Chapter 2
Subgroups of Dyspepsia

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INTRODUCTION
Dyspepsia is a common symptom with an extensive differential diagnosis and a heterogeneous pathophysiology. Its prevalence by itself implies a great health care problem, even though most do not seek medical care [1, 2]. Dyspepsia is responsible for substantial health care costs and considerable time lost from work [3]. The management of dyspepsia represents a major component of clinical practice at the primary care level, and 2% to 5% of family practice consultations are for dyspepsia [4].

The term dyspepsia is derived from the Greek word meaning bad digestion. The condition was described 2,000 years ago. It is a complex of symptoms referable to the upper gastrointestinal tract, but not all clinicians and researches agree on which symptoms should be included in its definition. Guidelines from UK and Canada use the term to mean all symptoms referable to the upper gastrointestinal tract, whereas Rome II definition from 1999 excludes patients with classic heartburn and regurgitation [5–7].

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An international committee of clinical investigators (Rome III Committee) defined dyspepsia as one or more of the following symptoms [1]:

- Postprandial fullness
- Early satiation (meaning inability to finish a normal size meal or postprandial fullness)
- Epigastric pain or burning

Patients with symptoms of dyspepsia who have not undergone any investigations are defined as having uninvestigated dyspepsia. Diagnostic investigation (upper gastrointestinal endoscopy, laboratory, and X-ray) reveals normal findings in 40% to 60% of individuals (functional dyspepsia group), and in the others, organic or structural causes of the symptoms can be found (Table 2.1) [8, 9].

**Table 2.1. Structural or biochemical causes of dyspepsia.**

<table>
<thead>
<tr>
<th>Structural or biochemical causes</th>
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<tbody>
<tr>
<td>Gastroesophageal reflux disease (GERD)</td>
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<td>Peptic ulcer disease</td>
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<td>Gastric or esophageal cancer</td>
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<td>Biliary pain</td>
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<td>Medications (including potassium supplements, digitalis, iron, theophylline, oral antibiotics, especially ampicillin and erythromycin, NSAIDs, corticosteroids, niacin, gemfibrozil, narcotics, colchicine, quinidine, estrogens, and levodopa)</td>
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<td>Gastroparesis</td>
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<td>Pancreatitis</td>
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<td>Carbohydrate malabsorption</td>
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<td>Infiltrative diseases of the stomach (e.g., Crohn’s disease, sarcoidosis)</td>
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<td>Metabolic disturbances (hypercalcemia, hyperkalemia)</td>
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<td>Hepatoma</td>
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<td>Ischemic bowel disease</td>
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<tr>
<td>Systemic disorders (diabetes mellitus, thyroid, and parathyroid disorders, connective tissue disease)</td>
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<tr>
<td>Intestinal parasites (giardia, strongyloides)</td>
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<td>Abdominal cancer, especially pancreatic cancer</td>
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**ORGANIC OR STRUCTURAL DYSEPSIA**

In patients with organic or structural dyspepsia, there are three major causes of dyspepsia: gastroesophageal reflux (with or without esophagitis), chronic peptic ulcer disease, and malignancy.
The prevalence of gastroesophageal reflux disease (GERD) is 25% in dyspepsia. Erosive esophagitis is found at endoscopy in 5% to 15% of the cases. The predominant symptom of GERD, heartburn, is not a reliable indicator in differentiation between GERD and dyspepsia. The probability of GERD in the setting of dominant heartburn is 54% [10].

A peptic ulcer is found in approximately 5% to 15% of patients with dyspepsia (see more in Chap. 10) [11].

Gastric or esophageal adenocarcinoma is found in less than 2% of all patients referred to endoscopy to evaluate dyspepsia [12]. Alarm features are used to try and identify patients who need early investigation with endoscopy (see Table 6.1). The sensitivity, specificity, positive, and negative predictive values vary greatly (see Chap. 8) [13].

Other causes of organic dyspepsia are rare. Classic biliary pain can be differentiated from dyspepsia by its clinical picture. It occurs as episodic acute and severe upper abdominal pain, usually in the epigastrium or right upper quadrant, and lasts for at least 1 h (often several hours or more). The pain may radiate to the back or scapula and is often associated with restlessness, sweating, or vomiting. Episodes are typically separated by weeks to months. Gallstones are sometimes implicated as the source of symptoms in patients with dyspepsia. However, such an association should be made cautiously, since gallstones may silently coexist in patients with dyspepsia [14].

Nonsteroidal anti-inflammatory drugs (NSAIDs) can cause dyspepsia. If dyspepsia occurs, their use should be discontinued whenever possible. A meta-analysis found a greater degree of risk reduction in dyspepsia when patients were on proton pump inhibitors [15].

Several other drugs have been implicated as causes of dyspepsia. The use of calcium channel blockers, methylxanthines, alendronate, orlistat, potassium supplements, acarbose, and certain antibiotics, including erythromycin and metronidazole, should also be considered as a potential factor [16].

Gastroparesis results from a range of muscular, neural, or rhythm disorders of the stomach. It is more common in women and in diabetic patients [17].

While chronic pancreatitis, celiac disease, and lactose intolerance may coexist with dyspepsia, they are uncommon causes of the condition [18–20].

Other rare causes of dyspepsia include infiltrative diseases of the stomach (Mb Crohn, eosinophilic gastritis, sarcoidosis), metabolic disturbances (hypercalcemia, hyperkalemia), intestinal
angina, intestinal parasites (giardia, strongyloides), hepatoma, and pancreatic cancer [12, 20].

