JOHNS HOPKINS ALL CHILDREN'S HOSPITAL

# Cannabinoid Hyperemesis Syndrome Clinical Pathway

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Owners: Michael Wilsey, MD; Paola Dees, MD

Johns Hopkins All Children's Hospital

# Cannabinoid Hyperemesis Syndrome Clinical Pathway

**Rationale:**

This clinical pathway was developed by a consensus group of Johns Hopkins All Children's Hospital (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 CHS
2. When to consider admission for further evaluation
3. When to consult Gastroenterology
4. When to consider escalation in treatment

**Background:**

The rates of cannabis use for both medicinal and recreational purposes continue 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 tetrahydrocannabinol (THC) in newer strains and the risk of these cannabis products being "laced" with other illicit substances have 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 [Stoner 2022].

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 CHS [Dosani 2021]. CHS is seen in patients with prolonged cannabinoid use, loosely defined as "weekly use for greater than three months" [Lonsdale 2021]. Convenient access to various forms in conjunction with variable standards of regulation increases consumer risk. This increased risk may also contribute to neuropsychiatric changes in a developing brain [Stoner 2022]. Medical use of cannabinoids is most directly associated with their antiemetic effects observed in chemotherapy users and their 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 the brain and 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" [Lonsdale 2021; Perisetti 2020].

In CHS, the proposed pathophysiology involves the overstimulation 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 usage leads to loss of endogenous thermoregulation, creating hypothermia, which further triggers nausea and vomiting and may explain the behavioral component of seeking hydrothermotherapy [Lonsdale 2021]. 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 history and physical (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-$HT_3$-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 (complete blood count (CBC), c-reactive protein (CRP), erythrocyte sedimentation rate (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”) [Pergolizzi 2018].

Table 1: Alternative Differential Diagnoses

| Gastrointestinal (GI) System | Central Nervous System |
|---|---|
| • Gastroenteritis<br>• CHS<br>• Inflammatory bowel disease<br>• Functional abdominal pain<br>• Cholecystitis<br>• Choledocholithiasis<br>• Cholelithiasis<br>• Constipation<br>• Small/large bowel obstruction<br>• Pancreatitis<br>• Appendicitis and diverticulitis<br>• Gastroesophageal reflux disease<br>• Peptic ulcer disease | • Elevated intracranial pressure<br>• Cerebral vascular accident<br>• Concussion<br>• Vertebral injury<br>• Vestibular concerns<br>• Migraines<br>• Dysautonomia<br>• Neuromyelitis Optica<br>• HPA axis hyperactivity |
| **Genitourinary System** | **Other Systems** |
| • Nephrolithiasis<br>• Urinary tract infection<br>• Pregnancy hyperemesis<br>• Ectopic pregnancy<br>• Ovarian/testicular torsion<br>• Menstrual cramps | • Metabolic/mitochondrial disorders<br>• Ingestion<br>• Endocrine (endocrine tumors, diabetic ketoacidosis, thyroid)<br>• Psychiatric (CWS, eating disorders, CVS, rumination syndrome) |

Abbreviations: CVS, cyclic vomiting syndrome; CWS, cannabis withdrawal syndrome; HPA, Hypothalamic-pituitary-adrenal

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 in recognizing and appropriately diagnosing all patients with CHS [Schey 2020]. In addition, data on the relationship between symptom resolution and cessation is incomplete. Further, there is no definition for clinically significant ‘cessation’ [Venkatesan 2019]. 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 [Lonsdale 2021]. These are summarized in Table 3.

Table 2: Rome IV Criteria for CHS

| |
|---|
| 1. Stereotypical episodic vomiting resembling CVS in terms of onset, duration, and frequency<br>2. Presentation after prolonged use of cannabis<br>3. Relief of vomiting episodes by sustained cessation of cannabis use |
| Supportive History: Pathologic bathing behavior (prolonged hot baths or showers) may help relieve symptoms |
| *Note*: Criteria fulfilled for the last 3 months, symptoms onset at least 6 months before diagnosis |

Table 3: Pragmatic Diagnostic Criteria for CHS

| |
|---|
| Major Criteria:<br>• Regular cannabis use for 3 months or more<br>• Onset or worsening of episodic nausea and vomiting resembling CVS, after the start of regular cannabis use<br>• Absence of other underlying medical conditions which could explain the symptoms, after all appropriate negative investigations |
| Supporting Criteria:<br>• Symptomatic relief with hot showers/baths<br>• Weight loss<br>• Change in bowel habit<br>• Abdominal pain |

