Original paper

Gastritis – facts and doubts

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Abstract

Introduction: Many clinicians consider chronic gastritis to be equivalent to *Helicobacter pylori* infection. However, it is known that there are numerous other causes of the condition.

Aim: Determination of the incidence of gastritis in patients with dyspepsia referred for diagnostic endoscopy of the upper part of the digestive tract, identification of the parts of the stomach most frequently affected by the inflammation, as well as the impact of an insufficient number of collected samples on the correct diagnosis.

Material and methods: Upper gastrointestinal endoscopy due to dyspepsia was performed in 110 patients. In the course of gastroscopy two biopsy specimens were collected for histopathological examination and towards *H. pylori* infection from the lesser and greater curvature in the antrum 3 cm from the pyloric sphincter, in the body – 4 cm proximally to the stomach angular incisure on the lesser curvature, and in the middle of the greater curvature, as well as in the subcardiac region on the side of the lesser and greater curvature.

Results: In patients with dyspepsia *H. pylori*-negative chronic gastritis is more common than gastritis with accompanying *H. pylori* infection. Collection of too small a number of biopsy specimens results in failure to detect inflammatory changes and/or *H. pylori* infection, which may be limited to one part of the stomach. Biopsy specimens of gastric mucosa should be collected in compliance with the assumptions of the Sydney System. *Helicobacter pylori* infection in people with dyspepsia is now being reported more rarely than in the past (36%).

Conclusions: In patients with dyspepsia chronic *H. pylori*-negative gastritis is more common than gastritis with an accompanying *H. pylori* infection. *Helicobacter pylori* infection is not always equivalent to the presence of chronic gastritis.

Introduction

Chronic gastritis is a process progressive in character, which begins with superficial, localised inflammatory infiltrations leading to gradual atrophy of the proper glands of the mucous membrane with possible intestinal metaplasia. Exponents of chronic gastritis include: infiltration from lymphoidal and plasmatic cells, and atrophy of the glands of the body and the antrum (with or without intestinal metaplasia). The activity of the inflammatory process is evidenced by the presence of eosinophilic and neutrophilic granulocytes, which may generate micro-abscesses in the lumina of glandular tubes. The above changes sometimes coexist with oedema of the stroma, minute extravasations, or shallow erosions, as well as dysplasia (generally low degree) of epithelial cells. Massive inflammatory infiltrations along with other lesions may lead to disturbances in the architectonics of gastric mucosa.

Chronic gastritis is primarily diagnosed microscopically on the basis of a histopathological examination of mucous membrane specimens. The presently applied Sydney System combines microscopic evaluation with the topography and aetiology of the inflammation. In addition, information about the stage and extent of a chronic inflammatory process can be provided by two other evaluation systems known as operative link for gastritis assessment (OLGA) and operative link on gastric intestinal metaplasia (OLGIM) [1, 2].

Many clinicians consider chronic gastritis equivalent with *Helicobacter pylori* (*H. pylori*) infection. However, it is known that there are numerous other causes of the condition. Gastritis without an *H. pylori* infection is frequent, being estimated at 21% of all inflammations [3], and the causes of the phenomenon are complex. The diagnosis of the inflammation is often made on the basis of an endoscopic picture, which is commonly overused by endoscopists and may result in unjustified pharmacotherapy. Endoscopic diagnosis of an inflammation may be accepted in cases where characteristic endoscopic features provide firm grounds for diagnosing an inflammation as it is in the case of erosive, atrophic, hypertrophic, haemorrhagic, or biliary inflammation.

Aim

The aim of the study was to determine the frequency of the presence of gastritis in patients with dyspepsia referred for diagnostic endoscopy of the upper segment of the digestive tract, to identify the parts of the stomach most frequently affected by the inflammation, as well as the impact of an insufficient number of collected samples on the correct diagnosis. In addition, we intended to find out how often chronic gastritis is not linked to a *H. pylori* infection and what the causes of this phenomenon may be, as well as how often a *H. pylori* infection is not accompanied by an inflammation. Another aim was to check the correlation between the presence of anti-*H. pylori* antibodies and the actual inflammation of the mucous membrane detected on microscopic examination of biopsy specimens.

