

REVIEW ARTICLE

Definition and Investigation of Dyspepsia

Consensus of an International *Ad Hoc* Working Party

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WHAT IS DYSPEPSIA?

The term "dyspepsia" derives from the Greek words "δυσ" (dus = bad) and "πεπτείν" (peptien = to digest). However, the term "digestion" is variously interpreted and may be used to describe very different processes, from chewing to defecation.

Many definitions of dyspepsia have been proposed over the last 25 years. For example, in 1968, Rhind and Watson described the term "flatulent dyspepsia" as "epigastric discomfort after meals, a feeling of fullness so that tight clothing is loosened, eructation, with temporary relief and regurgitation of sour fluid into the mouth, with heartburn" (1). In 1982, Crean and collaborators described dyspepsia as "any form of episodic or persistent abdominal discomfort or other symptom referable to the alimentary tract, excepting jaundice or bleeding" (2). Some authors use dyspepsia to indicate symptoms resembling those reported by peptic ulcer patients, ie, ulcer dyspepsia. In 1984, Thompson (3) described nonulcer dyspepsia as "chronic, recurrent, often meal-related epigastric discomfort initially suspected to be due to a peptic ulcer, but subsequently found not to be." In the same year, Lagarde and Spiro (4) dealt with the problem of functional dyspepsia and described functional dyspeptics as "those patients with intermittent upper abdominal discomfort in whom a reasonable clinical evaluation has failed to reveal a definite cause of their symptoms.

Because of this lack of agreement, it is not surprising that the word dyspepsia is still regarded with suspicion in the scientific literature, despite widespread use of the term in clinical practice.

Hence, the necessity to define dyspepsia and its variants more carefully in a way that will command general acceptance and avoid confusion with other syndromes, particularly with the "irritable bowel syndrome" which is now recognized as an entity with a group of definable symptoms (5, 6).

We suggest, therefore, that dyspepsia be defined as "episodic or persistent abdominal symptoms, often related to feeding, which patients or physicians believe to be due to disorders of the proximal portion of the digestive tract."

Diseases that may present with dyspepsia are listed briefly in Table 1. In an attempt to relate symptom pattern more precisely to particular diseases, the word dyspepsia may be qualified by other words or phrases, eg, (1) ulcer dyspepsia: the symptoms suggest a peptic ulcer; (2) nonulcer dyspepsia: ulcerlike symptoms when no ulcer is found; (3) flatulent dyspepsia: the symptoms of belching, distension, and early satiety are prominent; (4) biliary dyspepsia: used to describe recurrent biliary pain (biliary colic) as opposed to flatulent dyspepsia associated with gallstones; and (5) functional dyspepsia: defined below.

Dyspeptic symptoms are reported also by patients in whom no disease can be identified. This condition, generally described as functional dyspepsia, may be defined as dyspepsia that is not attributable to structural, drug-induced, alcohol-induced, or metabolic disease, but is thought to be related to disorders of upper gut function or to abnormalities of a patient's perception of normal function. Use of the term functional dyspepsia thus implies that reasonable clinical investigation has been carried out to exclude structural and metabolic disease. How far investigation should go is the dilemma faced by the practicing clinician (see Investigations section below)

Manuscript received May 26, 1988; accepted December 8, 1988.

The working party met initially in Cortina, Italy, in March 1986.

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DYSPEPSIA

TABLE 1. DISEASES FREQUENTLY ASSOCIATED WITH DYSPEPSIA

Structural diseases of the gastrointestinal system
Cholelithiasis
Chronic pancreatitis
Colorectal cancer
Esophagitis
Gastric and duodenal localised lesions (erosions, ulcers)
Gastric cancer
Malabsorption syndromes
Pancreatic cancer
Other intraabdominal malignancies
Structural disease involving other systems
Ischemic heart disease
Collagen diseases
Metabolic conditions
Diabetes mellitus
Hyper/hypo-(para)thyroidism
Electrolyte disorders
Drugs
Alcohol
Nonsteroidal antiinflammatory agents
Digitalis

DYSPEPTIC SYMPTOMS AND THEIR INTERPRETATION

The main symptoms occurring in dyspeptic patients are upper abdominal pain/discomfort, postprandial fullness, early satiety or an inability to finish a normal meal, anorexia, belching, nausea/vomiting, and heartburn/regurgitation. Patients may complain of associated symptoms, such as postprandial drowsiness and headache.

The symptoms of dyspepsia overlap to some extent with those of the irritable bowel syndrome; symptoms common to both include postprandial abdominal fullness and poorly localized abdominal pain and/or discomfort. However, patients with a predominant abnormality in bowel function (constipation or diarrhea) are usually given the diagnosis of irritable bowel syndrome.

