

Review

The Cyclic Vomiting Syndrome: A Report of 71 Cases and Literature Review

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Summary: This study reviews 71 patients who presented between 1968 and 1988 with recurrent, self-limited episodes of nausea and vomiting separated by symptom-free intervals and were diagnosed with cyclic vomiting syndrome (CVS). The length and symptomatology of episodes tended to be stereotyped and characteristic for each patient over time. The disorder may persist from months to decades. There is a coincident relationship between CVS, migraine, and irritable bowel syndrome. The differential diagnosis includes many diseases which may

mimic CVS. Management involves a responsive, collaborative doctor-patient relationship, sensitivity to stresses caused by the illness and to feelings and attitudes that may predispose to attacks, use of antiemetic agents to abort or shorten attacks, treatment of complications, and use of prophylactic agents in patients whose episodes are of sufficient frequency and severity to warrant their trial. **Key Words:** Cyclic vomiting—Recurrent vomiting—Migraine—Periodic syndrome—Irritable bowel syndrome.

Cyclic vomiting syndrome (CVS) is an uncommon disorder. It may be descriptively defined as recurrent, self-limited, fairly uniform episodes of intractable nausea and vomiting not caused by any identifiable organic disease. The episodes have rapid onset, persist for hours to days, and are separated by symptom-free intervals (1). Although many consider CVS to be a migraine equivalent, little is known about its etiology or pathogenesis. CVS has as yet no established diagnostic biochemical, radiologic, electroencephalographic, or anatomic markers, either during or between attacks, and no specific treatment or generally accepted management. Only three large series of patients have been reported in the English literature during the past 60 years (2-4) and no prospective studies have been published on the phenomenology or

treatment of this disorder. Future analyses may reveal more than one etiology for this syndrome.

The present report is a retrospective study from personal observations of 71 patients with CVS. Its purposes are to contribute descriptive data to the phenomenology of this disorder, to increase awareness of its existence, and to facilitate diagnosis and management of individual patients.

MATERIALS AND METHODS

The study included 71 consecutive patients referred to a pediatric gastroenterologist (DRF) between 1968 and 1988 who met the following criteria: two or more episodes of intractable, self-limited nausea and vomiting with no identifiable organic cause separated by symptom-free intervals. The initial assessment of each patient averaged 2 h. It included a history and physical examination, family history, and review of systems. Standardized questions were asked concerning the patient's intellectual, motor, emotional, and social development and current level of function. A psychosocial history of

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the patient, family, and their related interactions was obtained (5). Each child had diagnostic data reviewed and further tests were ordered as indicated. Follow-up ranged from 3 months to 15 years (mean, 3.9 years). Follow-up questionnaires regarding the patient's condition were sent to each family and 29 (41%) responded. The study describes the characteristics of these 71 patients and compares them with previously reported series.

CASE REPORT

The following patient had many frequently encountered features of CVS: Tom, 6.5 years old, was the older of two siblings. Past medical history was unremarkable except that he passed pellet stools from 7 months to 3 years of age, suggestive of an irritable bowel diathesis, and he was hospitalized at age 2.5 years for accidental laceration of his hand by a power saw. His parents described him as a high-strung boy concerned about doing well in school, careful with his personal possessions, who tended to worry excessively when relatives traveled by air. His "sensitivity" was exemplified by an episode of near-syncope and "clamminess" while in the Snow White pavilion at Disneyland. He was prone to car sickness. His parents described themselves as "real nervous types."

The first episode of cyclic vomiting occurred 2 days after Tom's fifth birthday when he awoke early in the morning with vomiting which lasted 1 day. He was then symptom free for 5 months, until the second episode which woke him early in the morning while on vacation. The vomiting again lasted a day and subsided spontaneously. He was then symptom free for 7 months until 1 day after his sixth birthday when he awoke in the morning with vomiting, vomited more than 25 times, and was well the next day. His 4th episode occurred after a symptom-free interval of 5 months; he was camping with his father and awoke with severe vomiting the morning they were to go on a horseback ride. The fifth episode occurred after a 2-month interval; he awoke with vomiting at midnight, was given an injection in an emergency room, slept for the rest of the night, but vomited twice after awakening. He returned to sleep without eating and awoke at 3:30 p.m. feeling well and hungry. The sixth, seventh, and eighth episodes each consisted of 1 day of vomiting after symptom-free intervals of 5 months, 1 year, and 4 months, respectively. The seventh and eighth episodes both occurred during the excite-

ment of visits by his cousins. He was lost to follow-up after 8.3 years of age.

RESULTS

Forty-five percent of the 71 patients were male. They ranged in age from 2.7 to 23.4 years at the time of referral. The age at onset of CVS ranged from 6 months to 18 years, with a mean of 6.9 years of age. Although CVS has been characterized as beginning in preschool and early school-aged children, our data suggest that an onset during preadolescence is not uncommon. Adult-onset cases have also been described (6).

Vomiting began at characteristic times specific for the individual in 79% of patients; 60% were awakened during the night and/or had symptoms on arising in the morning and 19% had episodes beginning at other characteristic times of the day. The remaining 21% had episodes which began at no characteristic times of day or night.

