

### **From the history of epidemiology of peptic ulcer disease in the 20th century: social factors and the prevalence**

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The dynamics of ulcer disease morbidity in Russia and the developed world from the end of the 19th to the beginning of the 21st century are analyzed. The recorded peaks of peptic ulcer disease morbidity in the 20th century coincide with World War I and World War II, as well as with the Great Depression. Materials from the seminal work "Experience of Soviet medicine in the Great Patriotic War of 1941–1945" help to clarify the particular characteristics of peptic ulcer pathomorphism during global conflict. A sustained reduction of morbidity began to be recorded from the mid-1950s, while the frequency of complicated forms of the disease remained unchanged. Against this background, groups of patients exhibiting signs of social deprivation stand out. They are characterized by an increase in the incidence of peptic ulcer disease, complicated progressions and poor treatment outcomes. The analysis of the specifics of such cases of peptic ulcer progression can be most justified from the standpoint of psychosomatic medicine, rather than the theory of infectious ulceration, as in this case the impact of persistent stress and/or depression in patients at risk is clearly demonstrated. The epidemiological aspects of peptic ulcer disease present an obvious model for the study of the relationship between the inherent psychosocial and behavioral characteristics of patients from the at-risk group, as well as external and socioeconomic factors in the occurrence of infectious disease. The dynamics of peptic ulcer disease from the 19th century to the 21st century show a distinct connection to global and local social conflicts, as well as an adherence to cyclic rhythms (circadian, annual, perennial) affecting biological systems. Violation of these circadian processes is reflected in both the development and pathomorphism of peptic ulcers. Thus, an analysis of the impact of global and local conflicts in peptic ulcer diseases from the perspective of the history of medicine is not just a "look back at the past," but also an attempt to rethink the etiopathogenesis of the disease.

**Keywords:** *peptic ulcer, morbidity, social factors*

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Peptic ulcer disease is a polyetiological, polypathogenetic chronic illness with polycyclic relapsing. It is characterized by seasonal recrudescence with the appearance of (typically) a single ulcer defect in the gastric mucosa and/or duodenum. Human beings are the only species affected with ulcer disease, and the number of ulcer patients and of the disease's vital complications drastically increase during military conflicts or macroeconomic difficulties that impact large groups of people [1]. Many generations of clinicians have diagnosed the influence of negative global socioeconomic factors and personal emotions such as fear, anger, despair and sadness on the development of peptic

ulcer disease [2–4]. In the course of the 20th century peptic ulcer morbidity indicators changed substantially throughout the world. The present work analyzes the impact of social factors on peptic ulcer morbidity in a historical context.

Until the 1800s peptic ulcer disease was apparently rare. A gastric ulcer was described for the first time in 1835 by J. Cruveilhier [5]. At the end of the 19th century this disease was diagnosed primarily in young women and duodenal ulcers began to appear only in the early 1900s, predominantly in men [2]. The Mayo brothers, the great American surgeons, noted the duodenal ulcer's rapidly increasing frequency in comparison to the gastric ulcer and the increasing number of this disease's complicated forms [6].

According to modern gastroenterology, the primary cause of peptic ulcer disease is the

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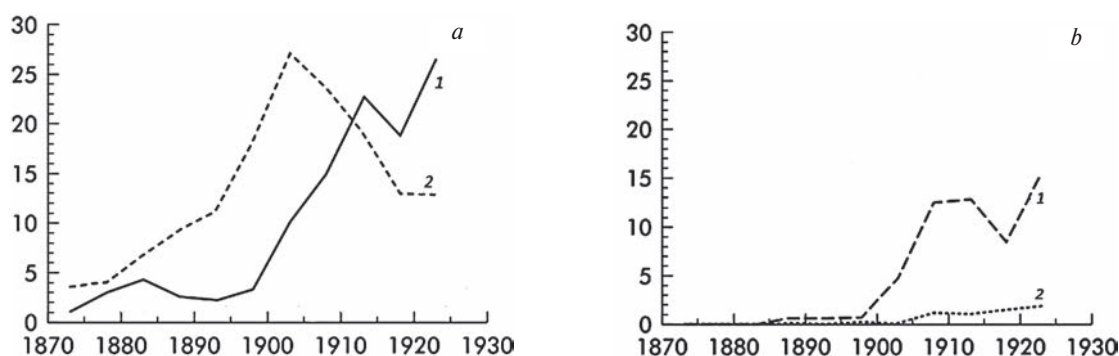