The symptoms of patients with functional dyspepsia include a variable combination of the symptoms listed above. Typically they occur during the day and only rarely at night. Bowel function is normal, in contrast to most patients with the irritable bowel syndrome, and frequently there is a personal or family history of stress (2).

The practical evaluation of such patients involves assessment of the symptoms and of nonverbal signals. Diagnosis from the history is frequently, although not always, possible; patterns of symptoms may be recognized and the inconsistency of certain symptom combinations may point to a functional rather than a specific diagnosis. However, the specificity of symptoms is often insufficient to differen-

tiate functional dyspepsia confidently from peptic ulcer disease, a distinction frequently required in gastroenterology outpatient clinics. Computer-assisted evaluations of several hundred of patients with dyspepsia (7) have determined the following as features likely to differentiate dyspepsia due to peptic ulceration from functional dyspepsia: (1) nocturnal pain, which is indicative of ulcer rather than nonulcer dyspepsia, particularly if it is relieved by milk or food; (2) ability to eat soon after vomiting, which is reported by ulcer patients but not those with functional dyspepsia; and (3) localization of upper abdominal pain to a small area of the epigastrium or right hypochondrium suggests ulcer disease; diffuse pain is more typical of functional dyspepsia.

In differentiating functional from biliary dyspepsia (ie, pain from the biliary system), the patient's ability to describe precisely the nature and number of characteristic attacks of right upper quadrant pain favors the diagnosis of gallstones. However, patients with gallstones can also have all the symptoms of flatulent dyspepsia.

HOW ARE THE SYMPTOMS PRODUCED?

Very little is known about the production of dyspeptic symptoms. Even in peptic ulcer disease there is a problem because large ulcers sometimes give no pain and small erosions may be very painful. Experiments in which acid or alkaline solutions are infused onto the mucosa have not been conclusive in defining the basis of pain (8, 9).

In functional dyspepsia, recent studies of gastric motility and emptying have shown abnormalities in a significant proportion of patients but not in all (10-12). The evidence for a relationship between symptoms and a motility disorder comes from three sources: (1) the correlation between symptoms and the disorder (10, 13), although this does not prove a causal relationship; (2) attempts to reproduce the symptoms and the motility disorder (14, 15); and (3) attempts to relieve the symptoms by altering motility without affecting other functions such as secretion (12, 16).

Sensation from the stomach and duodenum probably reaches the central nervous system via sympathetic pathways because all the symptoms can occur after complete vagotomy. Present knowledge on symptom production in dyspeptic patients is summarized in recent articles (17-19).

WHICH INVESTIGATIONS ARE APPROPRIATE?

An investigation may be described as useful if it reliably resolves an uncertainty about diagnosis or treatment in the mind of the clinician. In patients with dyspepsia, the reassurance provided by normal results is often considered to be as valuable as the identification of abnormality, and in consequence normal findings do not in themselves imply that a given investigation was unnecessary. However, this means that the cost effectiveness of individual investigations is difficult to quantify.

Evaluation of the patient with dyspepsia begins with a detailed history and physical examination and should include a dietary history and a brief psychological assessment that may indicate a need for early formal evaluation by a psychiatrist or psychologist. Investigation is undertaken in the light of this first clinical assessment (20–22).

First-Line Investigations that are Widely Available

Hematology (CBC) and Biochemistry (SMAC). Normal results are expected in most patients, but unexpected abnormalities are likely to be important and will often cause a plan of investigation to be modified.

Barium Radiology and Upper Gastrointestinal Endoscopy. These are undoubtedly the most widely employed and most important investigations for dyspeptic patients. In practice, considerations of access and availability may determine the choice between radiology and endoscopy, and most patients need not undergo both. When both techniques are readily available, endoscopy is usually preferable despite its greater cost. Endoscopy is essential for evaluation of the postoperative stomach and if malignancy is considered a serious possibility. For some disorders, however, the diagnostic yield from endoscopy is poor. Gastroesophageal reflux disease, for example, is detected endoscopically in only about 50% of patients with abnormal results on esophageal pH monitoring (23).

Mucosal Biopsies. Distal antral and duodenal biopsies may show erosion or inflammation (24, 25). Erosive gastritis or duodenitis may be responsible for symptoms (26), but the importance of nonerosive inflammation is uncertain. In this connection, the possible role of *Campylobacter Pylori* in causing inflammation and dyspeptic symptoms is of great current interest (27). Duodenal biopsies may

occasionally be diagnostic such as in detection of unsuspected coeliac disease or Whipple's disease.

Pentagastrin Stimulated Acid Secretion. Acid secretion studies have little place in modern clinical evaluation of dyspepsia.