The frequency of episodes ranged from one to 70 per year with an average of 12 per year.

Patients had episodes that were stereotypic for the individual in duration and symptomatology over long periods of time (months or years), although attacks became longer and/or more frequent in some cases. Eighty-five percent of patients had attacks of fairly uniform length and 15% had attacks of variable lengths (Fig. 1) Two patients suffered episodes lasting as long as 10 days.

Since "cyclic" implies a regular rhythmicity of recurrences, patients' histories were examined for this characteristic. Forty-eight percent had regular

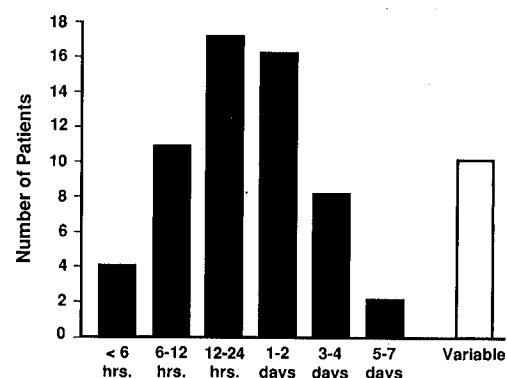


FIG. 1. Characteristic durations of episodes in 68 patients. The number of patients whose episodes clustered around various time limits are represented by solid bars. Patients whose episodes varied in duration are represented by the open bar.

recurrences, i.e., the intervals between attacks varied by less than the mean interval between attacks.

Many patients' episodes were accompanied by characteristic symptoms in addition to vomiting. Loose stooling at the onset and/or during the episodes was reported by 30% of patients. Headache was reported by 27%. Episodes were reportedly accompanied by fever in 23% of patients; it was usually low grade and remitted spontaneously. Patients were intensely miserable during episodes. Many complained of midabdominal and/or epigastric pain (1). They sometimes carried a towel or basin to spit, rather than swallow their saliva, or they held saliva in their mouths and refused to speak. They often preferred to rest in a darkened, quiet room. Two patients had tachycardia and mild hypertension (7). These abnormal vital signs were present throughout their attacks, even during sleep, and remitted as soon as the episodes subsided. No organic cause of this phenomenon was found. Hematemesis often occurred in patients with prolonged episodes. Endoscopy showed peptic esophagitis which was thought to have been the result, rather than the primary cause of vomiting.

Eighty percent of our patients identified specific conditions or events that seemed to trigger episodes (Table 1). Heightened emotional states were identified as triggers in 42 patients. Noxious emotional states, such as parental conflict, were cited by 54% of those patients; nonnoxious excitement, such as birthdays and holidays, was cited by 47% (8,9). Eight percent of our patients developed vomiting episodes during upper respiratory infections.

Each parent was asked to describe their child's

personality. Seventy-six percent of our patients were viewed as having one or more of the following traits: competitive, perfectionistic, high achieving, aggressive, strong willed, moralistic, caring, and/or enthusiastic.

The review of systems showed that, apart from symptoms associated with vomiting episodes, 67% of our patients had symptoms of irritable bowel syndrome (pellet stools, diarrhea induced by stress or fatty meals, recurrent abdominal pain syndrome) (10). Fifty-two percent had recurrent headaches, including 11% whose headaches were migrainous, as defined by Pinsky (11). Follow-up data regarding the prevalence of headaches were available for 27 patients. Forty-four percent reported headaches. Of the 22 children who had experienced headaches during and/or between attacks, 10 (45%) reported no headaches, six (27%) reported nonmigrainous headaches, and six (27%) reported migraines at the time of follow-up injury. Forty-six percent of patients had a history of motion sickness. Four patients (5.6%) had seizure disorders. Anticonvulsant agents benefited their seizure control, but did not seem to affect their cyclic vomiting episodes. There was no temporal relation between seizure and cyclic vomiting. One of our patients had cerebral palsy with developmental delay.

Family histories revealed that first and/or second degree relatives had irritable bowel syndrome in 62% of cases and recurrent headaches in 58%, including 40% whose headaches were migrainous. Three patients each had a parent with a history of CVS. Two patients' fathers awoke with transient vomiting and/or nausea every morning for months or years.

Figure 2 depicts the course of CVS in 29 patients for whom follow-up data were available. The duration of CVS is not clear in all cases, although 16 of 29 patients had been symptom free for more than a year at the time of follow-up.

TABLE 1. *Clinical features of CVS*

Recurrent, self-limited episodes of nausea, vomiting, and pallor	100%
Intervals between episodes are symptom free	100%
The duration and symptomatology of episodes are stereotyped and characteristic for each patient over time	85%
Episodes may be triggered by heightened emotional states and/or somatic stress	77%
Patients have typical personality features	76%
Episodes are accompanied by other autonomously mediated phenomena: headache and/or loose stooling and/or mild pyrexia and/or mild hypertension and tachycardia	67%
Family history of irritable bowel syndrome	62%
Episodes begin during the night and/or on arising in the morning	60%
Patients are prone to motion sickness	46%
Family history of migraine headaches	40%
Patients expectorate saliva or hold it in their mouths without swallowing for extended periods	13%