Material and methods

Study groups and methodology of research

The study covered 110 patients reporting subsequently for upper gastrointestinal endoscopy due to dyspepsia. Patients whose case history taken on examination revealed a possibility of neoplastic disease, reflux disease, liver cirrhosis, chronic cardiac insufficiency, long-term nonsteroidal anti-inflammatory drugs (NSAIDs), or acetylsalicylic acid therapy, as well as patients with abdominal organ changes on USG examination, were excluded from the study. Only patients who gave informed consent to the collection of additional biopsy specimens of the gastric mucosa and blood specimens for the presence of IgG anti-*H. pylori* antibodies with the use of the ELISA method (Instalert, sensitivity: 95.9%, specificity: 75.9%) were included in the study. The indicator of the participation in the study was 50%. Each patient completed, with the help of a trained nurse, a questionnaire concerning case history, *H. pylori* infection, and treatment of the infection as well as the medication used, including antibiotics, NSAIDs, acetylsalicylic acid (ASA), and proton pump inhibitors (PPI). Gastroscopy was performed by doctors from the endoscopy laboratory. In the course of gastroscopy two biopsy specimens were collected for histopathological examination and towards *H. pylori* infection from the lesser and greater curvature in the antrum 3 cm from the pylorus, in the body – 4 cm proximally to the angular incisure on the lesser curvature, and in the middle of the greater curvature, as well as in the subcardiac region on the side of the lesser and greater curvature. The consent of the Bioethics Committee by Medical University of Warsaw was obtained for the performance of the study on 23 March 2010.

The study group covered 62 males and 58 females. The age of the participants ranged from 18 to 88 years and did not differ for women and men (the mean age of women and men was 55.16 and 55.12 years, respectively).

Histopathological examination

Each of the collected biopsy specimens fixed in a 10% solution of neutralised formalin was, after proper orientation, immersed in paraffin. Slices of 5 µm thickness were cut and stained with haematoxylin and eosin as well as Giemsa with the purpose of detecting *H. pylori*.

Histopathological preparations were assessed by two independent pathologists who did not know the results of other *H. pylori*-detecting tests in a given patient. The principles of the revised Sydney classification were applied in the description and diagnosis. Each diagnosis contained topographic data (cardia, body, pre-pyloric region).

The assessment included:

- morphological features of the inflammation and its severity on a four-grade scale along with the depth of the inflammatory infiltration,
- presence and possible aggravation of intestinal metaplasia,
- presence and aggravation of mucous membrane atrophy,
- other features of damage to the epithelium, e.g. erosions, architectonics disturbances, dysplasia,
- changes in the stroma (oedema, extravasations),
- presence of *H. pylori*; aggravation of the infection on the four-grade scale.

Statistical analysis

The frequency of the appearance of individual subgroups and the errors of these frequencies were calculated from the binomial distribution. A comparison between the frequencies of occurrence was performed on the basis of *t*-Student distribution. An analysis was carried out of the interdependence between the studied features by determining the correlation coefficient and

the least-squares method. The results were deemed statistically significant at the *p* significance level equal to or lower than 0.05.

Results

The frequency of occurrence and the location of the inflammation in the gastric mucosa

In the studied group of 110 patients with dyspepsia, chronic superficial gastritis of any part of the stomach was detected in 85 (77%) patients, equally frequently in females and males. Thus, in the studied group of patients the histopathological examination revealed a normal picture of the mucosa of the whole stomach in 23% of the examined (20 patients) did not have the infection, and in one anti-*H. pylori* antibodies were found. Only 20 out of the 110 patients studied had neither inflammation nor current infection. Changes of an active kind were revealed in 35.5% of cases. Differences in the frequency of occurrence of both chronic and active inflammation in females and males were not statistically significant. Inflammation of the mucosa affected most frequently the antrum (67%) followed by the body of the stomach (61%) and, most rarely, the sub-cardia region (47%) (Figure 1). Inflammatory changes involving the whole stomach were found in 43 (39%) of the studied patients with dyspepsia and in 50.5% of all patients with inflammation.

An isolated inflammation of the sub-cardia region was not detected in any patient. Inflammation was rarely found in the body – 6% (7 patients, all without a *H. pylori* infection), being most common in the antrum – 12% (13 patients, including four with *H. pylori* infection). In 38.5% of cases, active type of inflammation did not coexist with an infection, although 66.7% of these patients were found to have antibodies. On the other hand, in active inflammations with *H. pylori* colonisation (61.5%), the presence of antibodies was detected in 83.3% of the patients.

