

GASTROESOPHAGEAL REFLUX DISEASE: A PSYCHOLOGICAL PERSPECTIVE OF INTERACTION AND THERAPEUTIC IMPLICATIONS

T. Kamolz

Public Hospital of Zell am See, Zell am See, Austria

Introduction

Never before has the interaction between gastrointestinal disorders and psychosocial factors been analysed more intensively than in the past two decades. Heartburn sufferers represent a heterogeneous group of patients with considerable symptom overlap. The biopsychosocial model of diseases is a remarkable step forward in the process of understanding more about GERD and GERD-like diseases. As shown, several psychological and social aspects have potentially important roles in the presentation and symptom perception of GERD. A primary causative role for these psychological factors remains unproven. However, factors such as stress and coping strategies, personality traits or psychiatric comorbidities interact through recognized psychophysiological or behavioural mechanism to affect the clinical presentation of GERD. Recognizing these possible levels of interaction has significant implications for those who want to understand the development and the sensitivity of GERD-related symptoms as well as diagnostics and selection of optimal treatment.

Gastroesophageal reflux disease (GERD) is a very common chronic condition, particularly frequent in primary care setting, with a high economic burden on Western society, and represents the most common disease of the upper gastrointestinal tract. Approximately 40% of the adult Western population suffer from GERD-related symptoms monthly. Persistent untreated GERD can lead to esophageal strictures, premalignant Barrett's esophagus, and a potential risk of adenocarcinoma of the esophagus [1], [2].

The primary symptoms of GERD are heartburn, epigastric pain or regurgitation, but it may also be associated with extrasophageal manifestations, such as asthma, chest pain and ortholaryngologic disorders.

However, more accurate anamnesis raises an additional spectrum of untypical symptoms which can be linked to GERD [3], [4]. Nevertheless, a symptom is how a person perceives and interprets a stimulus. Therefore, GERD symptoms and the perceived severity are more than the simple pathological reflux of gastric contents back into the esophagus. The purpose of this chapter is to analyse the relationship between GERD and possible psychological aspects such as stress or patients' personality.

A psychological perspective

In daily practice, significant discrepancies occur between endoscopic severity of GERD, and the patient's symptom experience and quality of life impairment. These discrepancies cannot be explained by simple morphologic findings, and usually are considered to be related to psychological factors according to a bio-psycho-social model of disease. Recent advances in the understanding of the interaction between psychological factors and the brain-gut axis, provide a challenging opportunity for all to establish a more comprehensive understanding of GERD. A bio-psycho-social model integrates the various physical and psychosocial factors that contribute to the patient's illness and offers a comprehensive and effective approach for the diagnosis and a multidisciplinary management of GERD.

Since the end of the 1970's, an increased number of studies have been performed in order to establish potential relations between the symptoms and causal factors of GERD on the one side, and psycho-physiological, as well as other psychologically relevant aspects

on the other. Recent studies have shown, that up to 60% of patients with GERD-related symptoms noticed an increase in complaints under conditions of stress [5], [6]. On the basis of pH monitoring of reflux patients, it could be established that less than 20% of the objective reflux episodes accompany subjective reflux symptoms, as seen from the patients point of view [7]. Contrary to this, complaints without objective results are perceived [8] whereby a slight correlation between acid exposure in the esophagus and symptom perception is acknowledged [9].

In recent years, numerous studies in this context have been performed in order to link possible psychophysiological factors such as psychological stress or personality aspects with reflux-associated processes. It must be noted that the majority of these studies proceeded under laboratory conditions and therefore did not take into consideration everyday stress situations, or partly were conducted with healthy individuals. In addition, some of the physiological stressors performed produced highly individual threshold values with respect to their perception, despite defined physical properties and well standardised research practices in relation to the sampling. Furthermore, the intensity of mental stressors depends from motivation as well as the intellectual potential and pre-experiences or expectational attitude are sample dependent. As a consequence of this, some results are under controversial discussion.

The impact of psychological stress on esophageal manometry

In the 1920th [10], [11] the first known tests with respect to changes in motility of the distal esophagus and laboratory induced stress had already been conducted by Jacobson. Approximately 40 years later, Rubin et al [12] conclude that non-propulsive contractions in the distal esophagus can be induced in 5 healthy individuals through burdensome questioning. An other survey [13] investigated the effects of the “cold-pressor-task”, noise disturbance of 100 dB and cognitive problem solving exercises on esophageal manometric values in 25 healthy individuals. A short-lived rise in pressure at the lower esophageal sphincter, followed by relaxation and changes in esophageal motility occurred under both physiological and cognitive stress conditions. Additionally, Ayres et al [14] found comparable results in pa-

tients with irritable colon, as did Anderson et al [15] in 19 patients with non-cardiac chest pain. A significant rise in amplitude of esophagus contraction occurred under a variety of stress conditions, whereby cognitive problem solving exercises proved to be more burdensome than noise disturbance. Other investigations [16], [17] proved that stress is accompanied by a postprandial slowing of sphincter relaxation or gives rise to intensified contraction of the hiatal crura whereby, in principle, a rise in sphincter pressure and reduced reflux occurs. From these results it is possible to infer, that different stress conditions lead to changes in esophagus motility and changes to the lower sphincter, and can thus be partly linked to reflux events. However, changes as a result of long-term stress on the function of the gastroesophageal junction have not been shown.