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 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 taking hot showers [Blumentrath 2017]. Current literature demonstrates the beneficial utilization of gastric emptying studies to aid in differentiating the diagnosis. With CHS, delayed gastric emptying is a potential sequela, whereas increased gastric emptying is commonly seen in CVS [Perisetti 2022]. 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 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 is 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 [Razban 2022]. Patients presenting with CHS usually demonstrate symptoms within 24 hours of consumption, compared to patients presenting with CWS who can present with symptoms anytime from 1 to 10 days after consumption [Razban 2022; Gorelick 2012]. Additionally, 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: Clinical History to Guide Clinical Decision-Making in CWS versus CHS

| | Cannabis Withdrawal | Cannabinoid Hyperemesis |
|---|---|---|
| Onset of symptoms from the last consumption of a 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<br><br>History of escalation of dosing to combat tolerance |
| The quantity of cannabis ingestion/use history correlates with the severity of presenting symptoms | Yes | No |

*Lab tests:*
*Key initial laboratory tests to consider*:

1. Urine drug screening (UDS):
    - 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 (CMP): important to assess for electrolyte disturbances, hypoglycemia, and acute kidney injury in the setting of dehydration/volume depletion

**Clinical Management**

*Fluid management*:
Intravenous fluid (IVF) resuscitation with bolus and maintenance fluids should be provided appropriately for the degree of dehydration in the patient. Studies in CHS have only included normal saline (NS). 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 [Noelle 2022].

*Medical management of hyperemesis*:
5-$HT_3$-receptor antagonists (ondansetron) are noted to be less effective in resolving emesis related to CHS; 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 presenting with vomiting will receive a dose of ondansetron in the Emergency Center (EC). Recent studies suggest that haloperidol is superior to ondansetron in decreasing nausea and abdominal pain and leading to shorter stays in the EC [Roberto 2021]. 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.

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 [Senderovich 2022]. 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 dose and route recommendations presented in this pathway are sourced from a cumulation of the reviewed literature, current Food and Drug Administration (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. 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 electrocardiogram (ECG) and metabolic screen before 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 displays abnormalities on their ECG, the patient should be transferred to the pediatric intensive care unit (PICU) for continuous cardiac telemetry.

Additionally, droperidol utilization has shown less antiemetic use and shorter length of stay (LOS) [Lee 2019]. Other publications purport shorter LOS than haloperidol [Chopra 2022].

If haloperidol or droperidol are 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/droperidol with adjunct topical therapies.

Table 5: Pharmacologic Considerations for the Management of CHS

| | Medication | Route | Dose |
|---|---|---|---|
| First-Line | ondansetron | Enteral, if not tolerated, start with IV | 0.3 – 0.4 mg/kg/dose (max dose: 8 mg) |
| Second-Line | haloperidol | Enteral/IM/ IV | 0.05 mg/kg/dose (max dose: 2 mg) |
| | droperidol | IM/IV | 0.05 mg/kg/dose (max dose: 2.5 mg) |
| Third-Line: | lorazepam | IV | 0.025 - 0.05 mg/kg/dose (max dose: 2 mg) |

Abbreviations: IM, intramuscular; IV, intravenous

*Medical management of abdominal pain:*
Abdominal pain management is focused on redirecting blood flow away from the viscera. Topical application of capsaicin cream (0.025%) or hydrothermotherapy 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 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 [Perisetti 2020]. When the patient has been admitted to the inpatient floor, they may choose to try hydrothermotherapy 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. Opioids are not advised.

*Initial clinical monitoring*:
Abdominal imaging is often obtained in the EC 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 CAR, RELAX, ALONE, FORGET, FRIENDS, TROUBLE (CRAFFT). Please see Appendix B for a HEADSS Exam for substance use concerns.

If an adolescent has multiple EC visits and/or hospital admissions for a confirmed diagnosis of CHS, it is recommended that the adolescent be 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. These patients must 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

Patient with signs/symptoms of intractable emesis, cyclical episodes of emesis for 24 – 48-hour duration, nausea, and non-specific abdominal pain, with history of cannabis use

Physical exam suggestive of acute abdomen*?

Yes

Consider STAT abdominal imaging, Surgery consult

No

Assess hydration status:
If acutely dehydrated, administer NS bolus 20 mL/kg (max 1000 mL); consider maintenance IVF

Obtain CBC, CMP, lipase, UA with reflex urine culture, UDS, and urine hCG

Supportive pain management

Perform HEADSS exam

Are findings suggestive of other gastrointestinal pathology?