Of 25 studied patients without inflammation in any part of the stomach, 20 (80%) patients did not show any evidence of *H. pylori* infection in any place – in one (5%) of them anti-*H. pylori* antibodies were present. In 71 patients without active inflammation, infection was not detected in 55, but serological examination was positive in 14 (25.5%) of the cases (Table I). Five of the infected patients showed no evidence of inflammation, and as many as 16 of the infected did not have active inflammation (though in 37% of them anti-*H. pylori* antibodies were detected).

Frequency and localisation of *Helicobacter pylori* infection

Helicobacter pylori infection in any of the six collected biopsy specimens of gastric mucosa was found in 40 (36%) patients. There were no statistical differences between the infected and the non-infected patients with respect to mean age or sex. The localisations of the infection in individual parts of the stomach are given in Figure 2, which shows the percentage distribution of *H. pylori* infection. In a few patients the infection was isolated and affected: the antrum in 6 patients, the body in 2 patients, and the cardia region in 4 patients. The bacteria were most frequently detected in: the antrum in 31 patients, the cardia in 29 patients, and the body in 26 patients.

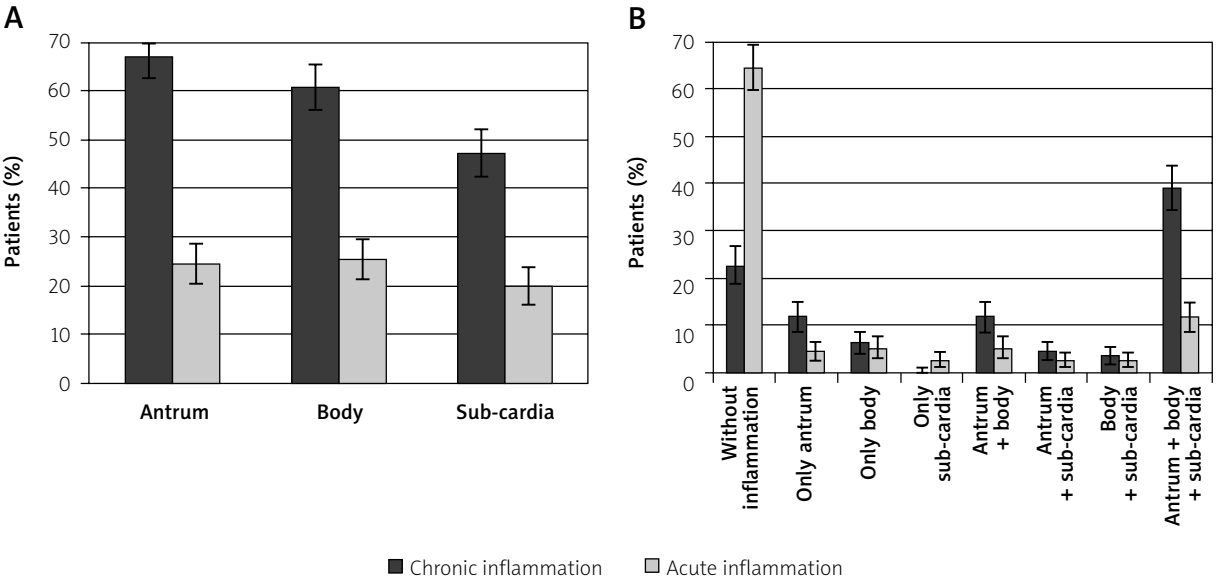

Figure 1. A – Percentage of patients with chronic gastritis and acute gastritis. **B** – Configuration of gastritis

Table I. Chronic gastritis and active gastritis and *H. pylori* infection

Inflammation	N	*H. pylori* (–)			Serology (+)		
		n	%	Error	*n*	%	Error
Active:							
No	71	55	77.5	5	14	25.5	5.9
Yes	39	15	38.5	7.8	10	66.7	12.2
Chronic:							
No	25	20	80	8	1	5	4.9
Yes	85	50	58.8	5.3	23	46	7
	N	***H. pylori* (+)**			**Serology (+)**		
		n	%	Error	*n*	%	Error
Active:							
No	71	16	22.5	5	6	37.5	12.1
Yes	39	24	61.5	7.8	20	83.3	7.6
Chronic:							
No	25	5	20	8	0	0	17.9
Yes	85	35	41.2	5.3	26	74.3	7.4

Co-existence of *Helicobacter pylori* infection and gastritis

In all parts of the stomach chronic inflammatory changes without an accompanying *H. pylori* infection were more common than inflammation with a co-existing infection. In active type inflammations there was a reverse situation. Healthy mucosa without evidence of inflammation or *H. pylori* infection was most rare in the antrum and more and more frequent towards the cardia, opposite to how it was in the case of inflammation with a co-existing infection (Figure 3).

