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## Abstract:-

Helicobacter pylori infection is acquired in child hood & plays a causative role in peptic ulcer disease, chronic gastritis, & in the gastric cancer development. Many treatment regimes have been developed to effectively treat this infection since early 1980s. International guidelines have allowed consensus on the best management & improved eradication rates. Increasing antimicrobial resistance has resulted in falling eradication rates with st&ard therapies during recent years. Here we review the guidelines & most recent studies in the treatment of Helicobacter pylori. Presently, the ﬁrst-line treatment remains clarithromycin, amoxicillin or metronidazole & proton pump inhibitor twice daily, but a number of recent studies have shown low eradication rates with this treatment. Increased duration of therapy has been recommended to overcome the falling eradication rates. However, conﬂicting ﬁndings have been reported on the beneﬁts of extending the length of traditional therapy. Sequential therapy may be an effective alternative to st&ard triple therapy in regions of increased antimicrobial resistance. Side-effects from traditional regimens is reduced by Probiotics & may improve eradication rates. A quinolone-based second-line triple therapy appears to be effective & well tolerated. Bismuth-based quadruple therapy is also an effective alternative if available. In the future, regional antimicrobial resistance & eradication rates will determine the best treatment for H. pylori . Here we focus on the latest advances in the treatment of H. pylori infection with emphasis on both indications for treatment & eradication regimens & co-therapy.

## .

## Introduction:

Helicobacter pylori (H. pylori) are a type of intestinal bacteria that cause the majority of ulcers in the stomach & duodenum. They thrive in highly acidic environments & have a unique way of adapting to the harsh environment of the stomach. H. pylori have been classified as low-potential carcinogens (cancer-causing substances) by the World Health Organization. Helicobacter pylori colonization is very common worldwide. Although all H. pylori-positive subjects have chronic active gastritis, it is estimated that only 20–25% of affected subjects develop clinically overt disease during their lifetime. 1 This ranges from gastric & duodenal ulcer disease to gastric adenocarcinoma & lymphoma, as well as more rare disorders, including a few extra-gastric disorders. H. pylori eradication has a major impact on the natural course of several of these disorders, in particular peptic ulcer disease & gastric mucosa-associated lymphoid tissue (MALT) lymphoma. The recognition of this effect & the development of effective treatment strategies have revolutionized the clinical approach to these patients. This is generally considered one of the most important new developments in gastroenterology in the past 25 years, which was supported by the award of the Nobel prize to Drs Marshall & Warren, who first recognized the clinical importance of this bacterium. 2 Ever since then, much effort has been spent on developing optimal treatment strategies for the clinical management of H. pylori-positive subjects, a process that is still ongoing. The evidence that H pylori infection causes peptic ulcer disease is compelling(3–5) Thus However, currently, the level of evidence supporting an association between specific symptoms due to H pylori infection in children & recurrent abdominal pain is insufficient to advocate testing & treating in this clinical context 6.. Furthermore, a similar prevalence of H pylori infection in children with & without functional abdominal pain was identified in case control trials 7 unfortunately; the reported treatment trials that lack controls do not provide additional supportive information. The role of H pylori in dyspepsia in adult patients is controversial. Although current guidelines for adults advocate a test & treat strategy, when nonnuclear dyspepsia treatment trials were assessed systematically, H pylori eradication had only a small effect on dyspeptic symptoms

