

JOHNS HOPKINS ALL CHILDREN'S HOSPITAL

Cannabinoid Hyperemesis Syndrome Clinical Pathway



JOHNS HOPKINS
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This pathway is intended as a guide for physicians, physician assistants, nurse practitioners and other healthcare providers. It should be adapted to the care of specific patient based on the patient's individualized circumstances and the practitioner's professional judgment.

Johns Hopkins All Children's Hospital
Cannabinoid Hyperemesis Syndrome Clinical Pathway

Rationale:

This clinical pathway was developed by a consensus group of JHACH physicians, advanced practice providers, nurses, and pharmacists to standardize the management of children hospitalized for **Cannabinoid Hyperemesis Syndrome (CHS)**. It addresses the following clinical questions or problems:

1. When to evaluate for Cannabinoid Hyperemesis Syndrome
2. When to consider admission for further evaluation
3. When to consult the Gastroenterology Clinical Team
4. When to consider escalation in treatment

Background

The rate of cannabis uses for both medicinal and recreational purposes continues to rise in the United States. Cannabis can now be purchased online and in stores across many states, and it can be consumed in various ways (e.g., smoked, inhaled, ingested). Additionally, the potency of THC in newer strains and the risk of these cannabis products being “laced” with other illicit substances has made cannabis use more dangerous. Despite this, cannabis use among pediatric patients has continued to increase, with many adolescents citing a reduction of perceived risk due to its recent legalization in most states.¹

In correlation with the increased usage of cannabis products, symptoms have emerged, including abdominal pain, intractable vomiting, and nausea, with patients seeking hot showers for symptom relief. This combination of symptoms has become recognized as “cannabinoid hyperemesis syndrome” or “CHS”.² CHS is seen in patients with prolonged cannabinoid use, loosely defined as “weekly use for greater than three months”.³ Convenient access to various forms in conjunction with variable standards of regulation increases the risk for the consumer. This increased risk may also contribute to neuropsychiatric changes in a developing brain.¹ Medical use of cannabinoids is most directly associated with its anti-emetic effects observed in chemotherapy users and its role as an appetite stimulant. In pediatric patients, cannabidiol has demonstrated efficacy as an adjunct in anti-convulsive therapy. However, the psychoactive THC component is removed in this formulation. The known benefits of cannabinoid-based products in pediatric patients are limited due to a lack of research, and the risks to a child’s developing brain are poorly understood.

Pathophysiology

Endocannabinoid receptors are present in both the brain and the gut. In normal physiology, it is proposed that THC stimulates these receptors and has a regulatory effect on the emetic center of the brain, intestinal secretions, motility, and perception of visceral pain. This explains why cannabis products have been used to relieve emesis and chronic pain.³⁻⁴

In CHS, the proposed pathophysiology involves the over-stimulation of these receptors and loss of the regulation of these processes. This “intoxication” of the endocannabinoid system

results in a paradoxical response to THC: intractable emesis, visceral pain, and anxiety. In addition, repeated cannabinoid use leads to loss of endogenous thermoregulation, creating hypothermia which further triggers nausea and vomiting and may explain the behavioral component of seeking hydro-thermotherapy.³ It is important to note that the pathophysiology of this over-stimulation of the endocannabinoid system differs from the withdrawal effects of THC use. For a more detailed description of the pathophysiology of CHS, please see [Appendix A](#).

Diagnosis

The following components of the H&P may support (but cannot confirm) the diagnosis of CHS:

- Intractable vomiting with no other identifiable cause
- Positive urinary THC screen
- The average duration of symptoms occurs for 3 – 4 days and occurs between periods when the patient is well and without symptoms
- The patient's symptoms do not respond to customary antiemetic and analgesic treatment like 5-HT₃-receptor antagonists (ondansetron)
- Hot showers are well known to the patient as a reliable therapy to ease symptoms
- Patient lacks symptoms that may suggest prompt surgical intervention: high fever, abrupt onset with it being the first occurrence of symptoms, rigid/guarding abdomen, bloody stools, bloody emesis, or abnormalities seen on baseline initial routine lab work (CBC, CRP, ESR, procalcitonin, etc.)

The diagnosis of CHS is ultimately a diagnosis of exclusion. The non-exhaustive list of differential diagnoses is due to the vague constellation of symptoms (nausea, cyclical/intractable emesis, and abdominal pain) that can also occur in many other pathologies (Table 1). Obtaining a complete and detailed history should include asking about long-term cannabis use (synthetic, edible, botanical, prescription “medical marijuana”).⁵

Table 1. Alternative Differential Diagnoses Considerations for Intractable Nausea/Vomiting and Abdominal Pain	
<p><i>Gastrointestinal System</i></p> <p>Gastroenteritis CHS IBD Functional Abdominal Pain Cholecystitis Choledocholithiasis Cholelithiasis Constipation SBO/LBO Pancreatitis Appendicitis and Diverticulitis GERD PUD</p>	<p><i>Central Nervous System</i></p> <p>Elevated ICP CVA Concussion Vertebral Injury Vestibular Concerns Migraines Dysautonomia Neuromyelitis Optica HPA Axis Hyperactivity</p>
<p><i>Genitourinary System</i></p> <p>Nephrolithiasis Urinary Tract Infections Pregnancy Hyperemesis Ectopic Pregnancy Ovarian/Testicular Torsion Menstrual Cramps</p>	<p><i>Other Systems</i></p> <p>Metabolic/Mitochondrial Disorders Ingestion Endocrine- Endocrine Tumors, DKA, Thyroid Psychiatric- Cannabis Withdrawal Syndrome, Eating Disorders, Cyclic Vomiting Syndrome, Rumination Syndrome</p>

Historically, the diagnosis of CHS in adult patients has been made using Rome IV criteria (Table 2). However, the current Rome IV criteria for CHS are not all-encompassing to recognize and appropriately diagnose all patients with CHS.⁷ In addition, data on the relationship of symptom resolution to cessation is incomplete. Further, no definition for defining clinically significant ‘cessation’ exists.⁸ Some patients are unwilling to accept cannabis use as the root cause of their disorder. The largest case study to date of pediatric and adolescent CHS instead offers pragmatic criteria that can provide firm clinical guidance.³ These are summarized in Table (3).

