

AN OBSERVATION ON CHRONOPATHOLOGY OF PEPTIC ULCER REVISITED

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Received after revision June 2006

Abstract

In 1952 Otto Bsteh, a well-known Austrian surgeon and teacher at the medical school in Vienna, published a book in which he summarised his experience on the development of peptic ulcer (1). Among other details he presented an observation on the circannual distribution of the incidence of ulcer perforation in an area where mainly farmer families lived. The peak of the circannual distribution appears in June to July and is explained as caused by the stress in connection with the time of harvest. This publication should remind us of the fact that, besides the recently discovered role of *Helicobacter pylori*, psychosomatic and chronopathological phenomena play an important role in the generation of the ulcer disease.

INTRODUCTION

The experience of old physicians and many studies about peptic ulcers of the gastric or duodenal mucosa show that the beginning as well as continuation of symptoms are related to time and time periods. The role of stress and, therefore, of psychosomatic effects mediated by the autonomic system was considered as important.

The discovery of the importance of *Helicobacter pylori* and the improvement of therapeutical success may lead to a neglect of the other influences, and in particular of the role of chronobiological or chronopathological mechanisms in the multifactorial aetiology of this disease.

In 1952 O. Bsteh, a well-known Austrian surgeon and teacher at the medical school in Vienna, published a book in which he summarised his experience on the development of peptic ulcer (1). He was chairman of the surgical department of the main hospital in this area, which is located in the town of Mistelbach, in the northern part of Lower Austria, close to the border of the Czech Republic. The patients who were treated in this hospital came from a quite homogeneous population of farmers. Therefore, his observations are important for the study of the chronopathology of occupational factors.

The role of psychosomatic and chronobiology

The innervation by the autonomic nervous system of the gastrointestinal tract makes this area of the body particularly sensitive to reactions to any kind of stress. Peptic ulcer had, for a long time, been considered as one of the most prominent examples of psychosomatic diseases. The development of specific antihistaminic drugs and of proton-pump inhibitors reduced the danger of the disease.

The discovery of the role of *Helicobacter pylori* by *Warren* and *Marshall*, published in 1984 (2), which was recently (2005) honoured by the Nobel Prize, started a new era of treatment of the ulcer disease.

Besides this obvious medical success, the role of psychosomatics as of an aetiological factor now appears to be non-existing. The final and definite cause, i.e. the complete aetiology of the disease, is assumed to be explained as bacterial infection with the further proof that the eradication of *Helicobacter* in many patients permanently healed the disease.

However, the observations by *Bsteh* (1) remind us that we should not forget the psychosomatic factors behind the scene, which are related to the autonomic nervous and endocrine control. The unique circannual distribution of ulcer perforation reported by *Bsteh* (1) points strongly to an influence of the autonomic system. It would be wrong to consider them as unimportant.

The observations by O. Bsteh (1)

In the years from 1936 to 1947 the number of inhabitants in the area was about 70000. At that time 1026 persons had been treated in the hospital. From the 1026 persons, 821 were treated surgically; the others received internal medical treatment.

The most severe event of peptic ulcer disease is perforation. *Bsteh* reports in his book 185 cases of perforation within 17 years. The numbers of perforations in individual years show a minor variation between 9 and 20 cases per year. The age of the patients was between 30 and 50 years.

The main reason why it appears worthwhile to present this short report about *Bsteh's* results is the observation of a clear circannual distribution. As can be seen in the following table, there is a unique and marked peak in the summer months of June and July.

| | |
|-----------|----|
| January | 6 |
| February | 2 |
| March | 8 |
| April | 9 |
| May | 15 |
| June | 30 |
| July | 34 |
| August | 22 |
| September | 17 |
| October | 18 |
| November | 12 |
| December | 12 |

Total 185 ulcer perforations in the years 1936 to 1947 (1)

In *Fig. 1* the circannual distribution of ulcer perforations is shown as a histogram.