## Epidemiology

Once the role of H. pylori in peptic ulcer disease was firmly established, it was imperative to find out more about the prevalence & distribution of the infection. To do this, investigators needed data about large populations of people all over the world & a way to make feasible such extensive testing. Clearly, the task of culturing bacteria from individuals would be impossible. Not only were specialized equipment & techniques necessary to grow the bacteria, but also the only way to obtain culture material from human sources was by endoscopy, hardly feasible for large-scale studies. The human immune system provided the answer. Researchers had discovered that specific anti-H. pylori antibodies could be detected in the blood serum of individuals who were infected with the organism. That enabled the use of a simple blood test for the important epidemiological studies. Researchers were able to expedite the investigations because they did not have to collect new tissue samples from each person; instead, they used blood samples that had already been collected in large numbers at clinics & blood banks, often for other studies & tests. This early research on H. pylori characterized much of the work to come. The data that emerged from the study of all these samples were unexpected. It showed that H. pylori is a common bacterial agent & at least 30-50% of the world’s population are colonized with it. Investigators discovered that the frequency of H. pylori presentation was highly variable from country to country & between socioeconomic & ethnic groups. Overall, they found a consistent pattern in most developing nations, where 70 to 90% of adults harbored the bacteria; most individuals acquired the infection as children, before age 10. In developed countries, on the other h&, fewer than 10% of children became infected & although a steady rate of colonization persisted with increasing age, less than half of 60-year-olds had acquired H. pylori. Clear associations could be made with conditions of poor sanitation & crowded living conditions such as those in orphanages or other institutions. In spite of this connection with the signs associated with poverty, the studies failed to establish whether or how transmission from one individual to another actually occurs. Obvious c&idates (e. g., oral-oral or fecal oral pathways) have been considered & investigated. But aside from minor modes of passage, such as through unsterilized endoscopy equipment & from African mothers who premasticate food for their children, researchers have been unable to identify a common means for transferring the infection from person to person. A surprising finding was that most infected individuals were generally asymptomatic & fewer than 20% of people (regardless of age) who tested positive for H. pylori had ulcers.

## Discussion:-

## symptoms

## symptoms & incubation time of an H. pylori infection:-

Getting an H. pylori infection is nothing like catching a common cold in that immediate consequences of an infection are rarely seen. In fact, it is possible to go many years without noticeable symptoms. When symptoms do occur, abdominal discomfort is the most common. This discomfort is usually a dull, gnawing ache that comes & goes for several days or weeks. It usually occurs two to three hours after a meal or in the middle of the night (when the stomach is empty) & is relieved by eating, drinking milk or taking antacid medications. Other symptoms include: heartburn, increased burping, weight loss, bloating & burping, & less common symptoms include: poor appetite, nausea & vomiting. Most people recover from their symptoms within two to three weeks of starting antibiotic therapy. Severe symptoms associated with serious ulcer-related problems may take longer to heal. H. pylori bacteria have been associated with many different diseases, including: duodenal ulcers, gastric (stomach) ulcers, stomach cancer & non-ulcer dyspepsia (indigestion). H. pylori infections have also been linked with causing gastritis (inflammation of the stomach) in adults & children. Infected persons have a two to six-fold increased risk of developing stomach cancer & lymphoma (cancerous tumors in the lymphatic tissue) compared with their uninfected equivalents. If an ulcer does cause bleeding, prolonged bleeding may cause anemia leading to weakness & fatigue. If bleeding is heavy, hematemesis (the vomiting of blood), hematochezia (the passage of feces containing blood), or melena (a condition marked by black, tarry stools or vomit composed largely of blood) may occur.

## Diagnosis:-

It is presumed that H. pylori infection should only be diagnosed when an eradicating therapy is indicated. We currently have a wide variety of methods for the diagnosis of this infection. The discussion has considered two viewpoints regarding diagnostic modalities for H. pylori infection: on the one h&, the diagnostic method to use in varying clinical situations; on the other h&, the current role of each individual diagnostic modality. A. Regarding diagnosis, agreed-upon recommendations for the following clinical settings will be discussed: a) Endoscopic diagnosis of normality & dyspepsia symptoms. b) Diagnosis of gastric or duodenal ulcer. c) In gastrointestinal bleeding secondary to peptic ulcer. d) In patients with a history of peptic ulcer. e) In the control of infection eradication. f) In patients currently or recently on antibiotics or antisecretory agents. B. Regarding diagnostic modalities, consensus has been reached on the current role of methods based on:

## Invasive methods:-.

Endoscopy test (Biopsy collection histology, rapid urease test, & culture)

