A Guide for Practitioners and Patients of *Helicobacter pylori*

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By

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Cambridge Scholars Publishing

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A: amoxicillin
AAD: antibiotic-associated diarrhoea
AB: Acinectobacter baumanni
ABR: antibiotic resistance
ACE: angiotensinj converting enzyme
ADH: aldegyxde degydrogenase
AGERERE: Appraisdal of Guidelines Research and Evaluation-Recommendations Excellence
AI: artificial intelligence
AMAG: autoimmune diffuse corporal gastritis
AMP: adenosin monophosphate
AMSTAR: A Measurement Tool to Assess Systematic Reviews
ATP: adenosin triphosphate
Bacteroides fragilis
bp: base pair
BAO: basal acid f output
BLI: blue light imaging
BMI: Body mass index
C: clarirhtomycin
CagA: cytotoxin-associated gene A
CA: carbonic anhydrase
CBS: colloidal bismuth subsalycilate b
CD: cluster differentiation
CDC: Center for Disease Control and Prevention
CLSI: Clinical and Laboratory Standards Inystitute
CMV: cytomegalovirus
CONSORT: Consolidated Standard of Reporting Trials
COPD: chronic obstructive pulmonary disease
COVID-19: coronavirus-induced disease 2019
C. pylori: Campylobacter pylori
CRP: C-reactive protein
CV: cardiovascular
CYP450: cytochrome P 450
D doxycyclin
DNA: dexoxyribonucleic acid
DPM: disintegration per minute
DU: duodenal ulcer
EAHP: European Association of Hospital Pharmacists
EARC: European Antimicrobial Resxistance Collaborators
EARS: European Antimicrobial Resistance Surveillance Program
EBM: evidence based medicine
EBV: Epstein-Barr virus
EC: Enzyme Classification
ECDC: European Centre for Disease Prevention and Control
ECL: enterochromaffin cell
EGF: epidermal growth factor
EHPSG: European Helicobacter pylori Study Group

EHMSG: European Helicobacter and Microbiota Study Group
ELISA: enzyme linked immunosorbent assay
EMAG: environmental multifocal atrophic gastritis
EoG: eosinophilic gastritis
ESO: esomperazole
EUCAST: European Commizttee on Antimicrobiasl Susceptibility Testing
F: furazolidone
FD: functional dyspepsia
FISH:fluorescent in-situ hydridization
FMA: faecal material transplantation
GC: gastric cancer
GG: granulomatous gastritis
GGT: gamma-glutamyl-transpeptidase
GP: general practitioner
GU: gastric ulcer
GVHD: grasft-versus-host disease
GWA: genome-wide analysis
HAART: highly active antiretroviral treatment
HCl: hydrochloric acid
HDDT: high-dose dual therapy
H&E: haematoxylin-eosin staining
HetEM: heterozygous externsive metasbolizer
H. felis: Helicobacter felis
H. heilmanni: Helicobacter heilmanni
HomEM: homozygous extensivce metaboliter
H. pylori: Helicobacter pylori
H. suis: Helicobacter suis
HIV: human immunodeficiency virus
HPF: high power field
HVS: herpes vireus simplex
H_2B: histamine H_2 receptor blocker
IARC: International Agency for Research of Cancer
IBD: inflammatory bowel disease
IM: intermediate metabolizer
ICAM: intercellular adhesion molecule
ICI: immune checkpoint inhibitors
IDA: iron deficiency anaemia
IEE: image-enhanced endoscvopy
IF: intrinsic factor
IgA: immunoglobuin A
IgE: immunoglobulin E
IFC: immunfluorescence
IgG: immunoglobuin G
IgM: immunoglobulin M
IHC: immunohistochemistry
ITP: idiopathic thrombocytopenic purpura
kB: kilobase
kD: kilodalton
L: lansoprazole
Lv: levofloxacin
LCI: linked color imaging
LG: lymphocytic gastritis
M: metronidazole
MS: meta-analysis
MACE: major cardiovascular events
MALDI-TOF-MS: matrix-assisted laser