FUNCTIONAL DYSPEPSIA
Functional dyspepsia (FD) is defined as at least a 3-month history of dyspepsia in the absence of any organic, systemic, or metabolic disease that is likely to explain the symptoms [1]. The pathophysiology of FD is unclear. Putative mechanisms include overlapping disorders of upper gastrointestinal motor and sensory function. Approximately 25% to 45% of the patients have delayed gastric emptying, 40% have impaired fundic accommodation, and visceral hypersensitivity occurs in about one third of the patients [21–23]. A specific symptom profile for these subsets of patients does not exist [24]. Psychological distress, including abuse, has been associated with dyspepsia, but a cause-and-effect relationship has not been established [25].

In the past 20 years, several attempts have been made to try to subclassify patients with FD to a subgroup with similar pathophysiological mechanisms and/or symptoms, what would be of help to physicians and researchers.

The Rome I and Rome II consensuses define FD as the presence of pain or discomfort in the upper abdomen in the absence of organic disease. The Rome II definition excluded patients with predominant heartburn and patients with irritable bowel syndrome. Symptoms must be present for at least 12 weeks, which do not need to be consecutive, within the preceding 12 months [7, 26].

The Rome II consensus subdivided patients with dyspepsia in three subgroups:

• Ulcer-like dyspepsia (pain centered in the upper abdomen is the predominant and most bothersome symptom)
• Dysmotility-like dyspepsia (an unpleasant or troublesome non-painful sensation or discomfort centered in the upper abdomen is the predominant symptom; this sensation may be characterized by or associated with upper abdominal fullness, early satiety, bloating, or nausea)
• Unspecified (nonspecific) dyspepsia (symptomatic patients whose symptoms do not fulfill the criteria for ulcer-like or dysmotility-like dyspepsia)

The Rome II subdivision has been criticized because of the difficulty distinguishing pain from discomfort, the lack of an
accepted definition of the term predominant, number of patients who do not fit into one of the subgroups, and especially the lack of stability of the predominant symptom even over short time periods [27–29].

The Rome III committee decreased the number of FD symptoms to four specific symptoms that originate from the gastroduodenal region [1]:

- Postprandial fullness
- Early satiety
- Epigastric pain
- Epigastric burning

At least one symptom must be present for at least the last 3 months with an onset of symptoms at least 6 months prior to diagnosis.

Other symptoms may coexist, such as bloating (may be derived from the bowel), nausea (often of central origin), vomiting, belching, and heartburn (esophageal origin).

The Rome III committee subdivided FD into two new diagnostic categories:

- Meal-induced postprandial distress syndrome (PDS), characterized by postprandial fullness and early satiety
- Epigastric pain syndrome (EPS), characterized by epigastric pain and burning

**Diagnostic Criteria for PDS (B1a)**
Must include one or both of the following:

1. Bothersome postprandial fullness, occurring after ordinary sized meals, at least several times per week
2. Early satiety that prevents finishing a regular meal at least several times per week

**Supportive Criteria**
1. Upper abdominal bloating or postprandial nausea
2. EPS may coexist

**Diagnostic Criteria for EPS (B1b)**
1. Pain or burning localized in the epigastrium of at least moderate severity at least once per week.
2. The pain is intermittent.
3. Pain not generalized or located in other abdominal or chest regions.
4. Pain not relieved by defecation or passage of flatus.
5. Not fulfilling criteria for gallbladder and sphincter Oddi disorders.

**Supportive Criteria**

1. The pain may be of a burning quality but without a retrosternal component.
2. The pain is commonly induced or relieved by ingestion of a meal but may occur while fasting.
3. PDS may coexist.

In the study of Hsu et al., there was a 34.2% overlap between EPS and PDS. Multiple linear regression analysis demonstrated that the diagnosis of PDS was independently associated with higher scores in overall psychopathological stress. In patients with EPS, the diagnosis was not associated with psychopathology [30].

The Rome III subdivision of FD was proposed under the assumption that different underlying pathophysiological mechanisms are present in each of the subgroups and, consequently, that different treatment modalities would be most suitable for each group. The future research will give us the answer whether this assumption is correct [31] (Fig. 2.1).

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**Fig. 2.1 Rome III subgroups of dyspepsia.**
**CONCLUSIONS**

Dyspepsia is a common symptom with an extensive differential diagnosis and a heterogeneous pathophysiology. Its prevalence for itself implies a great health care problem, even though most do not seek medical care. An international committee of clinical investigators (Rome III Committee) defined dyspepsia as one or more of the following symptoms: postprandial fullness; early satiation (meaning inability to finish a normal size meal, or postprandial fullness); epigastric pain or burning with at least a 3-month history in the last year. After diagnostic investigation (upper gastrointestinal endoscopy, laboratory, and X-ray), 40% to 60% of individuals have normal findings (functional dyspepsia group); in the others, organic or structural causes of the symptoms can be found. The Rome II consensus subdivided patients with dyspepsia in three subgroups: ulcer-like dyspepsia; dysmotility-like dyspepsia, and unspecified (nonspecific) dyspepsia. The Rome III committee subdivided functional dyspepsia into two new diagnostic categories: meal-induced PDS, characterized by postprandial fullness and early satiety, and EPS, characterized by epigastric pain and burning.

**References**

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