Yes

Consider differential

No

Consider CHS
Consult SW

Acute nausea and/or vomiting?

No

Yes

ondansetron and PO challenge once

Pass

Fail

Consider haloperidol or droperidol
(consider ECG and/or addition of diphenhydramine)

Does patient meet admission criteria**?

Decision to admit the patient:

- Consider a Gastroenterology consult on all patients
- Continue or start maintenance IVF
- Consider antiacids
- Supportive pain management

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, and state-specific resources
- Consider Gastroenterology referral
- Consider referral to Adolescent Medicine 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 EC visits without resolution
5. Uncontrolled pain

Abbreviations: hCG, human chorionic gonadotropin; PO, by mouth; SW, Social Work; UA, urinalysis

**EC 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 SW. A PO challenge is critical to determining whether the patient can be safely discharged or warrants admission.

***Consider admission for observation if the patient has been seen in EC multiple times with a similar presentation.***

| **DIFFERENTIAL** | **CHS** | **CWS** | **CVS** | **Rumination Syndrome** | **Eating Disorder** | **Gastroenteritis** |
|---|---|---|---|---|---|---|
| Pathophysiology | Functional GI Disorder | Substance Abuse Condition | Functional GI Disorders | Functional GI Disorder | Psychiatric Disorder | GI Disease |
| Symptoms | • Intractable vomiting<br>• Seeking a hot shower for relief | • Vomiting days to within 1 week of cannabis use | • (+) recurrent vomiting episodes<br>• (-) cannabis use<br>• (+/-) use of hot showers as a way to mitigate symptoms | • Frequent spit-ups or regurgitation of digested foods exacerbated by anxiety | • Vomiting secondary to active self-induction | • Nausea<br>• Vomiting<br>• Diarrheal disease<br>• Acute onset |
| Diagnosis | • Diagnosis of exclusion based on history, symptoms, and clinical exam | • Can occur after a single use, with cessation of symptoms after 1 week of cessation | • (+) increased gastric emptying | Rome IV criteria:<br>• Persistent or recurrent regurgitation of recently ingested food into the mouth with subsequent spitting or re-mastication and swallowing<br>• Regurgitation is not preceded by retching | • Disordered eating habits with purging secondary to body dysmorphia-related etiology<br>• Dependent on DSM criteria | • Acute onset with associated diarrhea with the potential infectious agent |

Abbreviations: DSM, Diagnostic and Statistical Manual of Mental Disorders

**Admission:**

Admission criteria include:

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

When the decision has been made to admit the patient:

- Consider a Gastroenterology consult on all patients to:
  - establish follow-up, especially given this is a diagnosis of exclusion
  - provide a multidisciplinary approach to management at the time of discharge
- Continue or start maintenance IVF
- Consider ordering antacids if gastritis is suspected
- Supportive pain management
- Admit as *Observation* status

**Inpatient Management:**

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

Patients should receive IVF for rehydration until they are hemodynamically stable and tolerating 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 ondansetron in EC triage. If the patient does 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 to 8 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 <u>not</u> be discharged with oral haloperidol.

Consults to Pediatric Psychology and SW 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 Patient Health Questionnaire (PHQ)-9 when sober and comfortable enough to provide an accurate response.

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# Inpatient Treatment Algorithm for Cannabis Hyperemesis Syndrome

*The patient was admitted to the floor from EC for the management of intractable emesis in the setting of suspected cannabis use*. Admitting team to perform a full H&P to assess for alternative or comorbid diagnoses.

If CHS remains the working diagnosis:

- Rehydrate with IVF as indicated
- Replete potassium < 3 mEq/L
- Continue topical capsaicin, if tolerated
- Offer hydrothermotherapy as needed
- Consult SW for substance abuse treatment resources
- Consult Psychology for motivational interviewing

↓

The patient is experiencing significant abdominal pain and/or is unable to tolerate PO due to vomiting

↓

Nausea/vomiting controlled with ondansetron?

YES → Continue maintenance IV hydration and IV ondansetron Q 6-8 hours as needed emesis

NO ↓

*Second-Line*: haloperidol
Continue adjunct therapies: topical capsaicin, hydrothermotherapy

Before giving haloperidol, assess risk for prolonged QT; may obtain ECG or start continuous cardiac monitoring if ECG is abnormal

If the patient develops acute signs of akathisia, rigidity, bradykinesia, dysphagia, or tremor, stop haloperidol and administer IV diphenhydramine

↓

Emesis and pain are adequately controlled?