Fig. 1. The gender particularities of treatment demand (in 1 million people) among English men (1) and women (2) who were diagnosed with the gastric ulcer (a) and the duodenal ulcer (b) (according to information in [11]).<sup>1</sup>

*Helicobacter pylori* (*H. pylori*) infection. However, even for apologists of the infectious theory of ulceration it is clear that *H. pylori* is a human infection that was widespread long before the end of the 1800s. This prevalence does not explain the growth of peptic ulcer disease or the transition from the dominance of the gastric ulcer to the escalated frequency of the duodenal ulcer through the suddenly increased contagium [7].

We must recognize the great clinical skills of the doctors from that era, whose intravital diagnoses were primarily based on the analysis of complaints, case histories and the insufficient information obtained from the physical examination of the patients: “For diagnosing ulcers anamnesis is everything while objective examination is nothing” [3]. In that period it was the surgeon carrying out the operation on the perforation or bleeding of the ulcer or the pathologist performing the postmortem examination who had the prerogative of making the final clinical diagnosis. In fact, since for a long time pathological diagnosis was considered the most reliable [8], the spread of the peptic ulcer disease was initially evaluated based on the autopsy results.

Citing S.P. Botkin, S.B. Geiro states that the gastric ulcer in the 1870s–1880s was very rare in St. Petersburg, Russia. (According to autopsies in the Obukhovskaya and Alexandrovskaya clinics, it constituted 0.1–0.05% of the cases.) [4] In other countries the gastric ulcer was found in 5% of all autopsies and the duodenal ulcer in 0.8% [9].

In the beginning of the 20th century doctors began diagnosing peptic ulcer disease (as well as its complicated forms) more frequently in Russia. The problem of the “round gastric ulcer” became

a program theme at the first congress of Russian therapists in 1909 and was reviewed at the joint therapist and surgeon conference [4].

During WWI (1914–1918), when multimillion-man armies had enlisted almost the entire combat-ready male population of the warring countries, the increase of ulcer patients was so significant that specialists even spoke of an “epidemic” of peptic ulcer disease [4]. Meanwhile, the duodenal ulcer was practically unmentioned. A typical reason for discharge was “inflammation and ulceration of the stomach” [10]. Founder of Russian neuropsychology Professor R.A. Luria wrote that “the war... increased the number of peptic ulcers not only because radiology has created the opportunity to diagnose them more frequently and more exactly than before, but also because some kind of source for the formation of the gastric ulcer... was implanted in those enormous neuro-psychic traumas that the large parts of the population acquired in the war” (citation in [4]).

Russian clinicians also noted the increase in the number of new diagnosed cases of peptic ulcer disease during the Russian Civil War (1918–1921), although in that period radiological diagnoses were usually an exception to the rule, while clinical diagnoses were based on the ascertainment of hematemesis (that is, the identification primarily of a complicated ulcer).

In the 1920s–1930s the level of treatment demand among ulcer patients in the USSR was stable. (In Leningrad it remained 0.3–1.3% of all hospitalized patients.) This indicator suddenly increased (doubling to 2.6–2.6%) from 1933 to

<sup>1</sup>The patients asked for treatment at the St. Bartholomew Hospital in London.