A dependence of this kind was not registered for an active type inflammation where active inflammation and *H. pylori* presence showed similar frequency in all parts of the stomach. In both chronic and active inflammation positive correlation was observed between the severity of the inflammation and the severity of the infection – the higher the grade of the inflammatory state, the higher the grade of the *H. pylori* infection (Figure 4).

In all parts of the stomach *H. pylori* infection was significantly more commonly associated with the presence of an inflammation both chronic and active. However, in 7% to 9% of cases in different parts of the stomach an active inflammation was not accompanied by infection (Table II).

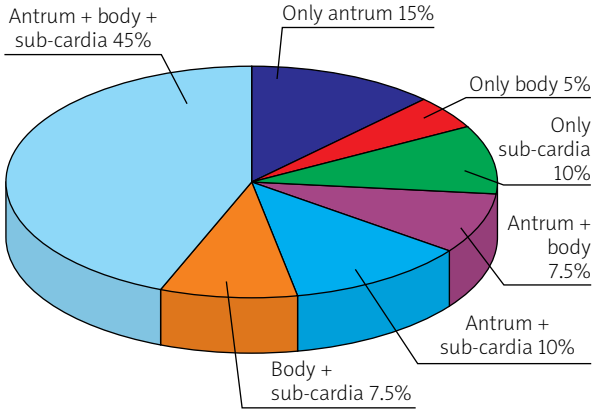

Figure 2. Localisation of *H. pylori* infection

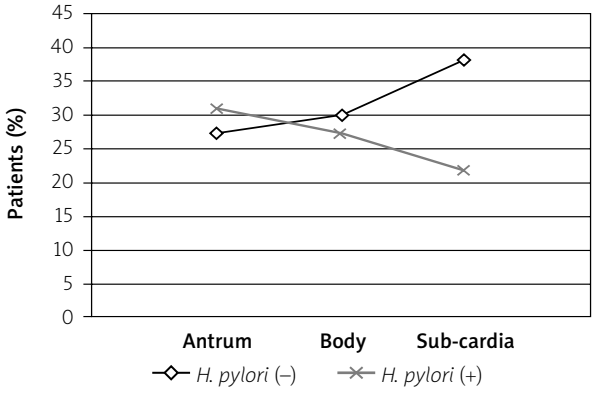

Figure 3. Coexistence of chronic gastritis in various sections of stomach and *H. pylori* infection

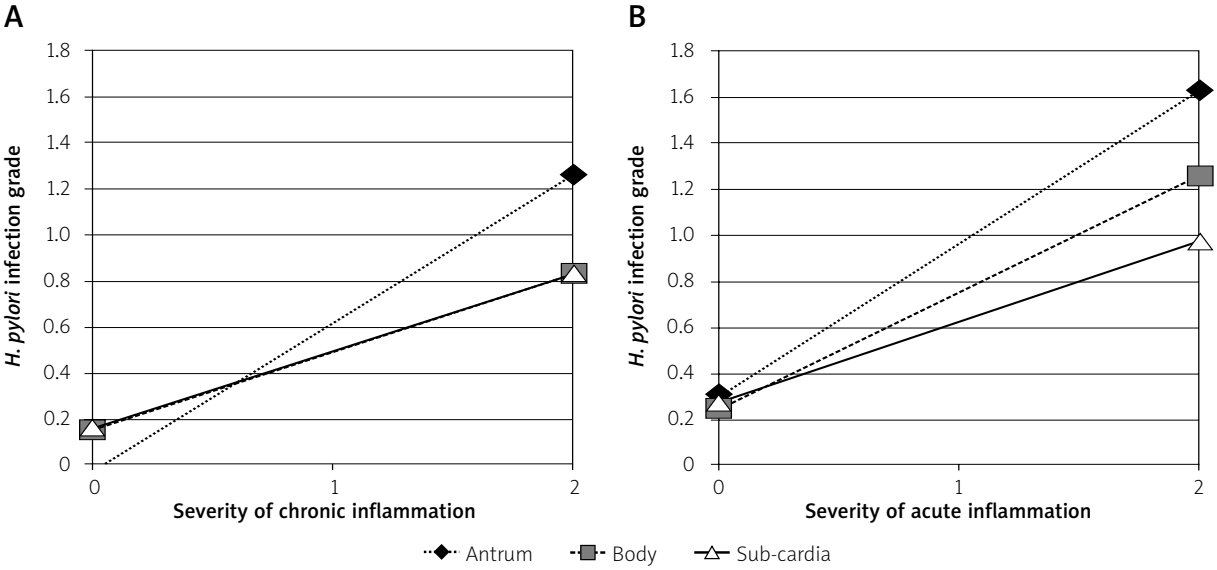

Figure 4. Correlation of inflammation score in various sections of stomach and *H. pylori* infection grade