desorption/ionization - time-of flight mass spectrometry
MALT: mucosa-associated lymphoid tissue
MAO: maximal acid outout
Mb: megabase
MIC: minimum inhibitory concentration
mRNA: messenger ribonucleic acid
MSM: male having sex with male
NAC: N-acetylcysteine
NBI: narrow band imaging
NCI: National Cancer Institute
NF: nitrofurantoin
NGS: next generation sequencing
NHANES: NatiinalHeaslth and Nutrition Survey
NIH: National Institute of Health
NSAID: non-steroidal anti-inflammatory drug
NTZ: nitazoxanide
μCI: microCurie
O: omeprazole
OMP: outer membrane protein
OMV: outer membrane vesicle
OR: odds ratio
ORF: open reading frame
OTC: over the counter
QUOROM: Quality of Reporting of Meta-analyses
P: pantioprazole
PAF: platelet activating factor
PCA: parietal cell antibody
P-CAB: potassium-competitive acid blocker
PCR: polymerase chain reaction
PG: prostaglandin
PG I-II: pepsinogen I-II
PPI: proton- pump inhibitor
PRISMA: Preferred Reporting items fot Systematic Review and Meta-analysis
PROSPERO: Prospective Register of Systematic Reviews
PTH: parathormone
PU: peptic ulcer
QUORUM: Quality of Reporting of Meta-Analyses
R: rabeprazole
RE.GA.IN.:Real-world Gastritis Initiative
RF: rifabutin
RIGHT: Reporting Items for Practic Guidelines on Healthcare
RNA: ribonucleic acid
rRNA: ribosomal ribonucleic acid
RR: relative risk
16S-RNA: 16 Svedberg ribonucleic acid
23S-5S RNA: 23 Svedberg 55 ribonucleic acid
SEQ: sequential therapy
SGT: susceptibility. guided treatment
SF: sitafloxacin
SHEA: Society for Healthcare Epuidemiology of America
SR: systematic review
STT: standard triple therapy
SUCRA: surface under the cumulative rank order
T: tetracycline
Tn: tinidazole
Taq: Thermus aquaticus
TFSS: type IV secretory system

TGF alpha: transforming growth factor alpja
TGZ: tegoprazan
TN: tinidazole
UBT: urea breath test
UC: ulcerative colitis
UNESCO: United Nations Educational, Scientific and Cultuiral Organization
UV: ultraviolet light
VPZ: vonoprazan
WLI: white-light imaging

FOREWORD

Forty-two years after its discovery, tens of thousands of articles and hundreds of textbooks, books and booklets have been dedicated to *Helicobacter pylori*, examining all the aspects of this typically 20th-century disease. So, why publish a new book on *Helicobacter pylori*? Because the available literature – from basic research to clinical aspects and the highly-acclaimed consensus statements – is often contradictory and the guidance difficult to implement in daily practice. As with any practitioner, I have frequently met outlier cases where no guidelines were applicable. The present material is not the regurgitated content of previous texts, but rather a combination of personal experience and the collective knowledge, consensus provisions and expert opinions regarding the diagnosis and treatment of the *Helicobacter pylori* infection. Thus, it is intended to be a balanced presentation of the most relevant literature and personal results and opinions, also emphasising the state of knowledge from my country, Hungary. In doing so, the most difficult problem was whom to include and whom to omit from the narrative, to obtain a readable and understandable text both for beginners, experienced practitioners and even specialists of the field. While the text is addressed to practicioner colleagues and patients, I tried to use a simple and comprehensible language and avoid sophisticated data on genetics, microbiology and other basic fields and statistical data, which are not well understood by the author and probably not by the reader either.

This book discusses *Helicobacter pylori* as an infectious disease and not its complications as peptic ulcers, gastric malignancies or extragastric manifestations, or complications such as peptic ulcer bleeding, perforation or pyloric obstruction.

The *H. pylori* topic is not an isolated field of research: it is deeply embedded in the whole story of gastroenterology. Therefore, short historical elements and timelines are introduced, to remind readers about the main predecessors of today's knowledge: many of whom are Nobel Prize winners.

Writing a single-authored book for professionals and lay people is not an easy task. Such undertakings are usually performed during a sabbatical year. This is not usual in my country, so the manuscript was written outside of my working hours, at weekends and on short holidays. It was

not my intention to write an *Encyclopaedia*, or to present a one-man-show, telling all about *Helicobacter pylori*, thus I compiled only a few chapters on topics in which I have gained personal expertise. The opinions expressed are those of a practising physician and not of an in-depth *Helicobacter* researcher, thus in some cases, they may differ from mainstream opinions and recommendations.