Psychological stress and pH-monitoring

Several investigations into possible relations between laboratory stress and pH monitoring produced negative results. Bradley et al [6] found no relation between distinct experimental stressors and objective parameters such as the number of reflux episodes, duration of the longest reflux phase or the total acid value of the test phase in 17 reflux patients. Whereas, other physiological parameters such as heart rate and blood pressure rose significantly, providing evidence as to the stressful nature of the test phase. In contrast to the above, patients with subjective links between stress and their reflux symptoms, a significant rise in exclusively subjectively perceived complaints experienced under test conditions. Others [18] achieved partly comparable results in healthy subjects, during the course of their investigations into postprandial reflux. Likewise, Sonnenberg et al [19] found no association of any sort between noise disturbance and acid secretion in the stomach, blood supply to the mucosa in healthy subjects.

Nevertheless, Holtman et al [20] reported interesting findings: the authors investigated the effect of mental stress on the gastric acid secretion with respect to personality traits. The trait “impulsiveness” was found to be a relevant one in healthy subjects. People with highly pronounced “impulsiveness” exhibited a significant rise in acid, whilst the acid values fell in people with less pronounced “impulsiveness”. These results lead

to the conclusion that stress evokes only limited changes in acid secretion. A change would most likely take place in the subgroup of GERD patients with a subjective interaction between stress and perceived symptoms and within the confines of emotion and a defined personality structure. A further moderating variable could be "fear" [21], [22]. This increases in times of stress and leads via the neuronal level, centrally, to a sensitising of physiological processes and thereby to increased symptom and pain perception. That such an event could eventually form the basis for sensitive esophagus or NERD (non-esophagitis reflux disease) in patients, is at the very least, under debate and the subject of current studies. Fundamentally, it is known that patients suffering from endoscopic negative reflux disease display a comparable symptom spectrum and with corresponding intensity, as well as identical disease profile to patients with an erosive disease [23].

Personality traits and symptom perception

As mentioned above, beside impulsiveness and fear, it seems that other characteristics such as social withdrawal, depression or somatisation can also be associated with changes in motility and gastric acid secretion [21], [22], [24]–[26].

Own results [27] on 100 reflux patients support the view that besides partly significant differences in personality, differences in the stress management strategies of routine daily life exist between stress sensitive and unspecified stress reflux patients. Stress sensitive patients favour an intensely active stress management; frequently show aggressive tendencies and are more likely to forego social support respectively display less tendency of flight when under stress. As far as their personality structure is concerned, they perceive themselves as highly achievement orientated, experience at the same time a greater number of physical complaints and tend toward psychosomatic misperceptions. Moreover, a part from more numerous and more stressful reflux symptoms, stress specific reflux patients report further gastrointestinal symptoms. These, despite successful surgical therapy performed in the light of intensifies or displaced symptoms, nevertheless come to the forefront. Significant differences with respect to the time of day (upright versus supine refluxers) at which events occur could also be confirmed.

Over 90% stress sensitive GERD patients can be described as daytime refluxers. Differences in objective parameters (DeMeester Score, esophageal manometry) have not been found. Velanovich et al [28] came to similar conclusions. The authors found no or only slight correlation between the pressure on the lower esophageal sphincter, results from pH monitoring, the degree of GERD and quality of life. Significant links were only found between the number of perceived complaints and quality of life.

Wright et al (under submission) report the data of an experimental investigation, examining whether exposure to psychological stress may produce an increase in objective reflux episodes or modify subjective perceptions of symptoms. The used experimental stressor induced a significant increase in cortisol and state anxiety, but was not associated with any increase in reflux episodes. However, the experimental group was unable to exactly identify their level of symptom severity. The authors conclude that their findings are relevant because they indicate that perception of anxiety or exposure to stress clearly affects the personal ability to interpret accurately the severity of perceived symptoms. Therefore, it might be possible if patients under antireflux medication, when they become stressed they may still perceive themselves to be experiencing reflux symptoms, even if medication was physiologically successful.

The results of a longitudinal study concerning to life stress on chronic symptoms of heartburn have been published by Naliboff et al [29]. In a group of 60 patients with current heartburn symptoms, the authors evaluated the presence of stressful life events retrospectively over a period of 6 months and prospectively for 4 months. In addition, symptom severity, quality of life, anxiety and depression as well as vital exhaustion were measured. Based on the results, they concluded that symptom severity appears to be most responsive to major life events and that vital exhaustion in relation to sustained stress may represent the psychophysiological symptom complex most closely associated with heartburn exacerbation. In contrast, affective and subjective stress ratings were not strongly related to heartburn severity. But depression showed a strong relation to heartburn medication use and anxiety to impaired quality of life. The authors finally suspected that potential mechanisms for these results include an increased level and frequency of esophageal acid

exposure, an inhibition of gastric emptying or a stress-induced hypersensitivity of the esophagus.

