment is the primary approach to dealing with oral ulcers. If their cause is known, then treatment of that condition is also recommended. Adequate oral hygiene may also help in relieving symptoms**.** Topical antihistamines, antacids, corticosteroids or applications meant to soothe painful ulcers may be helpful, as may be oral analgesics such as paracetamol or ibuprofen and local anesthetic lozenges, paints or mouth rinses such as benzocaine and avoiding spicy or hot foods may reduce pain. Ulcers persisting longer than three weeks may require the attention of a medical practitioner.

CORNEAL ULCER

A **corneal ulcer**, or **ulcerative keratitis**, or **eyesore** is an inflammatory or more seriously, infective condition of the cornea involving disruption of its epithelial layer with involvement of the corneal stroma. It is a common condition in humans particularly in the tropics and the agrarian societies. In developing countries, Children afflicted by Vitamin A deficiency are at high risk for corneal ulcer and may become blind in both eyes, which may persist lifelong [9].

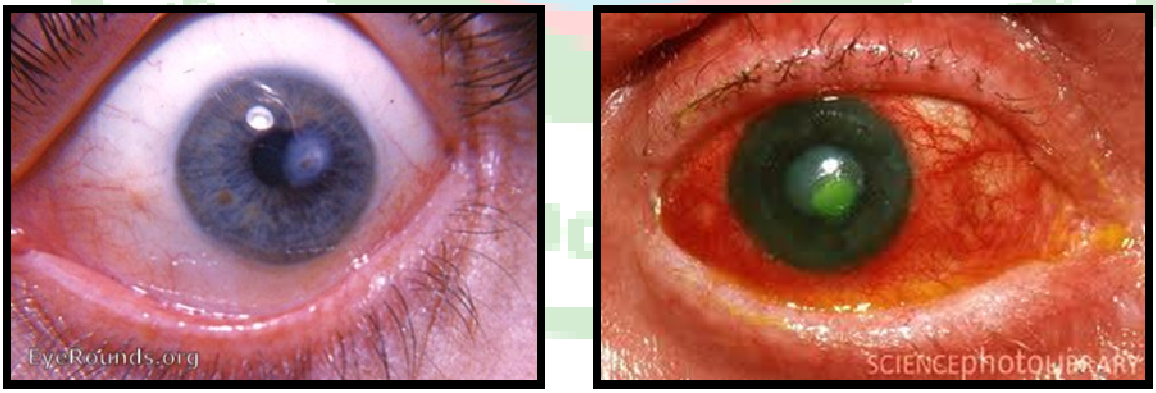

Fig 3: Corneal Ulcer

Symptoms

Corneal ulcers are extremely painful due to nerve exposure, and can cause tearing, squinting, and vision loss of the eye. There may also be signs of anterior uveitis, such as miosis (small pupil), aqueous flare (protein in the aqueous humor), and redness of the eye. An axon reflex may be responsible for uveitis formation — stimulation of pain receptors in the cornea

results in release inflammatory mediators such as prostaglandins, histamine, and acetylcholine.

Diagnosis

Diagnosis is done by direct observation under magnified view of slit lamp revealing the ulcer on the cornea. The use of fluorescein stain, which is taken up by exposed corneal stroma and appears green, helps in defining the margins of the corneal ulcer, and can reveal additional details of the surrounding epithelium [10]. Herpes simplex ulcers show a typical dendritic pattern of staining. Rose-Bengal dye is also used for supra-vital staining purposes, but it may be very irritating to the eyes. In descemetoceles, the Descemet's membrane will bulge forward and after staining will appear as a dark circle with a green boundary, because it does not absorb the stain. Doing a corneal scraping and examining under the microscope with stains like Gram's and KOH preparation may reveal the bacteria and fungi respectively. Microbiological culture tests may be necessary to isolate the causative organisms for some cases [11]**.** Other tests that may be necessary include a Schirmer's test for keratoconjunctivitis sicca and an analysis of facial nerve function for facial nerve paralysis.