DISCUSSION AND LITERATURE REVIEW

This review represents the largest personal clinical experience with CVS. Although this report does not advance our understanding of the etiology or pathogenesis of this disorder, it does supplement previous observations concerning the stereotypic nature of attacks (9,12), their precipitants (1,9,13), their duration (3), the time span between attacks (3), the personality features of patients (9), and the coincidence of migraine, irritable bowel syndrome,

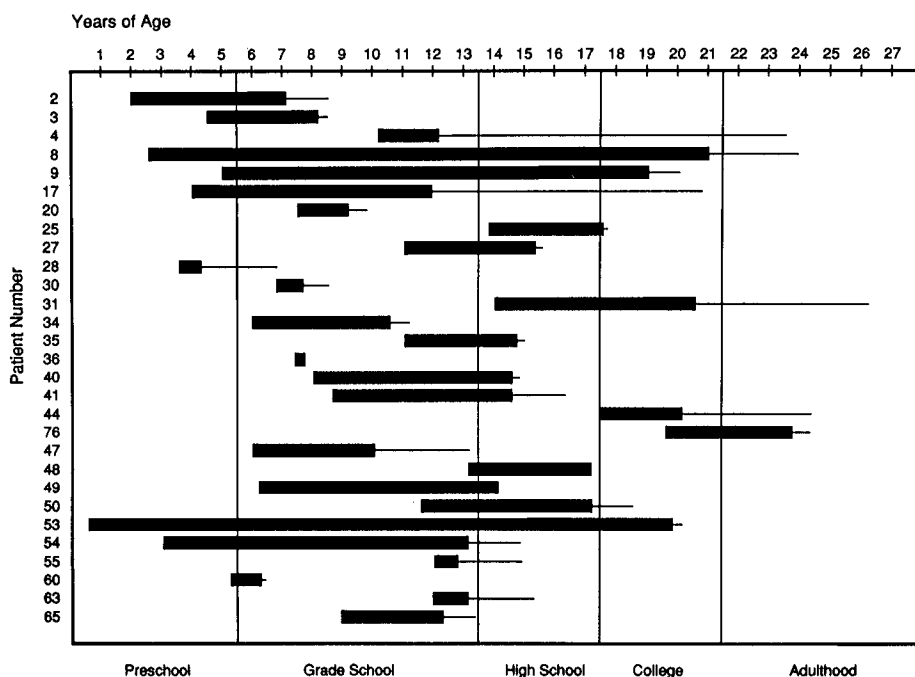


FIG. 2. The age at onset and the duration of CVS in 29 patients. The wide horizontal lines represent the age span from the first bout to the most recent bout of cyclic vomiting in each patient. The thin horizontal lines represent the time each patient was known to have been symptom free.

and motion sickness in patients and their families (14–16). This series of patients confirms what has been suggested in prior studies: each individual's attacks tend to follow a specific pattern that is internally consistent with respect to the duration and severity of each attack and the duration of symptom-free intervals between attacks. Notwithstanding this, there was a wide variation in these characteristics between patients.

The series described herein also adds to existing information concerning the occurrence of this syndrome at older ages. Our series differed from others in that the average age of onset (6.75 years) was almost double those reported by Smith (2) (3.7 years) and Hoyt and Stickler (3) (3.8 years). Whereas none of the patients in these latter two series had onset of symptoms beyond 12 years, 14% of the present series began later, including two who were young adults. Therefore, one cannot exclude the diagnosis of CVS on the basis of age alone.

Demographics

The prevalence of CVS is unknown and there are no data pertaining to its frequency (3,13). The average rate of presentation of our patients was 3.5 cases per year referred from the greater Los Angeles area. By comparison, CVS was diagnosed 3.25 times a year by Smith in New York from 1915 to 1935 (2), 3.7 times a year at the Mayo Clinic from

1945 to 1957 (3), 3.2 times a year at the Hospital for Sick Children in London from 1955 to 1965 (13), and 5.7 times a year at The Columbus Children's Hospital in Ohio from 1985 to 1991 (4). CVS was recognized more frequently at two German pediatric clinics where 20.9 and 29.6 cases per year were seen between 1945 and 1962 (17,18).

Etiology and Pathogenesis

The prevailing theory that CVS is a migraine variant or equivalent (19) is based on features shared by the two disorders (2–4,9,20,21). Both are episodic (1–4). The episodes in both disorders tend to be stereotypic for each patient (2,3), are often triggered by stress or excitement (9), and often begin during the night or morning (2,9,22–25). Migraine is familial (11), and the impression exists that migraine is also more common in the families of CVS patients, although this remains to be proved by prospective study (2,9,26). Motion sickness and irritable bowel syndrome (27,28) are more frequent in both disorders. A history of motion sickness was found in 46% of our CVS patients. This figure resembles the data of Barabas et al. (29) who found that 45% of their group of migrainous children reported motion sickness as compared with 5–7% of the nonmigrainous children they examined. The prevalence of irritable bowel symptoms between at-

tacks in our cyclic vomiting patients was two to three times that found in the general population (30,31). Recurrent abdominal pain syndrome (RAPS) is perhaps the commonest presentation of irritable bowel syndrome in school children (30,32,33), and children with RAPS are more likely to have frequent headaches and CVS (14-16,34). However, labeling CVS as a migraine equivalent adds little to our understanding because the pathogenesis of migraine remains uncertain (35). Therefore, rather than pigeonholing CVS as migraine, it might be more productive to study these syndromes as elements of a larger phenomenon, a hypothetical "dysautonomic" diathesis with characteristic personality traits. This might be done by examining the temperament (36,37), personality (12,38-43), autonomic reactivity (44-47), and experience (48,49) of patients and control groups. If patterns of association of these characteristics were found, they could lead to a better understanding of mind-body function and the mechanism of many functional disorders.