1935 and then decreased to the initial level at the end of the 1930s [4], on the eve of the Great Patriotic War.<sup>2</sup> The particularities of this period, which is marked by the sad statistics, are explained by the increased level of anxiety concerning potential political repression, when the anxiety level in many Russian families was extreme. For comparison, in England before the beginning of WWII the mortality rate from peptic ulcer disease was below 1% of all non-violent deaths [10].

Russian therapists and surgeons' mosaicked evaluation of the development of the peptic ulcer disease epidemic in Russia in the first half of the 20th century is detailed by more than a century of information on ulcer patient treatment demand provided by foreign gastroenterologists (for example, data from London's largest hospitals; see fig. 1 and 2).

The authors of works dedicated to the study of ulcer morbidity in the 19th-20th centuries admit that they cannot explain, from the viewpoint of the infectious theory, the drastic increase in treatment demands concerning this disease in the beginning and middle of the 20th century, the temporary gap between the peaks of demand in duodenal and gastric ulcer patients, the gender differences in the time they were recorded and the divergent trends in identifying gastric and duodenal ulcer in women [11–14]. The authors recorded a drastic increase in the number of gastric ulcer patients in the beginning of the 20th century with two peaks corresponding to WWI and the Great Economic Depression of 1929–1939. The rise of duodenal ulcer morbidity occurred in the prewar years, the WWII period and the subsequent devastation.

After the beginning of WWII, in the UK the mortality rate of first duodenal ulcer patients and then gastric ulcer patients increased tenfold [10]. Work by C.C. Spicer and his coauthor demonstrates the link between the bombing of England's industrial centers and the drastic increase in the frequency of perforated ulcers [15].

Similar processes occurred in the USSR. The classical multi-volume guidebook *The Experience of Soviet Medicine in the Great Patriotic War*

<sup>2</sup>The Great Patriotic War is a term used in Russia to describe what the Western world calls World War II, or the period (June 22, 1941 - May 9, 1945) when the Soviet Union fought against Nazi Germany and its allies along the Eastern Front.

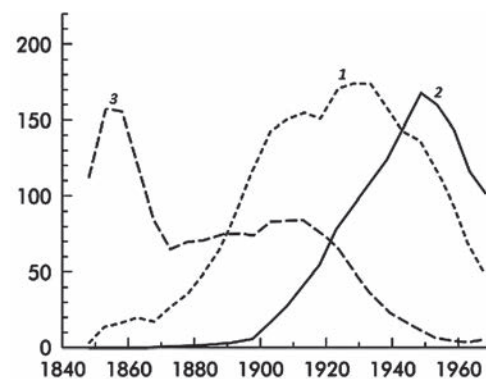


Fig. 2. The hospitalization of ulcer patients from the 1840s to the 1860s in London (according to [11]).

1 – gastric ulcer, 2 – duodenal ulcer, 3 – dyspepsia.

1941–1945 presents the results of the various analyses of ulcer morbidity in Russia from the second half of the 19th century to 1945 [4]. A precise analysis of medical statistics helps identify the influence of natural cyclical processes and the crude impact of social factors. It also explains the difference between peptic ulcer and duodenal ulcer morbidity.

The following particularities of the peptic ulcer “epidemic” during the Great Patriotic War are identified:

- ulcer patients in frontline evacuation hospitals made up 21.3–24.6% of all gastroenterological patients;

- the percentage of ulcer patients among all patients with gastroenterological diseases reached its peak (29.1%) in the first half of the war and then gradually declined (to 18.5%) by the fourth year of combat activity;

- the proportion of gastric ulcer patients to duodenal ulcer patients during the war was 1.07:1.00;

- general morbidity increased, primarily due to duodenal ulcer patients, the number of whom constantly grew and reached its peak in the fourth year of the war;

- the increase of duodenal ulcer morbidity began in the second year of the war and its prevalence occurred in the third, while the first two years of the war were dominated by gastric ulcer cases whose peak came in the third year of the war;