Table 2
Rome IV criteria for cannabinoid hyperemesis syndrome
<p>Stereotypical intractable and cyclical vomiting that resembles the onset, duration, and frequency parameters in (CVS)</p> <p>Patient is usually presenting with these symptoms after prolonged excessive cannabis use</p> <p>Relief of vomiting episodes by sustained cessation of cannabis use</p> <p>Supportive History:</p> <p>Pathologic bathing behavior (prolonged hot baths or showers) may help relieve symptoms</p>
<p>Note</p> <p>Criteria fulfilled for the last 3 months, symptom onset at least 6 months before diagnosis.</p>

Table 3
Pragmatic diagnostic criteria for adolescent cannabinoid hyperemesis syndrome [11]
<p>Major criteria (reported in all patients)</p> <ul style="list-style-type: none"> ~ Regular cannabis use for 3 months or more ~ Onset or worsening of episodic nausea and vomiting resembling CVS, after the start of regular cannabis use ~ Absence of other underlying medical conditions which could explain symptoms, after all appropriate negative investigations
<p>Supporting criteria (reported in majority of patients)</p> <ul style="list-style-type: none"> Symptomatic relief with hot showers/baths Weight loss Abdominal Pain Change in bowel habit

At this time, there are no confirmatory tests for CHS. Consequently, some patients may undergo extensive negative investigations. Appropriate testing and suspicion for CHS should be considered and remain high in any patient presenting with hallmark symptoms.

Differentiating Between Cyclical Vomiting Syndrome (CVS) and CHS

Both syndromes present with recurrent episodes of vomiting and nausea with abdominal pain. These syndromes can be difficult to differentiate, and both possess a unique feature in which symptoms may be relieved by the act of taking hot showers.⁹ Current literature demonstrates the utilization of gastric emptying studies can be beneficial to aid in differentiating the diagnosis between the two. With CHS, delayed gastric emptying is a potential sequela, whereas increased gastric emptying is commonly seen in CVS.¹⁰ Gastric emptying studies expose the patient to radiation. This should only be investigated if the patient has a history of symptoms in the absence of positive THC on a urine drug screen, or if the patient has been treated for CHS and continues to be symptomatic.

Differentiating Between Cannabis Withdrawal Syndrome (CWS) and CHS

In both CHS and CWS, the use of cannabis may appear to cause symptomatic relief. Once a history of cannabis use is established and the exclusion of other similar presenting pathologies made, key points in the patient’s history about the onset of symptoms and time of last consumption of cannabis can help the provider differentiate CWS and CHS.¹¹ Patients presenting with CHS usually demonstrate symptoms within 24 hours of last consumption compared to patients presenting with CWS who can present with symptoms anytime from 1 to 10 days after their last consumption.^{11,12} Additionally demonstrated correlations of reported systemic/psychological symptoms with key clinical history information are described in the table below to help guide provider clinical decision-making.

Table 4. Key clinical history information to help guide clinical decision-making in CWS vs. CHS¹¹

	Cannabis Withdrawal	Cannabinoid Hyperemesis
Onset of symptoms from last consumption of cannabis product	> 24 hours	< 24 hours
Symptomatic relief experienced with hot showers	No	Yes
Noticeable associated psychological symptoms (e.g., irritability, sleep difficulty, nervousness, restlessness, and depression)	Yes	No
Clinical course/pattern	No defined pattern; the patient may share symptoms that occur when attempting to abstain	Well described, 3 clear phases of symptoms History of escalation of dosing to combat tolerance
Quantity of cannabis ingestion/use history correlates with severity of presenting symptoms	Yes	No

Lab tests:

Key initial laboratory tests to consider:

1. **Urine drug screening:**
 - Of note, the urine drug screen used at JHACH tests for THC, the psychoactive cannabinoid
 - Patients taking cannabidiols (such as CBD oil or Epidiolex®) are not expected to test positive for THC on this assay
2. **Complete Metabolic Panel:** important to assess for electrolyte disturbances, hypoglycemia, and acute kidney injury in the setting of dehydration/volume depletion

Clinical Management

Fluid Management

Intravenous fluid resuscitation with bolus and maintenance fluids should be provided appropriately for the degree of dehydration in the patient. Studies in CHS have only included the use of normal saline. Maintenance fluids should aim to correct metabolic and electrolyte derangements. Excessive vomiting may result in hypokalemia, hypochloremia, hyponatremia, and contraction alkalosis. Additionally, if symptoms lead to prolonged periods of poor oral tolerance, patients may also present with signs of hypoglycemia. Severe electrolyte derangements increase the risk of cardiac arrhythmia, which may be exacerbated by the QT-prolonging effect of medications used in the treatment of CHS. If the patient's potassium level is < 3 mEq/L, repletion with IV potassium is indicated.¹³

Medical Management of Hyperemesis

In the treatment of emesis for CHS, 5-HT₃-receptor antagonists (ondansetron) are noted to be less effective in resolving emesis; approximately one-third of patients respond to enteral ondansetron. The failure of ondansetron to resolve symptoms is a hallmark feature of CHS. However, the use of ondansetron remains the first-line therapy as a response to ondansetron may allow the patient to be discharged home with enteral therapy. Additionally, it is anticipated that patients will receive a dose of ondansetron in EC triage if they present with vomiting. However, recent studies suggest that low-dose haloperidol is superior to ondansetron in decreasing nausea and abdominal pain and leading to shorter stays in the Emergency Center.¹⁵ Therefore, if a patient seen in the EC has demonstrated poor response to ondansetron in triage, then no further doses of ondansetron should be given.