A unique feature of the book is that the materials presented are based on high-quality systematic reviews and meta-analyses instead of individual studies, providing robust evidence of the topics discussed.

This work would not have been possible without the help of family members and colleagues. I would like to express my warm thanks to my wife, Adriana, who provided a solid background for writing and editing the text and translating foreign literature. Many thanks to Dr. Gábor Lotz (Semmelweis University, Institute of Pathology, Forensic and Insurance Medicine, Budapest) for providing the histologic figures. The help of Mrs. Alice Dobolyi (Semmelweis University, Budapest) was instrumental in obtaining literature from databases. Mrs. Jolán Józan's assistance in editing and correcting the text as well as drawing the figures and front cover was, as always, invaluable. The linguistic revision of the text by Mr. Douglas Arnott (EDMF Language Services, Budapest) is highly acknowledged.

I trust that the final product will be a useful source of information and, moreover, provide "how to do it" advice for all those involved in the diagnosis and treatment of the *Helicobacter pylori* infection. In other words: "*Habent sua fata libelli*".

CHAPTER ONE

EPIDEMIOLOGY: THEN AND NOW

1.1. Introduction

For thousands of years, humanity has been afflicted by infectious diseases causing severe epidemics and resulting in high rates of morbidity and mortality. Therefore, the survival of different populations was determined from antiquity to the 20th century by many epidemics such as the bubonic plague, yellow fever, malaria, small pox, cholera, and poliomyelitis. Most epidemics were caused by natural-born infectious agents. However, more recently intentionaly-induced diseases (anthrax, botulism, severe acute respiratory syndrome (SARS) and coronavirus (COVID-19)) have caused epidemics (Bolletz AJ, 2004, 1-15).

Another important survival factor was nutrition. Hunger and sub/malnutrition caused for centuries premature deaths, even in the Western world, and continue to do so today in underdeveloped regions. However, as stated by the American Nobel Laureate Robert Williams Fogel (1926-2003), in the past 2-3 centuries, and especially in the past 100 years, the so-called technophysio evolution has led to the progressive improvment of the human condition. Fogel described this phenomenon as the synergism between rapid technological change and the improvement in human physiology (Fogel RW, 2007, 20-42). As result, recent centuries have witnessed a decrease of morbidity and mortality from infectious diseases, an increase of BMI and average duration of life, and the progressive improvement of nutrient availability, with the end result of the current overweight and obesity endemia (both are considered risk factors for *H. pylori* infection). All these factors led to a synergism between the technophysio evolution and a decrease of infections. Consequently, we have to to integrate this phenomenon into the past and present epidemiology of *H. pylori* infection.

Epidemiological studies represent a significant proportion of the *H. pylori* research. A PUBMED/MEDLINE search for "*Helicobacter pylori*

and epidemiology" resulted 10,325 publications, representing 19.6% of the total publications on the bacterium (http://www. ncbi. nih. pubmed., accessed February 10, 2026). As in the case of other gastrointestinal diseases, epidemology studies with proper methods have examined the prevalence and incidence of *H. pylori* infection on the global and local scale, determining its medical, economical and social burden, risk factors, and patient-related outcomes (Richard Locke R III and Talley N, 2007, 5-7).

Current epidemiology of the infection cannot be understood without knowing the history of *H. pylori*. In brief, the bacterium occured as a commensal (non-pathogenic) agent approx. 65,000 years ago in apes living in subequatorial Africa and was transferred to humans during the Stone Age (Marshall Barry J, 2016, 4-5). Then, humans migrated throughout the world on different itineraries which are only in part known. Several theories emerged, based mostly on studies of archeological materials such as the coprolites of precolumbian mummies or Ötzi, the prehistorical man who lived approx. 5,200 years ago and was conserved in the Austrian Alps, in which *H. pylori* sequences were found along the gastrointestinal tract, using a metagenomic approach and targeted genome capture. The strain identified was the virulent cagA and vacA s1a/11 type (Mégraud Francis, 2016, Maixner F et al., 2016).

