



# Cyclic Vomiting Syndrome in Adults

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## Introduction

Cyclic vomiting syndrome (CVS) is a disorder with recurrent episodes of severe nausea and vomiting interspersed with symptom free periods. This syndrome was first described in the English literature in 1882 by Samuel Gee who reported a series of nine children ranging from 4 to 8 years in age. While CVS has been studied in pediatric populations, its occurrence in adults has been underappreciated. It is now thought that this crippling syndrome can occur in a variety of age groups including adults.

## The Condition

The symptom episodes of CVS tend to follow the same pattern for each individual patient over time. The symptom episodes are characterized by four phases:

1. The inter-episodic phase occurs between vomiting episodes when the patient is relatively symptom-free. This phase typically last weeks to months.
2. The pre-emesis phase occurs when the patient begins to sense the approach of an episode and has nausea of varying intensity but is still able to take oral medications. This phase lasts minutes to hours.
3. The emetic phase is characterized by intense, persistent nausea, vomiting, and other symptoms (abdominal pain, prostration, and lethargy). This phase lasts from hours to days.
4. The recovery phase begins with the settling down of nausea and ends when hunger, tolerance of oral intake and vigor returns to normal.

Unfortunately, patients with these symptoms may go for years without correct diagnosis. Initially, patients may be thought to have viral gastroenteritis. However, characteristically these patients often have repeated trips to Emergency Departments seeking relief of the vomiting and the often-accompanying abdominal pain and dehydration. Some of these patients may be thought to have gastroparesis, a disorder with chronic

nausea and vomiting. At University of Kansas, 5% of patients referred for evaluation of possible gastroparesis were diagnosed as CVS. Patients may undergo surgical procedures, such as removal of their gallbladder (cholecystectomy), which often fails to improve their symptoms. Patients with CVS suffer from an impaired quality of life due to the repeated episodes of severe vomiting. Both patients and their families often suffer economically and socially when the symptoms interfere with day-to-day life, schooling and job performance, which may sometimes lead to loss of employment.

Lack of awareness of this syndrome in adults often delays the diagnosis of CVS. There is a scarcity of studies describing the spectrum of CVS in adults. Lack of an appreciable number of patients at any one center has made it difficult to study the cause and processes involved in this disorder and to describe an organized treatment plan for these patients. Fortunately, this is being corrected, as more information is becoming available. Recently, criteria for the diagnosis of cyclic vomiting syndrome in adults were published by the Rome III study group on functional GI disorders.

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The following three criteria must be fulfilled for the last 3 months with symptom onset at least 6 months before diagnosis

1. Stereotypical episodes of vomiting regarding onset (acute and duration (less than 1 week).
2. Three or more discrete episodes in the prior year
3. Absence of nausea and vomiting between episodes

Supportive criteria for the diagnosis of CVS includes: History or family history of migraine headaches

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There have been several recent series of adult patients with cyclic vomiting syndrome. One recent series from the University of Kansas Medical Center described 31 adult

patients with CVS. Data collected from these patients provides insight into the clinical, psychological, and motility characteristics of CVS in adults. The most uniform feature of the patients in this series was the stereotypical nature of the nausea, vomiting, and abdominal pain with intermittent symptom free periods. These characteristics are similar to the pediatric experience, although the abdominal pain appears to be more pronounced in the adult patients than in pediatric patients. The ages of patients ranged from 18 to 62 years, indicating that many characteristics of CVS are similar irrespective of age of the patient.

### **Associated Conditions**

Migraine headache is reported to occur in many patients with CVS. A family history of migraine is also prevalent among CVS patients suggesting that CVS may be part of the spectrum of certain inherited disorders. Genetic mutations have been found that are associated with recurrent episodes of vomiting as well as migraine. Other conditions observed to coexist with migraine include mood disorders, panic disorder, and irritable bowel syndrome.

Depression and anxiety can be common findings in the patients, although it is difficult to distinguish whether these psychological disorders are a contributing factor, or the result of what can certainly be a stressful and mood depressing syndrome. One may also see a resemblance to panic disorder when patients are affected with unpredictable but stereotypical symptoms.

Marijuana use has also been proposed as a contributing factor in CVS. A large number (13 of 31) of the patients in the Kansas series reported daily marijuana use. During follow-up, 2 patients confirmed resolution of their symptom cycles after they completely quit using marijuana. However, 7 patients claimed that marijuana was actually improving their nausea symptoms. It is difficult to draw conclusions at this time about the role of marijuana. Marijuana has been shown to delay gastric emptying of a solid meal and repeated inhibition of gastric emptying with marijuana use could pre-dispose a patient to nausea and vomiting.