## Endoscopy

An endoscopy diagnoses an H. pylori infection by allowing tissue samples of the stomach & duodenum to be taken for testing. A thin, narrow, flexible, lighted tube with a tiny camera on the end is eased into the mouth & down the throat to the stomach & duodenum. Through this tube (the endoscope), the doctor can examine the lining of the esophagus (food pipe), stomach & duodenum. The endoscope can be used to take photographs of the ulcers or to remove tiny pieces of tissue to view under a microscope. The removal of tissue samples for observation is a process called a biopsy & the samples can be used to check for the presence of H. pylori. Non-invasive methods (endoscopy is not required )An H. pylori infection is diagnosed through blood, breath & stool tests in Non-invasive methodsBlood tests are the most common as they are one of the least invasive tests available. If a blood test comes back positive for H. pylori & further clarification is still available, will then proceed with other tests, such as the breath test , fecal antigens test or an endoscopy. The four tests are briefly described below. serology testsC-urea breath testfecal antigens test

## Serology tests:-

Blood tests will identify a Helicobacter pylori infection by detecting the presence of the antibodies that stick to the H. pylori bacteria. If the tests are positive (i. e. the antibodies are present) the bacteria are either currently present, or were present in the recent past (within the past three years).

## carbon-\_4-urea & carbon \_3-urea breath tests. 14

Urea breath tests are an effective diagnostic method for H. pylori & are quicker & simpler to perform than an endoscopy. By drinking a urea solution that contains a special carbon atom, the presence of the bacteria can be determined. If H. pylori are present, they will break down the urea in the solution, thus releasing the carbon. The blood carries the carbon to the lungs, where the patient exhales it. The breath test is 96 percent to 98 percent accurate & can also be used after treatment to see whether the treatment worked.

## Fecal antigens test:-15

Stool tests may be used to detect an H. pylori infection in a patient’s fecal matter. Studies have shown that this test, called the Helicobacter pylori stool antigen (HpSA) test, is accurate for diagnosing H. pylori. A positive test (a test that suggests an H. pylori infection) is when antigens, substances that when introduced into the body stimulates the production of an antibody, are found in the fecal matter. The antigens in this case would be the H. pylori bacteria cells.

## Table 1

Diagnostic Tests for Helicobacter pylori. 8-17TestSensitivity (%)Specificity (%)Usefulness

## INVASIVE

Endoscopy with biopsy. HistologyUrease activityCulture

## NONINVASIVE

Serology forimmunoglobulin GUrea breath testH. pylori stoolantigen> 9593 to 9770 to 808595-10091-98100> 951007991-9894-99Diagnostic strategy of choice in children with persistent or severe upper abdominal symptomsSensitivity reduced by PPIs, antibiotics, & bismuth-containing compounds. Sensitivity reduced by PPIs, antibiotics, bismuth-containingcompounds, & active bleedingTechnically dem&ingSensitivity & specificity vary widely; positive result may persist for months after eradicationReliability in children not adequately validated; not recommendedRequires separate appointments; sensitivity reduced by PPIs, antibiotics, & bismuth-containing compounds; reliable test for cure Best available noninvasive test in children but higher false-positive rates in infants & children youngerThan six years compared with school-age children& adolescents. Test for cure seven days after therapy is accurate; sensitivity reduced by PPIs, antibiotics, & bismuth-containing compounds Easy to perform independent of age; possible alternative to ureabreath test; monoclonal antibody-based test most reliable

## Treatment:-

Since the discovery of in the early 1980s many treatment regimes have been developed to effectively treat this infection. International guidelines have allowed consensus on the best management & improved eradication rates. In recent years, increasing antimicrobial resistance has resulted in falling eradication rates with st&ard therapies. In this article, we review the most recent studies & guidelines in the treatment of Helicobacter pylori.

## Traditional treatment:-

H. pylori infection is common even in asymptomatic individuals & has been shown to be a risk factor for gastric cancer. 18 Eradication of the organism can be difficult to achieve with conventional antibiotic therapies, requiring combinations of antibiotics, proton pump inhibitors & bismuth preparations. 19 Moreover, adverse effects are regularly associated with these conventional treatments. Garlic is one of the most extensively researched medicinal plants. 20 Its antibacterial action depends on allicin & is thought to be due to multiple inhibitory effects on various thiol-dependent enzymatic systems. 21 Allicin is formed catalytically by crushing raw garlic or adding water to dried garlic, when the enzyme allicinase comes into contact with allicin. Steam distillation of mashed garlic produces garlic oil containing methyl & allyl sulphides of allicin, having the practical advantage of being more stable than allicin itself.