Ultrasonography of Biliary Tract and Pancreas; Cholecystography. These investigations are generally accurate for gallbladder pathology [eg, sensitivity 98%, specificity 93–98% for cholelithiasis (28)] and ultrasonography is widely accepted as the preferred first line assessment of the pancreas (29). Of course, the presence of gallstones does not always mean that they are the cause of a patient's symptoms. With the increasing age of the population and wider availability of ultrasonography, detection of more asymptomatic gallstones can be anticipated.

Stool Inspection and Fecal Occult Blood Tests. In practice, these are undertaken in only a minority of patients with dyspepsia but may give support to a suspicion of associated irritable bowel syndrome or, if blood is present in the stool, establish a requirement for unequivocal diagnosis.

Further Investigation

Additional investigation may be considered for patients with persistent symptoms if clinical assessment and the investigations described above have not achieved a clear diagnosis. Functional dyspepsia is usually a proper diagnosis for such patients, and in many, treatment with one or more drugs has already been attempted. It is the persistence of unexplained distressing symptoms, unrelieved by medication, which justifies performance of further investigation in an attempt to identify abnormalities relevant to or responsible for the symptoms. However, a critical approach to interpretation of these investigations is essential.

Esophageal Manometry and Ambulatory pH Monitoring. These procedures are now available in many centers, but the tests still require careful interpretation in view of variability of techniques employed, uncertainty about what is normal and abnormal, the significance of abnormalities detected, and their relationships to patients' symptoms. The esophagus should be considered a possible source of dyspepsia, particularly if heartburn or epigastric discomfort are prominent symptoms. Provocation tests based on mechanical distension of the esophagus or intraluminal infusion of acid, alkali, or other substances are the subject of research interest but have no established diagnostic role at present.

Bernstein Test. The usefulness of the Bernstein test (8) is restricted by a sensitivity of 50% and a false-positive response rate of 10% in normal individuals (30).

Gastric Emptying Measurements. The chief indications for gastric emptying tests are unexplained postprandial fullness and recurrent vomiting. The measurement may also assist in the evaluation of symptoms in patients who have previously undergone gastric surgery. Radioisotopic techniques with a marker of the solid phase of the meal are preferable (31), but there is much debate on the comparative merits of the various methods that have been reported and on the best way to analyze the results. In addition, interpretation of an abnormal result in an individual patient may be compromised by a "chicken and egg problem": is an observed delay in gastric emptying responsible for dyspeptic symptoms or is there some other basis for the symptoms which themselves induce delayed gastric emptying? Despite these uncertainties, it is clear that a proportion of patients with unexplained dyspepsia exhibit abnormal gastric emptying (11, 12).

Measurement of Duodenogastric Reflux. Radionuclide methods adequately identify major abnormalities (32), particularly in the postoperative stomach. However, the significance of duodenogastric reflux and its causal role in dyspepsia remain uncertain.

Gastrointestinal Manometry. Manometric abnormalities of the stomach and upper small bowel have been found in more than 50% of patients with otherwise unexplained dyspepsia (33), but the cause-effect relationship remains unclear. Sophisticated motility investigation of this type is available in a few centers but does not yet have an established clinical diagnostic role.

Manometry of the Bile Duct. This may identify abnormalities of the sphincter of Oddi (34). The investigation may be helpful in individuals whose symptoms suggest a biliary origin but in whom gallstones are not present. If abnormal sphincter function is identified, sphincterotomy may be justified.

Formal Psychiatric Evaluation. Dyspepsia alone is not a sufficient indication for formal evaluation, although each patient should have a psychological assessment by the physician at the first interview. Formal psychiatric evaluation may be particularly indicated if the physician suspects personality disturbance, if there is a past history of psychological disorder, or if vomiting is a major feature among the constellation of symptoms reported.

Tests for Food Intolerance. These may be indicated in patients who attribute their symptoms to the ingestion of specific foods, although present evidence indicates that, with the possible exception of milk (lactose) intolerance, objective confirmation of intolerance to a particular food can seldom be obtained even when the clinical history seems clear (35, 36).

CONCLUSION

The dyspeptic patient presents a common and difficult problem in clinical practice. Careful evaluation of symptoms may be unrewarding; however, a thorough clinical and screening psychiatric evaluation are essential. Upper gastrointestinal endoscopy or upper gastrointestinal radiology and ultrasonic examination of the biliary tract and pancreas should be the first investigations. In patients in whom these are noncontributory and in whom symptoms persist, evaluation of upper gastrointestinal function (secretory, motor, provocation tests) may be indicated to determine the cause of functional dyspepsia and to allow appropriate management.

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