Diagnosis

The differential diagnosis of CVS includes illnesses that share symptoms presented in Table 1. One of the commonest pitfalls is the misdiagnosis of brain stem glioma as CVS (3). The vomiting of CVS resembles that of increased intracranial pressure in that both tend to occur in the morning, unrelated to food intake (23). Brain tumors are readily diagnosed in the presence of signs of increased intracranial pressure. Brain stem gliomas, however, may infiltrate the medulla without obstructing the flow of cerebrospinal fluid; they cause vomiting by direct encroachment of medullary vomiting centers and cranial nerve nuclei that control gastrointestinal motility (50-52). Therefore, a high index of suspicion is necessary to distinguish CVS from brain stem lesions not accompanied by signs of increased intracranial pressure. Magnetic resonance imaging is superior to computed tomography for diagnosis of posterior fossa tumors (24).

Urinary tract disease can resemble CVS. Obstructive uropathy is a relatively common cause of recurrent vomiting in children. Recurrent, self-limited episodes of abdominal pain and vomiting may be symptomatic of acute hydronephrosis occurring during periods of increased urine flow through a renal pelvis that is partially obstructed ("Dietl's crisis") (53). The symptoms may be epi-

sodic, like CVS, ending when the renal pelvis drains and recurring during subsequent diureses (54). Many children who vomit because of unilateral hydronephrosis localize their pain ipsilateral to their obstructed kidney. This differentiates them from CVS patients whose pain is midabdominal and/or midepigastric. However, other children with unilateral hydronephrosis localize their pain to the mid-abdomen (55,56) and this could prompt the misdiagnosis of CVS.

Transient leucocytosis without apparent infection may accompany some attacks (26) and, together with abdominal pain, vomiting, and hypoactive bowel sounds, may prompt a misdiagnosis of appendicitis (2,3).

CVS patients lose weight during episodes (2), but regain it promptly between attacks (3). Growth lag suggests the presence of chronic disease (57).

Every episode of vomiting in all CVS patients should be evaluated clinically for possible super-vening or previously missed organic disease before treatment of vomiting is begun (3). One more caveat may be helpful: Vomiting due to organic disease may be exacerbated by stress or excitement. Therefore, the view that nausea or vomiting is either organic or functional is a potentially disastrous oversimplification (58).

A search of the literature identified diseases (listed in Table 2) which might be mistaken for CVS because of intermittent vomiting by patients who seemed otherwise well during at least part of their illnesses. Among the tests to be considered in the differential diagnosis of CVS are those in Table 3.

Management

Children with CVS suffer bouts of alarming symptoms. The diagnosis is often missed because CVS is seldom encountered in general medical practice. As a result, the parents' feeling of not knowing what's wrong or what to do about it causes despair, anger, and the undoing of all sense of well-being. Making the correct diagnosis and explaining the syndrome may result in an immediate sense of relief followed by decreased frequency or severity of attacks. However, the disruptions caused by attacks may still overwhelm the family by depriving the parents of sleep, draining their financial resources, and causing them to miss work. A modus operandi should be developed in each case that is convenient for the family and minimizes frustrating waits in emergency rooms, hospitalizations, and ex-

TABLE 2. Disorders to be considered in the differential diagnosis of cyclic vomiting syndrome

Gastrointestinal
Peptic ulcer disease (59)
Pancreatitis (60)
Pancreatic pseudocyst (61)
Intestinal parasitism (62)
Recurrent subacute appendicitis (63,64)
Chronic idiopathic intestinal pseudo-obstruction (65)
Bochdalek's hernia (66)
Intermittent small bowel obstruction (67,68)
Central nervous system
Brain tumors causing increased intracranial pressure
Brain stem tumors, with or without increased intracranial pressure (50,51)
Subdural hematoma or effusions (69,70)
Abdominal epilepsy (71)
Hydrocephalus—slit ventricle syndrome (72,73)
Autonomic nervous system
Familial dysautonomia (74,75)
Urinary tract
Obstructive uropathies (53,54)
Endocrine
Pheochromocytoma (76)
Adrenal insufficiency (77)
Diabetes mellitus (78)
Metabolic
Ornithine transcarbamylase deficiency (79)
Medium chain acyl coenzyme A dehydrogenase deficiency (80)
Propionic acidemia (81)
Isovaleric acidemia (chronic intermittent form) (82)
Porphyria (83)

posure to caregivers who are unfamiliar with the patient and the disorder.