Treatment

Proper diagnosis is essential for optimal treatment. Bacterial corneal ulcer requires intensive fortified antibiotic therapy to treat the infection. Fungal corneal ulcers require intensive application of topical anti-fungal agents. Viral corneal ulceration caused by herpes virus may respond to antiviral like topical acyclovir ointment instilled at least five times a day. Alongside, supportive therapy like pain medications are given, including topical cycloplegics like atropine or homatropine to dilate the pupil and thereby stop spasms of the ciliary muscle. Superficial ulcers may heal in less than a week. Deep ulcers and descemetoceles may require conjunctival grafts or conjunctival flaps, soft contact lenses, or corneal transplant. **[8]** Proper nutrition, including protein intake and Vitamin C are usually advised. In cases of Keratomalacia, where the corneal ulceration is due to a deficiency of Vitamin A, supplementation of the Vitamin A by oral or intramuscular route is given. Drugs that are usually contraindicated in corneal ulcer are topical corticosteroids and anesthetics - these should not be used on any type of corneal ulcer because they prevent healing, may lead to super infection with fungi and other bacteria and will often make the condition much worse [12].

CONCLUSION

Ulcer is a very crucial issue worldwide. From the perspective of the different ulcer it was depict that development of the different category of ulcer in the population, mostly depends on the food habit. Ulcer is usually initiate with a sign of gastritis; it is very common in case of gastric ulcer & duodenal ulcer. In other cases, it was observed that the development of other category of ulcer was due to physiological & pathological causes. Most of the instances, some organisms *(H.Pylori)* were also the causative one for developing ulcer. Most common ulcer is gastric ulcer, whereas the corneal & genital are rare. Very common sign in ulcer is inflammation, severe pain (heart burn in case of gastric ulcer). From the point of view of the distinct type of GIT problems such as GERD (Gastro-Esophageal Reflex Disorder) & Zolliger-Ellision syndrome, the ulcer could be turn to cancer or

malignant tumor. So a very special care required to manage or treat that condition.

Different types of anti-ulcerant agents may used to treat ulcer including-H**2**-Blocker, PPIs (Proton Pump Inhibitors). Most widely used H2-Blocker is Ranitidine-150mg & PPIs is Omeprazole-20/40mg. Hence, it's clear that most of the people of whole world are suffered from different ulcer, so positive care & proper treatment/management need to check the problem & cure the patients from ulcer; otherwise it could be danger or life-threatening.

REFERENCES

1. *Gottsch J, Liu S, Stark W. Mooren's Ulcer and evidence of stromal graft rejection after penetrating keratoplasty. Am J Ophthalmol, 1992;113:412-417.*
2. *Brown S, Mondino B. Penetrating keratoplasty in Mooren's Ulcer. Am J Ophthalmol, 1980;89:255-258.*
3. *Hayes RJ, Schulz KF, Plummer FA. The cofactor effect of genital ulcers on the per-exposure risk of HIV transmission.Journal of Tropical Medicine and Hygiene, 1995;98: 1–8.*
4. *James, William D.; Berger, Timothy G. Andrews' Diseases of the Skin: clinical Dermatology. Saunders Elsevier, 2006,*
5. *Hill J, Potter P. Treatment of Mooren's Ulcer with cyclosporine A: Report of three cases. Br Ophthalmol, 1987;71: 11-15.*
6. *Orroth KK. Syndromic treatment of sexually transmitted diseases reduces the proportion of incident HIV infections attributed to these diseases in rural Tanzania. AIDS, 2000;14: 1429–1437.*
7. *Kinoshuita S, Ohashi Y, Ohji M. Long-term results of kerato epithelioplasty in Mooren's ulcer. Ophthalmology, 1991, 98:438-445*
8. *Hunt, RH. Helicobacter pylori: from theory to practice. Proceedings of a symposium. Am J Med, 1996; 100 (5A) supplement*
9. *Bowman W. Case the parts concerned in the operations of the eye (1849), cited by Nettleship, E: Chronic Serpiginous Ulcer of the Cornea (Mooren's Ulcer). Trans Ophthamol Soc UK 1902;22:103-104.*
10. *Brown S. Mooren's Ulcer: Histopathology and proteolytic enzymes of adjacent conjunctiva. Br J Ophthalmol, 1975;59:670-674,.*
11. *Genvert G, Sakauye C, Arentsen J. Treatment of marginal corneal ulcer with cryotherapy and conjunctival recession or resection. Cornea, 1984;3: 256-261.*
12. *Mondino BJ, Brown SI, Mondzelewski JP. Peripheral corneal ulcer with herpes zoster ophthalmicus. Am J Ophthalmol 1978;86:611-614.*