- gastric ulcer recurred in patients with long ulcer anamnesis and “new ulceration cases” [4] were characteristic of the duodenum;

- officers were affected mostly with the duodenal ulcer (more “fresh cases”) (1.67 duodenal ulcer cases to 1.00 gastric ulcer cases), while soldiers were affected mostly with the gastric ulcer (more “chronic” ulcer) (1.21 gastric ulcer cases to 1.00 duodenal ulcer cases);
- the average age of gastric ulcer patients was 36–45 and of duodenal ulcer patients 26–35; and
- pronounced exhaustion and nutritional marasmus led to an asymptomatic (unresponsive) trend in peptic ulcer disease, which manifested, first and foremost, in vital complications – ulcer bleeding and perforation.

The authors of the guidebook note the prevalence of gastric ulcer patients in the infantry and of duodenal ulcer patients in the communication troops, aviation and tank troops [4]. They attribute this fact to the drastic nervous stress in these troops of young officers. There are also indications that in peacetime peptic ulcer disease is characterized by pronounced periodicity, cyclical trends, rhythmic changes and repeatability of aggravation and remissions.

The gradual reduction of insolation, the end of vacation periods in peacetime, the transition to “winter” time from zone time and the beginning of the working year in the autumn months results in a peak of morbidity in the end of autumn/beginning of winter. The growth of insolation and the transition to “summer” time in March are also accompanied by an increase in the number of patients seeking treatment, although this rise in morbidity is usually less than the winter rise [16]. Thus, the disruption of the adaptation to cyclical natural processes is

related to the risk of developing an aggravated ulcer.

Similar trends were observed during the Great Patriotic War. During wartime the typical periodicity of ulcer aggravation or complication patients seeking treatment was preserved (that is, the cyclicity of ulcer trends did not change in comparison to peacetime). In the summer months no more than 5–6% of all patients were ulcer patients. The peak of treatment demand was observed in October-December and March. Seasonality was more characteristic of gastric ulcer patients and less pronounced in duodenal ulcer patients (fig. 3). At the same time the classical idea of the cyclical trend of peptic ulcer disease was not reflected in the infectious theory of ulceration.

Seasonality was especially pronounced in the first two years of the war and starting in the third year seasonal influences began relenting. Nevertheless, the autumn rise with a peak of hospitalization in December persisted in both types of ulcer localizations [4]. Military doctors attributed the declining trend of seasonal influence to exposure to combat circumstances. Thus, in the course of the defensive battles treatment demand decreased. The third and fourth years of the Great Patriotic War were characterized by a turnaround in the course of military actions: the Soviet troops began to liberate the occupied territories and transitioned to decisive attacks. During the offensive operations patients suffered more frequently from ulcer aggravation and complication.

The war experience demonstrates that the risk of casualties due to health problems is particularly

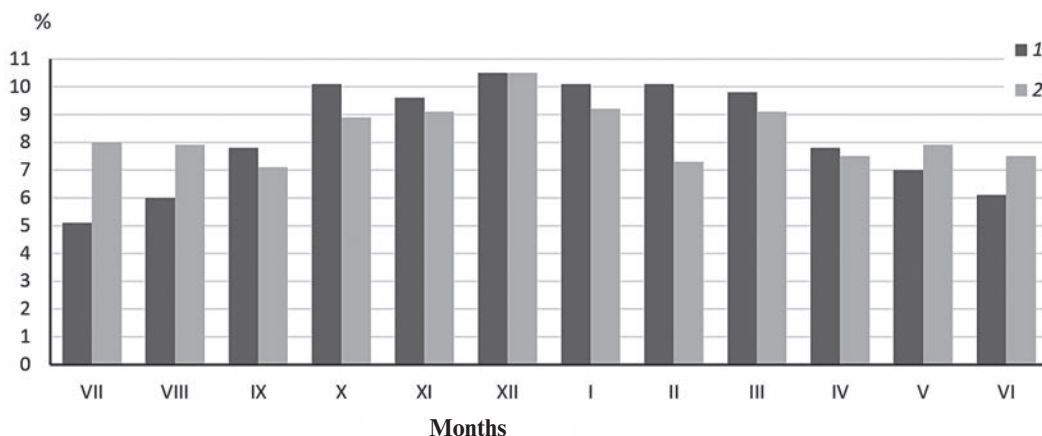


Fig. 3. The hospitalization of gastric ulcer patients (1) and duodenal ulcer patients (2) during the Great Patriotic War (according to information in [4]).