The Afrian origin of *H. pylori* is generally accepted (Linz B, Balloux F, Moodley Y et al., 2007). More controversial is the development and diversity of strains in the populations of Asia, Europe, and North and South America. It was supposed initially, that *H. pylori* was a kind of probiotic, with a beneficial effect for the host, which might be advantageous in periods of malnutrition. While moving from the African environment to regions with less friendly climates, the bacterium underwent genetic changes to acclimate to the new conditions. With the advent of genomics and proteomics, it was shown that migrations and the mixture of different populations resulted in several deleterious mutations in strains harbouring in Europe, Asia, Siberia and the Americas (Moodley Y et al., 2021). By adaptation to the local conditions, climate and nutrition, these admixtures explain in part the current geographic differences in prevalence and pathogenecity of *H. pylori* (Thorpe HA et al., 2022). Consequently, the current *H. pylori* is genetically heterogenous as a result of consecutive DNA rearrangments, and the insertion and deletion of strange sequences (Nyrén O, 2007, 125-127).

1.2. Incidence of *Campylobacter pylori* infection

Shortly after the discovery of the bacterium, studies were performed assessing the incidence of *Campylobacter pylori* infection in asymptomatic persons and diseased patients (Rathbone BJ et al. 1988). These studies used histology for identification of the bacterium, a method which actually is not very accepted for epidemiological studies and showed that in persons with normal mucosal structure, the bacterium was found in 0-41% of the cases, while in patients with chronic gastritis, the incidence was of 43-100%. The same studies showed that in gastric ulcet cases, the incidence was of 57-79% and in duodenal ulcer 27-100% of the patients. The type of populations, age limits and histological methods for diagnosing *C. pylori* were different, explaining the divergent values. Serologic studies dating from this era revealed an important feature of the infection, i.e., that its prevalence increased with age both in healthy blood donors and non-ulcer dyspepsia patients, being higher in dyspeptics than in healthy people. However, endoscopy is invasive and not a suitable method for epidemiological studies. These initial data were obtained in studies including small numbers of patients; data from healthy cases could underestimate and that from dyspeptics overestimate the real distribution of the bacteria in the general population.

1.3. Serology: a useful tool for epidemiological study of *Helicobacter pylori*

After acquisition of the infection, most patients – excluding those very young or immune-compromised – develop a strong immunologic response consisting of the occurence of antibodies (immunoglobins IgG, IgM, IgA and IgE). IgM antibodies occur firstly, as a sign of acute infection, IgG antibodies represent a sign of chronic infection and will later persist with the progression of chronic gastritis, while IgA is only seldom elicited as a marker of secretory immune response. IgE occurs mainly in children as an allergic reaction. Regarding antibodies to CagA, the virulence factor is a marker of a pathogenic strain but is only seldom used for epidemiological studies. All of these immunoglobulins can be determined using validated kits having different sensitivity and specificity. Serology, however, is a marker of a past and not an actually living *H. pylori* infection, because antibodies persist even after spontaneous or therapeutical eradication. In recent decades, serology became the recommended method for epidemiological studies, because it is non-invasive, cheap – as compared to endoscopy or breath test – and accurate, if validated locally. A positive

test must not have a therapeutic consequence as long as other, more accurate methods are available.

Approximately half of the world's population is infected with *H. pylori* (Parsonnet J, 1995): this early data was reconfirmed by a meta-analysis reassessing the worldwide prevalence of infection (Hooi, 2017). In developing counteries, by the age of 2 years, 60% of children are infected and at 10 years, this rate increases to 80-90% (Cseh, Áron et al., 2014). The incidence of new infections is estimated at 0-7%/year in adults and 0-1.7%/month in children 2 years old and 0.11-16%/year in those 2-18 years old (Sierra, Mónica et al., 2014). Evidence from these studies showed the considerable geographical and ethnical variance and the age-dependency of the infection. Studies from the past 2 decades revealed that in developed countries, but also in other regions, the prevalence of the infection is more or less sharply decreasing, probably due to economic-physiological progress, improved living conditions, nutrition and sanitation, large-scale national eradication policies, a decrease in smoking and other, less well known factors. The rate of decrease is slow, about 2-4%/year. A detailed presentation of worldwide distribution of *H. pylori* is available (Sierra, Mónica et al., 2014) and now is beyond the scope of this chapter: some relevant data are presented in Table 1-1, illustrating the timely trends of the infection. The current worldwide prevalence of the infection is presented in Figure 1-1. It is worth mentioning that there are no studies investigating the whole population of a given country, although there are large regional and ethnical variations even in a small country such as Hungary (Buzás GM, 2013, Lenke B, 2019). The most recent estimate of *H. pylori* prevalence was published in 2024, showing that between 1980 and 2022, the global prevalence reduced from 52.6% to 43.9% (decrease of 15.9%) in adults, but not in children and adolescents. The reduction was remarkable in the Western Pacific, Southeast Asian and African regions (Chen Yi-Cu et al., 2024).

