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WORKING TEAM REPORT

Identification of Sub-groups of Functional Gastrointestinal Disorders

D.A. DROSSMAN (Chairman)[1], W. GRANT THOMPSON[2], N.J. TALLEY[3], P. FUNCH-JENSEN[4], J. JANSSENS[5] AND W.E. WHITEHEAD[6]

[1]University of North Carolina, Chapel Hill, North Carolina, USA; [2]Ottawa Civic Hospital, Ottawa, Canada; [3]Mayo Clinic, Rochester, Minnesota, USA; [4] Aarhus Country Hospital, Aarhus, Denmark; [5]University of Leuven, Leuven, Belgium; and [6]Johns Hopkins University, Baltimore, Maryland, USA

The functional gastrointestinal disorders may be defined as a variable combination of chronic or recurrent gastrointestinal symptoms not explained by structural or biochemical abnormalities. The frequency and chronicity of these disorders, and the associated health care burden, attests to the need to develop reliable methods of diagnosis in order to provide cost-effective treatment. Based on existing epidemiological and clinical data, our multinational committee of clinician-investigators has set out consensus guidelines for the diagnosis of 21 functional gastrointestinal disorders attributed to the oesophagus, gastroduodenum, intestines, biliary tree and anorectum. We emphasise the importance of using symptom-based criteria with a minimum of diagnostic studies. The proposed criteria provide the basis for selecting patients for future epidemiological and clinical investigation. Future studies using these criteria will lead to their validation and/or modification.

INDEX TERMS: Functional Gastrointestinal Disorders, Diagnosis, Diagnostic Criteria.

The functional gastrointestinal disorders are defined as: "a variable combination of chronic or recurrent gastrointestinal symptoms not explained by structural or biochemical abnormalities. They include symptoms attributed to the pharynx, esophagus, stomach, biliary tree, small or large intestines, or anorectum" (1). These symptoms affect up to 35% of the population (2-4), and in Western society, a functional gastrointestinal disorder is diagnosed in over 40% of patients in gastroenterological practice (5, 6).

The chronicity of these disorders (7-9) and the associated health care burden (10-12) attest to the need for cost-effective methods for diagnosis and the development of effective treatments. Yet, current knowledge suggests that the aetiopathogeneses of functional gastrointestinal symptoms are multidetermined, vary from patient to patient and cannot easily be verified by physician-based measurements (13). Furthermore, current treatments are empiric, symptomatic, individualised, and not highly effective. While there is evidence that for many patients, the symptoms have physiological correlates, the differentiating features of these physiological data are not developed sufficiently to permit diagnostic specificity. Moreover, the same symptoms can often be found in diseases that have a recognised structural or biochemical (organic) basis. Currently, diagnosis of the functional gastrointestinal disorders is based on clinical assessment, and the prudent use of diagnostic studies to exclude other disorders. Therefore, we believe that identification of clinically meaningful sub-groups using symptom criteria based, when possible, on pathophysiological determinants, will lead to improved understanding of these disorders and, ultimately, more effective treatments.

Based on these premises, the charges to this committee which have resulted in this document were: (1) to identify and provide the rationale for discriminating clinical sub-groups of the functional gastrointestinal disorders; (2) to provide guidelines for diagnosis of these sub-groups that could be used in research and clinical practice; and (3) to make recommendations for future studies that would help improve diagnostic specificity and our understanding of these disorders, thereby leading to more effective treatments.

This report, developed by consensus of an international panel of clinical investigators, is a preliminary document for five subsequent papers that will review in more detail diagnostic and therapeutic aspects of the functional oesophageal, gastroduodenal, intestinal, anorectal and biliary gastrointestinal disorders. Furthermore, the committee has instituted a process by which these documents will be further modified in the future, based on validation of these criteria and the acquisition of new scientific information.

RATIONALE FOR IDENTIFYING CLINICAL SUB-GROUPS

The rationale for classifying the functional gastrointestinal disorders into clinical sub-groups has three bases:

Address for correspondence: Douglas A. Drossman, MD, Division of Digestive Diseases, University of North Carolina, CB# 7080, Burnett-Womack Bldg., Rm. 420, Chapel Hill, NC 27599-7080, USA.

1. Clinical experience.

Given that patients with functional GI disorders report a wide variety of symptoms affecting different regions of the gastrointestinal tract, we suspect that many of these disorders are due to disturbed sensory, motor or secretory function affecting different organs of the digestive system and in different ways. Thus, globus may be due to a disturbance of upper oesophageal sphincter function, and biliary dyskinesia to a disturbance of the sphincter of Oddi. Similarly, the mechanisms producing constipation are likely to be different from those producing diarrhoea.

Clinical experience supports our contention that to obtain reliable and valid information, future studies of the functional gastrointestinal disorders must use symptomatic criteria to define sub-groups for clinical and physiological assessment and treatment trials. The somewhat arbitary selection criteria in many clinical studies may have produced patient populations yielding mixed, inconclusive and poorly comparable data (13, 14).

2. Epidemiological data.

Surveys of patient and non-patient populations with functional gastrointestinal disturbances have shown that functional gastrointestinal symptoms are reported in varying combinations from oropharynx to anus (Table 1). Despite some overlap, epidemiological data support the clinical evidence that symptoms tend to aggregate into clusters (2-4, 15, 16). Statistical methods such as discriminant function and factor analyses of various populations can complement clinical experience to identify sub-groups of functional gastrointestinal disorders.

TABLE I. The functional gastrointestinal disorders.