Table II. Inflammation process in various sections of stomach and *H. pylori* infection

Inflammation	Antrum			Body			Sub-cardia		
	n	%	Error	*n*	%	Error	*n*	%	Error
Chronic:									
Infl. (–) Hp (–)	30	27.27	4.25	33	30	4.37	42	38.18	4.63
Infl. (–) Hp (+)	6	5.45	2.17	10	9.09	2.74	16	14.55	3.36
Infl. (+) Hp (–)	40	36.36	4.59	37	33.64	4.5	28	25.45	4.15
Infl. (+) Hp (+)	34	30.91	4.41	30	27.27	4.25	24	21.82	3.94
Active:									
Infl. (–) Hp (–)	61	55.45	4.74	60	54.55	4.75	62	56.36	4.73
Infl. (–) Hp (+)	22	20	3.81	22	20	3.81	26	23.64	4.05
Infl. (+) Hp (–)	9	8.18	2.61	10	9.09	2.74	8	7.27	2.48
Infl. (+) Hp (+)	18	16.36	3.53	18	16.36	3.53	14	12.73	3.18

Inflammatory lesions in gastric mucosa and abnormalities on endoscopic examination

A significant dependence was found between the inflammation of the antral part and duodenal ulcerative disease. Duodenal ulcer did not occur in patients without an inflammation in the antrum, while in patients with an inflammation of the antrum, duodenal ulcer was reported in 15% of cases.

Helicobacter pylori infection and the presence of IgG anti-*H. pylori* antibodies in the serum

The correlation between the histopathological examination towards *H. pylori* and serological examination amounted to a mere 65%. Twelve percent of patients with microscopically revealed infection did not have anti-*H. pylori* antibodies in the serum, while 22% of patients without the infection had these antibodies (Figure 5). Anti-*H. pylori* antibodies were present in 46% of the non-infected patients vs. 74.3% of the infected ones.

Helicobacter pylori infection and eradication, use of antibiotics or PPI

Among 70 patients without *H. pylori* infection 23 (33%) had received eradication therapy in the past, while among 40 currently infected patients 11 (27.5%) were receiving it at the time of study. Of the 70 patients referred to (20 without an inflammation and 50 with a chronic inflammation of any part of the stomach),

27 patients had taken antibiotics and at least 19 had taken proton pump inhibitors during the 6 months prior to the examination; data were not available for 18 patients (Table III). Patients with *H. pylori* infection used PPI more rarely but the difference was not statistically significant; however, the small number of PPI-taking patients may be responsible for this result.

Discussion

Chronic gastritis worldwide is most frequently caused by *H. pylori* infection. The spectrum of this infection-related disease ranges from an asymptomatic infection to peptic ulcer or gastric cancer. The course is prolonged, with a superficial inflammation transforming some cases into changes with a glandular atrophy or intestinal metaplasia character. The process is usually asymptomatic clinically but in some cases it may generate a clinical manifestation in the form of functional dyspepsia. In the studied group of patients with dyspepsia in whom its organic causes were excluded, the majority were most likely to be patients with functional dyspepsia. Although verification according to the Roman criteria was not conducted, clinical, endoscopic, and ultrasound examinations excluded organic causes of dyspepsia. As shown by other studies, functional dyspepsia dominates in patients with non-diagnosed dyspepsia [4].