There is currently limited strong-quality evidence that supports haloperidol as a treatment modality. Current evidence is derived mostly from case reports and case series, which lacks generalizability. The *Haloperidol versus Ondansetron for Cannabis Hyperemesis Syndrome* (HaVOC study) is a randomized controlled trial that demonstrated promising results as it was found to have low bias, appropriate blinding of participants, and appropriate randomization of cohorts.¹⁶ However, the study reviewed participants with an average age of 29 years, highlighting the need for higher quality evidence that outlines the effectiveness of therapy route, duration, and dosage in managing CHS symptoms among the pediatric and adolescent population. The evidence would be important in guiding the management of CHS symptoms for this age group. The dose and route recommendations presented in this pathway are sourced from a cumulation of the reviewed literature, current FDA pediatrics standard dosing, current FDA-recommended pediatric route administration, and clinical judgment.

Of note, there is a higher risk of QT-interval prolongation and torsade de pointes when haloperidol is administered intravenously, which is not a recommended or approved route of administration in the pediatric population. Caution is warranted when treating patients with congenital QT-prolonging conditions, familial long QT syndrome, hypothyroidism, concomitant QT-prolonging drugs, or underlying cardiac abnormalities. In patients with these preexisting conditions, physicians should obtain an ECG and metabolic screen before enteral or intramuscular administration and review the patient's medication history to determine potential risks or interactions.

If haloperidol must be given intravenously, and if the patient being treated displayed abnormalities on their ECG, the patient should be transferred to the PICU for continuous cardiac telemetry.

In the case that haloperidol is not effective, case reports have shown benzodiazepines may be effective, likely due to their similar effect on anxiolysis. This may be considered a third-line for patients who have failed ondansetron and haloperidol with adjunct topical therapies.

Table 5. Pharmacologic Considerations for the Management of CHS

	Route	Dose
First-Line: ondansetron	Enteral, if not tolerated, start with intravenous	0.3 - 0.4 mg/kg/dose (max dose 8 mg) Maximum daily dose: 32 mg/DAY
Second-Line: haloperidol	Enteral/ Intramuscular/ Intravenous	0.05 mg/kg/dose (max dose 2 mg), not exceeding the maximum weight-based dose: Patients ≤ 40 kg: 6 mg/DAY Patients > 40 kg: 15 mg/DAY
Third-Line: LORazepam	Intravenous	0.025 - 0.05 mg/kg/dose (max dose 2 mg)

Medical Management of Abdominal Pain

Management of abdominal pain is focused on redirecting blood flow away from the viscera. Topical application of capsaicin cream (0.025%) or hydrotherapy with warm water (a warm bath or shower) are both options that promote vasodilation and redirection of blood to the body's surface. A trial of capsaicin cream, if not already started in the EC, may be considered as an initial adjunct to medical treatment. It is recommended to use a small amount and observe for adverse reactions (e.g., blistering of skin, irritation). Treatment with capsaicin cream alone has not been shown to reduce abdominal pain.⁴ When the patient has been admitted to the inpatient floor, they may choose to try hydrotherapy with a warm shower; it is recommended that the water temperature not exceed 100° F (38° C).

Opioid administration for the treatment of abdominal pain in CHS may theoretically worsen the pain, as opioids have a known side effect of slowing gut motility. Narcotics are not advised.

Initial Clinical Monitoring

Abdominal imaging is often obtained in the EC setting to rule out other etiologies of abdominal pain and vomiting and is recommended if there is high clinical suspicion for possible causes of an acute abdomen. Repeat abdominal imaging is not recommended unless there is suspicion that the patient has developed esophageal injuries such as Mallory-Weiss tears or pneumomediastinum due to prolonged forceful vomiting.