On the basis of these reports, it does not seem to be a question of a “psycho-physiological” disease, as was previously thought, even if GERD-related symptoms are significantly more present in patients with psychiatric comorbidities [24], [30]. However, it is certain that GERD, that is, the perception of GERD symptoms as a result of psychological stress, a particular type of personality structure can be influenced in some of the patients. This knowledge should therefore be incorporated in the process of medical diagnosis and therapy of at least this element of patients.

NERD and “functional heartburn”

On the basis of current research, it has to be assumed, however, that NERD is fundamentally not the question of a pure psychological phenomenon. Quigley [31] offers a detailed review of non erosive reflux disease. Cohen and Snape [32] present a plausible hypothetical model of potential psycho-physiological and cognitive interactions between excitatory and inhibitory neuro-humeral substances with stress and their effect on the distal sphincter. Few neuro-physiological studies of the gastroesophageal junction [33], [34] describe nervous reflux and stimulation processes which are responsible for the perception of pain, vomiting or false sensations and which can at least, be indirectly linked to reflux events. Kellow et al [35] or Drossman et al [36] present reviews about fundamental principles of neuro-gastroenterology with respect to physiology and symptom perception.

In 1991, Pustorino et al [37] compared more than 60 patients with GERD-related symptoms, with or without endoscopic evidence of esophagitis, using the Middlesex Hospital Questionnaire to analyse personality traits and manometric findings. The authors did not find any significant differences in psychological traits or manometric data between patients with or without esophagitis, but significant differences between both groups and controls. Neurotic traits were significantly more pronounced in GERD-like patients than in healthy controls or patients without any digestive disorder. In addition, the authors found a close relation between psychological traits and manometric data. Therefore, they concluded that

psychological aspects play a role in the pathogenic process of GERD, even if other aspects may be necessary to develop an esophagitis.

In approximately 40% of NERD patients no evidence for a pathological acid burden on the distal esophagus has been found using pH monitoring. Despite existing parallels to GERD or NERD, the disease profile is described as “functional heartburn” and according to the “Rome II Consensus Report” is categorised under functional esophagus disorders [38]. As per definition, the diagnosis “functional heartburn” is given when primary symptoms (heartburn or chest pain) appear for a period of 12 weeks (within the previous 12 months) and without any pathological explanation such as GERD, achalasia or esophageal motility disorders. Contrary to patients with GERD, there is a significantly stronger link between acid exposure (whether low or normal) in the distal esophagus and the timely perception of symptoms in patients diagnosed with “functional heartburn” [39]. The real cause is unclear, however, hypersensitivity of the receptors in the esophagus to intraluminal stimuli is primarily suspected [39], [40] (hypersensitive esophagus). Shi et al [41] experimentally showed (intra esophageal balloon distention test) that mechanical stimuli lead to symptoms significantly earlier in these patients than in other individuals. Mixed reflux, as a further factor is also discussed [42]. Principally, psychological factors are also discussed alongside the various possible physiological explanations. In contrast to other functional gastrointestinal disorders very few studies exist [22], [43], [44] which concentrate exclusively on possible links between psychological factors and “functional heartburn”, rather, it is more than likely the case that partly highly controversial results exist. The most probable potential factors are stress or fear. Treatment is per se identical with all GERD but with limited success of common antireflux medication [45]. Furthermore, the prescribing of antidepressive medication or pain modulators in low doses are also under discussion.

Is there a possible link between psychological aspects and Barrett’s esophagus or carcinoma?

In general, gastroesophageal reflux disease is a risk factor for adenocarcinoma of the esophagus, and inci-

dence has significantly increased during the past 20 years. Adenocarcinoma may develop from Barrett esophagus which is associated with chronic reflux. Certain factors associated with Barrett's esophagus also hold for esophageal adenocarcinoma: greater severity of reflux symptoms, specific pattern of symptoms (particularly nocturnal), longer duration of symptoms, white race, and male gender or a high body mass index [46], [47]. However, the distribution of these factors over the time and also genders does not match the pattern of adenocarcinoma occurrence well.

It is known that psychological aspects are associated with an impaired immune function and an increased susceptibility to cancer [48], [49]. In this relation, less is known about a possible link between psychological aspects and GERD complications. Based on a MEDLINE research, only 2 studies were found in this relation: In a case report, Dessureault et al [50] reported from the association of Barrett's esophagus and invasive squamous cell carcinoma of the distal esophagus in a young woman with a history of self-induced psychogenic vomiting. This report illustrated the complicated associations between human behavior and pathogenic mechanisms involved in carcinogenesis.

Jansson et al [51] published the results of a nationwide Swedish population-based case-control study. Aim of the study was to evaluate and analyse if stressful psychosocial working conditions might be involved in the etiology of esophageal cancer. The authors hypothesized that eventually work-related stress could decrease the sphincter pressure of the lower esophageal sphincter, thereby promoting reflux, and finally esophageal or gastric cardia adenocarcinoma, respectively that work-related stressors could impair the immune system leading to cancer. As a result of their study, they did not find any associations between job strain and cancer risk, but a moderately strong association between having a covert coping style when treated unfairly at work and developing a tumor. In addition, they analysed that subjects reporting from low work place satisfaction have an almost 3-fold increased risk of an esophageal adenocarcinoma which might be explained by an increased occurrence of reflux secondary to stress response. Nevertheless, the authors concluded that these findings must be interpreted cautiously and that further investigations are needed.