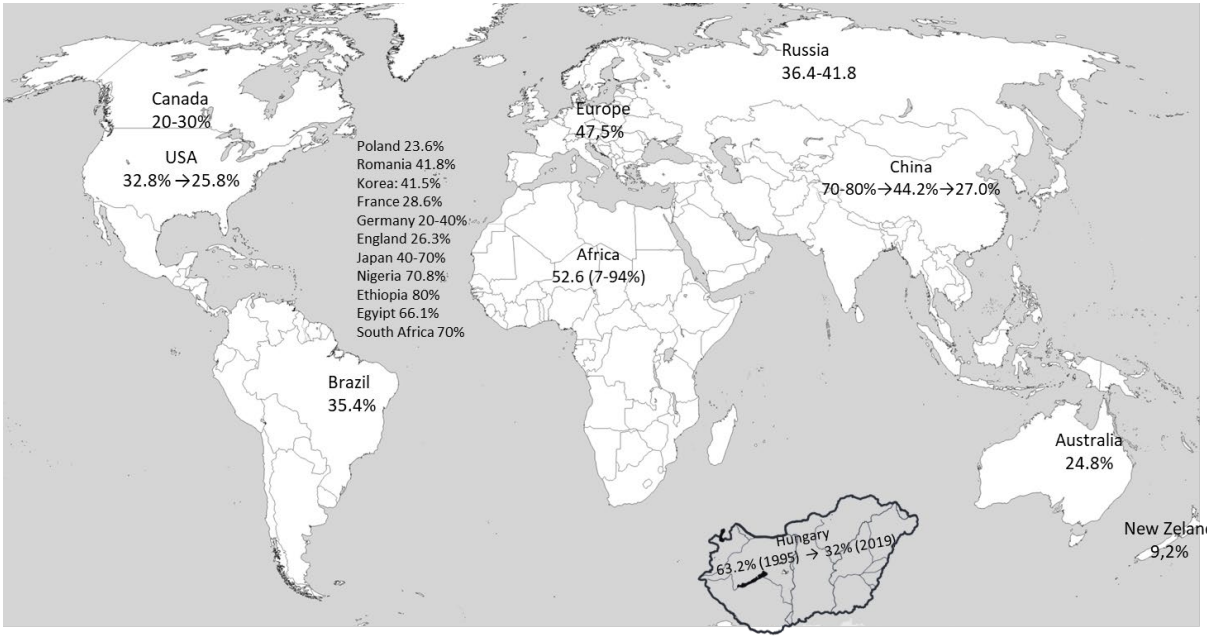

Figure 1-1. World chart presenting the current prevalence of *H. pylori* infection based on recent studies (2020-2025).

Table 1-1. Distribution of *Helicobacter pylori* prevalence: (1982-1995) and now (2000-2024)

Country	Period 1908-1995					Period 1995-2018				
	Year	Method	Nr. of cases	Prevalence (%)	Reference	Year	Method	No. of cases	Prevalence	Reference
USA	1988-1991	Serology	7495	32.5	Perez-Perez GI, 1991	1999-2018	Serology	913,328	25.8	Shah SC et al. 2024
Germany	1996	Serology	260	36.9	GlasbrenneRB, 1986	2017	Serology	516	28.9	Franck C et al. 2017
China	1983-1994	Serology	556,674	58.3	Ren S et al. 2022	2017	Serology	51,299	31, 9	Yu et al. 2022
Japan	1982-1988	Serology	1,687,895	50-70	Wang et al. 2017	1980-2003	Serology	1,880,004	10.0-24.6	Wang et al. 2017
Hungary	1995	Serology	400	63.2	Tamássy K et al. 1995	1997-2012	Serology	1,001	32.0	Lenke B et al., 2019