- A. Functional Oesophageal Disorders
  - A1. Globus
  - A2. Rumination syndrome
  - A3. Functional chest pain of presumed oesophageal origin
  - A4. Functional heartburn
  - A5. Functional dysphagia
  - A6. Unspecified functional oesophageal disorder
- B. Functional Gastroduodenal Disorders
  - B1. Functional dspepsia
    - B1a. Ulcer-like dyspepsia
    - B1b. Motility-like dyspepsia
    - B1c. Reflux-like dyspepsia
    - B1d. Unspecified functional dyspepsia
  - B2. Aerophagia
- C. Functional Bowel Disorders
  - C1. Irritable bowel syndrome
  - C2. Functional constipation
  - C3. Functional diarrhea
  - C4. Burbulence
  - C5. Unspecified functional bowel disorder
- D. Chronic Functional Abdominal Pain
- E. Functional Biliary Pain
  - E1. Sphincter of Oddi dyskinesia
- F. Functional Anorectal Disorders
  - F1. Functional incontinence
  - F2. Functional anorectal pain
    - F2a. Levator syndrome
    - F2b. Proctalgia fugax
  - F3. Pelvic floor dyssenergia
  - F4. Unspecified functional anorectal disorder

3. Assessment of treatment trial.

Existing therapeutic trials have used a variety of non-specific criteria (for example, combining irritable bowel syndrome patients having predominant diarrhoea with those having constipation). This increases the likelihood that a medication with a specific physiological effect will not be found effective (13). The use of clearly specified symptom-based criteria permits the identification of patient sub-groups that can be targeted to the predicted effects of the treatment. An example in psychiatry is the evidence that panic disorder is distinct from generalised anxiety, and is more closely linked to depression. Patients with panic disorder respond better to anti-depressants than patients with generalised anxiety.

LIMITATIONS IN DEVELOPING DIAGNOSTIC CRITERIA

The use of symptom-based criteria to diagnose functional gastrointestinal disorders poses certain limitations:

1. The functional gastrointestinal disorders exist on a continuum, and symptoms may overlap.

The committee recognises that many, if not most of the functional gastrointestinal disorders are interrelated in their pathophysiology and clinical expression. Furthermore, these disorders exist on a continuum, and many patients will have clinical features that overlap. Therefore, it is expected that the separation into symptomatic sub-groups is to some degree an arbitrary process. The criteria proposed herein should be considered in terms of their potential benefit for research and as guidelines for diagnosis and clinical care, however, they cannot replace clinical judgment in making a diagnosis (17).

2. Functional gastrointestinal disorders may coexist with other diagnoses.

The high prevalences of the functional gastrointestinal disorders ensures that they will often coexist with other diseases, or even other functional disorders producing similar symptoms. A diagnosis of a functional gastrointestinal disorder by any criteria is not sufficient to exclude the possibility of a concurrent disease, and vice versa. Furthermore, when two or more disorders producing similar symptoms coexist (e.g. ulcerative colitis and irritable bowel (18)), clinical judgment is needed to determine the safest and most rational treatment.

3. The symptom-based criteria vary in the extent to which they correlate with known organ dysfunction.

Some disorders are strongly associated with physiological abnormalities (e.g. sphincter of Oddi dyskinesia, functional incontinence); in others, organ dysfunction is presumed but not proven (e.g. irritable bowel); and in others the symptoms correlate more with behavioural than physiological factors (e.g. chronic abdominal pain). The committee recognises that clinical syndromes lack pathophysiological specificity, and several aetiological processes may produce the same symptoms. In view of this, the committee believes that patient symptoms should be the basis for diagnostic criteria, since this is what is presented to the clinician. It will be task of future investigation to identify the biological and behavioural factors underlying these symptoms.

4. The diagnoses are based on exclusion of known structural or biochemical disorders.

By definition, a functional gastrointestinal disorder is in part determined by the exclusion of an underlying pathophysiological mechanism, particularly those that may be amenable to more specific treatment. For example, before 1965, patients with lactose intolerance were considered to have irritable bowel, but recognition of intestinal lactase deficiency permitted the possibility of a different disease classification with more specific treatment (19). For the purpose of this document, the finding of a discrete motility disturbance in the absence of a structural or biochemical abnormality would classify it as a functional disorder. Therefore, diffuse oesophageal spasm, but not achalasia, would be considered a functional gastrointestinal disorder.

5. There are no "gold standards" of validation.

Physician-based measures to categorise and validate the functional gastrointestinal disorders do not exist, although there are candidate physiological markers for some of these disorders. Diagnosis is based on patient symptoms, which are not usually precise enough to discriminate patients with different pathophysiological mechanisms. Furthermore, individuals with similar pathophysiological processes may report different complaints (and vice versa), and investigators will have different interpretation of these complaints based on training, experience, and personal bias. Division of patients according to symptom criteria is a pragmatic exercise, which can serve as a basis to test the validity of physiological markers through future studies and treatment trials.

6. Recommendations apply to a patient population.

Our recommendations pertain to patients with functional gastrointestinal disorders who request treatment. We recognise that most persons with functional gastrointestinal symptoms do not see physicians (2, 3). There are little clinical, physiological or outcome data about non-patient populations with functional gastrointestinal symptoms. While further investigation of non-patients with functional intestinal symptoms will enhance our understanding of these disorders, there is no justification for making clinical recommendations for this population.

ARE PSYCHOSOCIAL FACTORS IMPORTANT IN THE DIAGNOSIS OF THE FUNCTIONAL GASTROINTESTINAL DISORDERS?

Research on the psychosocial aspects of patients with functional gastrointestinal disorders has yielded three general observations:

1. Psychological stress exacerbates gastrointestinal symptoms.

Psychological stress or emotional responses to stress can affect gastrointestinal function and produce symptoms in healthy subjects (3, 4, 20), and does so to a greater degree in patients with functional gastrointestinal symptoms (21-25). However, psychological stress cannot distinguish between organic and functional disorders, since it can precede the onset and exacerbation of all illness. Identification of psychological stressors that can exacerbate these disorders may help in planning teatment.

2. Psychological disturbance exists to a greater degree in patients with functional gastrointestinal disorders than for non-patients with these disorders, other medical populations, and normals.

Patients with functional gastrointestinal disorders have greater psychological disturbance than otherwise healthy subjects or some other medical comparison groups (26-39). However, having functional gastrointestinal symptoms does not imply that a psychological disorder exists. Rather, psychological factors have an added effect on how symptoms are perceived, and acted upon (e.g. the decision to seek medical attention) (40, 41). It is understandable, therefore, that frequent clinic attenders, regardless of medical diagnosis, have greater psychosocial disturbance (42). The implication for the clinician and investigator is that an understanding of psychosocial factors in these illness are relevant to treatment because they may: (1) precipitate onset or exacerbation of gastrointestinal symptoms; (2) precipitate overt anxiety or depression; and (3) may cause increased concern about illness and lead a patient to seek treatment. Research of psychopharmacological and behavioural interventions in patients is needed to complement ongoing studies directed at gastrointestinal function.