## Recent developments in treatment of H. pylori infection:-

The treatment of Helicobacter pylori remains a challenging clinical problem despite extensive research over the last 25 years. Increasing antimicrobial resistance & falling eradication rates are the result of the widespread use of antibiotics. However, in clinical practice eradication rates are lower H. pylori than 80% for many of the st&ard treatment regimes. A number of factors such as duration of treatment, choice of antibiotics, new drug combination, improved patient compliance, & novel agents may help to improve eradication rates.

## Indications for Treatment:-

## Strongly Recommended Indications:-

From the very beginning of H. pylori research, it was clear that this infection is closely associated with peptic ulcer disease 22 & that H. pylori eradication significantly reduces ulcer recurrences. 23 Nevertheless, it took more than a decade before peptic ulcer disease became generally accepted as an indication for H. pylori eradication therapy. Nowadays, this has become thoroughly embedded in daily clinical practice worldwide. Indications for eradication include uncomplicated as well as complicated ulcer disease, & both pertain to patients with current ulcer disease as well as to patients with a history of ulcer disease. In uncomplicated ulcer disease, a seven- to 10-day course of eradication therapy is sufficient for ulcer cure without further acid-suppressive therapy. However, most clinicians prefer to continue acid-suppressive therapy for several weeks. Other strongly recommended indications for H. pylori diagnosis & treatment are gastric MALT lymphoma, atrophic gastritis, previous treatment for gastric cancer unless a complete gastrectomy has been performed, patients with first-degree relatives with gastric cancer & subjects who wish to be treated after consultation with their physician. 24 The level of evidence for these indications varies. Obviously, there is no evidence for the last indication listed, patient’s wishes. First-degree relatives of patients with gastric cancer are known to have an increased risk of this same disease, & have in the past been noted to have a higher prevalence of pre-neoplastic lesions in comparison with matched controls. 25 Atrophic gastritis may improve after H. pylori eradication. 26 Even though there is concern that H. pylori eradication at this stage may not reduce the already elevated risk of gastric cancer, H. pylori eradication is nevertheless recommended. 24-27 Further studies have to clarify which patients with pre-malignant lesions in this respect benefit from H. pylori eradication. Finally, 60–65% of gastric MALToma patients are in complete remission one year after H. pylori eradication therapy as sole treatment. Predictors of response to eradication therapy are lymphoma confined to the (sub-)mucosa of the stomach without extragastric disease, & the absence of a translocation with fusion of the API2 & MALT1 genes. MALTomas with this translocation show no or minimal response to H. pylori eradication therapy. 28

## Other Indications:-

H. pylori eradication provides a modest but significant benefit in patients with non-ulcer dyspepsia (see Table 2). 29 Meta-analysis data suggest that31-34 patients need to be treated to cure one patient with non-ulcer dyspepsia. Despite these unfavorable numbers, H. pylori test-&-treat strategies are considered appropriate both for patients with uninvestigated dyspepsia in the absence of alarmsymptoms & for patients with investigated non-ulcer dyspepsia. 30 In both groups, treatment should be accompanied by a clear explanation to the patient that the effect of treatment may become apparent only after a considerable time interval. Profound acid-suppressive therapy affects the pattern & severity of H. pylori gastritis, favoring a corpus-predominant pangastritis. 31 This may accelerate the loss of gastric gl&s, leading to atrophic gastritis. In patients with reflux disease requiring long-term acid-suppressive therapy, H. pylori eradication decreases gastritis without impairing the efficacy of acid suppression. 32 The Maastricht guidelines for the management of H. pylori infection therefore advise considering H. pylori eradication in long-term proton pump inhibitor (PPI) users. 24