Only 20 out of the 110 studied patients had neither inflammation of the mucous membrane nor *H. pylori* infection. The fact that an inflammation in some part of the stomach was found in 85 probands may support the idea that inflammation plays a role in the pathogenesis of functional dyspepsia. The inflammatory process involved all parts of the stomach to the same extent, being most frequent in the antrum and least frequent in the sub-cardia region. Earlier studies indicated that the inflammatory process begins in the antrum and then spreads to the remaining parts of the stomach [5]. However, the whole stomach was affected by the inflammation in 40% of the patients. Moreover, sporadically (in 12% in the antrum (13 patients, including only four with *H. pylori* infection) and in 7% in the body) the inflammation took an isolated form, which may imply

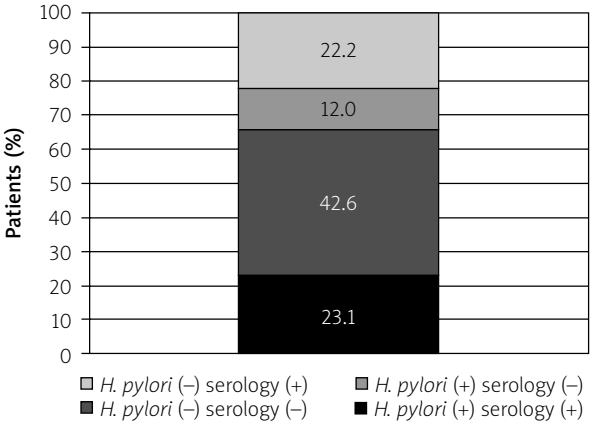

Figure 5. Infection with *H. pylori* and presence of IgG serum anti-*H. pylori* antibodies

either the presence of undetected focal changes in other parts of the stomach or the existence of other factors responsible for the limitation of the inflammation to any particular part of the stomach.

The updated version of the Sydney System recommends that five biopsy specimens are collected from the gastric mucosa: two from the antrum (3 cm from the pylorus on the lesser and greater curvature), one from the angle, and two from the body – from the lesser curvature 4 cm above the angular incisure and from the middle part of the body on the greater curvature. This procedure allows proper assessment of the status of *H. pylori* and chronic inflammation but may not suffice to detect pre-neoplastic lesions, which are generally multifocal [2, 6]. The question arises: which part of the stomach is most representative to detect chronic inflammation, atrophic changes, or intestinal metaplasia? Some believe that these changes are most frequently observed in the region of the angular incisures of the stomach [7] while others think that the inflammatory process commences in the mucosa of the antrum where it is most explicitly expressed and from where it spreads in the direction of the body [5, 8]. Endoscopists often do not collect any biopsy specimens or only single ones, often from randomly chosen places. In the past suggestions also appeared that a biopsy specimen should not be collected from a macroscopically normal mucosa due to economic conditions. However, it is known that the

Table III. Absence of *H. pylori* infection treatment with antibiotics and PPIs

Inflammation	N_{antib}	Antib(+)	Antib(–)	%Antib	Error	p_{antib}	N_{IPP}	PPI(+)	PPI(–)	%PPI	Error	p_{PPI}
Infl. (–) Hp (–)	20	6	14	30	10.2	NS	12	2	10	16.7	10.8	NS
Infl. (–) Hp (+)	5	3	2	60	21.9		4	2	2	50	25	
Infl. (+) Hp (–)	50	21	29	42	7	NS	40	17	23	42.5	7.8	NS
Infl. (+) Hp (+)	35	8	27	22.9	7.1		32	10	22	31.3	8.2	

correlation between the macroscopic and microscopic picture is poor [9, 10]. If, in spite of everything, the examiner decides to limit the number of biopsy specimens, against the assumptions of the Sydney System, he/she should collect them from the antrum and from the angular incisures on the lesser curvature.

In patients with an erosive inflammation of the oesophagus without an *H. pylori* infection gastritis was detected in 75–90% of cases [11], while in patients with functional dyspepsia or a non-erosive form of the reflux disease without an *H. pylori* infection, gastritis was found in 56–69% of patients [12]. In turn, in a large group of Portuguese patients subjected to gastroscopy in order to detect *H. pylori* infection, superficial inflammation of gastric mucosa was detected in 77% of cases [13].

