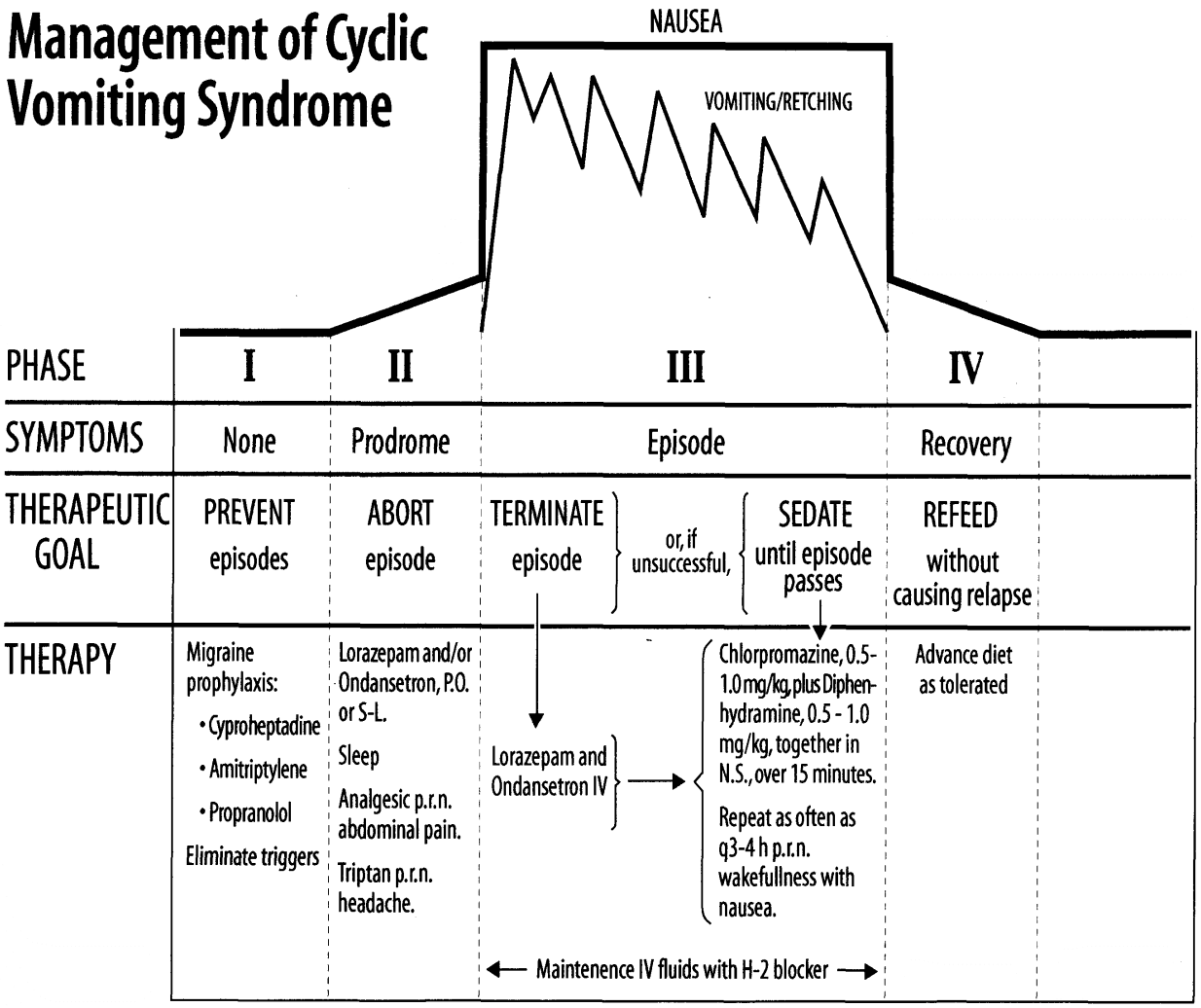
Empiric Guidelines for the Management of Cyclic Vomiting Syndrome

There is as yet, no standard, evidence-based treatment regimen for CVS. Management must be individualized and "fine-tuned" during the course of the patient's illness. The following guidelines are offered not as a recipe, but as a conceptual framework from which to begin. Management strategy is based on the four phases of CVS. Treatment is applied according to the phase the patient is in at the time of presentation. Each phase has its goal and treatment options aimed at achieving the goal.



PHASE I is the nausea-free interval between episodes. Appropriate treatment includes migraine prophylaxis if episodes are frequent, long or difficult to abort. A daily dose of amitriptylene h.s. propranalol or cyproheptadine may lessen the frequency or duration of episodes. In addition, try to identify and ameliorate conditions that may predispose to or trigger episodes, such as chronic sinusitis, clinically significant anxiety, PMS, motion sickness or metabolic stress (e.g. prolonged caloric deprivation in patients who may have a defect in fatty acid oxidation).