Patients whose episodes last a day or less seldom require parenteral fluid and electrolyte replacement. However, episodes lasting more than a day are likely to cause considerable weight loss, fluid and electrolyte depletion, and peptic esophagitis. Esophagitis and intracellular electrolyte deficits should be treated promptly and vigorously because these complications can themselves cause nausea and thus prolong cyclic vomiting attacks. Esophagitis, manifested by hematemesis and retrosternal pain, should be treated with sufficient intravenous ranitidine to raise the pH of the patient's vomitus above 4–5. If the patient is able to swallow 0.5–1 g of powdered sucralfate suspended in about 15 ml of water, it may adhere to and protect inflamed esophageal mucosa as it flows down, and again as it is vomited up through the esophagus. Patients usually can indicate when their esophagitis pain improves.

Potassium losses may be profound, even when serum potassium levels are in the low-normal range. The patient may be receiving "maintenance" potassium input intravenously while losing much more in expectorated saliva and vomited gas-

tric juice. Magnesium, may also be required in above-maintenance amounts (84). Inappropriate secretion of antidiuretic hormone may occur during prolonged nausea (85).

Pharmacotherapy

Although no controlled studies have been published concerning drug therapies to shorten or prevent recurrences, personal experience and anecdotal reports suggest some useful strategies. Induction of sleep has been considered beneficial (2). Lorazepam, a benzodiazepine with antiemetic, anxiolytic, and sedative properties (86), has suppressed or shortened attacks of cyclic vomiting (87) when given at a dose of 0.05–0.2 mg/kg intravenously over a few minutes, as soon as possible after the onset of vomiting. Sedation and decreased nausea may occur within minutes. The patient should then be allowed to sleep in a darkened, quiet room and observed without being awakened. If the patient wakes with renewed vomiting, the dose may be repeated every 6 h three or four times. This is comparable to the doses of lorazepam used in status epilepticus (88,89) and requires similar precautions

TABLE 3. Diagnostic studies in the differential diagnosis of CVS

Blood studies
CBC with differential and RBC morphology
Electrolytes, blood urea nitrogen, creatinine, glucose
Tests of hepatic function (AST, ALT, alkaline phosphatase, bilirubin, serum protein, and albumin)
Blood ammonia
Amylase and lipase
Blood lead
Pregnancy test
Urine studies
Urinalysis with microscopic examination of sediment
Urine culture
Urine for amino acids, organic acids, catecholamines, porphobilinogen, aminolevulinic acid, uroporphyrin, and coproporphyrin
Stool studies
Occult blood
Stool leucocytes
Ova and parasites
Radiologic studies
Ultrasonography of liver, biliary tract, pancreas, kidneys, and adrenal glands
Chest roentgenograms
Abdominal roentgenograms
Barium study of upper GI tract and small bowel
Contrast enema study
MRI of brain
Other studies
EEG

for management of respiratory arrest which occasionally occurs after rapid infusion of benzodiazepines. This use of lorazepam is similar to the use of diazepam for vomiting crisis in familial dysautonomia (75). When patients are aware of the approach of a vomiting episode, lorazepam, 1–2 mg. p.o. or sublingually may abort the attack. Ondansetron, a new serotonin antagonist, also deserves evaluation as an antiemetic to interrupt cyclic vomiting episodes. It has relatively few side effects and is non-sedating. Phenothiazines (e.g., chlorpromazine), butyrophenones (e.g., haloperidol), or benzamides (e.g., metoclopramide [Reglan] or trimethobenzamide [Tigan]) may be effective in the suppression of vomiting, but may cause extrapyramidal reactions. It is our impression that the sooner antiemetic treatment is begun, the easier it is to effect a remission. Therefore, we try to administer antiemetic therapy within an hour of onset of an attack. Long-term propranolol (25) or amitriptyline have been used for prophylaxis of CVS with apparent success in many cases.

Many patients are intensely hungry at the end of vomiting episodes. Some are able to immediately resume an unrestricted diet, while others suffer recurrence of symptoms after eating their first meal. Some adult patients with cyclic nausea and vomiting were found to have abnormal gastric myoelectrical function when studied during symptom-free periods (6). Patients with such gastric dysrhythmias tolerate liquids better than solid food (90). Therefore, we limit the resumption of feedings to isotonic or hypotonic nutrient liquids in children who have had recurrences of nausea after eating solid food at the end of an attack of cyclic vomiting.

Psychiatric Aspects of Management

CVS, like migraine, is probably best viewed as functional, i.e., a disorder caused by organ dysfunction rather than underlying organic or mental disease. Parents of children with CVS may fear for their child's life, and their unallayed fears may cause them to unrealistically view their child as vulnerable and fragile (91). The child's and/or family's psychopathology may also cause stress that directly triggers cyclic vomiting (13). Moreover, cyclic vomiting may be utilized for somatizing, the process by which a patient consciously or unconsciously uses bodily symptoms for psychological purposes or personal advantage (92). For example, marital conflict may precipitate an episode of vomiting

which then shifts the parents away from conflict and toward caring for their sick child. Cyclic vomiting, as the child's defense against the anxiety caused by his parents' hostility toward each other, may thereby be reenforced and unwittingly perpetuated. A mental health referral should be considered when emotional factors contribute to the severity of the patient's CVS, but made only after the parents have come to accept it as potentially helpful. The referring physician should remain involved in the management of all vomiting episodes and responsible for assessment of worrisome symptoms of any etiology (93).