## Table2:

Indications for Helicobacter pylori Eradication 24Strongly recommendedConditionPeptic ulcer disease, Gastric MALT lymphoma , Atrophic gastritis, Partial gastrectomy for gastric cancer, First-degree relatives of gastric cancer patientSubject’s own wishOther indicationsNon-ulcer dyspepsia, Long-term PPI use, Long-term NSAID use, Unexplained iron deficiency anaemia, Thrombotic thrombocytopenic purpuraMALT = mucosa-associated tymphoid tissue; NSAID = non-steroidal anti-inflammatory drug; PPI = proton pump inhibitor. Apart from an interaction with acid suppressants, H. pylori infection may also interact with non-steroidal anti-inflammatory drug (NSAID) use, but this relationship is complex. H. pylori & NSAIDs both independently increase the risk of development of gastro duodenal ulcer disease. H. pylori eradication may reduce the incidence of ulcers in those with both H. pylori infection & NSAID use, 33 but eradication therapy is inferior to PPI therapy for the prevention of ulcer bleeding in NSAID users, 34 & also has no additional effect to PPI therapy for maintaining remission in chronic NSAID users with previous ulcer disease. 35 Based on these data, the most recent European guidelines conclude that H. pylori eradication may be of value for long-term NSAID users but is insufficient to prevent ulcer disease. Furthermore, they conclude that when an ulcer occurs in a patient with a persistent need for NSAID therapy, prevention of recurrent ulcers & ulcer complications should preferentially be achieved by means of PPI maintenance therapy instead of H. pylori eradication. The effect of H. pylori eradication may be larger in aspirin users. Thus, an H. pylori test-&-treat strategy is advised for long-term aspirin users to prevent ulcer disease & in long-term NSAID users who are also treated with a PPI to prevent an accelerated loss of gastric gl&s. 24All of these effects of H. pylori eradication, cure & prevention of ulcer disease, improvement of dyspepsia, remission of MALT lymphoma & prevention of NSAID-associated damage occur within weeks to months after therapy. This is also true for the healing of gastritis, which more slowly can be accompanied by a certain regression of atrophic gastritis, probably without much effect on pre-existent intestinal metaplasia. 26 These short-term observations supported the enthusiasm to assume that H. pylori eradication would also have a rapid preventative effect on the occurrence of gastric adenocarcinoma. However, the first long-term intervention studies showed that any effect of H. pylori eradication on prevention of gastric cancer in the first five years after eradication therapy appears confined to subjects without pre-existent atrophic gastritis & intestinal metaplasia. 27 This supports the concept of a point of no return, beyond which the contribution of persistent H. pylori colonisation decreases. This is in line with observations that the colonization density of H. pylori decreases with progressive gl& loss & intestinal metaplasia, so that in fact a considerable proportion of gastric adenocarcinoma patients have completely lost their previous infection. Therefore, prevention of gastric cancer by wide-scale H. pylori test-&-treat programmes is currently not an accepted strategy. The feasibility of such an approach needs to be demonstrated by further data, which, among others, need to provide insight into the optimal timing of treatment, the magnitude of effect, side effects & optimal treatment regimens. Finally, there is accumulating evidence that some patients with unexplained iron-deficiency anaemia as well as patients with idiopathic thrombocytopenic purpura benefit from H. pylori eradication. 36, 37 There is no indication for H. pylori treatment in other extra-intestinal diseases. All of the indications mentioned above, in particular peptic ulcer, nonnuclear dyspepsia & unexplained iron-deficiency anaemia, are also indications for H. pylori diagnosis & treatment in children. 24

## Treatment Regimens:-

Recent developments in the treatment of H. pylori infection include three main aspects: The disappearance of bismuth products off the market in various countries of the world; An abundance of new data on alternative treatment regimens, in particular for second-line treatmentThe use of non-antimicrobial agents along side eradication treatment to improve the eradication effect &/or to ameliorate side effects. The aim of treatment of Helicobacter pylori is eradication of the bacterium from the foregut. Treatment is difficult because of the bacterium's habitat & acquired resistance to commonly used antibiotics. Dual therapy, the 2 week combination of omeprazole or ranitidine bismuth citrate & either amoxicillin or clarithromycin, eradicates H. pylori in 50-80% of patients. Classical triple therapy is commonly associated with side effects, is highly dependent on patient's compliance, & is significantly less effective in the presence of metronidazole-resistant strains of H. pylori, where eradication may be 50%. One week, twice daily, proton pump inhibitor (PPI)-based triple therapy regimens eradicate about 90% of H. pylori & are associated with mild side effects. Second line regimens include 7 days treatment with omeprazole & 3 times daily amoxycillin & metronidazole or a PPI-based quadruple therapy regimen. In some cases, the bacterium defeats all attempts at eradication.