3. Having a functional gastrointestinal disorder may produce psychosocial effects.

Previous experience with illness, current life stressors, personality style, coping strategies and the quality of social support will affect how an individual responds to an illness. These factors are particularly important in the adjustment to chronic illness, such as with the functional gastrointestinal disorders (43).

The committee believes that physicians should identify and respond to contributing psychosocial factors in all patients in order to plan more effective treatments. However, no evidence currently exists to

warrant the inclusion of psychological criteria in the diagnosis of the functional gastrointestinal disorders (42).

CLASSIFICATION OF THE FUNCTIONAL GASTROINTESTINAL DISORDERS

Based primarily on symptom localisation and description, and in some cases, evidence for motility disturbance, we have classified the functional gastrointestinal disorders into six major syndromes[1] (Table I). These major syndrome categories are also subclassified using more restrictive criteria. Since some patients may have symptoms that do not meet the more restrictive criteria, we have created an "unspecified" category.

These diagnostic criteria apply *only* if: **(1) symptoms are chronic or recurrent for at least three months; and (2) the symptoms are not attributable to other gastrointestinal disease based on adequate medical evaluation.** However, we recognise that in some cases clinical judgment will prevail when symptoms are due to a functional gastrointestinal disorder coexisting with another disease. Furthermore, the recommendations for diagnostic studies are the judgments of the committee members.

A. Functional Oesophageal Disorders

The functional oesophageal disorders are functional gastrointestinal disorders attributed to the esophagus. They include symptoms of globus, chest pain, regurgitation, dysphagia, heartburn or any combination.

A1. Globus is the sensation of a lump in the throat. It is not to be confused with dysphagia (difficulty in swallowing), for it exists when the individual is not swallowing. Globus may develop or exacerbate during emotional states, resembling the normal reaction of being "choked up" during experiences of sadness, grief, or pride (44), and may be relieved by weeping (45).

(a) *Symptom criteria for globus* —
1. The sensation of lump in the throat at the level of the cricopharyngeal cartilage for at least three months; *and*
2. symptoms occur between meals (even when not swallowing); *and*
3. no dysphagia (improved or unchanged with swallowing).

These symptoms may be associated with strong emotion.

(b) *Diagnostic studies* — If the symptom criteria are met, and the physician is reasonably confident that no other gastrointestinal or cervical disease exists to explain the symptoms, diagnostic studies usually are not needed. If suspicion of dysphagia exists, direct pharyngeal examination, video or cine-fluoroscopy of swallowing, an oesophagram, endoscopy or oesophageal manometry may be considered.

(c) *Physiological data* — A motility disturbance involving the hypopharynx or upper oesophageal sphincter is suspected, though not well documented. In one study (46) elevated upper oesophageal sphincter pressures were reported in nine patients with globus. Oesophageal reflux has been implicated in the production of this symptom (47), though it is not present in most of these patients.

A2. Rumination syndrome is a learned maladaptive habit, classified in children as an eating disorder, in which a person rechews regurgitated gastric contents and then either expectorates or reswallows it (48, 49). The behaviour usually ceases within an hour of eating, when the gastric contents become too acidic to be palatable. The disorder has also been described among children and adults with personality disturbance. However, there is no characteristic psychological profile or psychiatric diagnosis reported. Patients who seek treatment may report weight loss and symptoms of regurgitation, and the physician may falsely assume that the symptoms are due to oesophageal reflux or vomiting.

(a) *Symptom criteria for rumination* —
1. Chronic or recurrent regurgitation and rechewing of partially digested gastric contents for at least three months; *and*
2. no nausea, vomiting or signs of distress.

Rumination may stop when the contents turn acidic.

(b) *Diagnostic studies* — Diagnosis depends on identifying the characteristic clinical features in the absence of other organic oesophageal or gastric disease. In the patient never previously evaluated, medical conditions such as oesophageal stricture, reflux oesophagitis, gastrointestinal obstruction or gastro-oesophageal motor disorders may need to be excluded. Diagnostic studies may include cine or videofluoroscopy, upper gastrointestinal series, endoscopy, or oesophageal manometry.

Other disorders which may be confused with rumination syndrome include reflux oesophagitis and bulimia. Reflux oesophagitis is distinguished by the fact that: (1) solid food is rarely brought back up; (2) reflux may occur at any time, not primarily after meals; and (3) reflux symptoms are more common when lying down or bending over, whereas rumination is not. Bulimia is distinguished by: (1) absence of rechewing and reswallowing digesta; and (2) primary motivation is to control weight.

Rumination is frequently found in institutionalised, retarded individuals, or neglected children. In these cases, remination is often seen in association with other self-stimulatory behaviour, such as head-banging and masturbation.

(c) *Physiological data* — The disorder appears to be a learned maladaptive habit. The process is usually initiated by a belch or swallow at which time the

[1] A *syndrome* is defined as a set of symptoms (or signs) which are found in association with each other more often than would be expected by chance. Such a symptom cluster suggests the presence of a morbid process, but does not prove its existence.

lower oesophageal sphincter pressure is lowered creating a common channel between the stomach and oesophagus. At the same time diaphragmatic and rectus muscle contractions raise the intra-abdominal pressure thereby leading to regurgitation. When the upper oesophageal sphincter is relaxed, food is ejected into the mouth. Manometric studies are normal until rumination begins, at which time a simultaneous pressure spike-wave is seen at all manometric sites (50). The findings are unlike true rumination in animals since reverse peristalsis does not occur.

A3. Functional chest pain of presumed oesophageal origin (51) is characterised by episodes of midline, angina-like chest pain thought to emanate from the oesophagus, in which structural abnormalities are excluded. Some degree of dysphagia may be present as well; if present, it makes the oesophagus more suspect and a motility disorder more likely. If an associated motility disorder is found, it infrequently falls into the classic pattern of diffuse oesophageal spasm, and more frequently is defined as a "non-specific oesophageal motor disorder" characterised especially by high amplitude peristaltic contractions. Although the usual sensation felt in relation to oesophageal reflux is heartburn, reflux may be accompanied or not, by oesophageal motility disorders. Sometimes reflux, motility disturbances or a combination may induce chest pain in the same individual.