Counseling on Substance Use

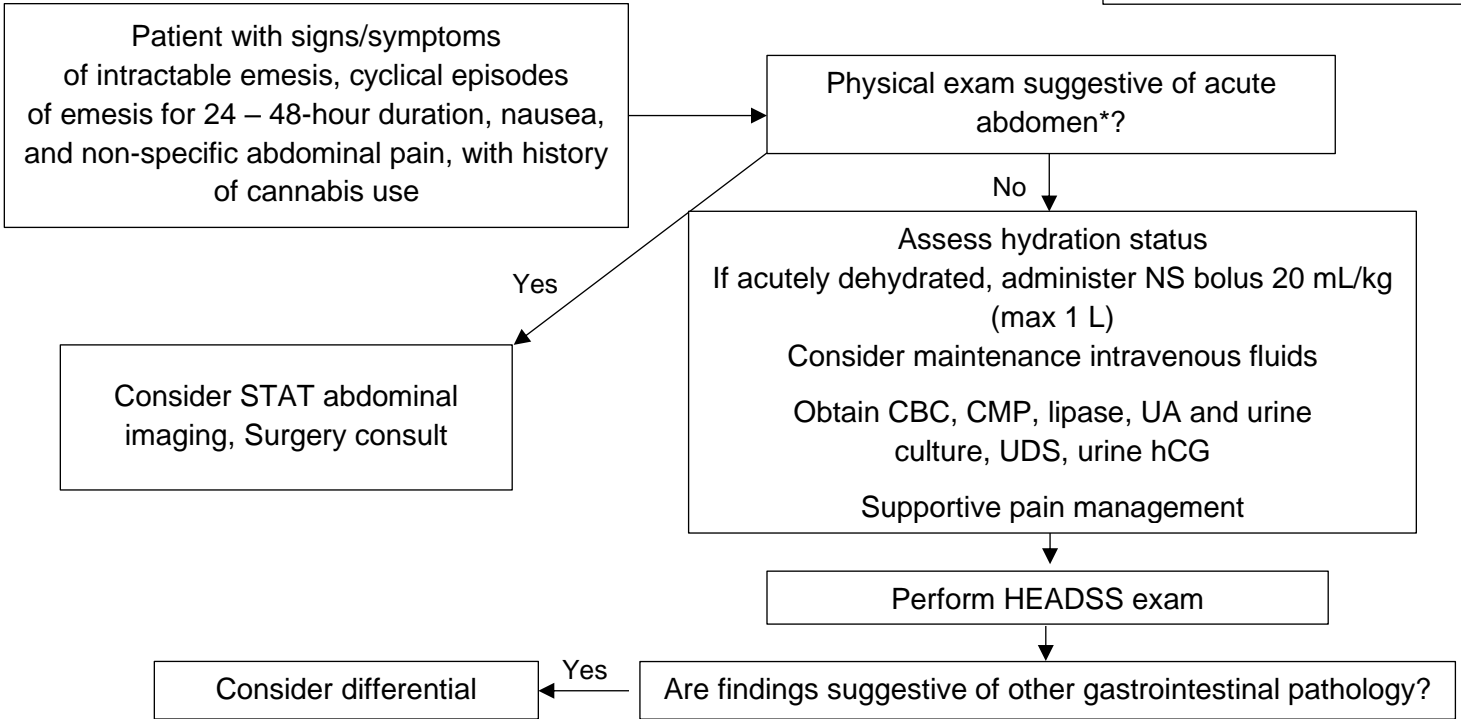
It is important to counsel patients who present with CHS that the only known effective long-term treatment for CHS is abstinence from all forms of cannabinoid consumption. The recurrence of CHS symptoms is high in patients who resume using THC products. Adolescents should be screened for the use of other illicit substances at the time of presentation. Recommended screening tools include the CRAFFT questionnaire. Please see [Appendix A](#) for a [HEADSS exam](#) that is for substance use concerns.

If an adolescent is noted to have multiple emergency center visits and/or hospital admissions for a confirmed diagnosis of CHS, it is recommended that the adolescent is referred to a rehabilitation program that focuses on substance abuse disorder.

With the increasing use of “medical marijuana,” many adolescents identify their use of marijuana as a treatment for nausea, untreated anxiety and/or depression, and chronic pain. It is important that these patients be counseled that marijuana use has been found to worsen these conditions, and alternative treatment options should be discussed with their primary pediatrician.

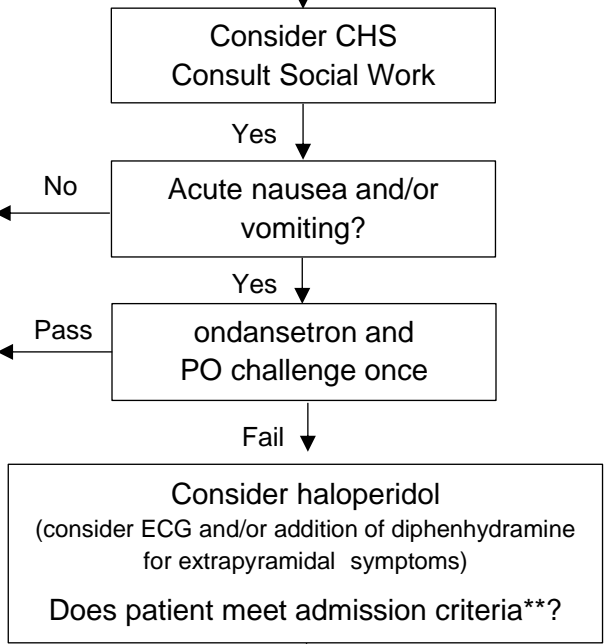
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Emergency Center CHS Clinical Pathway

*Signs of an acute abdomen include rigidity, guarding, non-distractible pain, distension, vital sign instability, and/or fever



- Discharge Criteria**
- Able to tolerate PO intake
 - Adequate pain control
 - Adequate hydration
 - Controlled emesis (with or without medication)
 - Provide education on disease, abstinence from cannabis, state-specific resources
 - Consider GI referral
 - Consider referral to Adolescent Med Clinic and Psychology for substance use counseling
 - Consider blocking note based on patient preference

- **Admission criteria**
1. Intractable vomiting
 2. Dehydration and requirement for IVF
 3. Failed PO challenge
 4. Multiple ER visits without resolution
 5. Uncontrolled pain



- Decision to admit the patient:**
- Consider GI consult on all patients
 - Continue or start maintenance IV fluids
 - Consider proton pump inhibitor
 - Supportive pain management
 - Admit as Observation status

Emergency Center Management

Patients with signs and symptoms of intractable emesis, cyclical episodes of emesis, and non-specific abdominal pain with a history of cannabis use warrant further evaluation. If not already performed, a thorough HEADSS exam is critical to ascertain a diagnosis of CHS. Once an acute abdomen or other differential has been excluded, initial management includes assessment of hydration status, rehydration, lab work as detailed above, as well as supportive pain management. A consultation should be placed with Social Work. A PO challenge is critical to determining whether the patient can be safely discharged or warrants admission.

