CLINICAL GUIDELINE

Cannabinoid Hyperemesis Syndrome (CHS)

Evaluation and Emergency Department Management (Age 12+)

Children's MINNESOTA

Aim: to standardize the diagnosis and management of Cannabinoid Hyperemesis Syndrome in adolescents

Patient presents with acute vomiting and dehydration + history of recurrent episodes of intractable nausea/vomiting and non-specific abdominal pain

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Detailed H&P including HEADSSS exam (Note 1)

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Physical exam suggestive of acute abdomen (Note 2)

Yes → **Off Guideline**

No ↓

High suspicion for CHS?
(See Note 3 for Rome IV diagnostic criteria and Note 4-5 for differential diagnoses)

No → Work up as indicated.
Off Guideline if alternative etiology identified
(See Notes 4-5)

Yes ↓

- **Start IV fluids**
- **Obtain EKG**
- **Initial labs to consider: CBC, CMP, lipase, urinalysis, urine pregnancy test, urine drugs of abuse screen-** *drug screen needn't be performed for CHS diagnosis if history is definitive and can be negative in CHS, see Note 6*

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Do labs suggest alternative etiology for vomiting?

Yes → **Off Guideline**

No ↓

Is QTc prolonged? (Males >460, females >480, Note 12)

Yes →

First line medications to consider (Note 7):
- Olanzapine ODT
- Aprepitant PO
- Capsaicin topically 0.075%
- Lorazepam IV or PO

If ineffective, consider Sumatriptan as a second line medication (Note 8)

No →

First line medications to consider (Note 7):
- Droperidol IV
- Aprepitant PO
- Olanzapine ODT
- Diphenhydramine IV
- Capsaicin topically 0.075%
- Lorazepam IV or PO
- Ondansetron IV or ODT

If ineffective, consider second line medications (Note 8)

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1. **Were the medications effective?**
2. **Can the patient tolerate liquids, maintain oral hydration and tolerate oral medications?**

Yes → **Discharge home AFTER:** ***Counsel patients:*** *cessation of cannabis use is the only definitive cure for CHS* (see Note 9 for discharge referral resources)
- Social work/Toxicology consulted for substance abuse counseling/resources
- Referral to Adolescent Medicine or Psychology; consider referral to GI or Integrative Medicine Clinic
- Prescribe discharge medications (see Note 10-11)
- If prolonged QTc, appropriate follow up in place (see Note 12)

No → Admit to inpatient
(Inpatient Management on Page 2)

EXCLUSION GUIDELINES

Patients **excluded** from this guideline:
- Concern for sepsis or acute abdomen
- Patients <12 years old
- Pregnant patients

Disclaimer: This guideline is designed for general use with most patients; each clinician should use their own independent judgment to meet the needs of each individual patient. This guideline is not a substitute for professional medical advice, diagnosis or treatment.

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Inpatient Management (Age 12+)

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EXCLUSION GUIDELINES

Patients **excluded** from this guideline:

- Concern for sepsis or acute abdomen
- Patients <12 years old
- Pregnant patients

Patient admitted with acute vomiting and dehydration due to suspected hyperemetic phase of Cannabinoid Hyperemesis Syndrome? *(see page 1 of the clinical guideline for work-up)*

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Treatment of CHS

- **Hydration:** NS bolus (if needed), then D5NS + 20mEq KCl/L @ 1-1.5 maintenance (Note 13)
- **Pain/Nausea: Patients with CHS may require multiple anti-emetic medications used in combination. First line medications to consider** (Note 7): *Minimize medications with * if patient has prolonged QTc (Note 12)*
  - **Aprepitant**: 125 mg day 1, then 80 mg days 2 and 3, then 80 mg 2x/week until emesis resolves
  - **Olanzapine** 5-10 mg PO BID prn
  - **Capsaicin** 0.075% TID to back of arms or abdomen
  - ***Droperidol** IV 1.25 mg Q6H prn (can increase to max of 2.5 mg/dose if needed)
  - ***Ondansetron** 0.15 mg/kg IV or ODT Q6H (max 8 mg/dose) -- *often ineffective in patients with CHS, ONLY order if trial dose efficacious*
  - ***Diphenhydramine** 1 mg/kg IV Q6H prn (max 50 mg/dose) OR *Hydroxyzine 25-50 mg PO prn
  - **Lorazepam** 1 mg IV or PO Q6H prn (can increase to max of 2 mg/dose if needed)
  - **Famotidine** 0.5 mg/kg IV BID (max 20 mg/dose)
- **Consults:** Social Work and/or Toxicology Consult (when available) for substance abuse treatment/resources + Integrative Medicine on all, consider Psychology consult
- **If concurrent nicotine addiction:** see Note 11 for dosing of nicotine replacement therapy
- **If QTc prolonged:** see Note 12

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Treatment effective in aborting hyperemetic phase and patient clinically improving?