The impact of psychological factors on medical treatment concepts

From the medical point of view, there are two fundamentally different treatment concepts, which can each be followed when indications are clearly defined. In the present chapter, the potential option of endoscopic treatment procedures has been excluded. Generally, the aim of any GERD therapy, besides the achievement of a disease free state, and thereby an improvement in patients quality of life as seen from the patients point of view, is the healing of esophagitis, the prevention of the development of progressive disease and also prevention with respect to the development of a potential Barretts' esophagus. This fundamental aim of therapy can be achieved with the use of antacids, prokinetics, H₂ antagonists and/or proton pump inhibitors. The signal to discuss surgical therapy is only given if suffering is particularly high and quality of life is severely impaired; if complications of GERD have arisen; if a causal functional defect is evident and lastly, if general health of the patient is good enough to withstand an operation [2].

Accompanying medical therapy, patients are in most cases obliged to initiate particular behavioural changes in order to achieve a further improvement in the disease profile [52]. However, no prospective randomized studies exist, which unequivocally and wholly support the efficacy of these theoretical improvement measures. Here, it is primarily a question of behaviour related measures of everyday habits, and a consequence of this is the emergence of the first possible psychologically oriented interventions. It is common known that it is not always easy, despite medical advice, to effect behavioral change or the abandonment of daily rituals (e.g., weight reduction, eating behaviour, stress management). This is often only achievable through appropriate psychological intervention.

Independently from the medical treatment option, the patients' view and expectations in a therapy becomes an important factor in relation to compliance and therefore also for efficacy. Own data [53] show, that patients expectations in a PPI therapy are as follows: The leading expectations have been: (1) an improvement (61%) or elimination (33%) of perceived symptoms; (2) healing of esophagitis (50%); (3) in 46% of the patients a return to normal daily life and in 44% an improvement of quality of life respectively. A

number of 36% expected no further therapy following this initial treatment, 34% no side-effects of PPI treatment, and only 4% had no real expectations in a prescribed antireflux medication. The same as for medical treatment, an improvement of symptoms is the leading expectation of patients in a possible antireflux operation [54]. In contrast, none of the surgical patients expect an elimination of all perceived symptoms. This result is in relation to previous findings suggesting that even if not all symptoms are eliminated, patients satisfaction with treatment can be high and quality of life may be improved [55], [56].

Nevertheless, GERD is a chronic condition and the majority of the patients' need a life-long medication to treat their symptoms. In this relation it has to be stated that a long-term use of drug therapy is always a question of patients expectations and compliance, even if a "on demand" therapy is under debate. As previously shown [57], approximately 25% of GERD patients referred to pre-surgical examination are not compliant in relation to medical prescriptions, and about 40% are just partly compliant. The reasons for being non-compliant are, in general, a rejection of any kind of medication use, less information about GERD, low severity of GERD, but also an aspect of patients' personality which also affects quality of surgical outcome. In general, next to medical compliance also the aspect of health care seeking has to be seen in relation to patients' personality. As shown by Johnston et al [58], health care seeking in heartburn suffers is in relation to factors such as increased phobia, obsessionality, somatization, and less social support when compared with heartburn suffers who had never sought medical help. Therefore, aspects such as health care seeking or compliance with prescribed medication are associated with psychological and social factors.

Interventions from a psychological view

Several studies have been conducted from a psychological point of view. These investigated the effect of biofeedback on the lower esophageal sphincter pressure and on reflux symptoms [59]–[61]. Due to the high technological cost involved, most of these were single case studies. Gordon et al [61] used biofeedback to alter the resting pressure of the lower esophageal sphincter from 2.7 mmHg to 8.7 mmHg in only 10 sittings in a

patient who had been suffering from GERD-related symptoms for 8 years. At the same time, reflux symptoms and also the number of single reflux events were significantly reduced. The effect of hypnosis induced deep relaxation on gastric acid secretion was investigated and a reduction in the latter was evident [62]. This technique is nevertheless concerned with a selective method which presupposes a special choice of patient and is therefore of only limited application.

Only one systematically applied investigation was concerned with the effect of progressive muscle relaxation (originally by Jacobson) on reflux events. This relaxation technique is easy to learn, efficient and is successfully practised in phobia therapy, stress management or on patients with gastrointestinal disorders. McDonald-Haile et al [63] were able to show that progressive muscle relaxation, leads to a reduction in subjective symptoms, as well as to an objectively lower acid exposition in the esophagus. Additionally, an anxiolytic effect was also achieved. Unclear, however, is the exact mode of operation of this relaxation on reflux events. According to the authors, in the context of perceptual changes, not only is it possible to directly influence the gastroesophageal junction and the hiatal crura, it is also possible to influence these areas via an anxiolytic change in the form of a moderation process.