May consider admission for observation if the patient has been seen in Emergency Center multiple times with the similar presentation

<i>DIFFERENTIAL</i>	Cannabis Hyperemesis Syndrome	Cannabis Withdrawal Syndrome	Cyclic Vomiting Syndrome	Rumination Syndrome	Eating Disorder	Gastroenteritis
Pathophysiology	Functional GI Disorder	Substance Abuse Condition	Functional GI Disorders	Functional GI Disorder	Psychiatric Disorder	Gastrointestinal Disease
Symptoms	<ul style="list-style-type: none"> Intractable vomiting Seeking a hot shower for relief 	<ul style="list-style-type: none"> Vomiting days to within 1 week of cannabis use 	<ul style="list-style-type: none"> (+) recurrent vomiting episodes (-) cannabis use (+/-) use of hot showers as a way to mitigate symptoms 	<ul style="list-style-type: none"> Frequent spit-ups or regurgitation of digested foods exacerbated by anxiety 	<ul style="list-style-type: none"> Vomiting secondary to active self-induction 	<ul style="list-style-type: none"> Nausea Vomiting Diarrheal disease Acute onset
Diagnosis	<ul style="list-style-type: none"> Diagnosis of exclusion based on history, symptoms, and clinical exam 	<ul style="list-style-type: none"> Can occur after a single use with cessation of symptoms after 1 week of cessation 	<ul style="list-style-type: none"> (+) increased gastric emptying 	Rome IV criteria: <ul style="list-style-type: none"> Persistent or recurrent regurgitation of recently ingested food into the mouth with subsequent spitting or re-mastication and swallowing Regurgitation is not preceded by retching 	<ul style="list-style-type: none"> Disordered eating habits with purging secondary to body dysmorphia-related etiology Dependent on DSM criteria 	<ul style="list-style-type: none"> Acute onset with associated diarrhea with the potential infectious agent

Emergency Center Medications Table

Medication	Route	Dose	Comments
acetaminophen	Enteral/Rectal	10 – 15 mg/kg/dose (max dose 1000 mg)	Max 90 mg/kg/DAY or 4000 mg/DAY
capsaicin	Topical	0.025% topical	Monitor use and placement, as may result in burning of the skin
haloperidol	Enteral/ Intramuscular/ Intravenous	0.05 mg/kg/dose (max dose 2mg)	
ibuprofen	Enteral	10 mg/kg/dose (max dose 800 mg)	Max 2400 mg/DAY
lansoprazole	Enteral	1 mg/kg/dose (max dose 30 mg)	
LORazepam	Intravenous	0.05 mg/kg/dose (max dose 2mg)	
ketorolac	Intramuscular/ Intravenous	0.5 mg/kg/dose (max dose 30 mg)	Max of 5 days
ondansetron	Enteral/Intravenous	0.3 – 0.4 mg/kg/dose (max dose 8 mg)	
pantoprazole	Intravenous	1 mg/kg/dose (max dose 40 mg)	