NO → If patient has refractory abdominal pain or nausea/vomiting:

*Third-Line*: lorazepam

↓

If patient remains symptomatic:

↓

**Further Suggestions:**

- Consult Gastroenterology
- Consider ordering a urine carboxy-THC (THC-COOH)
  - Significant if > 100 ng/mL

Reconsider differential diagnoses and include other specialists as indicated

**Opioids should be avoided in the treatment of abdominal pain in CHS, as they are often ineffective and may even worsen abdominal pain in CHS**

YES ↓

May repeat dose every 6 – 8 hours if patient continues to have nausea/vomiting and responds appropriately

Consider repeat CMP to ensure electrolytes normalize

↓

Does patient meet criteria for discharge?

1. Demonstration of PO tolerance for at least 12 hours or 2 meals
2. Symptoms controlled with oral ondansetron and/or topical capsaicin

↓

Consider observation for 24 hours, as some patients may seek premature discharge due to cannabis withdrawal symptoms

↓

**Discharge:**
Counsel patients on cessation of cannabis use as the only definitive cure for CHS

Include education with Smart phrase “CHSAVS” in discharge papers

**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 the 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 Appendix C)
- 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 concerning threats to the patient's (or other vulnerable persons') safety.
2) Adolescent patients may request that documented information 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 HEADSS exam concerning the limits of patient confidentiality of conversations and documentation.

*Coding recommendations for cannabis hyperemesis*:
Cannabis use, specify:
a) Nondependent abuse vs. dependence: What is the patient's pattern of use?
b) Intoxication: Was the patient under the influence during the encounter

c) In remission: Indicate whether the patient is in remission (based on the provider's clinical judgment)
d) Withdrawal: Presence or absence of withdrawal symptoms
e) Specificity regarding any cannabis-induced disorders (e.g., 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*

Owner(s): Michael Wilsey, MD; Paola Dees, MD

Also Reviewed by:

Specialists: Dr. Michael Wilsey
Hospitalists: Paola Dees, MD; Kimberly Collins, MD
Emergency Center: Lisa Odendal, MD; Courtney Titus, PA-C
Resident Physicians: Tian Mauer, MD; Isabel Hendrickson, MD; Caroline Clark, DO; Carolena Trocchia, MD
Pharmacists: Corey Fowler, Pharm.D., BCPPS

Clinical Pathway Management Team: Joseph Perno, MD; Courtney Titus, PA-C

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*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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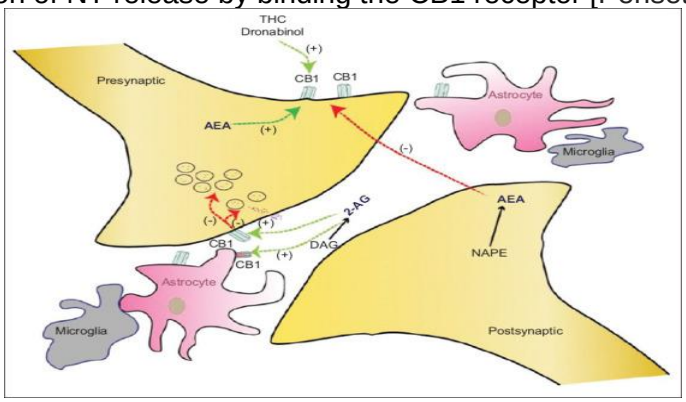
**Appendix A:** CHS Pathophysiology

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 are present throughout the body, but they particularly exert a significant portion of their effects on the brain. These receptors influence the HPA axis to impact the emetic center, along with the cerebellum, hippocampus, and hypothalamus, which control and influence 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) and arachidonoylglycerol (2-AG) are enzymes produced by membrane lipids with significantly higher levels within the brain. They 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 [Perisetti 2020]




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 emesis [Perisetti 2020]. 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 to 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.

**Appendix B:** HEADSS Exam (*example questions as detailed in reference below)*

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. https://journalofethics.ama-assn.org/article/headss-review-systems-adolescents/2005-03

**Appendix C:** Cannabinoid Hyperemesis Education for Patients and Caregivers

*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 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 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, a 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 the potency of cannabis products may be the problem. However, everybody 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.

How is CHS treated?

The abdominal pain and vomiting in CHS do 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" for 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 a hotline that is useful for teens who are also struggling with mental health.
- 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.northtampabehavioralhealth.com/