In contrast to medical therapy, surgical intervention studies substantiate the effect of psychological factors on the subjective quality of the results [64], [65]. Personality traits seem to play an essential role in the subjective assessment of stress on postoperatively essential adaptation processes (e.g., eating behavior) as well as in the subjective assessment of dysphagia and satisfaction with surgery. As previously shown [65], the subjective degree of swallowing problems after laparoscopic anti-reflux surgery is predictable by patients personality in relation to the possibility to cope with a postoperative situation. The used construct "locus of control" showed that patients with an increased believe in luck or fate respectively a low degree of personal abilities suffered from a significantly higher degree of subjective dysphagia but without any objective evidence.

Also in respect to patients' personality, using the same construct as described before, the initial degree of compliance with former antireflux medication seems to be a good predictor of surgical outcome. Own data [66] have shown that surgically treated pa-

tients with former non-compliance with medication are eventually limited good candidates for surgery. In contrast to compliant patients, these group of patients significantly suffered from higher a degree of dysphagia and other so called surgical side-effects (e.g., gas-related problems), needed postoperatively more additional medical intervention including redo-surgery, and quality of life improvement or patients' satisfaction was comparable negatively affected. In relation to these findings, initial results of an existing intervention study substantiate with respect to this the positive effect of an additional, psychological intervention on surgical patients [67].

The effect of psychiatric comorbidities on treatment

Finally, an essential aspect should be pointed out: It is certain that a not inconsiderable number of psychiatric disorders can appear as comorbidity to gastrointestinal diseases [68]–[70]. As Avidan et al [30] have show, GERD-related symptoms significantly occur more frequently in patients with than without a diagnosed psychiatric disorder. The reflux symptoms are not associated with any specific type of psychotropic medication, type of psychiatric disorder, the lifestyle did not influence the presence of reflux symptoms and, in general, may reflect a reduced threshold for or distorted perception of symptoms. In this respect, prevalence between 5% and 20% are put forward according to disorder profile. Depression and panic disorders are in the forefront [71]. The literature alludes to possible associations with the emergence of panic disorder where there are existing functional esophageal disorders, just as there can be with GERD [72], [73]. In this relation, Stanghellini [74] has shown that the most notable factors for the development of upper gastrointestinal symptoms, including GERD-related symptoms, were found to be various indicators of psychological stress and psychiatric disorders.

Behavioural techniques exist in the treatment of panic disorders with GERD symptoms. Own results, also, surprisingly substantiate a positive effect of laparoscopic antireflux surgery in GERD patients with comorbidity of a panic disorder. In this way, the elimination of anxiety disorders in one third of these patients was achieved within the first few postoperative

months [75]. In contrast, other psychiatric comorbidities in GERD patients are able to affect surgical outcome negatively [76]–[78]. As previously published [78], GERD patients with major depression as a comorbidity, when treated with laparoscopic Nissen fundoplication, show a significant lower quality of life improvement and a higher degree of swallowing problems or postoperative adaptation problems in comparison to patients who underwent a Toupet fundoplication. The authors concluded that eventually a Toupet fundoplication, independently from manometric findings, could be beneficial in such a group of patients with psychiatric comorbidities to improve subjective surgical outcome. However, further investigations in this field are needed and could be helpful for all, gastroenterologists as well as surgeons, to find an optimal procedure resulting in a high level of patients satisfaction and quality of life improvement. In conclusion, GERD patients with psychiatric disorders are rarely satisfied with the results of antireflux surgery. Moreover, these patients demonstrated less symptomatic relief than patients without psychiatric disorders. These results suggest that even patients who might otherwise be candidates for antireflux surgery may have a poor symptomatic outcome, if they also have psychiatric comorbidities. Antireflux surgery in these patients should be approached with great trepidation!

Conclusion

Gastroesophageal reflux disease (GERD) can be traced back to disorders of the gastroesophageal junction. But several psychological factors and psychiatric disorders interact through recognized psychophysiological or behavioural mechanisms to affect the clinical presentation and treatment outcome. Even if many aspects are still unknown, the following is conceivable: that well defined personality factors moderate the effect of stress on the gastroesophageal junction, just as they can influence the perception and assessment of symptoms. Additionally, psychiatric disorders as comorbidities can also accompany GERD. For this reason, it is necessary to consider if an extension of hitherto psychological interventions could be helpful in patients with a subjective link between reflux and stress on an emotional personality related level, or in patients with attendant psychiatric disorders. This broadening relates both to the conserva-

tive use of antireflux medication and to surgical therapy, since a postoperative shift in symptoms can occur. The effectiveness of psychological interventions in several gastrointestinal patient groups could already be shown in the past. Whereas evidence for their effectiveness in patients suffering with GERD is partly still outstanding and should be investigated in the future especially as several individual promising starts have been made.