high during an offensive. Undoubtedly the servicemen knew and remembered this. The emotional charge resulting from the successful advance (including the joy related to the liberation of occupied territories) was added to the fear of a possible serious wound or death, whether one's own and one's fellow servicemen's. Thus the frequency of patients complaining about a characteristic pain in their stomachs in critical moments of the offensive operations increased. Nutritional and neuro-psychological factors were the primary causes of the ulcer's development and complication in this period [4].

If an ulcer is aggravated in the hungry, exhausted and anxious, it supposedly must heal in the sated, rested and relaxed. This theory was confirmed by the treatment of ulcer patients. Because of the limited therapeutic opportunities available during evacuation, aggravated ulcers were treated successfully with bed rest, regular hearty meals and sleep medication without any anti-ulcer therapy. This method proved to be effective in 84% of the cases [4].

We see essentially the same results in the new phase of clinical medicine development. Thus, a low limit of permissible effectiveness of *H. pylori* eradication (80%) is included *a priori* in the Maastricht Consensus on Ulcer Therapy, while the "acceptable" frequency of annual recurrences with the standardized treatment of combining antibiotics is still 10–20%. But recurrences can be reduced with other medicine without resorting to anti-helicobacter therapy through the use of psychotropic drugs – up to 5% – and immunomodulators – up to 12.5% [17, 18].

Diagnostics of peptic ulcer disease during the Great Patriotic War were based on clinical data and results from laboratory and radiological studies. Primary radiological diagnostics were mostly produced in evacuation hospitals on the home front (42.3–45.5%) and much less during the earlier stages of evacuation (especially during the first years of the war).

The structure of the complicated ulcer in the USSR during the WWII was characterized mainly by bleeding (56%) and perforation (35% of all patients with complicated forms of peptic ulcer disease). Bleeding was encountered 4 times more in gastric ulcers, and perforation 2 times more, than in duodenal ulcers. Perforation complicated the course of the ulcer in 6.2% of the patients,

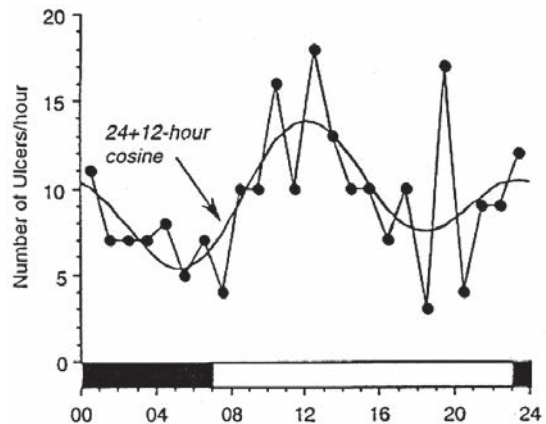


Fig. 4: The frequency of ulcer perforation during the day (according to [19]).

The x-axis shows the time of day (in hours).

bleeding in 14.5% and pyloric stenosis – as rare as it is today – in 1–2% of the patients. The reduction of the number of gastric ulcer patients and the increase in the number of duodenal ulcer patients was clearly seen in cases of bleeding: in 1941 gastric ulcers bled 12 times more than duodenal ulcers, whereas in 1943 the proportion was 2:1 [4]. In total 7.3% of peptic ulcer disease patients were operated on (11.4% of gastric ulcer patients and 3.1% of duodenal ulcer patients).