PHASE II, the prodrome, is the interval that starts when the patient begins to feel symptoms signalling the approach of an episode, but is still able to retain oral medications. It ends with the onset of vomiting. The prodrome might last days, minutes, or may not occur at all in patients who wake from sleep already vomiting. To treat it, discern its constituent symptoms and relieve each as quickly as possible, before the prodromal phase gives way to the episode.

For *nausea,* try ondansetron (Zofran) liquid, tablets or ODT's (oral disintegrating tablets) at 0.3 – 0.4 mg/Kg/dose. (This is twice the dose recommended for chemotherapy patients.) *Anxiety* potentiates nausea. Lorazepam (Ativan) is anxiolytic, anti-emetic and promotes sleep. It works well together with ondansetron. Lorazepam tablets are almost tasteless and dissolve in the mouth without the patient having to drink. If the predominant prodromal symptoms are those of acute anxiety (e.g. chills and/or hot flushes, sweating, trembling, palpitations, pounding heart, dyspnoea, light headedness), alprazolam (Xanax), a rapidly acting anxiolytic, 1 to 2 mg p.o. taken immediately, may abort the anticipated vomiting.

For midline *abdominal ache* (the predominant symptom in abdominal migraine), try ibuprofen p.o. or, if necessary, hydromorphone (Dilaudid), 3mg at a dose of about 0.08 mg/Kg/dose by rectal suppository. For *headache* with features of common or classical migraine, try ibuprofen or sumatriptan (by tablet or nasal spray). A proton pump inhibitor (e.g. Prilosec or Prevacid) may lessen *epigastric distress and heartburn*. Some patients experience *loose stooling*, a symptom that prevents use of suppositories. If diarrhoea is troublesome, loperamide (Imodium) p.o. and/or hyoscyamine S-L may help. Mild-to-moderate *hypertension and tachycardia*, caused by adrenergic discharge originating in the hypothalamus, may begin during the prodrome. Propranolol (Inderal), 0.1 – 2.0 mg/Kg/dose p.o., may lessen these effects.

PHASE III, the episode itself, is characterized by intense nausea and vomiting. Typical behavioural states are: 1) subdued, but responsive; 2) an immobile, unresponsive state referred to as "conscious coma"; and 3) writhing and moaning. Patients who are subdued but responsive usually prefer to lie down, but may be able to walk about, watch TV or attempt to play between bouts of vomiting. Patients in "conscious coma" lay motionless, eyes closed, and are so unresponsive that it is difficult to know whether they are awake or asleep. Patients who writhe and moan between bouts of vomiting have intense abdominal ache and/or severe retrosternal pain.

The possible acute complications of untreated episodes include hypovolemic shock, electrolyte depletion, tetany, hematemesis, and secretion of inappropriate anti-diuretic hormone (SIADH). The nausea of CVS episodes is agonizing. Therefore, treatment of CVS episodes must be prompt. If treatment is delayed, the patient's extreme distress predisposes them to fear the next episode, and, since anticipatory anxiety can cause nausea, their fear may cause more frequent attacks. Episodes that cannot be aborted should be treated without delay, ideally within an hour of onset. "Watchful waiting" or long waits in treatment facilities are counter-therapeutic.

To treat Phase III, cannulate a vein, draw whatever diagnostic blood samples are necessary, consider the need for a normal saline bolus, and start maintenance IV fluids. If the possibility of an underlying metabolic defect such as MCAD has not

been ruled out, the IV fluid should contain 10% glucose during the first 24 hours; the response or lack of response to IV glucose has diagnostic and therapeutic implications. Otherwise, 5% dextrose in 0.5 N saline with KCl and an H-2 blocker can be used for IV fluid maintenance. As soon as IV access is established, attempt to *terminate* the episode by giving lorazepam by slow IV push (0.05- 0.1mg/Kg , maximum 3 mg/dose) and ondansetron (0.3-0.4 mg/Kg/dose) by IV piggyback over 15 minutes. The patient will respond in one of three ways: 1) the nausea clears and doesn't return; 2) the nausea clears, but returns within minutes or hours; or 3) the nausea doesn't clear. In the first case, cap or remove the IV, give 4 to 8 mg p.o. of ondansetron and send the patient home. In the second and third cases, termination has failed and there is no way to give relief other than to *sedate* the patient. The brain, not the GI tract, is the origin of cyclic vomiting and sleep stops such vomiting. It also makes patients unaware of their nausea, giving them an escape from what would otherwise be relentless misery. Preferred sedative drugs are non-addictive and non-emetogenic. Chlorpromazine combined with diphenhydramine usually work well: mix chlorpromazine (0.5 – 1 mg/Kg/dose) with diphenhydramine (0.5 – 1 mg/Kg/dose) in 50 cc of normal saline and infuse over 15 minutes. This combination of sedatives should be repeated as needed for wakefulness with nausea, as often as q 3-4 hours for as long as the episode lasts.