References

- [1] Armstrong D (1994) Reflux disease and Barrett's oesophagus. *Endoscopy* 26: 9–19
- [2] Dent J, Brun J, Fendrick AM et al (1999) An evidence-based appraisal of reflux disease management – the Genval Workshop report. *Gut* 44: 1–16
- [3] Klauser AG, Schindlbeck NE, Müller-Lissner SA (1990) Symptoms in gastro-oesophageal reflux disease. *Lancet* 335: 205–208
- [4] Heading RC, Castell DO (2003) Clinical spectrum and diagnosis of gastroesophageal reflux disease. In: *The esophagus* (Castell DO, Richter JE, eds). Philadelphia: Lippincott, pp 381–388
- [5] A Gallup survey on heartburn across America (1988) The Gallup organisation. New York: Princeton
- [6] Bradley A, Richter JE, Pulliam TJ et al (1993) The relationship between stress and symptoms of gastroesophageal reflux: the influence of psychological factors. *Am J Gastroenterol* 88: 11–19
- [7] Baldi F, Ferrarini P, Longanesi A et al (1989) Acid gastroesophageal reflux and symptom occurrence. Analysis of some factors influencing their association. *Dig Dis Sci* 34: 1890–1893
- [8] Johnson DA, Winters C, Spurling TJ et al (1987) Esophageal acid sensitivity in Barrett's esophagus. *J Clin Gastroenterol* 9: 23–27
- [9] Singh S, Richter JE, Bradley LA, Haile JM (1993) The symptom index: differential usefulness in suspected acid-related complaints of heartburn and chest pain. *Dig Dis Sci* 38: 1402–1408
- [10] Jacobson E (1925) Voluntary relaxation of the esophagus. *Am J Physiol* 72: 387–392
- [11] Jacobson E (1927) Spastic esophagus and mucous colitis. *Arch Int Med* 39: 433–438
- [12] Rubin J, Nagler R, Spiro HM, Pilot ML (1962) Measuring the effect of emotions on esophageal motility. *Psychosom Med* 24: 170–176
- [13] Young LD, Richter JE, Anderson KO et al (1987) The effects of psychological and environmental stressors on peristaltic esophageal contractions in healthy volunteers. *Psychophysiology* 24: 132–141
- [14] Ayres RCS, Robertson DAF, Naylor K, Smith CL (1989) Stress and oesophageal motility in normal subjects and patients with irritable bowel syndrome. *Gut* 30: 1540–1543
- [15] Anderson KO, Dalton CB, Bradley LA, Richter JE (1989) Stress induces alterations of esophageal pressures in healthy and non-cardiac chest pain patients. *Dig Dis Sci* 34: 83–91
- [16] Penagini R, Bartesaghi B, Bianchi PA (1992) Effect of cold stress on postprandial lower esophageal sphincter competence and gastroesophageal reflux in healthy subjects. *Dig Dis Sci* 37: 1200–1205
- [17] Mittal RK, Stewart WR, Ramahi M et al (1992) Psychological stress increases tonic and phasic activity of the crural diaphragm and impairs relaxation of the lower esophageal sphincter. *Gastroenterol* 102: A487
- [18] Cook IJ, Collins SM (1986) Does acute emotional stress influence frequency or duration of gastroesophageal reflux in human subjects? *Gastroenterol* 90: A1380
- [19] Sonnenberg A, Donga M, Erckenbrecht JF, Wienbeck M (1984) The effect of mental stress induced by noise on gastric acid secretion and mucosal blood flow. *Scand J Gastroenterol* 19: 45–48
- [20] Holtman G, Kriebel R, Singer MV (1990) Mental stress and gastric acid secretion: do personality traits influence the response? *Dig Dis Sci* 35: 998–1007
- [21] Baker LH, Lieberman D, Oehlke M (1995) Psychological distress in patients with gastroesophageal reflux disease. *Am J Gastroenterol* 90: 1797–3
- [22] Johnston BT, Lewis SA, Collins SA et al (1995) Acid perception in gastro-oesophageal reflux disease is dependent on psychosocial factors. *Scand J Gastroenterol* 30: 1–5
- [23] Tew S, Jamieson GG, Pilowsky I, Myers J (1997) The illness behavior of patients with gastroesophageal reflux disease with and without endoscopic esophagitis. *Dis Esophagus* 10: 9–15
- [24] Nielzen S, Pettersson KI, Regnell G, Svenson R (1986) The role of psychiatric factors in symptoms of hiatus hernia or gastric reflux. *Acta Psychiatr Scand* 73: 214–220
- [25] Clouse RE, Lustman PJ (1983) Psychiatric illness and contraction abnormalities of the esophagus. *N Engl J Med* 309: 1337–1342
- [26] Feldman M, Walker P, Goldschmidt M, Cannon D (1992) Role of affect and personality in acid secretion and serum gastrin concentration. *Gastroenterol* 102: 175–180
- [27] Kamolz T, Bammer T, Wykypiel H Jr, Pointner R (1999) Streßverarbeitung und Persönlichkeitsstruktur