(a) *Symptom criteria for functional (non-cardiac) chest pain of presumed oesophageal origin* —
1. Midline chest pain with or without dysphagia for at least three months; *and*
2. no evidence for oesophagitis, cardiac or other disease to explain symptoms.

A relationship between swallowing (e.g. hot or cold liquids) and symptom development provides clinical support for the diagnosis.

(b) *Diagnostic studies* — It may be difficult to exclude the possibility of cardiac disease (51). Given the complexity and expense of cardiac evaluation, the decision for this type of evaluation must be determined on an individual basis. With regard to the exclusion of other oesophageal disorders, diagnostic studies may include a barium X-ray of the oesophagus (possibly including video or cineradiography) and/or oesophagoscopy and oesophageal manometry. This is especially important if the patient has dysphagia. Conventional manometry before and after provocation, sensitivity studies (e.g. acid perfusion, or balloon distension (52, 55) and prolonged pH and pressure recording with indication of occurrence of pain episodes, may also be indicated (52-57).

(c) *Physiological data* — In patients referred to gastroenterologists, the frequency for an oesophageal disturbance associated with non-cardiac chest pain, either acid reflux and/or an oesophageal motility disturbance, is between 20% and 60%. This depends on the criteria used to accept the oesophagus as the source of the pain (58, 59). It is also recognised that during a period of observation, motility disturbances may occur without pain and vice versa (60). This generally poor correlation suggests that other, less well-studied factors, such as oesophageal wall ischaemia (61), alteration in oesophageal wall tension (62), abnormalities in sensation (63, 64), or CNS/psychological factors (38, 65) may also be involved.

A4. Functional heartburn is the usual sensation felt in relation to oesophageal reflux, but here it occurs in the absence of gross structural changes (e.g. oesophagitis or stricture), and there is no evidence of pathological gastro-oesophageal reflux.

(a) *Symptom criteria for functional heartburn* —
1. A burning retrosternal discomfort or pain for at least three months; *and*
2. the symptom is relieved by antacids; *and*
3. associated with eating foods, emotion, lying down, or bending; *and*
4. there is no correlation between the symptoms and gross oesophagitis or acid reflux.

(b) *Diagnostic studies* — If clinically indicated, diagnostic evaluation would include the more sensitive measures of acid reflux and its effects, including oesophagoscopy and 24-hour pH monitoring. The committee recommends that if the patient has evidence for microscopic oesophagitis without gross changes of oesophagitis and without evidence of significant reflux, the disorder should still be considered functional hearburn.

A5. Functional dysphagia refers to dysphagia which occurs in the absence of structural changes (e.g. mass lesion, benign stricture) or achalasia. The underlying motility disorder may be diffuse oesophageal spasm or other symptomatic motility disorders. Sometimes the motor disturbance is intermittent and may only be apparent during a meal.

(a) *Symptom criteria for functional dysphagia* —
Difficulty in swallowing solids or liquids in the absence of anatomical obstruction or histopathologial findings to explain a motility disorder (e.g. primary or secondary achalasia) for at least three months.

A motility disturbance may sometimes be diagnosed by prolonged pressure monitoring, and in other cases there is no motor disturbance.

A6. Unspecified functional oesophageal disorder.

(a) *Symptom criteria for unspecified functional oesophageal disorder* —
Symptoms attributed to the oesophagus in the absence of other disease, and which do not fit into the previously described categories.

B. Functional Gastroduodenal Disorders

The functional gastroduodenal disorders are functional gastrointestinal disorders that are attributed to the stomach or duodenum.

B1. Functional dyspepsia describes episodic or persistent symptoms localised to the epigastrium or upper abdomen and attributed to the gastroduodenum. They may include upper abdominal pain or discomfort, bloating, early satiety, nausea or vomiting. The symptoms may or may not be related to meals, or exercise. These symptoms may coexist with, but can often be distinguished from the symptom of heartburn (66).

(a) *Symptom criteria for functional dyspepsia* — Chronic or recurrent upper abdominal pain for at least three months, or discomfort without X-ray or endoscopic evidence of other disease (acid-peptic or neoplastic disease of stomach or oesophagus, pancreas or hepato-biliary system) to explain the symptoms.

(b) *Diagnostic studies* — Diagnostic evaluation may not be indicated for transient or short-lived episodes of dyspepsia. For chronic or recurrent symptoms, or when other factors are considered, such as new symptoms in an older patient, the recommended diagnostic study is endoscopy. It is preferred over barium contrast studies to rule out acid peptic disease, and when indicated, to enable the taking of biopsies (75, 76). A complete blood count and biochemical tests may be obtained, though generally, these tests have low diagnostic yield. Abdominal ultrasound has not been of diagnostic benefit for ambulatory patients who do not have symptoms suggestive of biliary colic (77-79). Radionuclide gastric emptying and gastrointestinal motility studies may help provide new information in future research studies (67, 71), but are not at this time recommended for clinical practice.

(c) *Physiological data* — gastroduodenal dysmotility has been observed in a proportion of patients with functional dyspepsia seen in tertiary referral centres (80-84); the prevalence of motility disorders in other symptom sub-groups, and in the general community is unknown. Prokinetic agents, including metoclopramide (85), domperidone (86) and cisapride (82, 83, 87) have been shown in randomised, double-blind, controlled trials to be superior to placebo, thereby supporting the possibility of a motor disturbance in a sub-group of patients with functional dyspepsia. However, this has not always correlated closely with accelerated gastric emptying, and specific symptom improvement has been quite variable. The results of randomised, double-blind, placebo-controlled trials of H_2-receptor blockers in functional dyspepsia have been conflicting (88-92).

Functional dyspepsia may be classified by symptom criteria into sub-groups:

B1a. Ulcer-like dyspepsia is the sub-group in which the symptoms strongly suggest that an ulcer is present (67-69).

(a) *Symptom criteria for ulcer-like dyspepsia* — Criteria for functional dyspepsia and two or more of (70):
1. pain relieved by food or antacids;
2. periodic pain;
3. post-prandial pain;
4. pain that wakens the patient from sleep.

B1b. Motility-like dypepsia describes symptoms that suggest an underlying motility disturbance (67, 71-74).