## First-line therapy:-

First-line therapy should be with dual therapy classic triple therapy & alternative triple therapy by using a proton pump inhibitor or ranitidine bismuth citrate, combined with clarithromycin & amoxicillin or metronidazole.

## Dual therapy:-

Dual therapy refers to the combination of omeprazole or ranitidine bismuth citrate (RBC) & either amoxycillin or clarithromycin. These regimens were reported to overcome problems that had bedeviled classic triple therapy, such as side effects, MRS of H. pylori & patient's compliance with more complex regimens.

## Omeprazole & amoxicillin:-

Most of the work dealing with dual therapy uses omeprazole & amoxycillin (Table 3), is published as abstracts & is based on small,

## Table 3

Dual therapy with AmoxycillinOmeprazoleAmoxycillinRanitidine bismuth citrateAmoxycillinDosing20-40 mg twice daily750 mg 3 times daily or 1 g twice daily400-800 mg twice daily500 mg 4 times dailyDuration2 weeks2 weeksH. pylori eradication50-85%65%Side effectsdiarrhoeadiarrhoeaUncontrolled, non-r&omised studies38. The results suggest that the daily dose of amoxicillin should be at least 2 g; the frequency of administration appears to be less important than the ompliance with the treatment regimen. In combination with amoxycillin, omeprazole is more effective when given twice daily & at higher than normal doses. Thus, eradication with omeprazole 20 mg or 40 mg once daily with amoxycillin 2 g daily for 2 weeks varies between 0% & 28%, but on 20—40 mg twice daily in combination with amoxycillin 1 g twice daily (or 500 mg, 4 times daily) for 2 weeks, eradication was 50-90%6. However, recent data from large, double-blind, r&omised controlled trials of 2 weeks' treatment with omeprazole (20 or 40mg twice daily) & amoxycillin (500 mg or lg 3 times daily) reported H. pylori eradication of only 39-46%39. There are less data on lansoprazole or pantoprazole, in combination with amoxycillin, but preliminary studies suggest that the results with these newer PPIs are similar38

## Omeprazole with clarithromycin:-

Inhibition of acid secretion with PPIs increases the intragastric pH to 5. 0 or more & significantly decreases the minimum inhibitory concentration (MICJ0) of amoxycillin & clarithromycin making them more effective. The combination of various dosages & duration of omeprazole38, lansoprazole40 or pantoprazole41 with clarithromycin for H. pylori eradication have been studied (Table 4). The frequency of dosing with clarithromycin is important. Thus, clarithromycin 500 mg given twice daily in combination with omeprazole 40 mg was apparently less effective, with eradication reported as 56%43, compared with 63-81% on clarithromycin 500 mg, 3 times daily38, 44. Side effects occur in up to half of patients treated with clarithromycin & omeprazole & become more common as the dose & frequency of clarithromycin increase, the commonest being taste disturbance. Clarithromycin is a relatively expensive antimicrobial agent, & a 2 week combination of omeprazole

## Table 4

Dual therapy with clarithromycinOmeprazoleClarithromycinRanitidine bismuth citrateClarithromycinDosing40 mg once daily 500 mg 3 times dairy400 mg twice daily 500 mg twice dailyDuration2 weeks2 weeksH. pylori eradication80%80%Side effectsDiarrhea, taste disturbancesDiarrheataste disturbances

## Ranitidine bismuth citrate:-

Ranitidine bismuth citrate (RBC) is a new chemical compound that combines the antisecretory activity of ranitidine with mucoprotective & H. pylori suppressive effects of bismuth. Dual therapy with RBC (400 mg twice daily) & amoxycillin (500 mg 4 times daily) or clarithromycin (250 mg 4 times daily or 500 mg twice daily) for 2 weeks is licensed for H. pylori eradication. RBC with amoxycillin will eradicate H. pylori in about 65% of cases45, but with clarithromycin 500 mg twice daily, the figures become about 80% (Tables 3&4)46-48. Unfortunately, any possible advantages of twice daily dual therapy with RBC & clarithromycin are outweighed by the need for 14 days' treatment & high treatment cost.