Observations concerning the time course of peptic ulcer disease have, in the early phase of research, mainly focused on the fact that the disease proceeds in time periods and intervals. According to *Bsteh (1)*, one period during which the symptoms of the disease, such as pain, vomiting, melaena, are present lasts about 6 weeks. An interval of about half a year follows until the next outbreak of symptoms starts.

For clinical purposes *Bsteh* demands to observe the oscillations of symptoms during periods as the “ulcer day” and “weeks of the ulcer”. These observations were noted in each patient’s documents. However, they were not statistically evaluated.

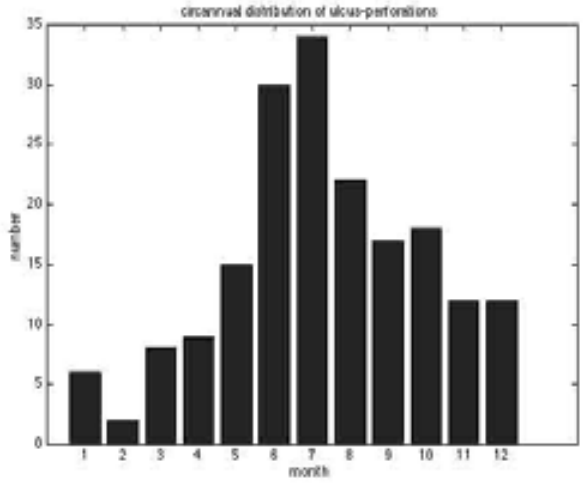


Fig. 1
Circannual distribution of ulcer perforations as described by *Bsteh (1)*

Other observations (3,4,5,6,7)

In his "Textbook of Internal Medicine" (1949), the Viennese Professor of Internal Medicine, *Ernst Lauda* (3), who was a very experienced practical physician, describes his observations on patients regarding the "grand periods" whose duration "may vary between 14 days and several months". – without statistics and references. He attributes the circannual peak of symptoms in patients from Vienna to spring and autumn.

As concerns the circadian distribution of pain, he attributes it as well to some possible endogenous rhythm such as to the periodicity of food intake. He states that after a meal there usually follows a "pain-free" interval of 2 to 3 hours. Independent of food intake, a typical time of pain starts between about midnight and 2 am.

In 1986 and 1987 *Moore* and *Halberg* (4,5) studied persons with active gastric ulcer and concluded that the circadian rhythm of unstimulated gastric acid secretion, observed in the clinically healthy and in the active ulcer groups, is unrelated to changes in plasma gastrin levels. Gastric acidity has a marked circadian periodicity, with high rates occurring during the evening and low ones early in the morning.

According to *Savarino et al.* (6), who studied a population in the city of Genova (Italy) in the years 1987 to 1992, the occurrence of duodenal ulcer is characterised by seasonal variations, which the authors describe as "poorly understood". They furthermore considered the question if and how variations of acidity and *Helicobacter* were synchronous. They examined whether these two important variables had similar seasonal fluctuations in patients with duodenal ulcer. The authors evaluated circadian gastric pH in 319 patients with duodenal ulcer during the years 1987 to 1992. The *Helicobacter pylori* infection was observed by histology in 171 patients examined in the period from 1990 to 1992. It was observed that the fluctuation of duodenal ulcer occurrence during the course of a year showed an evident increase in autumn (October to December) and in winter (January to March). The authors furthermore concluded that there was no parallel circannual fluctuation of duodenal ulcer, gastric acidity, and *Helicobacter pylori* infection.

For duodenal ulcer perforation, the circannual pattern was characterised by a 6-month rhythm, with significantly higher incidence in May-June-July and in November-December periods in most subgroups. A circaseptan rhythm was not found.

The authors summarise their conclusions: While it is likely that exogenous environmental and/or societal factors play a significant role, variations in ulcer perforation may be related to endogenous biological rhythms. The circadian pattern of duodenal perforation follows that for gastric acidity.