### **Pathophysiology of CVS**

The cause of CVS is not known. However, important advances are being made in the clinical understanding of this disorder which may open the way for new treatments. Investigations have focused on an underlying disturbance of stomach function in CVS. Additionally, investigation is underway evaluating abnormalities of brain-gut axis in CVS. Current

research involves several other areas. Genetic studies suggest a mitochondrial component in the pathogenesis of migraine and CVS with a maternal inheritance pattern. Hormonal abnormalities have been identified involving the hypothalamic pituitary system adrenal system (HPA axis), and more recently, corticotropin-releasing factor (CRF).

There have been several studies on stomach function in CVS. Twenty-three of 30 patients (77%) in the Kansas series that underwent gastric emptying tests using a low fat meal were found to have rapid emptying mimicking a “dumping syndrome” disorder. Dumping syndrome happens when undigested food from the stomach fills the upper end of the small intestine too quickly causing nausea, abdominal pain, and other symptoms. Interestingly, one patient with rapid gastric emptying in between the vomiting episodes was found to have delayed gastric emptying during a symptomatic period. Rapid emptying was also observed in 17 out of 21 (81%) adults with CVS in another study.

Gastric nerve function was assessed in 11 patients of the Kansas series using electrogastrography (EGG), a test which measures the electrical signals that control the contractions in the muscles of the stomach. Seven out of 11 (64%) demonstrated an abnormal EGG. The major electrical abnormality was a particular abnormal rhythm (tachygastric) thought to be increased during occurrences of nausea and vomiting. These data on gastric emptying and nerve function in the muscles within the stomach emphasize a possible role for the stomach in CVS and emphasizes the role of brain-gut pathways.

### **Treatment**

Treatment of cyclic vomiting syndrome remains largely empiric because of its obscure pathogenesis and the lack of controlled therapeutic trials. In general, the treatment approach to a patient with CVS should include consideration of lifestyle changes including avoidance of potential triggering factors, prophylactic drug therapy to prevent subsequent episodes, abortive and/or supportive care treatment during acute episodes, and support of the family.

Medication treatment for patients with CVS is often divided into acute treatment of the vomiting episodes and chronic treatment to try to prevent the episodes. There is a lack of data on the outcomes of patients, particularly adult patients with CVS, to different types of treatment.

A variety of agents are often tried to reduce the nausea and vomiting during the vomiting phase. Antiemetic agents can

reduce the severity of episodes and are best used in conjunction with sedatives. This may include the antiemetic agents – prochlorperazine (Compazine) and ondansetron (Zofran). Patients with CVS may respond well to intravenous lorazepam (Ativan), an anti-anxiety medication. Antimigraine triptans can also be used to try to abort episodes. Tricyclic antidepressants, although not classified as antiemetic agents, can prevent nausea and vomiting since they appear to influence the brain's regulation of the vomiting process. Tricyclic agents play a favorable role in migraine, depression, anxiety, and the abdominal pain associated with irritable bowel syndrome. They appear to be appropriate therapy to try for the potentially complex disease mechanisms of CVS. One study by Prakash et al. showed that tricyclic antidepressant therapy in a low dose (25–50 mg per day) in 17 CVS patients was associated with complete remission in nearly 1 out of 5 patients and partial response in over one-half of the patients. In the Kansas study, 27 patients were treated with a high dose of the antidepressant amitriptyline, and 93% of the patients showed a favorable response with decreased frequency and severity of their symptoms; one-quarter achieved full remission. Patients also reported improvement in their mood and anxiety symptoms, as well as prevention and treatment of migraine. Prophylactic antimigraine and anticonvulsive agents are also used to prevent episodes.

A multi-disciplinary approach has been found useful in treating children. This includes a supportive doctor-patient relationship, social and psychological counseling, use of medications to stop or shorten the acute attacks, use of medications to be used chronically to prevent the attacks, and the treatment of complications that might arise. This approach is now being tried in adults. It is helpful to have an organized approach to treat these patients in the emergency room where they often need to go for treatment of the acute vomiting phase. Since the patients often present with stereotypical symptoms, repeat evaluation of the patient is often not needed. A physician letter for the patient to have that describes the syndrome and the appropriate personal treatment is often helpful for patients. Having the assurance of a planned, quick, predictable, effective treatment serves to facilitate early intervention for patients should they need emergency treatment and often helps to diminish anticipatory anxiety of the patients. Anticipatory support and early treatment intervention are cornerstones to the treatment of CVS.

## Summary

Cyclic vomiting syndrome can occur in adults as well as children and is an increasingly recognized disorder. Important advances are being made in our clinical understanding of this disorder. New treatments are becoming available. Long-term outcomes and the natural history of cyclic vomiting syndrome in adults will require more studies.

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