What seems to be worthwhile is the surprisingly low percentage of infections among study group patients subjected to gastroscopy due to dyspepsia – only 36%. Studies conducted over 20 years ago on similar groups of patients revealed the presence of the infection in 92% of patients in 1988 and 71% and 68% in 1992 [14, 15]. This is in compliance with a general downward trend in the incidence of *H. pylori* infection in developed countries but stands in contradiction to current seroepidemiological studies covering adult Poles in whom the incidence of infections amounts to over 84% [16]. In patients with dyspepsia one could expect an even higher percentage of infections, this discrepancy being hard to explain. By comparison, a similar percentage (37.7%) of infections among patients with functional dyspepsia according to the Rome III Diagnostic Criteria was reported by Wei *et al.* [17]. There are suggestions that inflammation of gastric mucosa can be the cause of at least some of the functional dyspepsia cases [18, 19], and inflammation with *H. pylori* infection involving mainly the antrum with symptoms of functional dyspepsia promises easing of the complaint after effective eradication [20]. Inflammation of the antrum can be associated with fasting epigastric pain and inflammation in the sub-cardia region with motility disorders [21]. On the other hand, research carried out by Bucklay and Klupińska *et al.* in *H. pylori* infected patients did not reveal any difference in the histopathological condition of the mucosa between patients with dyspepsia and asymptomatic persons [22, 23].

In both chronic and active inflammation with co-existing *H. pylori* infection there was a positive correlation of the severity of the inflammation (score) and the infection, which remains consistent with the hitherto held knowledge on the subject. The active type of inflammation usually proceeds with intensive *H. pylori* colonisation, while in the study group of patients in over 38% an active inflammation did not co-exist with an infection in a relevant part of the stomach. This situation might be explained in terms of the focal character of the appearance of bacteria, which can be a source of error even in regional assessment of the mucosa. Other causes of the appearance of multinucleated cells in an inflammatory infiltration should also be considered. One can also speculate that an active inflammation survives in spite of the elimination of the infection as the presence of anti-*H. pylori* antibodies was reported in the majority of the patients concerned.

If an active inflammation was detected in any part of the stomach, *H. pylori* infection anywhere in the stomach was also reported in approximately 65% and in approximately 45% when the inflammation was inactive. Can *H. pylori* infection localised anywhere induce inflammation in the whole stomach and not only in the infected region? An answer to this question would require a study with a collection of a much larger number of biopsy specimens.

In their research Nordenstedt *et al.* detected in 40.7% of gastroscopy patients aged 40–80 years histopathological features of gastritis. In 20.5% of all cases with an inflammation, inflammatory changes were not accompanied by *H. pylori* infection [3]. In our study as many as 50 (58.8%) patients had inflammation without an infection, with 46% of them having anti-*H. pylori* antibodies, which seems to indicate a past infection. There were no statistical differences between the infected and the non-infected in the ingestion of proton pump inhibitors.

Inflammation without *H. pylori* infection appeared most commonly in the form isolated to one part of the stomach rather than in the form of an inflammation with *H. pylori* infection (37% only in the antrum and in 32% only in the body). In this study *H. pylori*-negative gastritis was found equally frequently in the antrum and in the body and a little less frequently in the sub-cardiac region (36%, 33%, and 25%, respectively). American studies did not reveal any significant differences in the appearance of atrophy and intestinal metaplasia between inflammation with and without *H. pylori* infection. In our study, due to very few cases of inflammation with intestinal atrophy and metaplasia, these differences were not assessed.

In 5 patients with microscopically detected *H. pylori* infection, inflammatory changes were not detected in any part of the stomach, which cannot be explained unless in terms of inflammation which remained undetected in spite of the collection of many biopsy specimens, or immunological disturbances.

Ulceration of the duodenum was not detected in any patient with an inflammation in the antrum, while in patients with antral inflammation duodenal

ulcer was detected in 15% of cases. This confirms the well-grounded opinion that the presence of an inflammation with a dominant antrum involvement increases the risk of the development of ulcerative duodenal disease [24, 25].

In the study by Nordenstedt *et al.* [3], patients with *H. pylori*-negative gastritis taking PPI or H2 inhibitors were significantly more common. In our study patients with an inflammation and with an *H. pylori* infection were found to be taking proton pump inhibitors slightly less often, but the difference was not statistically significant. Antibiotics and antisecretory drugs can lower the density of bacteria and lead to their transformation from a typical spiral-shape to colloidal forms, which are illegible on microscopic examination. Only the polymerase chain reaction (PCR) method detects *Helicobacter pylori* in both forms.

Causes of gastritis other than *H. pylori* infection include: PPI use – animal studies showed that long-term PPI treatment causes inflammation. Most likely as a result of bacterial proliferation in the stomach [26]. In turn, PPI use may falsify the detection of *H. pylori* infection.