1.4. Birth-cohort effect and the *Helicobacter pylori* infection

The birth-cohort theory was coined by Wade Hampton Frost (1880-1938) during the study of tuberculosis and was applied to the peptic ulcers in the 1960s by Mervyn Susser (1921-2014) and Zena Stein (1922-2021). They demonstrated that the mortality of people with peptic ulcers decreased with successive birth cohorts (defined as groups of patients born in periods of 5-10 years). Later, Amnon Sonnenberg, working in Germany and the USA, showed that the birth-cohort effect could also be demonstrated in IBD and gastric and colorectal cancers in several countries (the UK, Switzerland, Japan, and New Zeeland). In the case of *H. pylori*, the prevalence of the infection paralelled that of peptic ulcer disease, with an increase in patients born during the 19th and the first half of the 20th centuries, followed by a gradual decrease in the second part of the past century up to recent days. The birth cohort effect is thought to be a consequence of lifestyle changes related to industrialization and urbanization. How it is related to the above-mentioned techno-physio development remains to be elucidated. The phenomenon was demonstrated both in developed countries, as well as in Greece, Portugal, China, and Japan (Sonnenberg, A. 2022, Yi, X. 2017, Inoue, M. 2017).

In a central district of our capital Budapest, the prevalence of *H. pylori* decreased from 71.3% to 32.6% between 1998 and 2012. In this period, the prevalence decreased gradually in the 10-year cohorts born between 1920 and the 1990s. Interestingly, this started around the 1970s, more than a decade before *H. pylori*'s discovery (Buzás, György M. et al., 2013) (Figure 1-2).

However, the birth-cohort effect can not be considered a definitive phenomenon: data from The Netherlands showed that although the *H. pylori* prevalence decreased in children born between 1978 and 1993 from 19% to 9%, recent data suggest that the seropositivity from 1993 to 2005 remained stable at 9%, while cagA$^+$ antibodies were present only in 0.9% of cases, suggesting a tendency of the disappearence of this pathogenic strain, at least in Western countries (den Hoed CM et al., 2011, 3-5).

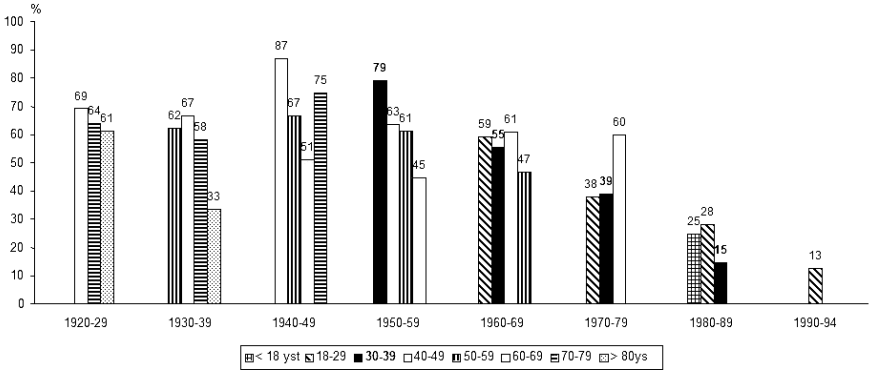

Figure 1-2. Birth-cohort effect of *H. pylori* prevalence in the 9th district of Budapest, Hungary between 1935 and 1990 (Courtesy of Academic Publishing House, Budapest, Hungary).

1.5. Sources of infection

Initially it was believed that the human stomach was the unique reservoir of the bacterium. Countless later studies demonstrated, however, that many other potential sources exist: the main data are summarized in Table 1-2. If we look on the data, our environment is seemingly full of *H. pylori*! The situation is, however, not so bad: transmission of the bacterium from animals to humans is limited by several factors (see below). There are plenty of data proving the transmission of infection from animals to human, but nobody knows if humans can infect animals with *H. pylori*. Big animal keepers have a higher prevalence of *H. pylori* than controls not involved in meal preparation, but this is probably due to serologic cross-reactivity between *H. pylori* and other bacteria like *Campylobacter jejuni*, so frequent in animals. Seroepidemiological studies also failed to demonstrate a higher prevalence of *H. pylori* in pet owners (Mitchell, Hazel M., 2001)