Just like uncomplicated ulcers, complications of the ulcer (perforation and bleeding) also demonstrated seasonality: almost 60% of the diagnosed complications developed at the end of autumn and beginning of winter. In 42.9% of the patients bleeding appeared in the three winter months (in December in 35.6% of the cases). The time of complication development preserved a daily rhythm: almost half of the perforations (43%) manifested from 6:00 a.m. to 12:00 p.m. [4].

A similar periodicity of perforations can be observed today (fig. 4). It is obvious that the quantity of perforations throughout the day is distributed unevenly, has a 24-hour period and is approximated by the cosine formula with two peaks (the maximum rise takes place at 12:00 p.m. and 12:00 a.m.) [19].

“Many patients with perforations” – that is, 3/4 of servicemen patients – “were operated on; primarily their ulcers were sewn up” [4]. The surgical method was employed in 28.5% of profusely bleeding cases with gastric resection being performed on 52.4% of the patients and

“various palliative operations” performed on the rest [4].

Mortality from the perforated ulcer corresponded to prewar figures (16–17%) and mortality with bleeding ulcers was close to contemporary indicators (12% with a gastric ulcer and 1.2% with a duodenal ulcer). Specialists attributed the high mortality indicators to late hospitalization. Similar indicators were observed in Moscow in 2007–2008 among patients who were hospitalized within 24 hours and higher indicators in perforated ulcer cases (15.2–16%). In these years general postoperative mortality in cases of gastroduodenal bleeding was 12.6–12.1% (with a decreasing trend) [20].

People who died from peptic ulcer disease constituted 2.2% of all deaths resulting from various diseases (in the USSR before the Great Patriotic War this indicator was 1.1%) [4]. During autopsies of servicemen who died from the peptic ulcer disease doctors discovered large and giant ulcers (5–19 cm in diameter in 14% of the cases and more than 10 cm in 5.4% of the cases). But those that were predominant (in 88% of the cases) were single ulcers (multiple ulcers appeared two times more than in the prewar period): in 50% of the cases they were callous ulcers and in 1/3 of the cases they were penetrative ulcers. In the first two years of the war multiple ulcers occurred more frequently (7.6%) than in 1943–1944 (5.9%). The cause of death in 59.8% of the patients was ulcer perforation, in 26.2% of the patients it was ulcer bleeding and in 0.9% it was cicatricial-ulcerative stenosis [4].

In England and Wales mortality from peptic ulcer disease among women in 1939–1942 was 2–3 times lower than among men, but higher than in the prewar period [10]. We are not aware of any equivalent studies of the civilian (predominantly female) population in the USSR during the Great Patriotic War.

The more serious the psychological trauma, the longer its consequences will persist. Heavy stress and depression symptoms increase the risk of developing an ulcer within 9–15 years [21].

The clinical consequences of the largest military conflict of the 20th century left a profound trace on both sides of the front. Former prisoners of war also contracted peptic ulcer disease several years after the end of the war. This is characteristic of both the soldiers from the Allied armies [22]