Keep the patient's room darkened and quiet. Minimize waking the patient for vital signs and other procedures as much as possible. Concerned parents understandably feel the need to evoke a response from their sick, uncommunicative child and may repeatedly ask, "Are you OK?" Although children need to know that their parents are available and supportive, they feel burdened by such demands for responsiveness. Family and hospital personnel should avoid causing this kind of distress as much as possible. If the patient does not remain asleep for at least 3 hours at a time, either increase the dose of IV chlorpromazine towards 1 mg/Kg/dose or give the patient a spot dose of IV lorazepam (0.05 -0.1 mg/Kg/, maximum 3mg) by slow IV push. Reliance on lorazepam alone for sedation, or too frequent administration of it, causes a state resembling alcohol intoxication that may prolong recovery by a day or two. Chlorpromazine and diphenhydramine don't seem to cause as much "hangover."

Hematemesis is common. It is often due to "prolapse gastropathy" in which there is bleeding of the mucosa of the proximal stomach as intense retching forces the cardia up into the lower oesophagus where it is squeezed and bruised. Although hematemesis of this type seldom causes serious blood loss, it does not preclude bleeding from the oesophageal mucosa or from Mallory-Weiss tears. Monitor the pH of vomitus. If it remains below 4.5, increase the IV dose of H-2 blocker. Intense nausea may be accompanied by SIADH. Monitor urine specific gravity; if it remains high in the presence of adequate hydration, check for low serum osmolality and hyponatremia and restrict water input until lab values return to normal.

Many patients experience intense thirst which compels them to drink, even though they know it will come back up almost immediately. If compulsive drinking is followed by self-induced vomiting during episodes, don't mistake this behaviour for bulimia! Drinking dilutes acid and bile, thereby making the vomitus less of a contact irritant to the oesophagus and mouth. Emesis can be induced more easily from a full stomach than an empty one. The transient lessening of nausea that follows self-induced vomiting makes this comfort-seeking behaviour worth the trouble for some

patients. Keeping the patient n.p.o. is almost impossible. Sedation eliminates the drink-and-vomit behaviour. Intense nausea may cause patients to spit-out rather than swallow their saliva. They may carry a pan or towel in which to expectorate. Others are prevented from speaking by a mouthful of saliva they are unwilling to swallow. Sedation eliminates these behaviours.

During episodes, some patients may behave in ways that offend their caregivers. Older patients who have a strong panic component to their distress may pace about or smoke. They may behave rudely, becoming hostile and demanding. Such obnoxious behaviour should not be taken as a personal affront. It is symptom-behaviour in an individual who is suffering misery they cannot get rid of. They are sharply intolerant to perceived delays in treatment of their distress. Give them relief and, even more important, provide them with a plan of treatment they can access reliably when they need to, and the abusive behaviour ceases.

Neutrophilia without a left shift is sometimes present during attacks, even in the absence of infection. It is probably caused by stress-induced demargination. It, together with abdominal pain and vomiting, can mimic appendicitis or pyelonephritis. Occasionally, increased serum amylase of salivary origin mimics pancreatitis.

PHASE IV. The recovery phase begins when vomiting is over and the nausea begins to subside. It ends when the patient's appetite, tolerance for food, and vigour become normal. Recovery tends to be prolonged when inadequate management of the episode permitted severe fluid and electrolyte deficits and marked weight loss. Some patients are able to tolerate a regular diet as soon as their nausea lifts. Others may suffer a resumption of nausea and vomiting if they take more than clear liquids initially. It doesn't take long for patients to learn when and what they can eat and drink. Allow them to decide. Prophylactic medications should be resumed as soon as recovery is complete.

CVS patients and their families have many fears concerning their mysterious, unpredictable disorder. One fear is that the illness might never go away. They need to be assured that, although there may be several or several hundreds of episodes during a course lasting months or decades, CVS, effectively managed, resolves in almost every case.

Another fear is that their physician might lose interest and become less accessible. Physicians want to help patients and it is understandable if they become discouraged when they feel unable to help the patient who is not improving. If the physician does lose interest because the challenge seems so daunting, he or she may deprive the patient of what is most essential and most valued under the circumstances: continuation of a relationship with perhaps the only physician who is caring, accessible and willing to collaborate with them in their struggle for well-being.
Until the time when CVS becomes curable, we must not allow ourselves to be defeated by failure.

David R. Fleisher, MD, Associate Professor, Department of Child Health, University of Missouri, School of Medicine, Columbia, Missouri, USA