(a) *Symptom criteria for motility-like dyspepsia* — Criteria for functional dyspepsia and two or more of:
1. nausea and/or vomiting;
2. early satiety and/or anorexia;
3. post-prandial abdominal bloating and/or a feeling of distension;
4. excessive belching (71, 72).

B1c. Reflux-like dyspepsia describes upper abdominal pain or discomfort accompanied by heartburn and/or acid regurgitation.

(a) *Symptom criteria for reflux-like dyspepsia* — Criteria for functional dyspepsia and symptoms attributed to heartburn or acid regurgitation. It is unclear whether this entity is distinct from gastro-oesophageal reflux disease. However, the presence of heartburn or acid regurgitation alone in the absence of upper abdominal pain or discomfort does not, in the opinion of the committee, constitute the syndrome of dyspepsia.

B1d. Unspecified functional dyspepsia.

(a) *Symptom criteria for unspecified functional dyspepsia* — Symptoms fulfilling the criteria for functional dyspepsia but which do not fit into the previously described categories.

B2. Aerophagia describes the repetitive pattern of swallowing air and belching, often to relieve a sensation of abdominal distension or bloating. After belching, the patient may obtain transient relief, yet this is soon associated with the urge to repeat the process.

(a) *Symptom criteria for aerophagia* — Symptoms for at least three months of repeatedly swallowing air and belching to relieve a sensation of abdominal distension or bloating.

C. Functional Bowel Disorders

The functional bowel disorders are functional gastrointestinal disorders having symptoms attributed to the mid to lower gastrointestinal tract. They include symptoms of abdominal pain, bloating or gaseousness, bowel dysfunction or any combination.

C1. Irritable bowel syndrome (IBS) is defined here by more restrictive criteria than may have been used previously. Terms such as spastic or irritable colon are no longer recommended. At the Rome International Congress in 1988, the irritable bowel syndrome was defined as "a functional gastrointestinal disorder attributed to the intestines and associated with symptoms of: (a) abdominal pain, and/or (b) disturbed defaecation, and/or (c) bloatedness or distension" (1).

(a) *Symptom criteria for irritable bowel* —
Continuous or recurrent symptoms for at least three months of:
1. abdominal pain or discomfort, relieved with defaecation, or associated with a change in frequency or consistency of stool; *and*[1]
2. an irregular (varying) pattern of defecation at least 25% of the time (three or more of):
   (i) altered stool frequency;
   (ii) altered stool form (hard or loose/watery stool);
   (iii) altered stool passage (straining or urgency, feeling of incomplete evacuation);
   (iv) passage of mucus;
   (v) bloating or feeling of abdominal distension.

(b) *Diagnostic studies* — As with all the functional gastrointestinal disorders, care should be taken to avoid unneccessary investigation which may be costly or harmful. Blood may be drawn for a complete blood count and erythrocyte sedimentation rate. Sigmoidoscopy is recommended to exclude inflammation or to diagnose concurrent disorders such as melanosis coli. Further testing depends upon the individual situation and may be influenced by the age of the patient, the nature and duration of symptoms, the region of practice, cost and other factors. Tests may include stool examination for occult blood, leucocytes, ova and parasites, and further colon investigation.

(c) *Physiological data* (93, 94) — While baseline motility studies usually show no difference from normal subjects, patients with IBS may differ from normals by having increased motor reactivity in response to various stimuli including meals, cholecystokinin, balloon distension of the rectosigmoid and psychological stress. Other studies report patients to have an enhanced rectal sensitivity to balloon distension, suggesting increased activity of afferent receptors or a reduced rectal compliance. It is presumed that these findings explain the observation the IBS patients report more frequent or severe bowel symptoms in response to meals or psychological stress, and have relief of pain with defaecation. The mechanisms for increased motor reactivity and/or increased sensitivity to environmental stimuli and symptom generation are not well understood, and current investigative efforts are addressing the possibility of altered smooth muscle myoelectric activity or abnormalities in CNS and enteric neurotransmitters or their receptors.

It is most likely that IBS may be sub-classified (for example) into those having predominant constipation due to motor dysfunction from disturbances in enteric nervous system functioning, predominant diarrhoea with dysfunction relating to incomplete bile salt absorption at the ileum, or predominant bloating due to motility disturbance or impaired absorption of carbohydrates. Sub-groups may also be identified by using provocative physiological stimuli. For example, a sub-group of IBS patients appear to have a hypersensitive rectum characterised by symptoms of rectal urgency, low pain thresholds to rectal distension, higher anxiety scores, and a greater tendency to have diarrhoea (95-97) than do IBS patients without increased rectal sensitivity. The selection of patients for study using physiologically-based symptom criteria would permit more valid and reliable results when pharmacological interventions are directed toward these proposed mechanisms.

C2. Burbulence or **gaseousness** refers to symptoms attributed to the intestines which may include a feeling of *abdominal fullness*, bloating, or *distension*, *borborygmi* (audible bowel sounds) and *farting*.

When partial or intermittent bowel obstruction, incomplete digestion of nutrients (e.g. lactose, sorbitol, fructose) (98,99) and bacterial overgrowth are excluded, burbulence may be due to air swallowing, or a motility disturbance. These symptoms are very common in the population and often accompany or exacerbate symptoms of functional dyspepsia, and irritable bowel. Exaggerated concern or frequent reporting of these symptoms by patients may be related to psychological disturbance (e.g. hypochondriasis).

(a) *Symptom criteria for burbulence ("gassy bowel")* —
1. symptoms of gaseousness, abdominal distension, borborygmi or farting for at least three months; *and*
2. symptoms are unrelated to maldigestion (e.g. lactase deficiency) or excess consumption of poorly digestible but fermentable foodstuffs (sorbitol, wheat bran), or other gastrointestinal diseases producing similar symptoms; *and*
3. insufficient criteria for functional dyspepsia, irritable bowel syndrome or other functional bowel disorders.

(b) *Diagnostic studies* — Supportive historical data include evidence for air swallowing or exacerbation of symptom reporting during times of anxiety. Diagnostic studies are usually not required but may include breath studies to exclude malabsorption of carbohydrates or a plain abdominal X-ray during an episode to estimate the quantity of bowel gas and to exclude bowel obstruction.

(c) *Physiological data* — Most patients with burbulence do not have increased quantities of gas or alteration in the composition of intestinal gas. Their symptoms may relate to their perception of disordered intestinal motility (100), or abnormal perception of normal bowel gas content.