Although we agree with Reinhart et al. (94) that cyclic vomiting may be a reaction to psychological stress and that attention to psychosocial factors is imperative, we disagree with labeling it psychosomatic, i.e., due to a primary neurotic illness (95). The implication that a bodily symptom having no discernible underlying organic disease means that the patient, necessarily, has something "wrong in the head," may damage doctor-patient rapport and reduce the clinician's efficacy. By viewing the etiology of CVS nonspecifically, as functional rather than psychiatric, we avoid that implication and the risk of offending those patients who are, in fact, emotionally well, as well as those who have significant psychological and family pathology, but are unable to utilize formal mental health resources. If the clinician avoids setting up the "psychosomatic" barrier from the start, he or she remains in a position to deal with mental health issues, including their resistance to a needed mental health referral, during management of the child's functional disorder (92).

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REFERENCES

1. Gee S. On fitful or recurrent vomiting. *S Bart Hosp Rep* 1882;18:1–6.
2. Smith C. Recurrent vomiting in children. *J Pediatr* 1937;10:719–42.
3. Hoyt C, Stickler G. A study of 44 children with the syndrome of recurrent (cyclic) vomiting. *Pediatrics* 1960;25:775–80.
4. Pfau B, Li BUK, Murray R, et al. Cyclic vomiting in chil-