Table 1-2. Sources of *Helicobacter pylori* infection

Class	Source	Comment	Reference
Animals	Swine	*H. pylori*-like microrganisms (*H. heilmanni, H., suis*) were isolated from pigs. Gnotobiotic piglets develop gastritis after *H. pylori* infection. Culture of the bacterium from abbatoir pigs failed.	Fox, JA, 1992
	Cow	*H. pylori* was positive by PCR in 32% of gastric biopsies of cow.	Momtaz H et al., 2014
	Cat	Spiral bacteriums were isolated from cat stomach more than a hundred years ago. *H. pylori* isolated from cats has genetic similarity with human strains. Due to close contact with humans, especially children (salivation, regurgitation permanent washing up, faeces), cat owners family members could have higher rates of infection.	Tailleau E et al., 2022
	Sheep	Sheep shepherds and breeders have higher *H. pylori* prevalence, although the bacterium can be isolated only by PCR,	Momtaz H et al., 2014
	Dog	Are frequently infected with *H. pylori, H. heilmanni* and *H. felis,* (61-86%) producing mild and limited gastritis. *H*. species are present in saliva and faeces. The physiologically high HCl secretion of dogs can rather supress than eradicate these infections.	Tailleau E et al., 2022
	Monkey	Spiral bacteria were first isolated from monkey stomach in 1939. Rhesus and Japanese macaques develop chronic gastritis after infection with *H. pylori* cultures, Strains isolated from baboons. Rhesus and macaco stomach have genetic similarities with human bacteria. Because of rare contact of humans with monkeys, their role as source of infection is minimal.	Fox, JA, 1992
	Housefly	*H. pylori* was isolated from body surface, intestine and faces of houseflies, their role is considered important in developing regions.	Grübel, P et al., 1997, Mitchell, HM, 2001

		Newer data consider that flies are not a vector of infection. Fly midgut contains oxyntic cells resembling human parietal cells, ensuring a local pH of 3.1, favourable for survival of *H. pylori*.	
Drinking water	Internal or external water supply, bottled mineral water	Children drinking of or swimming in external water are more prone to infection in Peru and Colombia; studies from Korea, China and Bangladesh do not support this data. Later, the bacterium was found in Mexico, the USA, Iran and other countries. *H. pylori* survives in coccoid form in water for several days, quite enough for an eventual ingestion. It also survives for some hours in distilled and chlorinated water. The bacterium forms biofilm in water pipes.	Nyren, O, 2004, Quiaglia, C et al., 2018
Foodstuffs	Crude and prepared food	*H. pylori* was indentified by culture or DNA-based methods in foodstuffs. It survives in cow, sheep pasteurized milk for 5-12 days, 7 days in ground beef, 3. 4 days in vegetables. It was isolated by PCR, culture or FISH from cow, buffalo, goat and camel meat, raw chicken, ready-to-eat tuna, olive, vegetable or fruit salads, and many other products. Some authors consider therefore *H. pylori* as a foodborne pathogen, although at individual level, it is difficult to establish, when and how was acquired the infection.	Quaiglia, 2018, Montaz, 2014

1.6. Transmission of infection

H. pylori infection can be transmitted from human to human through several routes: arguments have been raised pro and against each. The faecal-oral route is probably the most accepted (Mégraud, Francis, 1995, Hazel, Stuart, 2001 and Nyrén, Olof, 2004). During colonization, *H. pylori* is attached to the surface epithelial cells and with their desquamation, it is cleared into the small bowel. It is now known, how the bacterium, after acid acclimation, survives in the alcaline small bowel and colon content.

Culture of *H. pylori* from faeces is difficult and cumbersome; however, the bacterium can be identified from faeces by FISH, PCR or by its mono- or policlonal antigens. the latter methods do not differentiate between living or unviable organisms. Coccoidal forms of the bacterium are, in contrast, viable for a long time in faeces and fresh water. The modes of transmission are multiple: ingestion of contamined material from partner, siblings, household objects, sharing of the bed in overcrowded families, or even self-contamination. Most infections are acquired during early childhood: epidemiological studies showed in many populations the stepwise increase of infection prevalence beginning from 3-4 years until the teenage period. This is explained by the lack of adequate native and acquired immunological defense as well as the lower level of gastric acid secretion at these ages. Infection or reinfection with *H. pylori* in adulthood is unusual, as long as the patient is immuno-competent and is living under adequate personal and environmental hygiene.