Admission

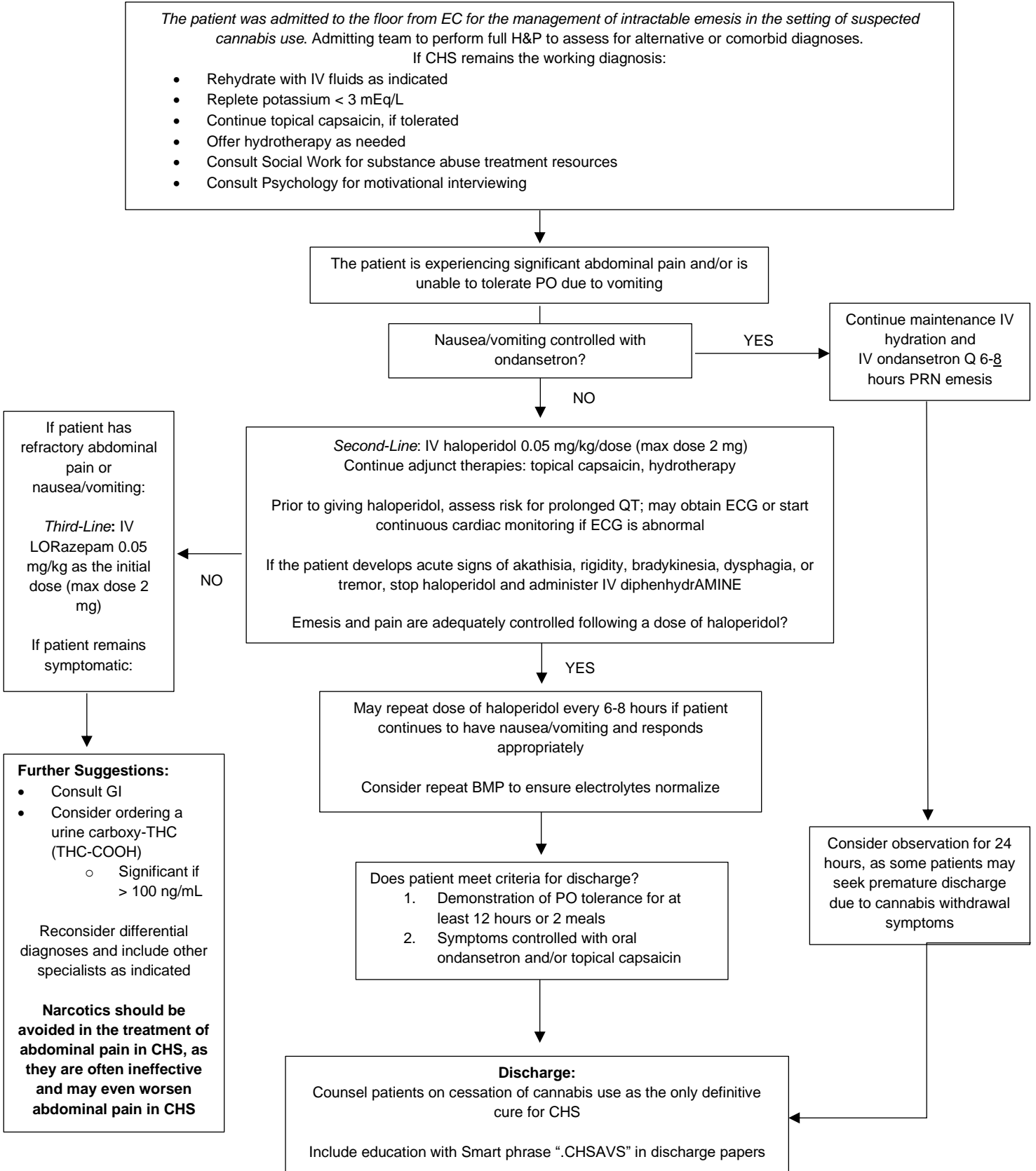
Admission criteria include:

1. Intractable vomiting
2. Dehydration and requirement for IVF
3. Failed PO challenge
4. Multiple ER visits without resolution
5. Uncontrolled pain

When the decision has been made to admit the patient:

- Consider GI consult on all patients in order to: **why*****
 - establish follow-up, especially given this is a diagnosis of exclusion
 - provide multidisciplinary approach to management at time of discharge
- Continue or start maintenance IV fluids
- Consider ordering proton pump inhibitor if gastritis suspected
- Supportive pain management
- Admit as **Observation** status

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Inpatient Treatment Algorithm for Cannabis Hyperemesis Syndrome:



Inpatient Management

Clinical management of admitted patients focuses on adequate rehydration and monitoring for effectiveness and adverse reactions from medical treatment.

Patients should continue to receive IV fluids for rehydration until they are hemodynamically stable and able to tolerate adequate oral hydration. Determination of when to trial oral intake of fluids or food is at the discretion of the inpatient team and the patient.

It is anticipated that patients will receive at least one dose of ondansetron in EC triage. If the patient did not respond to ondansetron and remains symptomatic, they should receive one dose of haloperidol and be observed for response. Patients may continue to receive haloperidol every 6 hours until they can tolerate oral medications. At that time, the team may continue an observation period to ensure the patient can successfully continue oral medications and oral hydration outpatient. Patients should not be discharged with oral haloperidol.

Consults to Pediatric Psychology and Social Work are recommended for all patients. These specialists provide resources for substance abuse programs and support for mental health needs. All patients admitted to the floor should be screened for depression with a PHQ-9 when sober and comfortable enough to provide an accurate response.

Discharge

Discharge from the floor should be considered when patients meet the following criteria:

- Ability to tolerate 8 hours and two meals without vomiting
- Ability to tolerate adequate oral hydration without IV supplementation for at least 8 hours
- Abdominal pain that is adequately controlled with over-the-counter analgesics at recommended standard dosages
- Emesis that is adequately controlled with oral ondansetron at recommended dosage and frequency
- Clinically improved hydration status, as judged by the team (vital sign stability, adequate urine output)

Providers should be aware that some patients who are experiencing substance use disorder may endorse a sudden improvement in their symptoms and become very insistent on discharge. This may happen when patients experience an intense craving to resume substance use upon discharge. Providers should therefore provide cautious counseling to patients and their caregivers on the likelihood of re-admission for CHS with resuming cannabis use.

Upon discharge, it is highly recommended that patients be given the following resources:

- Education on the diagnosis and prevention of CHS (see pamphlet)
- Referral to Adolescent Medicine or Pediatric Psychology for Substance Abuse Disorder

Documentation Reminders

With the enactment of the 2021 Cares Act, all provider notes, diagnoses, and patient-answered surveys may be viewed by the adolescent patient's proxy if requested. Providers should discuss with the adolescent patient the boundaries of confidentiality, including the following:

- 1) As mandatory reporters, we must report information that is concerning for threats to the patient's (or other vulnerable persons') safety.
- 2) Adolescent patients may request that certain information that is documented in the visit note be kept confidential between the patient and the healthcare provider. However, if the patient's legal guardian requests access to blocked notes, these notes are likely to be shared with the proxy.
- 3) The proxy may ascertain information on substance use by the diagnosis listed in the patient's medical chart and/or AVS.

As such, providers are advised to be forthcoming with adolescents before their HEADSSS exam concerning the limits of patient confidentiality as it pertains to conversations and documentation.