C3. Functional constipation may be considered as separate from irritable bowel syndrome if the symptoms are not associated with an alternating bowel pattern.

[1]The committee recognises that some investigators may require abdominal pain as an essential criterion, and others may not. The decision to permit either categories 1 or 2 will be left to the investigator.

(a) *Symptom criteria for functional constipation* — Two or more for at least three months of:
1. straining > 25% of the time[1];
2. hard stools > 25% of the time;
3. incomplete evacuation > 25% of the time;
4. two or fewer bowel movements in a week.

Abdominal pain is not required, loose stools are not present, and there are insufficient criteria for irritable bowel syndrome.

(b) *Diagnostic studies* — Diagnostic evaluation will depend on the nature of the symptoms, associated conditions, physical findings, the age of the patient and expense. Thyroid function studies are recommended. Sigmoidoscopy of colonoscopy may be required to exclude structural abnormalities (e.g. obstructing mass, anal fissure). With functional constipation, an X-ray of the abdomen five days after ingestion of radio-opaque markers may help determine the pattern of delayed transit. In certain circumstances, rectal manometry or defaecography may of clinical value.

(c) *Physiological data* — Functional constipation can result from at least three physiological mechanisms: (1) colonic inertia, in which there is increased compliance and decreased phasic contractile activity; (2) increased segmental contractions in the sigmoid colon leading to retention of faeces; and (3) outlet delay caused by failure to relax the anal sphincters and pelvic floor during defecation (e.g. pelvic floor dyssenergia, *see* F3). Physiological studies such as whole gut transit time, sigmoid motility, and pelvic floor electromyography during attempted defaecation can help distinguish these sub-types.

Severe functional constipation may relate to disturbances in the enteric nervous system, its neurotransmitters or receptors, or the CNS-ENS axis. Some of these patients have been shown to have morphological changes within the myenteric and submucus plexii in colectomy specimens (101). Normal defaecation is coordinated by centres in the pons and the sacral cord, and requires conscious sensation of the arrival of faecal material in the rectum. Stimulation of anterior sacral nerve roots will cause a coordinated contraction of the distal colon and relaxation of the sphincter, suggesting the existence of a control centre at this site. Lesions in the brain and spinal cord may impair defaecation and should be considered in the differential diagnosis. It is possible, therefore, that severe chronic constipation may be related to disease of the enteric nervous system or to unidentified lesions within the central nervous system.

C4. Functional diarrhoea is also considered separate from irritable bowel syndrome if the symptoms are not associated with abdominal pain or an alternating bowel pattern.

[1]"Per cent of the time" relates to a three months or longer period.

(a) *Symptom criteria for functional diarrhoea* — Two or more for at least three months of:
1. loose, watery stools more than 75% of the time;
2. three or more bowel movements/day > 25% of the time;
3. increased stool volume compared to the community norm[2].

Abdominal pain and hard stools are not present, and there are insufficient criteria for irritable bowel syndrome.

(b) *Diagnostic studies* — Functional diarrhoea raises a wider set of diagnostic possibilities than with most other functional gastrointestinal disorders including enteric infections, maldigestion or bowel disease. Evaluation may first begin with examination of the stool and, possibly, quantification of a 24-hour stool collection with stool electrolytes assay to evaluate for a high volume secretory or osmotic type of diarrhoeal disorder. A 72-hour collection may also be obtained for stool fat if malabsorption is suspected. Sigmoidoscopic or in some cases, colonoscopic examination is performed, and rectal biopsy is at times helpful. Finally, laxative abuse is an often overlooked, though not uncommon cause of undiagnosed diarrhoea (102).

(c) *Physiological data* — Patients with functional diarrhoea may have one or more as yet undiscovered mechanisms for their symptoms. There is on current evidence that functional diarrhoea is related to a neurological disorder.

C5. Unspecified functional bowel disorder.

(a) *Symptom criteria for unspecified functional bowel disorder* —
At least three months of bowel symptoms in the absence of other disease that does not fit into the previously described categories.

D. Chronic Functional Abdominal Pain

Chronic functional abdominal pain describes pain attributed to the abdomen which may range from frequently recurrent to continuous pain of greater than six months' duration. This disorder exists when no disease specific process (e.g. chronic pancreatitis, abdominal wall pain, chronic bowel obstruction) is found, and when there is no predictable relationship of the pain to physiological events (e.g. eating, bowel movement, exercise). When the pain is persistent over a long period of time, there is a strong relationship to psychological disturbance (103) and a diagnosis of Somatoform Pain Disorder (DSM-III 307.80) should be considered (104).

[2]If the measured stool volume is > 350 ml/day (in Western societies), further evaluation should be considered to exclude osmotic or secretory processes.

(a) *Symptom criteria for chronic functional abdominal pain* —
1. Frequently recurrent to continuous abdominal pain for at least six months which may vary in severity;[1] *and*
2. incomplete or no relationship of pain with physiological events (e.g. pain not affected by eating or defaecation); *and*
3. some loss of daily functioning; *and*
4. insufficient criteria for other functional gastrointestinal disorders that would explain the abdominal pain.

Patients with chronic functional abdominal pain are also characterised by illness behaviours such as dissatisfaction with medical care, the persistent seeking of further investigations and disability. These patients are also refractory to usual treatments used for the functional gastrointestinal disorders.

(b) *Diagnostic studies* — Diagnostic testing will depend on the nature of the symptoms, the past medical history, behavioural observations, the types of studies previously performed, and the cost and risk of the procedures. Testing is based on the presence of abnormal data (blood in stool, abnormal liver chemistries), rather than by the patient's demands or the physician's uncertainty.

(c) *Physiological data* (105,106) — Pain is a sensory, emotional and cognitive experience that is modulated by biological and psychosocial processes. Nociception is influenced by neural mechanisms in the dorsal horn of the spinal cord and by descending corticofugal pathways that facilitate or inhibit caudad transmission to the CNS. This permits memory, attention and other psychological processes to modify the pain experience. There is evidence that reports of *chronic* pain are more strongly influenced at the CNS affective and evaluative levels than by peripheral sensory pathways. Therefore, in the absence of obvious disease, chronic pain may still be attributed to the abdomen, but have little or no peripheral nociceptive input.

