بسم الله الرحمن الرحيم


# شبكة المعلومـــــات الجامعية

# التوثيق الالكتروني والميكروفيلم

شبكة المعلومات الجامعية

# جامعة عين شمس

## التوثيق الالكتروني والميكروفيلم

## ﴿ قـــســـم ﴾

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# بعض الوثائق الأصلية تالفة


# بالرسالة صفحات

# لم ترد بالأصـــل

# THE ROLE OF HELICOBACTER IN CANCER STOMACH AND DUODENUM

**THESIS**

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# INTRODUCTION

## Historical review of H. pylori

The search for gastric spiral organisms started since Salmon first described spiral organisms on the surface of human gastric mucosa in 1896. Several studies in the next four decades confirmed the presence of similar organisms in the human stomach.[1]

In 1938, Doenges reported "spirochetes" in the human stomach in necropsy specimens with a prevalence rate of 43%, but he was unable to detect a relationship between the presence of the organisms and various gastric diseases.[2]

In 1940, Freedberg and Barron, using silver staining techniques, studied 35 partial gastrectomy specimens and found spirochetes in 37% after a long search in the gastric mucosa. They concluded that the bacteria colonizing the tissues near the benign or malignant ulcers are non-pathogenic opportunists.[3]

An extensive histologic study of gastric biopsy results from 1000 subjects by Palmer in 1954 failed to confirm the previous report, although the more specific silver stain was omitted. Palmer concluded that others have been describing bacterial contaminants introduced by swallowing following death.[4]

Over a similar time period many authors have documented the presence of endogenous urease activity localized to the stomach in animals and humans. Interest in the role of gastric urease was kindled by the report

of Fitzgerald and Murphy in 1950 who emphasized the association of the enzyme and ulcer disease.[5]

An extensive review by Kornberg in 1955 concluded that gastric urease was localized mainly in the corpus of the stomach and was of bacterial origin.[1]

Interest in gastric bacteria waned until 1975 when the advent of fiberoptic biopsy techniques permitted biopsy of the antrum, Steer and Clain-Jones used the electron microscope to demonstrate the presence of bacteria with ulcer disease but not from normal individuals. Unfortunately, their cultures grew pseudomonas aeruginosa, a probable contaminant from the endoscope, and their findings failed to stimulate immediate interest.[4]

In 1983, Warren, an Australian pathologist in a western Australian Hospital, reported the finding of an unidentified curved bacillus in close contact with the gastric epithelium in biopsy samples showing active chronic gastritis. He pointed the direction toward a possible bacteriologic factor in the genesis of gastritis and peptic ulcer disease.[6]

In an accompanying report Marshal et al (1986) described the culture of these bacteria from an antral biopsy specimen using a Campylobacter isolation technique.[3,5] The organism was named Campylobacter pyloridis, then was known as Campylobacter pylori (C. pylori).[7]

After these initial reports many other groups in many parts of the world have confirmed these findings. Moreover it was found that this organism produced urease.[5]

However, Goodwin et al (1985) found that the major ultrastructure features and cellular fatty acids of C. pylori were very different from those of all other Campylobacters and this suggested that C. pylori did not belong to this genus.[8]

In addition, Geis et al (1990) analyzed C. pylori stains by gas liquid chromatography and reported that the unusual composition of C. pylori phospholipids and lipopolysaccharide fatty acids may have important implications for the taxonomy of the organism.[9]

Also the methylated menaquinone 6 (MK-6) which is characteristic of all other Campylobacters is absent in C.pylori. The guanine + cytosine (G+C) content of C.pylori is 36-38 mol% compared to other Campylobacters which is 35-44 mol%.[10] In addition, the polyacrylamide gel electrophoresis (PAGE) study of the protein profiles of 15 different strains of C.pylori had shown similar protein bands, however different from those of Campylobacter reference strains.[11]

Moreover, C.pylori differed from other Campylobacters in various biochemical characteristics. It possesses a powerful urease, extracellular superoxide dismutase and catalase in large amounts whereas some aquatic Campylobacters produce a weak urease enzyme and others a small amount of extracellular or intracellular catalase. C.pylori shows a strong phosphatase activity in phenolphthalein phosphate test, while other Campylobacters are negative.[12]

Also, C.pylori is very sensitive to many antibiotics as amoxycillin, benzyl penicillin and erythromycin, whereas other Campylobacters are 10 to 100 times more resistant to these antibiotics.[13]

In October 1989 the new genus name Helicobacter was first published encompassing nine distinct species. Its name refers to the morphology of the organism which is helical in vivo but often rod-like in vitro (bacteria staff). Sheathed flagellae and urease enzyme production are characteristic features of all members of the Helicobacter genus[14] and the definitive taxonomic data of this genus has been proved by recent analysis of partial 16 srRNA sequences. They are classified under the relevant host.[15]

Five Helicobacter species have been isolated from the stomach, three from the lower gut and one from both sites. The distribution is illustrated in table I.

H. pylori was the first clinically significant organism in the genus. The morphological and phenotypical properties of most species of the Helicobacter genus are markedly similar to those of H.pylori except for H.roppim which shows some phenotypic differences.[14]

## Study of H. pylori

Humans and primates appear to be the primary hosts for the H. pylori bacterium. In humans the organism has only been found in places where an acid secreting gastric mucosa is present; whether normally present in the stomach or metaplastic in the duodenum, Barrett's

**Table (0): Species of Helicobacter genus.**

| Species | Site of isolation | Host | Diseases |
|---|---|---|---|
| H. pylori | Stomach | Humans | Gastritis |
| H. mustelae | Stomach | Ferret | Gastritis |
| H. felis | Stomach | Cat and dog | Gastritis |
| H. nemestrinae | Stomach | Big tailed macaque | Gastritis |
| H. acinomyx | Stomach | Cheetahs | Gastritis |
| H. cinaedi | Lower gut | Humans | Gastroenteritis |
| H. fennelliae | Lower gut | Humans | Gastroenteritis |
| H. muridarum | Lower gut | Rats and mice | Gastroenteritis |
| H. rappim | Stomach and lower gut | Humans and beagle dogs | Gastroenteritis |

oesophagus,[1] Meckel's diverticulus and in the rectum.[16] Also H. pylori can be isolated from faeces[17] and dental plaque.[18]

Most investigators agreed that the human stomach, mainly the antrum, was the largest reservoir. The organism was typically located within or beneath the gastric layer of the mucus adjacent to the gastric type epithelial cells, in the gastric pits, in the necks of the gastric glands and tended to congregate near intracellular junctions.[19]

Gastric bacteria resembling H. pylori have been observed in a variety of animals including rodents, primates and swine. Isolates from ferrets are clearly dissimilar to those from humans, but organisms from swine and other primates appear similar if not identical to those from humans.[20] DNA of the animals gastric bacteria amplified with H. pylori specific primers, yielded polymerase chain reaction (P.C.R.) products identical to those from human isolates of H. pylori. So the results of P.C.R. amplification and partial 16 srRNA gene sequence analysis strongly supported the contention that the gastric organisms previously recovered from a pig, a baboon and a rhesus monkey were H. pylori.[20]

No environmental reservoir of H. pylori has been identified. Results of seeding experiments indicated that motile H. pylori might survive in chilled river water or milk for several days but clinical relevance of this observation remained unclear.[21]