Coding Recommendations for Cannabis hyperemesis

Cannabis Use, specify:

- a) Nondependent abuse vs dependence: what is patient's pattern of use?
- b) Intoxication: was patient under the influence during the encounter
- c) In remission: indicate whether the patient is in remission (based on provider's clinical judgement)
- d) Withdrawal: presence or absence of withdrawal symptoms
- e) Specificity regarding any cannabis-induced disorders such as: anxiety disorder, delirium, delusions, hallucinations, perceptual disturbance, psychosis, sleep disorders, or sexual dysfunction.

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Outcome Measures:

- Readmissions
- Return visits to EC
- Length of stay

Clinical Pathway Team
Cannabinoid Hyperemesis Syndrome Clinical Pathway
Johns Hopkins All Children's Hospital

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Disclaimer

Clinical Pathways are intended to assist physicians, physician assistants, nurse practitioners, and other healthcare providers in clinical decision-making by describing a range of generally acceptable approaches for the diagnosis, management, or prevention of specific diseases or conditions. The ultimate judgment regarding the care of a particular patient must be made by the physician in light of the individual circumstances presented by the patient.

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Appendix A: CHS Pathophysiology

CHS is related to the effect of THC on the cannabinoid receptors of the gastrointestinal and neurologic systems. This dual-system influence contributes to CHS's categorization as a functional disorder of the gut-brain axis. The endocannabinoid system receptors consist of cannabinoid type 1 (CB1) and cannabinoid type 2 (CB2), both of which are present within the GI tract. CB1 receptors exist throughout the body but particularly exercise a sizable portion of their effects on the brain. These receptors influence the hypothalamus-pituitary-adrenal gland (HPA) axis to impact the emetic center, along with the cerebellum, hippocampus, and hypothalamus which controls and influences thermoregulation. CB2 receptors exist within the ileum and along lymphoid cells of the GI where they regulate cytokine release modulating pain response. Therefore, the endocannabinoid system regulates gastric motility, gut secretions, and the modulation of visceral pain. Anandamide (AEA) & 2-AG (arachidonoylglycerol) are enzymes produced by membrane lipids with significantly higher levels within the brain, which will inhibit neurotransmitter release by binding to CB1 leading to their downstream effects (Figure 1).

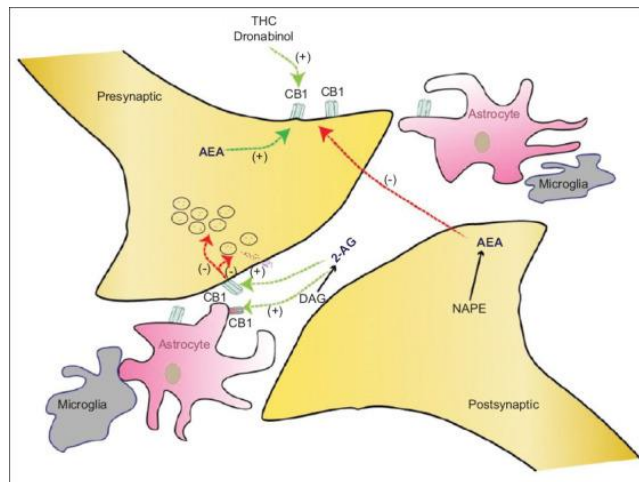


Figure 1. AEA inhibition of NT release by binding the CB1 receptor [Source]

The endocannabinoid receptors (namely CB-1) have a neuromodulatory effect on the HPA axis, regulating emesis by providing negative feedback as decreased effects of this pathway during stress cause increased HPA activity via the Vagus nerve, leading to emesis⁴. Tetrahydrocannabinol, or THC, is the predominant active ingredient in cannabis causing its primary psychoactive effect. This is a lipophilic compound that gets stored in the fat cells of chronic users. During times of active stress, lipolysis occurs causing a re-release of THC into the bloodstream where it exerts its effect on CB1 and CB2 receptors creating a system of re-intoxication. This then overstimulates the emetic centers leading to intractable vomiting.

The proposed mechanism of action for abdominal pain in CHS involves the release of Substance P, a neurotransmitter and pain modulator that also plays a role in gastrointestinal function. It is theorized that the TRVP1 receptor in the vomiting centers of the brain is upregulated by chronic THC use, which leads to unmitigated emetic drive and release of substance P from the Area Postrema, one of the vomiting centers of the brain. Release of Substance P not only leads to visceral hyperalgesia but also the stress-induced release of ACTH and subsequently cortisol. ACTH has a hypothermic effect, and cortisol leads to lipolysis, which may result in the release of lipophilic THC that has been stored in adipose tissue.

HEADSS Exam- example questions as detailed in the AMA Journal of Ethics, March 2005

Home: Where do you live? Who lives at home with you? Do you have any pets? Do you feel safe at home? Do you feel safe in your neighborhood? Are there any guns or other weapons at home? *How are they stored? Do you have access to them?*

Education: *(Note: Often teens are more comfortable answering questions about school than their home life, so you may choose to begin with these questions in your HEADSS assessment.)*

Where do you go to school? What grade are you in? What do you like or not like about school? What is your favorite or least favorite class? Do you feel safe at school? What are your grades like? Do you have an IEP (individual education plan) in place? What do you want to do after finishing school?

Activities/Employment: What do you do for fun? What do you and your friends do together? Are you in any clubs or teams? Do you have a job? *What is your work environment like?* Do you drive? Do you exercise?

