

For the Primer, visit [doi:10.1038/nrdp.2017.81](https://doi.org/10.1038/nrdp.2017.81)

➔ Functional dyspepsia is a common functional gastrointestinal disorder that is characterized by discomfort or pain in the upper abdomen with no apparent organic cause. The three subtypes of the condition are: postprandial distress syndrome (PDS), epigastric pain syndrome (EPS) and a subtype with features of both PDS and EPS.

DIAGNOSIS

The diagnosis of functional dyspepsia is based on clinical symptom definitions, as most recently described in the Rome IV criteria. The three subtypes are characterized by their predominant symptoms: PDS by meal-induced dyspeptic symptoms (such as postprandial fullness and early satiety), EPS by epigastric pain or burning that do not exclusively occur after a meal, and overlapping PDS and EPS by combined symptoms.

Dysphagia or odynophagia

Overt gastrointestinal bleeding

New-onset dyspepsia at >55 years of age

Evidence of iron-deficiency anaemia

Persistent vomiting

Unintentional weight loss

Palpable abdominal or epigastric mass or abdominal adenopathy

Family history of gastric or oesophageal cancer

! The presence of alarm symptoms urges further diagnostic work-up, such as endoscopy and ultrasonography, to exclude organic causes of diseases

PATHOPHYSIOLOGY

GASTRO-DUODENAL MOTILITY
Abnormal motility patterns during digestive or interdigestive periods

GASTRO-DUODENAL SENSITIVITY
Hypersensitivity to both mechanical and chemical stimuli

GASTRO-DUODENAL INFLAMMATION
Impaired permeability of the duodenal epithelial barrier, duodenal eosinophilia and subtle mucosal inflammation

Functional dyspepsia is a multifactorial disorder in which different pathophysiological mechanisms play a part, and each one could contribute to all subtypes

ENVIRONMENTAL FACTORS
For example, infections, antibiotic and NSAID use, smoking and overweight

INTESTINAL MICROBIOTA
Conflicting evidence on the role of small intestinal bacterial overgrowth

PSYCHOSOCIAL FACTORS AND BRAIN MECHANISMS
Psychiatric traits (such as anxiety and depression) and states (such as negative mood and stress)

GENETIC FACTORS
Polymorphisms in genes involved in serotonergic, adrenergic and immune functions

EPIDEMIOLOGY

The prevalence of functional dyspepsia varies substantially between countries (5–40%) and is difficult to establish precisely, as its features can overlap with those of other functional gastrointestinal disorders, such as irritable bowel syndrome.

QUALITY OF LIFE

Quality of life measures that are specific for functional dyspepsia take into account the aspects of the disease that are most meaningful to patients (for example, dietary problems). Somatization (multiple, stress-related symptoms of unknown origin) is a major risk factor for impaired quality of life.

Rx MANAGEMENT

Dietary adjustments are recommended for all patients, which include avoiding foods that could trigger symptoms and changing dietary patterns (for example, snacking frequently instead of having regular-sized meals). *Helicobacter pylori* infection should be treated first in those who are infected. Pharmacotherapy should specifically treat the predominant symptoms of each subtype of functional dyspepsia. For example, prokinetic drugs and fundus-relaxing drugs are recommended for PDS, whereas acid-suppressive drugs are recommended for EPS.

OUTLOOK

Progress in the understanding of the pathophysiology of functional dyspepsia has led to a paradigm shift: from a condition that is poorly defined by symptoms and functional abnormalities of uncertain aetiology to a disease that manifests because of the interaction of endogenous and exogenous factors. This new model proposes that in genetically predisposed individuals, enteric infections or food antigens damage the intestinal barrier, setting off an immune response that causes local inflammation and functional gastro-duodenal disturbances. This localized response may evolve to a systemic immune response that could also induce extra-intestinal symptoms, such as anxiety. New treatment options are emerging based on these concepts.