- dren: a migraine equivalent? [Abstract]. *Gastroenterology* 1992;102:S23.
5. Stein M. Interviewing in a pediatric setting. In: Dixon S, Stein M. *Encounters with children*, Chicago: Year Book Medical Publishers, 1987:29-37.
 6. Abell T, Chung H, Malagelada J. Idiopathic cyclic nausea and vomiting—a disorder of gastrointestinal motility? *Mayo Clin Proc* 1988;63:1169-75.
 7. Sato T, Igarashi N, Minami S, et al. Recurrent attacks of vomiting, hypertension and psychotic depression: a syndrome of periodic catecholamine and prostaglandin discharge. *Acta Endocrinol (Copenh)* 1988;117:189-97.
 8. Hammond J. The prognosis for severe cyclical vomiting in childhood. In: Cumings J, ed. *Background to migraine*. New York: Springer-Verlag, 1973:112-5.
 9. Farquhar HG. Abdominal migraine in children. *Br Med J* 5-12-56;1082-5.
 10. Thompson W. The irritable bowel: one disease, or several, or none? In: Read N, ed. *Irritable bowel syndrome*. London: Grune & Stratton, 1985:3-14.
 11. Prensly A. Migraine and migrainous variants in pediatric patients. *Pediatr Clin North Am* 1976;23:461-71.
 12. Heiner D, Blitzer J. Familial paroxysmal dysfunction of the autonomic nervous system (a periodic disease), often precipitated by emotional stress. *Pediatrics* 1957;20:782-93.
 13. Hammond J. The late sequelae of recurrent vomiting of childhood. *Dev Med Child Neurol* 1974;16:15-22.
 14. Lanzi G, Balottin U, Ottolini F, et al. Cyclic vomiting and recurrent abdominal pains as migraine or epileptic equivalents. *Cephalalgia* 1983;3:115-18.
 15. Lanzi G, Ballotin U, Fazzi E, et al. The periodic syndrome in pediatric migraine sufferers. *Cephalalgia* 1983;3(Suppl 1):91-3.
 16. Lundberg P. Abdominal migraine—diagnosis and therapy. *Headache* 1975;15:122-5.
 17. Lorber J. Causes of cyclical vomiting. *Dev Med Child Neurol* 1963;5:645.
 18. Lang K. On the importance of central nervous damage in periodic vomiting in childhood. *Monatschr Kinderheilk* 1963;111:161-7.
 19. Hockaday J. Migraine and its equivalents in childhood. *Dev Med Child Neurol* 1987;29:258-70.
 20. Jernigan S, Ware L. Reversible quantitative EEG changes in a case of cyclic vomiting: evidence for migraine equivalent. *Dev Med Child Neurol* 1991;33:80-5.
 21. Mortimer M. The VER as a diagnostic marker for childhood abdominal migraine. *Headache* 1990;30:642-5.
 22. Menkes J. *Textbook of child neurology*, 3rd ed. Philadelphia: Lea & Febiger, 1985:660.
 23. Menkes J. *Textbook of child neurology*, 3rd ed. Philadelphia: Lea & Febiger, 1985:534.
 24. Menkes J. *Textbook of child neurology*, 3rd ed. Philadelphia: Lea & Febiger, 1985:538.
 25. Symon D, Russell G. Abdominal migraine: a childhood syndrome defined. *Cephalalgia* 1986;6:223-8.
 26. Millichap J, Lombroso C, Lennox W. Cyclic vomiting as a form of epilepsy in children. *Pediatrics* 1955;15:705-14.
 27. Thompson W. *The irritable gut*. Baltimore: University Park Press, 1979:41-48.
 28. Stone R, Barbero G. Recurrent abdominal pain in childhood. *Pediatrics* 1970;45:732-8.
 29. Barabas G, Matthews W, Ferrari M. Childhood migraine and motion sickness. *Pediatrics* 1983;72:188-90.
 30. Apley J, Naish N. Recurrent abdominal pain: a field survey of 1000 school children. *Arch Dis Child* 1958;33:165-70.
 31. Thompson W, Heaton K. Functional bowel disorders in apparently healthy people. *Gastroenterology* 1980;79:283-8.
 32. Cullen K, Macdonald W. The periodic syndrome: its nature and prevalence. *Med J Aust* 1963;2:167-73.
 33. Oster J. Recurrent abdominal pain, headache and limb pains in children and adolescents. *Pediatrics* 1972;50:429-36.
 34. Apley J. *The child with abdominal pains*, 2nd ed. Oxford: Blackwell Scientific Publications, 1975:17.
 35. Welch K. Migraine—a biobehavioral disorder. *Arch Neurol* 1987;44:323-7.
 36. Thomas A, Chess S. *Temperament and development*. New York: Brunner/Mazel, 1977.
 37. Wender E, Palmer F, Herbst J, et al. Behavioral characteristics of children with chronic nonspecific diarrhea. *Am J Psychiatry* 1976;133:20-5.
 38. Menkes M. Personality characteristics and family roles of children with migraine. *Pediatrics* 1974;53:560-4.
 39. Waters W. Migraine and symptoms in childhood: bilious attacks, travel sickness and eczema. *Headache* 1972;55-61.
 40. Passchier H, vander Helm-Hylkema H, Orlebeke J. Personality and headache type. *Headache* 1984;24:140-6.
 41. Blaszczyński A. Personality factors in classical migraine and tension headache. *Headache* 1984;24:238-44.
 42. Ryan W, Kelly M, Fielding J. The normal personality profile of irritable bowel syndrome patients. *IJMS* 1984;153:127-9.
 43. Boyce W, Jemerin J. Psychobiological differences in childhood stress. I. patterns of illness and susceptibility. *Dev Behav Pediatrics* 1990;11:86-94.
 44. Jemerin J, Boyce W. Psychobiological differences in childhood stress. II. cardio-vascular markers of vulnerability. *Dev Behav Pediatrics* 1990;11:140-50.
 45. Kopel F, Kim I, Barbero G. Comparison of rectosigmoid motility in normal children, children with recurrent abdominal pain, and children with ulcerative colitis. *Pediatrics* 1967;39:539-45.
 46. Fielding J, Regan R. Excessive cold pressor responses in the irritable bowel syndrome. *IJMS* 1984;153:348-50.
 47. Lacey J, Bateman D, Van Lehn R. Autonomic response specificity. *Psychosom Med* 1953;15:8-21.
 48. Dalessio D, ed. *Wolff's headache and other head pain*, 4th ed. New York: Oxford Univ. Press, 1980:403-17.
 49. Engle G, Reichsman F. Spontaneous and experimentally induced depressions in an infant with a gastric fistula. *J Am Psychoanal Assoc* 1956;4:428-52.
 50. Sarkari N, Bickerstaff E. Relapses and remissions in brain stem tumors. *Br Med J* 1969;2:21-3.
 51. Frank Y, Schwartz S, Epstein N, et al. Chronic dysphagia, vomiting and gastroesophageal reflux as manifestations of a brain stem glioma. *Pediatr Neurosci* 1989;15:265-8.
 52. Lassiter K, Eben A, Davis C, et al. Surgical treatment of brain stem gliomas. *J Neurosurg* 1971;34:719-25.
 53. Elder J, Duckett J. Dietl's crisis. In: Gillenwater J, Grayhack J, Howards S, et al., eds. *Adult and pediatric urology*. Chicago: Year Book Medical Publishers, 1987:1555.
 54. Koff S, Hayden L, Cirulli C, et al. Pathophysiology of ureteropelvic junction obstruction. *J Urol* 1986;136:336-8.
 55. Kelalis P, Culp O, Stickler G, et al. Ureteropelvic obstruction in children: experiences with 109 cases. *J Urol* 1971;106:418-22.
 56. Balman A. Ureteropelvic junction obstruction as a cause for intermittent abdominal pain in children. *Pediatrics* 1991;88:1066-9.
 57. Hoffman H, Becker L, Craven M. A clinically and pathologically distinct group of benign brain stem gliomas. *Neurosurgery* 1980;7:243-8.
 58. Gonzalez-Heydrich J, Kerner J, Steiner H. Testing the psychogenic vomiting diagnosis. *Am J Dis Child* 1991;145:913-16.
 59. Gryboski J, Walker W, eds. *Gastrointestinal problems in the infant*, 2nd ed. Philadelphia: W.B. Saunders, 1983:237.
 60. Whitten D, Feingold M, Eisenklam E. Hereditary pancreatitis. *Am J Dis Child* 1968;116:426-8.