E. Functional Biliary Tract Pain

This term typically refers to symptoms of right upper quadrant pain associated with physiological dysfunction within the biliary system, in the absence of structural disease (e.g. cholelithiasis, biliary stricture).

E1. Sphincter of Oddi dyskinesia is the disorder most frequently identified. It is reported to occur in 5-35% of patients with post-cholecystectomy pain without organic disease (107). Sphincter of Oddi dyskinesia cannot always be distinguished from sphincter of Oddi fibrosis or other anatomical abnormalities. It is defined as right upper quadrant biliary-like pain usually in a patient who is status post-cholecystectomy, and who has the simultaneous finding of sphincter of Oddi dysmotility. Recently several other sub-groups have been proposed that may produce functional biliary-type pain even with an intact gallbladder: atony (108), hyperkinetic gallbladder, functional stenosis of the cholecysto-choledochal juction, and increased pain sensitivity of the common bile duct and/or papilla (tender papilla) (109). Further research is needed to determine whether these disorders should be classified a separate entities or are part of the same spectrum of disorder involving biliary tract muscle functioning.

(a) *Symptom and laboratory criteria for sphincter of Oddi dyskinesia* —
1. Episodic right upper quadrant or epigastric pain in the absence of other gastrointestinal disease for at least three months, that is severe (interferes with daily activites); *and*
2. lasts one to several hours; *and*
3. symptoms are associated with:
   (i) liver enzyme abnormalities; and/or
   (ii) dilated and/or delayed drainage of common bile duct.

Diagnosis may be achieved by identifying abnormal manometric findings with sphincter of Oddi manometry. Using a low-compliance hydraulic capillary infusion system (110) several findings are reported to be associated with sphincter of Oddi dyskinesia: (a) increased baseline pressures (111-113); (b) increased number of retrograde waves and/or dyscoordination (112, 114); and (c) increased phasic wave amplitude (113, 115), paradoxical response to CCK-analogues (114, 116, 117), and/or tachyoddia (114, 118). Manometry may also help differentiate between structural and functional obstruction at the papilla. In structural stenosis, the pressure increase is usually seen over a short segment and administration of nitroglycerine does not relax the sphincter of Oddi as it does in functional obstruction. Although these manometric findings are reported in sphincter of Oddi dyskinesia (107, 113, 114), alternative and less invasive diagnostic methods are under evaluation (dynamic cholescintigraphy and ultrasound) (119, 120).

(b) *Diagnostic studies* — There are done primarily to exclude other diseases and include: oesophagogastroduodenoscopy, abdominal ultrasound, endoscopic retrograde cholangio-pancreatography, urinalysis, and complete blood count.

(c) *Physiological data* — Functional pain from the biliary system may arise from increased pain sensitivity, ischaemia due to muscular spasm or increased luminal pressure secondary to hindered bile flow. For patients with sphincter of Oddi dyskinesia, cholecystectomy may alter the physiological reflex that normally produces sphincter of Oddi relaxation wtih increases in gallbladder and/or common duct pressure (107, 121, 122). Furthermore, the inhibitory action of CCK on sphincter of Oddi action appears absent (114, 116, 117) indicating that the sphincter of Oddi may have been denervated.

[1]The committee recommends six months to conform to the criteria used for other (non-GI) chronic pain syndromes.

F. Functional Anorectal Disorders

The functional anorectal disorders are functional gastrointestinal disorders attributed to the anorectum. They consist of several syndromes often involving the striated pelvic floor muscles, and which are not explained by established neurological conditions such as pudendal neuropathy or cerebrospinal disease. Symptoms may include anorectal pain or discomfort, dyschezia, rectal urgency, incontinence or constipation.

F1. Functional incontinence is defined as the intermittent uncontrolled passage of more than 10 ml of faeces in the absence of structural or neurological disease. Incontinence should be distinguished from seepage: the leakage of small amounts of faecalent material from the anal canal sufficient to cause dampness and staining of the undergarments. Functional incontinence (frequently called encopresis) should be also be distinguished from neurological causes of faecal incontinence (e.g. peripheral neuropathy, CNS injury), structural causes of incontinence (e.g. separated or severely scarred external anal sphincter), and from occasional faecal soiling associated with watery diarrhoea. The most common cause of functional incontinence is faecal impaction (96% of patients with incontinence have a hard mass of stool in the rectum) (123-125). Faecal impaction results in a more obtuse anorectal angle and in reduced sensation for rectal distension (126). Incontinence may also be associated with inappropriate relaxation of the anal sphincter or impaired rectal sensitivity.

(a) *Symptom criteria for functional incontinence* —
1. Recurrent faecal soiling for at least three months of more than 10 ml of stool in an individual over two years of age who has no evidence for neurological or structural aetiologies; *and* 2 or 3 as in
2. Faecal impaction or megarectum or megacolon on barium enema;
3. Clinical findings suggesting non-structural anal sphincter dysfunction:
   (i) elevated threshold for perception of rectal distension; *or*
   (ii) poorly functioning internal anal sphincter.

(b) *Diagnostic studies* — Diagnostic studies are performed to rule out the neurological or structural bases for incontinence. Sigmoidoscopy is often done to exclude anorectal disease. Anorectal manometry or electromyography (EMG) can determine whether maximum squeeze pressures are within normal limits and whether the sphincter is symmetric. Balloon distension can detect abnormal sensory threshold or compliance (as seen following ischaemic bowel disease or abdominoperineal pull-through surgery), which may contribute to faecal incontinence. Defaecography may provide supportive information, such as when abnormal descent of the perineum is found.

(c) *Physiological data* — Functional incontinence usually occurs secondary to constipation and represents an overflow phenomenon. Incontinence may occur in two ways: (1) by causing funnelling of the rectum into the anal canal; and (2) by reducing sensation for movement of stool into the rectum (126). Some reports suggest that faecal impaction also causes tonic inhibition of the internal anal sphincter (127). Physiological assessment may show inappropriate relaxation of the sphincter in response to the arrival of gas or faecal material into the rectum (128), or impaired rectal sensitivity (129).