No → **Consider:**
- Evaluating for alternative etiology (Note 4)
- Trialing second-line medications (consider QTc prolongation risk) (Note 8)
- Consulting GI

Yes → **Does patient meet discharge criteria:**
- Ability to tolerate liquids and two meals without vomiting (~6-8 hours of oral tolerance without IV supplementation)
- Emesis and abdominal pain adequately controlled with oral and topical medications (Note 10)
- Clinically improved hydration status

No → ↑ Treatment of CHS

Yes → **Discharge:**

Counsel patients: *cessation of cannabis use is the only definitive cure for CHS*
(see Note 9 for discharge referral resources)
- Referral to Adolescent Medicine or Psychology
- Consider referral to GI or Integrative Medicine Clinic
- Prescribe discharge medications (see Note 10-11)
- If prolonged QTc, appropriate follow up in place (see Note 12)

Disclaimer: This guideline is designed for general use with most patients; each clinician should use their own independent judgment to meet the needs of each individual patient. This guideline is not a substitute for professional medical advice, diagnosis or treatment.

Cannabinoid Hyperemesis Syndrome (CHS) Notes

Note 1. Thorough History. A complete history should be obtained with special attention to:

- **Duration of symptoms**:
  - **CHS prodromal phase** can last months-years: often characterized by early morning nausea, fear of vomiting, and frequent abdominal discomfort, but patients **maintain** normal eating habits. Patients may continue or further increase cannabis use hoping it will relieve nausea
  - **CHS hyperemetic phase** is characterized by paroxysmal bouts of vomiting that can be incapacitating, sometimes associated with nonspecific abdominal pain, average duration is 3-4 days, weight loss is common (>50% report weight loss >5kg)
- **Relieving factors:** Hot showers/baths classically provide temporary relief in CHS; however, such hydro-thermotherapy can also be relieving in patients with cyclic vomiting syndrome. If the patient has had CHS exacerbations in the past, then inquire which pharmacotherapy has been previously beneficial. Typical antiemetics like Ondansetron are often ineffective
- **Onset of symptoms** and time of last cannabis consumption: usually patients with CHS present symptomatically within 24 hours of last consumption
- **Cannabis use**: inquire about cannabis product used (e.g. synthetic, edible, vaping, botanical, prescription), duration, quantity and frequency of use. Most patients with CHS have consumed cannabis at least weekly for months-years, often with a history of escalation of dosing.
- **Mental health evaluation:** ask about co-abuse of other substances, assess for addiction, inquire about history of mental health concerns and treatment, and assess patient's current state of mental health
- **Red flag symptoms** that suggest alternative etiology include (see note 4 for ddx): high fever, abrupt onset with this episode being the first occurrence of symptoms, history of bloody stools

Note 2. Signs of an acute abdomen may include: guarding, rigidity, non-distractable pain, abdominal distension, vital sign instability, and/or fever

Note 3. Rome IV Criteria for CHS diagnosis (of note, criteria were developed for diagnosing adults)**:**

1. Stereotypical episodic vomiting resembling cyclic vomiting syndrome in terms of onset, duration, and frequency, i.e. two or more periods of unremitting paroxysmal vomiting, lasting hours to days, and separated by weeks-months with return to baseline health between episodes of vomiting
2. Presentation after prolonged use of cannabis
3. Relief of vomiting episodes by sustained cessation of cannabis use

Criteria fulfilled for the last 3 months with symptom onset at least 6 months prior to diagnosis

Note 4. Differential diagnoses to consider for intractable nausea/vomiting and abdominal pain – *this list is not exhaustive and cannabinoid hyperemesis syndrome is ultimately a diagnosis of exclusion. Even if a patient has a history of cannabis use or a positive tox screen, alternative pathologies should be considered.*

- **Gastrointestinal system etiologies:** gastroenteritis, peptic ulcer disease, appendicitis, gallbladder pathology (e.g. cholecystitis), Inflammatory Bowel Disease, cannabinoid hyperemesis syndrome, bowel obstruction, pancreatitis, cyclic vomiting syndrome (CVS)
- **Central nervous system etiologies**: elevated ICP, concussion, vertebral injury, migraines, dysautonomia, vestibular concerns
- **Genitourinary system etiologies**: nephrolithiasis, pregnancy hyperemesis, ectopic pregnancy, pelvic inflammatory disease, ovarian/testicular torsion, UTI
- **Metabolic/endocrinological etiologies**: toxin ingestion, metabolic/mitochondrial disorders, DKA, thyroid disease, endocrine tumors
- **Psychiatric etiologies:** cannabis withdrawal syndrome **(see note 5),** eating disorder, rumination syndrome

Note 5. Key clinical history information to help differentiate cannabis withdrawal from cannabinoid hyperemesis

	Cannabis Withdrawal	Cannabinoid Hyperemesis
Symptomatic relief with hot showers/baths?	No	Yes
Onset of symptoms from last cannabis consumption	>24 hours	<24 hours
Associated psychological symptoms, e.g. irritability, restlessness, insomnia, nervousness	Yes	No
Clinical course/pattern	No defined pattern. Symptoms occur when patient attempts to abstain.	Three clear phases of symptoms (prodrome, hyperemetic, recovery). Possible hx of escalation of THC dose to combat tolerance.
Quantity of cannabis consumed correlates with severity?	Yes	No