- bei Patienten mit und ohne streßassoziierter Symptomatik der gastroösophagealen Refluxkrankheit. *Z Gastroenterol* 37: 265–270
- [28] Velanovich V, Karmy-Jones R (1998) Measurement gastroesophageal reflux disease: relationship between health-related quality of life score and physiologic parameters. *Am Surg* 64: 649–653
- [29] Naliboff BD, Mayer M, Fass R et al (2004) The effect of life stress on symptoms of heartburn. *Psychosom Med* 66: 426–434
- [30] Avidan B, Sonnenberg A, Giblovich H, Sontag SJ (2001) Reflux symptoms are associated with psychiatric disease. *Aliment Pharmacol Ther* 15: 1907–1912
- [31] Quigley EM (2001) Non-erosive reflux disease: Part of the spectrum of gastro-oesophageal reflux disease, a component of functional dyspepsia, or both? *Eur J Gastroenterol Hepatol* 13: S13–S18
- [32] Cohen S, Snape WJ Jr (1977) The role of psychophysiological factors in disorders of oesophageal function. *Clin Gastroenterol* 6: 569–579
- [33] Goyal RK, Skarupta JN, Saha JK (1992) Properties of esophageal mechanosensitive receptors. In: *Advances in the innervation of the gastrointestinal tract* (Holle GE, Wood JD, eds). Elsevier, pp 523–537
- [34] Grundy D (1992) Extrinsic reflex pathways in the upper gastrointestinal tract and their central processing. In: *Advances in the innervation of the gastrointestinal tract* (Holle GE, Wood JD, eds). Elsevier, pp 539–546
- [35] Kellow JE, Delvaux M, Azpiroz F et al (1999) Principles of applied neurogastroenterology: physiology/motility-sensation. *Gut* 45: 17–24
- [36] Drossman DA, Creed FH, Olden KW et al (1999) Psychosocial aspects of functional gastrointestinal disorders. *Gut* 45: 25–30
- [37] Pustorino S, Guerrisi O, Calipari G et al (1991) Psycho-emotional distress and gastroesophageal reflux syndrome. *Minerva Gastroenterol Dietol* 37: 1–9
- [38] Clouse RE, Richter JE, Heading RC et al (1999) Functional esophageal disorders. *Gut* 45 (Suppl 11): 31–36
- [39] Janssens JP, Vantrappen G (1992) Irritable esophagus. *Am J Med* 92: 27–32
- [40] Trimble KC, Pryde A, Heading RC (1995) Lowered oesophageal sensory thresholds in patients with symptomatic but not excess gastro-oesophageal reflux disease: evidence for a spectrum of visceral sensitivity in GORD. *Gut* 37: 7–12
- [41] Shi G, Tatum RP, Joehl RJ, Kahrilas PJ (1999) Esophageal sensitivity and symptom perception in gastroesophageal reflux disease. *Curr Gastroenterol Rep* 1: 214–219
- [42] Vaezi MF, Richter JE (1999) Importance of duodeno-gastro-esophageal reflux in the medical outpatient practice. *Hepatogastroenterol* 46: 40–47
- [43] Norton GR, Norton PJ, Asmundson GJ et al (1999) Neurotic butterflies in my stomach: the role of anxiety, anxiety sensitivity and depression in functional gastrointestinal disorders. *J Psychosom Res* 47: 233–240
- [44] Johnston BT, Lewis SA, Love AH (1995) Stress, personality and social support in gastro-oesophageal reflux disease. *J Psychosom Res* 39: 221–226
- [45] Fass R, Tougas G (2002) Functional heartburn: the stimulus, the pain, and the brain. *Gut* 51: 885–892
- [46] Chang JT, Katzka DA (2004) Gastroesophageal reflux disease, Barrett esophagus, and esophageal adenocarcinoma. *Arch Intern Med* 164: 1482–1488
- [47] Shaheen N, Ransohoff DF (2002) Gastroesophageal reflux, Barrett esophagus, and esophageal cancer: scientific review. *JAMA* 287: 1972–1981
- [48] Garssen B (2002) Psycho-oncology and cancer: linking psychosocial factors with cancer development. *Ann Oncol* 13: S171–S175
- [49] Kiecolt-Glaser JK, Robles TF, Heffner KL et al (2002) Psycho-oncology and cancer: psychoneuroimmunology and cancer. *Ann Oncol* 13: S165–S169
- [50] Dessureault S, Coppola D, Weitzner M et al (2002) Barrett's esophagus and squamous cell carcinoma in a patient with psychogenic vomiting. *Int J Gastrointest Cancer* 32: 57–61
- [51] Jansson C, Johansson ALV, Jeding K et al (2004) Psychosocial working conditions and the risk of esophageal and gastric cardia cancers. *Europ J Epidemiol* 19: 631–641
- [52] Meinig A, Classen M (2000) The role of diet and lifestyle measures in the pathogenesis and treatment of gastroesophageal reflux disease. *Am J Gastroenterol* 95: 2692–2697
- [53] Kamolz T, Pointner R (2004) What do heartburn sufferers expect from proton pump inhibitors when prescribed for the first time? *Minerva Gastroenterol Dietol* 50: in press
- [54] Kamolz T, Pointner R (2002) Expectations of GERD patients in the outcome of laparoscopic antireflux surgery. *Surg Laparosc Endosc Percutan Techn* 12: 389–392
- [55] Contini S, Bertelé A, Nervi G et al (2002) Quality of life for patients with gastroesophageal reflux disease 2 years after laparoscopic fundoplication. *Surg Endosc* 16: 1555–1560
- [56] Klapow JC, Wilcox M, Malinger AP et al (2002) Characterization of long-term outcomes after Toupet fundoplication. *J Clin gastroenterol* 34: 509–515