Drugs: *(Note: Often teens are more willing to talk about their friends than themselves, so it can be helpful to start with those.)*

Do any of your friends smoke or drink? Do you know anyone who smokes or drinks? Have you ever tried? Have you ever used other drugs (cocaine, methamphetamine, ecstasy, heroin)? *How often do you drink or use drugs? Have you ever had a blackout?*

Suicidality: Have you ever been so sad you thought about hurting yourself? *Have you ever tried?* Have you ever run away from home? Have you ever cut yourself intentionally?

Sex: Have you ever dated anyone? Boys, girls, or both? Have you ever had sex? Has anyone ever touched you in a way you did not want to be touched or forced you to do something you did not want to do sexually? *Are you dating anyone now? Are you sexually active now? When did you last have sexual intercourse? Have you ever had a sexually transmitted infection?*

Reference:

Katzenellenbogen, R. (2005, March 1). *HEADSS: The "Review of Systems" for adolescents*. Journal of Ethics | American Medical Association. Retrieved April 16, 2023.
<https://journalofethics.ama-assn.org/article/headss-review-systems-adolescents/2005-03>

Cannabinoid Hyperemesis Education for Patients & Parents

May be included in AVS with the Smartphrase “.CHSAVS”

You were diagnosed with Cannabinoid Hyperemesis Syndrome. This is a side effect of cannabis use that is becoming more common in people who use cannabis products. Not many people know about Cannabinoid Hyperemesis Syndrome, and you likely have some questions.

What is cannabinoid hyperemesis syndrome (CHS)?

CHS has other names, including “weed sickness,” “scromiting” (screaming and vomiting), and “cannabis poisoning.” CHS happens when a person smokes or ingests cannabis products and develops vomiting and abdominal pain as a side effect of the THC in marijuana. Most patients who get CHS have been using marijuana for at least a year. The symptoms can develop quickly or slowly over several weeks, starting with:

- 1. Nausea may start out mild and get worse over days to weeks. At this stage patients often use more marijuana to try and treat the nausea, but this makes symptoms worse.*
- 2. Abdominal pain may also start out mild and become very severe; some patients may also start to feel anxious.*
- 3. Vomiting can be persistent and uncomfortable, lasting for days. Vomiting in CHS often does not respond to the most common anti-nausea/vomiting medications. Some patients cannot eat or drink and require hospitalization for dehydration.*

How do you know I have CHS?

The doctor will diagnose CHS based on your symptoms and history of cannabis use. Sometimes the symptoms of CHS are mistaken for food poisoning, stomach bug, or even appendicitis, so your doctor will first make sure you do not have any of these problems. Your doctor may also want to test your blood or urine for marijuana or other substances.

What causes CHS?

The exact cause of CHS is still unknown. Current research suggests a receptor in the brain has a role in regulating nausea and appetite, and THC in marijuana can activate this receptor. This may explain why some cannabis products help people with nausea and increase appetite, by

enhancing the activity of this receptor. However, sometimes cannabinoids may overwhelm and then inactivate the receptor, leading to nausea. This same receptor is also present in the stomach and intestines, and in CHS it alters the normal rhythmic movement of the intestines, causing painful abdominal cramping, reflux, and vomiting.

I know other people who have used marijuana, and they do not have CHS. Why did I get sick?

It is not understood why certain people experience CHS and others do not. Some research suggests that increasing potency of cannabis products may be the problem. However, every body is different, and some people's bodies metabolize drugs, foods, and cannabis products differently. Some people may routinely use cannabis products for years without symptoms, while others may experience CHS after they have been using marijuana for only a short period of time.

How is CHS treated?

The abdominal pain and vomiting in CHS does not always respond to the typical anti-nausea and anti-vomiting medications. Some patients with severe abdominal pain and vomiting may need to be hospitalized and get fluids and medications through an IV to make sure they do not become dehydrated. Many patients find that hot showers may help alleviate some of their symptoms, but the only true "cure" to CHS is to stop using cannabis products.

Can I get CHS again?

Patients who experience CHS are likely to have these symptoms again in the future if they continue to use cannabis products. There is no known "safe" amount of THC or cannabis that can be used without causing CHS symptoms.

How can CHS be prevented?

The only way to prevent CHS is to stop using cannabis products. This can be difficult, because many patients feel like they need to use cannabis to control symptoms such as pain, anxiety, and depression. Unfortunately, cannabis products may worsen these symptoms, and long-term use can have negative consequences on the developing adolescent brain. Fortunately, there are safe and effective ways to treat anxiety, depression, and abdominal pain without the addictive and destructive consequences of chronic cannabis use. Talk to your doctor about safe and effective treatment options. If you or a friend are having trouble quitting cannabis, please consider contacting your doctor and asking for help.

Resources for Adolescents who are fighting Substance Use Disorder:

Johns Hopkins Adolescent Medicine Clinic: 727-767-TEEN (8336). Schedule an appointment with our Adolescent Medicine Pediatricians.

Mobile Crisis Response Team: 727-362-4424. This is hotline that is useful for teens who are also struggling with mental health, and can help provide resources for treatment options in your community.

Rockland Treatment Center: <https://www.rocklandtreatment.com/>

Turning Point of Tampa: <https://www.tpoftampa.com/>

River Oaks Treatment Center: <https://americanaddictioncenters.org/treatment-centers/river-oaks>

PAR Academy (Operation PAR): <http://www.operationpar.org/services/adolescent-services/>

Baycare Substance Use Services: <https://baycare.org/services/behavioral-health/substance-use-services>

North Tampa Behavioral Health: <https://www.norhtampabehavioralhealth.com/>