## Classic triple therapy:-

Classic triple therapy (Table 3) consists of a bismuth compound (colloidal bismuth subcitrate (CBS) or bismuth subsalicylate, BSS), metronidazole & either amoxycillin or tetracycline. There are wide variations in the dosage & treatment schedules used in these regimens, with eradication results varying from 30-95%25. It is difficult to account for these differences, except by invoking the customary factors of dissimilarities in patient populations, incidence of metronidazole resistance, degree of compliance with the treatment & the like. Triple therapy given for less than 7 days has not been successful & when given for longer than 14 days appears to give no further therapeutic advantage6. Classic triple therapy is significantly less effective against pretreatment MRS of H. pylori, with most eradication results falling between 30% & 60% in this group of patients49, 50.

## Table 5

Triple therapy combinations with amoxicillin & metronidazoleOmeprazoleAmoxycillinMetronidazoleRanitidine bismuth citrate, Amoxycillin, MetronidazoleColloidal bismuth subcitrateTetracycline or amoxicillin, MetronidazoleDosing40 mg once dally500 mg 3 times daily400 mg 3 times daily300 mg once daily750 mg 3 times daily500 mg 3 times daily120 mg 4 times daily500 mg 4 times daily200-400 mg 4 times dailyDuration7 days12 days2 weeksH. pylori eradication95% in MSS75% in MRS90% in MSS50% in MRS60-90% in MSS50% in MRSSide effectsdiarrhoea, nauseadiarrhoea, nauseadiarrhoea, nausea

## Alternative triple therapy regimens:-

Antisecretory drugs have been tried in place of bismuth as part of a triple therapy with some success (Table 5). Thus, ranitidine 300 mg daily combined with metronidazole 500 mg 3 times daily & amoxycillin 750 mg 3 times daily for 12 days was shown to eradicate around 90% of H. pylori51. However, this regimen is far less effective against MRS of H. pylori, where eradication is around 50%51, 52. The combination of omeprazole 40 mg53, lansoprazole 30 mg54 or pantoprazole 40mg55. with amoxycillin 500 mg 3 times daily & metronidazole 400 mg 3 times daily for 1 week is an effective triple therapy, with H. pylori eradication in around 90% of the patients.. Thus, in areas with a high prevalence of MRS & CRS of H. pylori, 1 week's treatment with omeprazole, amoxycillin & metronidazole may be the first choice.

## second-line therapy:-

Subsequent second-line therapy should use quadruple therapy with a proton pump inhibitor, bismuth, metronidazole & tetracycline.

## Quadruple therapy:-

Quadruple therapy (Table 6) for H. pylori eradication must entail more compliance problems & side effects than the simpler regimens56, 57. Despite this, 98% H. pylori eradication has been reported using a 1 week combination of omeprazole (20 mg twice daily given for 10 days), CBS (120 mg 4 times daily), tetracycline (500 mg 4 times daily) & metronidazole (500 mg 3 times daily)57. Compliance was remarkably high in this well performed study, & all patients were followed-up. Only 7. 7% of the pretreatment H. pylori isolates were metronidazole resistant, & this may account for the very high eradication reported. Similar results have been reported using lansoprazole-based quadruple therapy regimens58. Twice daily quadruple therapy (bismuth subsalicylate, tetracycline 500 mg, metronidazole 500 mg & lansoprazole 15 mg) for 10 days was reported to be effective against MSS of H. pylori (95% eradication), but was significantly less effective against MRS of H. pylori (40% eradication) & is, therefore, of no benefit over simpler & shorter twice daily regimens59.