The oro-oral transmission is mainly restricted by the transfer of bacterium from the oral reservoir in the environment. The bacterium was repeatedly isolated from dental and subgingival plaques and saliva. The genotype of these bacteria with those isolated from gastric biopsies showed similarity in 56-82% of the cases. The oral cavity is a sanctuary place for *H. pylori*, which may contribute to the progresion of gingivitis, eradication failure or reinfection (Zhang, Lin et al., 2022). Patients must be educated to maintain a rigorous oral hygiene and mouth rinse with clorhexidine solution, available in pharmacies.

The gastro-oral transmission is considered of less importance. It can mainly occur during childhood when infected vomited material often contaminates objects in the environment.

Indifferent of route of transmission, *H. pylori*, contrasting with other bacteria, does not cause diaarrhoea, as strains of *Salmonella, Escherichia coli, Shigella* and *Vibrio cholerae*do. Most new infections are asymptomatic, excepting cases of acute gastritis, as happened to Marshall in his self-experiment by ingesting a *H. pylori* culture, which probably had a much higher bacterium number than those of foodstuffs, water or other sources (Marshall, Barry J, 1984).

1.7. Clustering the infection in families and couples

A peculiar feature of *H. pylori* infection is its pronounced tendency to intrafamiliar clustering, The phenomenon was first demonstrated by a serological and histological study of children and their family members in Toronto (Drumm, Brenden et al., 1990), where the parents of *H. pylori*

positive children were also positive in 74% of the cases, while in those of children not infected, the prevalence was only 24%. Successive older studies showed that the grade of clustering is highly variable, being of 38% in England, 60% in Romania, 67% in Italy, 68% in the USA (Mataly, HM et al., 1991) 87% in Greece, and 67% is Saudi Arabia (A-Kanwy, BA et al., 2000), and these data were reconfirmed in recent years by studies from China (87.23%) (Yu, Xue-Chun et al., 2022) and Turkey (95%) (Palanduz, Aye et al., 2018). Intrafamilial clustering was observed in children of infected parents (Drumm, Malaty, Yu, Xue-Chum, 2022) as well as in spouses of infected patients. In an early study it was shown that being a partner of an infected person increased the risk of being infected, but this was explained by age and ethnicity (Perez-Perez, Guillermo I, 1991). In the USA, the prevalence of *H. pylori* was 68% in spouses of infected persons and 9% of *H. pylori* negative cases (Maraly, HM et al., 1991). In Germany, *H. pylori* was determined in 670 couples by a ^{13}C-urea breath test. The prevalence of infection in women was 34.9% if the partner was infected and 14.5% if he was non-infected (Brenner, Hermann et al., 2006). In Saudi Arabia, the seroprevalence in spouses of seropositive persons was 45%, compared with 19.2% in seronegative cases (Al-Knawy, BA et al., 2000). In central China in 282 families the infection rate of both spouses was 34.8%; 17.2% of the couples were uninfected and 47.5% had only one spouse infected. Genetic studies have shown in Swedish families that the type of *H. pylori* strain is concordant in spouses and siblings in 81% of the cases (Kivi, Mårten et al., 2003), while in China this proportion was 94% (Yu, Xue-Chun, 2003). A minor proportion of cases were infected with multiple strains.

The higher incidence of *H. pylori* in spouses of infected persons raises the possibility of sexual transmission. Attempts have been made to isolate the bacterium from genital organs. Shortly before the discovery of *H. pylori*, flagellated rods of bacteria having corkscrew motility were isolated from the vagina (Holst, E. et al., 1982), and later, *H. pylori* was found by PCR in vaginal secretion, but the organism was never later cultivated (Martin de Argila, C et al., 1998). Italian authors found in a case-control study, that the prevalence of *H. pylori* is 74.5% in sexual partners (girlfriend, boyfriend or spouse) of infected patients, while the prevalence was only of 32.3% in the uninfected control parteners (Sgambato, Dolores et al., 2018). A hypothesis was formulated that *H. pylori* could be transmitted sexually, with the vagina acting as a reservoir (Eslick, Guy D., 2000); later it was supposed that the bacterium could be transmitted via oral-anal intercourse as well. Oral-anal contact is a good source of probiotics (Lewin R.A., 2004) and may contain also *H. pylori* (Eslick, Guy