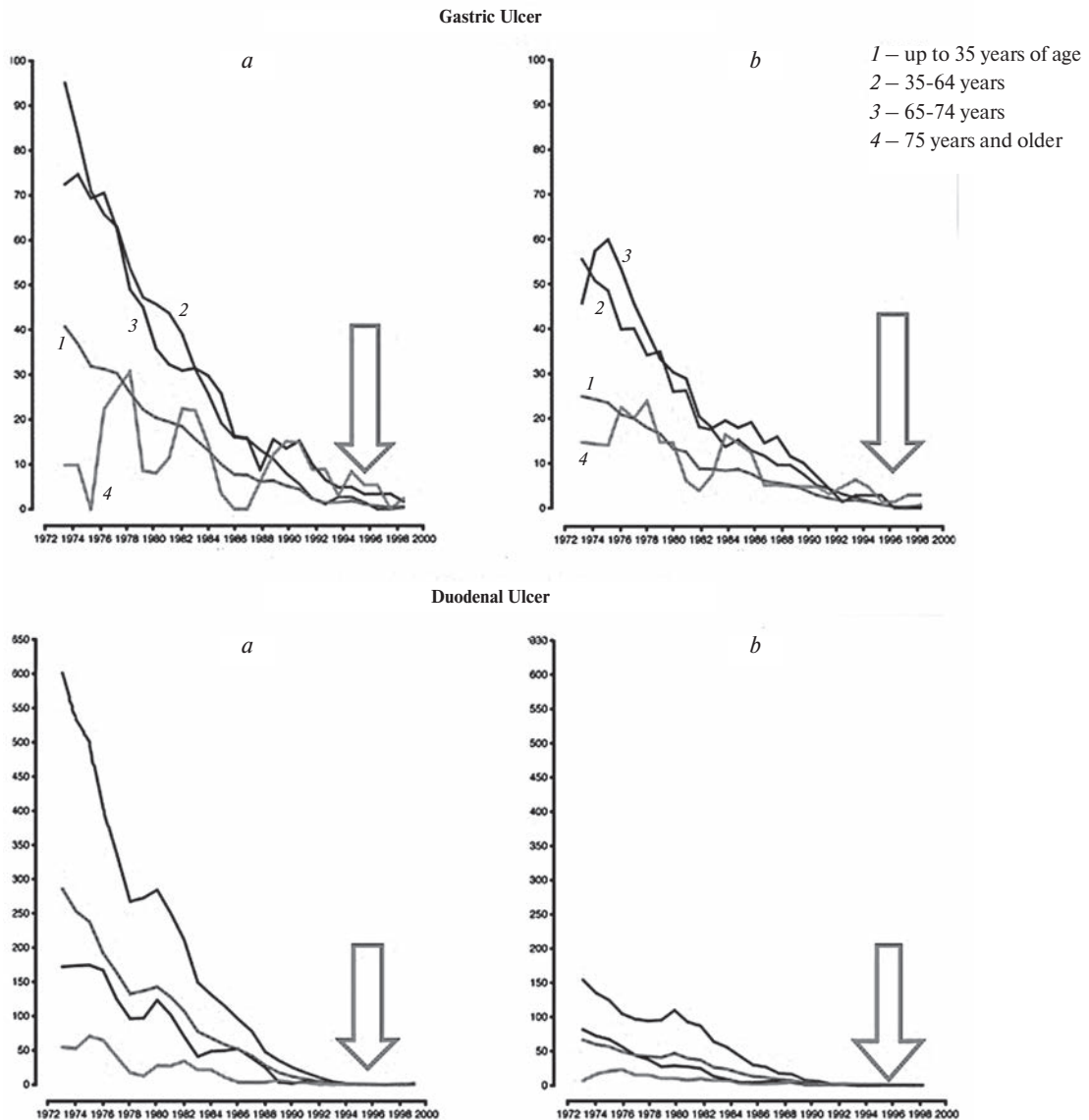
and the former Japanese prisoners of war [23]. The same predisposition was later discovered among US servicemen who fought in the Vietnam War [24].

Collective disasters, both natural and artificial (those conditioned by social factors), can provoke the formation of peptic ulcer disease. On the morning of January 17, 1995, an earthquake measuring 7.5 on the Richter scale shook the area between the Japanese cities of Osaka and Kobe in the southern part of the Honshu Island for 20 seconds. More than 6,400 people died and 26,000 survivors were extracted from the ruins of buildings, almost all of whom needed medical assistance. This catastrophe resulted in a drastic increase in the number of bleeding gastric ulcer patients [25]. In 1991 the severe economic crisis in Bulgaria provoked a sharp increase in treatment demand from patients with active and complicated forms of peptic ulcer disease [26].