- [57] Kamolz T (2002) Analysis of medical compliance in gastro-oesophageal reflux disease patients referred to pre-surgical examination. *Digest Liver Dis* 34: 183–189
- [58] Johnston BT, Gunning J, Lewis SA (1996) Health care seeking by heartburn sufferers is associated with psychosocial factors. *Am J Gastroenterol* 91: 2500–2504
- [59] Schuster MM (1983) Disorders of the esophagus: application of psychophysiological methods in treatment. In: *Psychophysiology of the gastrointestinal tract* (Hözl R, Whitehead WE, eds). New York: Plenum, pp 33–42
- [60] Shay SS, Johnson LF, Wong RKH et al (1986) Rumination, heartburn, and daytime gastroesophageal reflux: a case study with mechanism defined and successfully treated with biofeedback therapy. *J Clin Gastroenterol* 8: 115–126
- [61] Gordon A, Gordon E, Berelowitz M et al (1983) Biofeedback improvement of lower esophageal sphincter pressures and reflux symptoms. *J Clin Gastroenterol* 5: 235–237
- [62] Klein KB, Spiegel D (1989) Modulation of gastric acid secretion by hypnosis. *Gastroenterol* 96: 1383–1387
- [63] McDonald-Haile J, Bradley LA, Baily MA et al (1994) Relaxation training reduces symptom reports and acid exposure in patients with gastroesophageal reflux disease. *Gastroenterol* 107: 61–69
- [64] Watson DI, Chan ASL, Myers JC, Jamieson GG (1997) Illness behavior influences the outcome of laparoscopic antireflux surgery. *J Am Coll Surg* 184: 44–48
- [65] Kamolz T, Bammer T, Pointner R (2000) Predictability of dysphagia after laparoscopic Nissen fundoplication. *Am J Gastroenterol* 95: 408–414
- [66] Kamolz T, Granderath FA, Pointner R (2003) The outcome of laparoscopic antireflux surgery in relation to patients' subjective degree of compliance with former antireflux medication. *Surg Laparosc Endosc Percutan Tech* 13: 155–160
- [67] Kamolz T, Granderath FA, Bammer T et al (2001) Psychological intervention influences the outcome of laparoscopic antireflux surgery in patients with stress-related symptoms of gastroesophageal reflux disease. *Scand J Gastroenterol* 36: 800–805
- [68] Walker EA, Katon WJ, Jemelka RP, Roy-Bryne PP (1992) Comorbidity of gastrointestinal complaints, depression, and anxiety in the Epidemiologic Catchment Area (ECA) Study. *Am J Med* 92: 26–30
- [69] Hochstrasser B, Angst J (1996) The Zürich Study: XXII. Epidemiology of gastrointestinal complaints and comorbidity with anxiety and depression. *Eur Arch Psychiatry Clin Neurosci* 246: 261–272
- [70] Mayer EA, Craske M, Naliboff BD (2001) Depression, anxiety, and the gastrointestinal system. *J Clin Psychiatry* 62: S28–S37
- [71] Lydiard RB, Greenwald S, Weissman MM et al (1994) Panic disorder and gastrointestinal symptoms: findings from the NIMH Epidemiologic Catchment Area project. *Am J Psychiatry* 151: 64–70
- [72] Wiklund I, Butler-Wheelhouse P (1996) Psychosocial factors and their role in symptomatic gastroesophageal reflux disease and functional dyspepsia. *Scand J Gastroenterol* 220: S94–S100
- [73] Locke GR 3rd, Weaver AL, Melton LJ 3rd, Talley NJ (2004) Psychosocial factors are linked to functional gastrointestinal disorders: a population based nested case-control study. *Am J Gastroenterol* 99: 350–357
- [74] Stanghellini V (1999) Relationship between upper gastrointestinal symptoms and lifestyle, psychosocial factors and comorbidity in the general population: results from the Domestic/International gastroenterology Surveillance Study (DIGEST). *Scand J Gastroenterol* 231: 29–37
- [75] Kamolz T, Bammer T, Granderath FA, Pointner R (2001) Laparoscopic antireflux surgery in GERD patients with concomitant anxiety disorders. *Dig Liver Dis* 33: 659–664
- [76] Velanovich V (2003) The effect of chronic pain syndromes and psychoemotional disorders on symptomatic and quality of life outcomes of antireflux surgery. *J Gastrointest Surg* 7: 53–58
- [77] Velanovich V, Karmy-Jones R (2001) Psychiatric disorders affect outcomes of antireflux operations for gastroesophageal reflux disease. *Surg Endosc* 15: 171–175
- [78] Kamolz T, Granderath FA, Pointner R (2003) Does major depression affect the outcome of laparoscopic antireflux surgery. *Surg Endosc* 17: 55–60