Past *H. pylori* infection. Effective eradication results in granulocyte infiltration withdrawal and gradual reduction of the lymphocyte infiltration [27]. Changes in the type of glandular atrophy and intestinal metaplasia subside slowly or not at all – research findings have so far been inconclusive [28, 29]. In practice, the effectiveness of eradication is most frequently assessed with the help of a histopathological examination and a urease test, which are considered to be highly sensitive and specific. The high sensitivity of the histopathological examination can be disturbed by a small number or a small size of biopsy specimens. Conventional methods are of adequate sensitivity, where the density of bacteria is high. A respiratory test is of sufficient sensitivity in the evaluation of the effectiveness of the eradication also with moderate or focal colonisation [30]. Only the PCR method allows the detection of even very few bacteria present in specimens of mucosa. Thus, in the study by Patel *et al.*, 4 weeks after eradication with a triple combination drug therapy, *H. pylori* was detected in only 16% of patients on the histopathological examination and in 12% on the urease test, while the PCR method revealed the presence of the same bacterial strains in as many as 92% of patients [31]. In these patients such an insidious infection can support an inflammatory state then wrongly considered to be *H. pylori* negative. In the context of the study referred to, the question arises as to whether complete eradication is actually possible.

A positive serological examination towards *H. pylori* was reported more frequently in the infected patients, but the non-infected patients had anti-*H. pylori* antibodies in half of the cases. The infection in these patients might have undergone eradication or might have resolved spontaneously. According to study results the disappearance of antibodies during a 1-year follow-up period was found in 7.5% of patients [32].

Anti-*H. pylori* antibodies persist in the serum for several years [33] or even life-long [34]. A year after effective eradication 50% to 60% of patients remain seropositive, although the concentration of IgG anti-*H. pylori* antibodies decreases in the course of the first year by approximately 50% [35, 36].

The serological examination detecting anti-*H. pylori* antibodies is sensitive and specific within 80% to 90% in spite of the fact that the immunological reaction on the mucosal surface is moderate due to the niche localisation of bacteria [30]. Moreover, this immunological response can depend on the exposure time, nutritional status, and cross-reactions with other antigens (e.g. *Campylobacter*). In this study the compliance of the microscopic examination towards *H. pylori* infection was merely 65%. In 12% of the infected patients antibodies were not detected, and in 22% of the patients without infection antibodies were present, which seems to imply a past infection. This is another argument against giving indications for eradication only on the basis of determining antibodies, which seems to be common practice because a positive serological test does not provide definite evidence of an actual infection.

From 40 actually infected patients 11 (27.5%) had undergone eradication, which testifies to the rather low effectiveness of the applied therapies.

Other causes of inflammation of gastric mucosa without *H. pylori* infection include:

– Viral infection (*Cytomegalovirus, Herpes simplex*) and bacterial infection (*Mycobacterium avium*), which can involve gastric mucosa and lead, though very rarely, to an inflammation [3].
– Chemical or reactive inflammation. The more appropriate term used for the so-called chemical or reactive inflammation caused by a bile and pancreatic juice reflux to the stomach or by exogenous substances such as NSAIDs, ASA, alcohol, or chemotherapeutics where the inflammatory infiltration is minimal, is gastropathy [27]. It should be remembered that gastropathy and other forms of inflammation may co-exist, particularly in the presence of *H. pylori infection*.
– Autoimmune inflammation – characterised by the presence of antibodies against parietal cells and/or external factors.

Rare causes include post-radiation and eosinophilic inflammation, inflammation in the course of collagenosis, Crohn disease, sarcoidosis, or stress-induced in-

flammation (reported primarily in intensive care units). These forms of inflammation are relatively easy to differentiate on the basis of histopathological examination of specimens [3]. The clinical significance and prognosis in gastritis independent of *H. pylori* is unknown.

Conclusions

In patients with dyspepsia chronic *H. pylori*-negative gastritis is more common than gastritis with an accompanying *H. pylori* infection. Collection of too few biopsy specimens results in failure to detect inflammatory changes and/or *H. pylori* infection, which may be limited to one part of the stomach. Biopsy specimens of gastric mucosa should be collected in compliance with the Sydney System. *Helicobacter pylori* infection in patients with dyspepsia is less common these days than in the past. Anti-*H. pylori* antibodies can be found in almost half of patients with dyspepsia not infected with these bacteria. In over 1/3 of cases active inflammation occurs without *H. pylori* infection. *Helicobacter pylori* infection is not always equivalent to the presence of chronic gastritis.

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Conflict of interest

The authors declare no conflict of interest.

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