F2. Functional anorectal pain — Two types of anorectal pain syndromes have been described: *levator syndrome* and *proctalgia fugax*. They can be distinguished based on their clinical features, including symptom frequency (chronic or recurring versus infrequent), duration (long-lasting or continuous versus fleeting), and quality (aching pressure sensation versus sharp pain). However, indirect evidence suggests that both may be associated with spasm of the striated pelvic floor muscles.

F2a. Levator syndrome is described as a chronic or recurring aching or pressure that is localised to the rectum (130-132).

(a) *Symptom criteria for levator syndrome* —
Chronic or recurrent rectal pain or aching for at least three months.

The pain may radiate to the back or gluteal area and may be associated with sensations of rectal fullness or incomplet evacuation.

(a) *Diagnostic studies* — The rectal examination may reveal tenderness of the levator sling muscle, often palpated anteriorly on the left. Sigmoidoscopy is recommended to exclude anatomical lesions.

(c) *Physiological data* — The specific causes of this syndrome have not been well documented, although the most accepted mechanism relates to presumed spasm of the levator ani muscle which is identified by rectal examination (130).

F2b. Proctalgia fugax is described as a sudden severe pain in the anal area lasting several seconds or minutes, then disappearing completely (133).

(a) *Symptom criteria for proctalgia fugax* —
1. Recurrent episodes of midline pain localised to the lower rectum for at least three months; *and*
2. episodes last from seconds to no more than 20 minutes; *and*
3. there are no symptoms between episodes; *and*
4. there is no evidence for anorectal disease.

The symptoms may waken the patient from sleep.

(b) *Diagnostic studies* — The diagnosis is usually made from the history, since it is rare to have the opportunity to do a physical examination during an attack. An anoscopy and sigmoidoscopy should be done to exclude the possibility of anal fissure, thrombosed haemorrhoids or prostatitis.

(c) *Physiological data* — There are inadequate data to understand the pathophysiology of proctalgia fugax, though it is presumed that symptoms arise from spasm of the pelvic floor muscles.

F3. Pelvic floor dyssynergia — also called anismus or obtructed defaecation, this can be a sub-group of functional constipation (*see* C3). It is defined as difficulty in evacuating the rectum due to paradocal contraction of the pelvic floor during attempts to defaecate (134). Pelvic floor dyssynergia should be distinguished from structural causes of obstructed defaecation which may also cause dyschezia; these structural anomalies include intra-anal intussusception (blockage of the anal canal with the anterior rectal wall), and rectocele or enterocele. Rectocele may be suspected in female patients who report that pressing against the posterior vaginal wall facilitates defaecation, but the symptoms of intussusception are indistinguishable from pelvic floor dysynergia. The differential diagnosis depends on demonstrating a paradoxical contraction of the striated pelvic floor muscles during attempts to defaecate. Lesions of the cauda equina and low spinal cord and Hirchsprung's disease must be excluded as causes of dyschezia (135-138).

(a) *Criteria for pelvic floor dyssynergia* —
1. Difficulty with defaecation (dyschezia) for at least three months; *and*
2. EMG, manometric or radiological evidence for inappropriate contraction of pelvic floor muscles during attempts at defaecation (134).

(b) *Diagnostic studies* — Obstructing lesions causing dyschezia can be excluded with sigmoidoscopy (e.g. neoplasm, anorectal disease) or defaecography (e.g. enterocele, rectocele or intra- anal intussusception). EMG or anorectal manometry is required to diagnose sphincter dyssynergia. Radiological evidence after five days for "hang-up" of opaque markers (139) in the rectosigmoid area can be performed as a screening test and is supportive of the diagnosis.

(c) *Physiological data* — Pelvic floor dyssyncrgia is a diagnosis dased on a physiological finding: paradoxical contraction of the pelvic floor during attempted defaecation, in the absence of any known structural or neurological abnormality.

F4. Unspecified functional anorectal disorder.

(a) *Symptom criteria for unspecified anorectal disorder* —
Symptoms consistent with the functional anorectal disorders which do not fit into the previously described categories.

RECOMMENDATIONS FOR FUTURE WORK

1. Validation of recommended criteria

These criteria are presented as preliminary, and it is presumed that future studies will improve upon the existing categories as new data accumulate. The committee would hope that this will lead to standardised nomenclature for research that will permit better comparison of data across institutions. There are three investigational approaches that are recommended to validate these criteria:

(a) *Epidemiological studies* — Epidemiological studies are needed to determine the relative frequencies of the functional GI disorders in population-based and clinical samples. Factor analysis of symptom reports is one method that can be used to confirm or modify the validity of the symptom categories proposed in this document. Also, by identifying the clinical and physiological differences between patients and non-patients with functional gastrointestinal disorders, it will be possible to determine the factors associated with health care seeking.

(b) *Validation by physicians* — Despite the difficulties inherent with empirically based diagnoses, experienced physicians can make a diagnosis of functional gastrointestinal disorders with reasonable consistency, and this remains the "gold standard" of validation. It is recommended that the criteria proposed by this committee be tested by gastroenterologists in clinical practice.

(c) *Physiological assessment* — There is a lack of consistency for physiological measures to characterise these disorders, and it is possible that the patient populations previously studied are symptomatically too heterogeneous to yield meaningful findings. It is recommended that future physiological assessments be done with patients defined by these criteria. These studies may lead to improvements in the proposed symptom-based categories.

2. Additional assessments

(a) *Outcome studies* — Prospective assessments are needed to determine the natural outcome of patients with functional gastrointestinal disorders. Do symptoms continue or regress? Are there associations between these disorders? It would also be important to identify the predictors of poor clinical outcome.

(b) *Treatment trials* — The use of the proposed criteria are recommended for treatment trials, since more carefully defined patient populations are more likely to yield meaningful results.

(c) *Multidisciplinary studies* — Studies that include psychosocial and quality of life outcome variables in addition to physiological measures are needed for at least two reasons: (1) For patients with chronic illness, or recurrent symptoms, factors such as daily function, global well-being and psychosocial status (e.g. anxiety, depression) are important measures of health status and are sensitive outcomes to evaluate the efficacy of an intervention. Quality of life studies have not yet been performed among patients with functional bowel disorders; (2) Psychosocial factors are important predictors of clinical outcomes among patients with chronic illness. This is particularly relevant for studies performed in referral centre populations where patients tend to have a history of refractoriness to physiological interventions and have a higher prevalence of psychological disturbance.

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