However, the cataclysms in the various regions of the world can no longer influence the trend towards a decline of peptic ulcer disease morbidity after WW II which was observed in the 1950s first in the US and then in Western Europe [27, 28] and Japan [29].

The “golden billion” countries achieved stable economic growth in the 1960–1970s. The so-called social state was built in this period in which the healthy provide for the sick, the young for the old and the wealthy for the poor. The state system of aid, taxes and benefits helps former outcasts be part of such a society. Society discards the artificial identification of various minorities, and discrimination according to sex, age, profession, income level, nationality, religion, skin color and country of residence is eliminated. These circumstances certainly reduce tension in society, prevent a substantial part of social conflicts and indirectly result in the reduction of peptic ulcer disease morbidity. However, these processes did not affect the developing countries of Southeastern Asia and Africa, which currently have the highest indicators of morbidity and mortality from peptic ulcer disease.

The declining morbidity trend in the largest developed countries of the world was preserved at the end of the 20th and beginning of the 21st centuries [11, 13]. The decline of morbidity and the decrease in the number of patients with serious complications of peptic ulcer disease resulted in the



**Fig. 5. The number of gastric ulcer and duodenal ulcer operations in English men (1) and women (2) from 1970 to 2000 (according to [14]).**

The vertical arrow indicates 1996, the year of the First Maastricht Consensus (the beginning of the "anti-helicobacter era").

decrease of operations both in Europe and in the U.S. These trends, which were observed back in the second half of the 20th century (they appeared long before the introduction of new techniques for treating ulcers – “heliotropic anti-ulcer eradication therapy”, which includes antibiotics and antisecretory drugs), were preserved even after the First Maastricht Consensus was adopted in 1996 and the new doctrine on treating peptic ulcer disease was introduced [10, 14, 30] (fig. 5).

The decline of peptic ulcer disease morbidity in various regions of the world is uneven, manifesting in men and women in different ways, with gastric

and duodenal ulcers developing at different speeds [31–34]; and, most importantly, it is not related to the introduction of antisecretory drugs in clinical practice (H<sub>2</sub> antagonists and Proton-pump inhibitors) [35–37]. It is believed that this trend does not affect people over the age of 65 [36] and develops faster in cities than in rural regions [28]. Prevalence stabilization and a certain growth of complicated forms of peptic ulcer disease are also being observed, despite the performance of standard anti-helicobacter eradication therapy [14, 35, 37–39]. This trend, in the opinion of several authors, does not have a clear explanation

that would satisfy everyone [31]. However, an analysis of the presented results helps determine that complicated forms of the disease and high post-operative mortality are characteristic primarily of patients with a low level of social interaction (social deprivation) and with serious accompanying diseases [35]. Such patients can also be seen in countries with high standards of living. For example, these particularities of peptic ulcer disease are inherent in residents of the Hong Kong districts where people live permanently on the water in junks [40].

It has been objectively established that pronounced stress, anxiety and/or depression symptoms impede a clinical and endoscopic healing of the duodenal ulcer, something that negatively affects predictions of peptic ulcer disease development in the course of several years [41, 42].

Consequently, the epidemiological aspects of peptic ulcer disease serve as an apparent model for studying the relation between the immanent psychosocial, behavioral and external socioeconomic factors and the infectious factors in the occurrence of the disease. And the more categorical the unequivocal arguments in favor of a helicobacter etiology of the ulcer disease, the more meticulous should be the analysis of the causes of the disease's morbidity dynamics in the near future.

Thus, in the course of the 19th–20th centuries, during peacetime and wartime, the dynamics of peptic ulcer disease morbidity demonstrated a clear link to global and local social conflicts, as well as a dependence on the cyclical rhythms (daily, annual and perennial) that influence biological systems. The violation of these circadian processes is seen both in the development and the pathomorphism of peptic ulcer disease.

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