## Table6

Quadruple therapyPPIColloidal bismuth subcitrateTetracyclineMetronidazoleDosingonce daily - twice daily120 mg 4 times daily500 mg 4 times dally400-500 mg 4 times daily/3 times dailyDuration7 daysH. pylori eradication85-95%Side effectsDiarrhoea, nausea

## Flow chart of first line & second line therapy

## First line therapy

Ppi(RBC) b. d+ Clarithromycin 500mg b. d(C)+ amoxicillin 1000mg b. d(A) orMetronidazole R 500mg b. d(M) for a minimum of 7 daysIn case of failure

## Second line therapy

PPI b. d+ bismuth subsalicylate/subcitrate 120 mg q. d. s+ Metronidazole R 500mg t. d. s+ tetracycline for minimum 7 daysIf bismuth is not available , PPI based triple therapy should be usedsubsequent failures should be h≤d on a case-by-case basis. l patients failing second line therapy in primary care should be referred

## Non-antimicrobial Co-therapy:-

Various non-antimicrobial products have been studied for their effect on H. pylori when taken either alone or as co-therapy with triple therapy. These products include normal foods or food components, such as cranberry juice, ginger, oregano & broccoli sprouts, 60 food additives such as lactoferrin & various probiotics. The purpose of their use was either to reduce the side effects of eradication therapy or to improve the efficacy of this therapy, or both. Several normal foods or food extracts may have some bactericidal activity in vitro, but their effect on H. pylori in vivo is still questionable. Studies with lactoferrin, a glycoprotein with antibacterial characteristics, in addition to PPI triple therapy have yielded conflicting results, 61, 62 & have thus far not proved that this compound is of benefit for H. pylori eradication therapy. Along this line, Japanese researchers have studied the effect of administration of specific IgY-anti-Helicobacter antibodies to healthy volunteers. 63 These antibodies were isolated from eggs of chickens vaccinated with H. pylori antigen, & were shown to reduce the H. pylori colonization density. Further studies with specific antibodies are ongoing. Finally, various research groups have studied the effect of Probiotics strains on H. pylori. In vitro experiments showed that Lactobacillus strains, in particular L. casei Shirota, L. brevis & L. gasseri, can suppress H. pylori growth. 64-66This effect requires viable Lactobacilli. 64 Additional in vivo experiments suggested that these Lactobacillus strains when given for three to four weeks may decrease H. pylori colonisation density measured by urea breath testing, but do not lead to eradication. 64, 66 Combination of probiotics with triple therapy may decrease side effects of the triple combination, in particular diarrhoea & nausea, but has noconsistently reported effect on eradication rates. 67, 68. Currently, the ﬁrst-line treatment remains clarithromycin, amoxicillin or metronidazole & proton pump inhibitor twice daily, but a number of recent studies have shown low eradication rates with this treatment. Increased duration of therapy has been recommended to overcome the falling eradication rates. However, conﬂicting ﬁndings have been reported on the beneﬁts of extending the length of traditional therapy. Sequential therapy may be an effective alternative to st&ard triple therapy in regions of increased antimicrobial resistance. Probiotics reduce side-effects from traditional regimens & may improve eradication rates. A quinolone-based second-line triple therapy appears to be effective & well tolerated. Bismuth-based quadruple therapy is also an effective alternative if available. In the future, regional antimicrobial resistance & eradication rates will determine the best treatment for H. pylori clarithromycin (Biaxin). Bismuth subsalicylate (Pepto-Bismol) may cause a temporary grayish-black discoloration of the stool.

## Conclusion:-

Treatment of H. pylori infections has become routine in gastroenterology practice. Generally accepted indications for treatment are peptic ulcer disease, gastric MALT lymphoma, atrophic gastritis, previous partial gastrectomy for gastric cancer, Other common indications are nonulcer dyspepsia, long-term PPI use & unexplained iron-deficiency anaemia, as well as idiopathic thrombocytopoenic purpura. Increasing evidence suggests that st&ard triple therapy may no longer be the most effective ﬁrst-line treatment in certain regions. Two-week therapy may be more effective than 1 week but may not overcome bacterial resistance. Sequential therapy appears to be an effective alternative. Adjuvant therapy with probiotics & bovine lactoferrin can reduce side-effects & may improve eradication rates.. Non-antimicrobial therapy, in particular with probiotics, may reduce the side effects of triple therapy & simultaneously increase the efficacy of treatment, either by a direct effect on H. pylori or by improvement of therapy adherence due to reduction of side effects. All together, eradication treatment can lead to high eradication rates in H. pylori-infected subjects.