Interpretation and Discussion

As far as the problem of circannual cycle is concerned, which was probably for the first time clearly described by O. *Bsteh* in 1952 (1), there appears to be some difference, as compared with other research groups. In this short overview, one further textbook description (3) and two additional studies were mentioned which were performed more recently, in 1996 and 1998.

Bsteh (1) finds a clear peak in June to July.

Lauda (3) mentions spring and autumn as typical times for the outbreak of ulcer disease.

Savarino et al. (6) finds a high incidence in October to December and in January to March.

Svanes et al. (7) finds a circasemiannual periodicity with peaks in May to July and November to December.

The group of patients who were observed by *Bsteh* (1) in the hospital of Lower Austria were mainly farmers. In his book he speaks of a "homogeneous group". His interpretation of the main peak of ulcer perforation is derived from the fact that the highest physical and psychological load in farmers is connected with the time before and during the harvest season. During this time, in addition to the daily load, the time of sleep is reduced. Furthermore, during this time climatic events, heat, rain, and thunderstorms, as well as variation of barometric pressure may have influence on the autonomic nervous system.

Besides environmental factors and endogenous rhythms a third influence is important: *Bsteh* (1) discusses in detail the importance of personal constitution and, particularly, the increased "vagotonic" setting of the autonomic control.

Savarino et al. (6) observed that there was no parallel circannual fluctuation of duodenal ulcer, gastric acidity, and *Helicobacter pylori* infections in the studied patients. In addition, it seems noteworthy that, according to *Halberg* (4,5), the circadian time course of plasma gastrin is not in phase with the acidity in the gastric fluid. In other words, there appears no synchronisation between the variables of ulcer, acidity, plasma gastrin, and *Helicobacter* infection.

Svanes (7) mentions that exogenous environmental and/or societal factors play a significant role. He adds the important remark that "the variations in ulcer perforation may be related to endogenous biological rhythms."

It can be concluded that there exist endogenous rhythm generators which, in the presence of pathogenetic factors, permit the arising of symptoms in daily, weekly, and annual periods. It seems noteworthy that, in each of the four publications mentioned here, the timing is different, which may be due to the different occupational

activities of the patients. The phase of periodicity of the ulcer disease is influenced by societal and environmental stress factors. If there are broader peaks or even two distinct peaks in the circannual frequency distribution of certain symptoms of ulcer disease, this may be due to the mixing of different populations, or of groups with different occupations.

The opinion that by the explanation of one of the causes of a disease the complete aetiology has been found is certainly a mistake. Even before the discovery of *Helicobacter* it was clear that the ulcer disease must have several co-operating causes. And even if one of the necessary conditions can now be abolished, the other set of conditions still may be of importance.

The role of a vagotonic shift of the autonomic nervous system was already well known in the older literature. There is no question that acidity of the gastric secretion and the presence of *Helicobacter* belong to essential preconditions of gastric ulcer. However, it seems that there are still many open questions about the interaction of further aetiological components.

A c k n o w l e d g e m e n t

Support MSM 0021622402.

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NOVÝ POHLED NA CHRONOPATOLOGII PEPTICKÉHO VŘEDU

S o u h r n

V roce 1952 Otto Bsteh, známý rakouský chirurg a učitel na lékařské fakultě ve Vídni, publikoval knihu, ve které shrnul své zkušenosti s vývojem peptického vředu. Mimo jiné publikoval pozorování cirkanuální distribuce výskytu perforace vředu v oblasti, kde žily hlavně rolnické rodiny. Vrchol cirkanuální distribuce se objevil mezi červnem a červencem a autor jej vysvětluje působením stresu souvisejícího s obdobím sklizně. Tato publikace by nám měla připomenout, že vedle nedávno odhalené úlohy *Helicobacter pylori* mají také psychosomatické a chronopatologické faktory významnou úlohu v rozvoji ulcerózní choroby.

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