61. Silverman A, Roy C. *Pediatric clinical gastroenterology*, 3rd ed. St. Louis: C.V. Mosby Co., 1983:851.
62. Green M. *Pediatric diagnosis*, 4th ed. Philadelphia: W.B. Saunders, 1986:219.
63. Lee A, Bell R, Griffen W, et al. Recurrent appendiceal colic. *Surg Gynecol Obstet* 1985;161:21-4.
64. Crabbe M, Norwood S. Recurrent and chronic appendicitis. *Surg Gynecol Obstet* 1986;163:11-13.
65. Anuras S, Anuras J. Clinical manifestations of severe gastrointestinal motility disturbance. *J Intens Care Med* 1988; 3:99-108.
66. Hight D, Hixson S, Reed J, et al. Intermittent diaphragmatic hernia of Bochdalek. *Pediatrics* 1982;69:601-4.
67. Green M. *Pediatric diagnosis*, 4th ed. Philadelphia: W.B. Saunders, 1986:217.
68. Jahin Y, Stone A, Wise L. Mesenteric hernia. *Surg Gynecol Obstet* 1980;150:747-54.
69. Til K. Subdural haematoma and effusion in infancy. *Br Med J* 1968;3:400-2.
70. Weil M. Infections of the nervous system. In: Menkes J, ed. *Textbook of child neurology*, 3rd ed. Philadelphia: Lea & Febiger, 1985:322-3.
71. Mitchell W, Greenwood R, Messenheimer J. Abdominal epilepsy. Cyclic vomiting as a major symptom of simple partial seizures. *Arch Neurol* 1983;40:251-2.
72. Coker S. Cyclic vomiting and the slit ventricle syndrome. *Pediatr Neurol* 1987;3:297-9.
73. Nowak T, James H. Migraine headaches in hydrocephalic children: a diagnostic dilemma. *Child Nerv Syst* 1989;5:310-14.
74. Linde L, Westover J. Esophageal and gastric abnormalities in dysautonomia. *Pediatrics* 1962;29:303.
75. Axelrod F. Familial dysautonomia. In: Gellis S, Kagan B, eds. *Current pediatric therapy*, 13th ed. Philadelphia: W.B. Saunders, 1990:94.
76. Stackpole R, Melicow M, Uson A. Pheochromocytoma in children. *J Pediatr* 1963;63:315-30.
77. Valenzuela G, Smalley W, Schain D, et al. Reversibility of gastric dysmotility in cortisol deficiency. *Am J Gastroenterol* 1987;82:1066-8.
78. Feldman M. Nausea and vomiting. In: Sleisenger M, Fordtran J, eds. *Gastrointestinal disease*, 4th ed. Philadelphia: W.B. Saunders, 1989:227.
79. Berry G. Disorders of amino acid metabolism. In: Walker W, Durie P, Hamilton J, et al., eds. *Pediatric gastrointestinal disease*. Philadelphia: B.C. Decker, 1991:948-50.
80. Coates P, Hale D, Stanley C, et al. Genetic deficiency of medium-chain acyl coenzyme A dehydrogenase. *Pediatr Res* 1985;19:627-76.
81. Rezvani I, Auerbach V. Propionic acidemia. In: Behrman R, Vaughn V, eds. *Nelson's textbook of pediatrics*, 13th ed. Philadelphia: W.B. Saunders, 1987:292-3.
82. Sweetman L. Branched chain organic acidurias. In: Scriver C, Beaudet A, Sly W, et al, eds. *Metabolic basis of inherited disease*, 6th ed. New York: McGraw-Hill, 1989:795.
83. Stein J, Tschudy D. Acute intermittent porphyria. *Medicine* 1970;49:1-16.
84. Harris I, Wilkinson A. Magnesium depletion in children. *Lancet* 1971;2:735-6.
85. Rowe J, Shelton R, Helderman H, et al. Influence of the emetic reflex on vasopressin release in man. *Kidney Int* 1979;16:729-35.
86. *AMA drug evaluations*, 6th ed. New York: John Wiley & Sons, 1986:272.
87. Puls L. A recurrent vomiting syndrome in children. *Contemp Pediatrics* Sept 90;8-11.
88. Leppik I, Derivan A, Homan R, et al. Double-blind study of lorazepam and diazepam in status epilepticus. *JAMA* 1983; 249:1452-4.
89. Holmes G. *Seizure disorders*. In: Gellis S, Kagan B, eds. *Current pediatric therapy*. 13th ed. Philadelphia: W.B. Saunders, 1990:75-6.
90. McCallum R. Motor functions of the stomach in health and disease. In: Sleisenger M, Fordtran J, eds. *Gastrointestinal disease*, 4th ed. Philadelphia: W.B. Saunders, 1989:675-713.
91. Green M, Solnit A. Reactions to the threatened loss of a child: a vulnerable child syndrome. *Pediatrics* 1964;34:58-66.
92. Ford C. *Somatizing disorders—illness as a way of life*. New York: Elsevier, 1983:1-2.
93. Ford C. *Somatizing disorders—illness as a way of life*. New York: Elsevier, 1983:255-7.
94. Reinhart J, Evans S, McFadden D. Cyclic vomiting in children: seen through the psychiatrist's eye. *Pediatrics* 1977; 59:371-7.
95. Pearce J. Migraine: a psychosomatic disorder. *Headache* 1977;17:125-8.