Note 6. Urine drugs of abuse screen:

1. At Children's MN, the "Drugs of Abuse Screen, Urine" results in ~1 hour. In contrast, the "Drug Screen, Comprehensive Urine (MedTox)" on urine or blood results in ~10-14 days and is rarely indicated. The "Drugs of Abuse Screen, Urine" includes a test for Tetrahydrocannabinol (THC), but will not detect CBD, cannabidiol (Epidiolex), or synthetic cannabis. A drug screen cannot be used in place of a thorough history.
2. **New versus residual marijuana use:** Since marijuana is lipophilic and has a long elimination half-life, it can be detected in urine for weeks to months after stopping usage. If a patient has a positive urine drug screen, but history is indeterminate, and a provider needs to distinguish between new usage of marijuana versus residual positivity, they can use a urine creatine normalized carboxy-tetrahydrocannabinol concentration at two points in time and calculate a decision ratio based on these values. At Children's MN, this can be obtained by ordering "miscellaneous lab" and specifying in the comments "Mayo Lab: Mayo Test Code = THCCR" on two separate urine samples and then using the Mayo Lab Manual to interpret the results.

Note 7. Pharmacological Management of CHS – Consider first for nausea/vomiting in CHS hyperemetic phase

Suggested medications to try first in CHS- dosing and tips. Medications with different mechanisms may be utilized in combination.
If the patient has a history of known CHS, initiate treatment, trialing what has worked for them in the past.

Medication	Dose	Notes	QTc prolonging?*
Droperidol	1.25 mg IV Q6 hours prn (can increase to max of 2.5 mg/dose if needed).	If using, monitor for extrapyramidal side effects and order prn Benadryl. Some institutions recommend Haloperidol as a first-line, however based on expert pharmacist opinion, Droperidol is being recommended at Children's MN due to lower risk of potential QTc prolongation and extrapyramidal side effects **If scheduled, providers should order Q48H EKGs for monitoring**	Mild
Olanzapine	5-10 mg ODT BID prn	IV route not yet FDA approved in pediatrics, IM is also an option in an urgent situation	Rare
Aprepitant	125 mg PO day 1, then 80 mg PO days 2 and 3, after that 2x/week until symptoms cease	Time to onset: 1 hour	None
Diphenhydramine	1 mg/kg IV Q6H prn (max 50 mg/dose)	May not be helpful in CHS. Should be ordered prn if using Droperidol to treat rare extrapyramidal side effects	Rare
Hydroxyzine	25-50 mg q6h PO prn (max 100mg/dose)	May be useful for concurrent anxiety	Mild
Capsaicin	0.075% TID prn	May not be tolerated. Use gloves for application to back of arms or abdomen. Thoroughly wash hands after application. Avoid face and eyes. Discontinue if any skin irritation/burning.	None
Lorazepam	1 mg IV or PO Q6H prn (can increase to max of 2 mg/dose if needed)	Preferable not to discharge home with Lorazepam due to risk for abuse in the outpatient setting.	None
Famotidine	0.5 mg/kg IV or PO BID (max 20 mg/dose)		Rare
Ondansetron	0.15 mg/kg IV or ODT Q6H (max 8 mg)	May not be helpful in CHS. Consider a trial dose and schedule Ondansetron only if benefit observed. Could also try granisetron (2 mg IV BID), a similar 5-HT3 antagonist.	Mild

**Risk factors for QTc prolongation include using multiple QTc prolonging medications together, hepatic dysfunction, electrolytes abnormalities (hypomagnesemia, hypokalemia, hypocalcemia), congenital long QT syndrome, left ventricular failure, bradycardia, or recent cardioversion. See Note 12.*

Note 8. Pharmacological Management of CHS – Consider second for nausea/vomiting in CHS

Medication	Dose	Notes	QTc prolonging*?
Prochlorperazine	5 mg PO or IV Q6H prn	If using, monitor for extrapyramidal side effects and order prn Benadryl.	Rare
Sumatriptan	20 mg intranasal once prn	May repeat once after 1 hour if partial response	None
Amitriptyline	0.5 mg/kg/day (max 200 mg/day)	Caution in patients with any depression or suicidality risk given the high mortality/morbidity of any overdose	Significant

**Risk factors for QTc prolongation include using multiple QTc prolonging medications together, hepatic dysfunction, electrolytes abnormalities (hypomagnesemia, hypokalemia, hypocalcemia), congenital long QT syndrome, left ventricular failure, bradycardia, or recent cardioversion. See Note 12.*

Note 9. Discharge Resources

- Referrals for patients with substance abuse disorder may include: Psychology and/or Adolescent Medicine clinic
- For intensive outpatient addiction treatment, consider looking into Hazelden at the Plymouth location: https://www.hazeldenbettyford.org/treatment/models/specialized-programs/teens-young-adults
- For faith-based treatment for boys, consider Teen Challenge (https://www.mntc.org/)
- For assistance finding a local treatment facility for mental or substance use disorders: https://findtreatment.gov/locator
- If concurrent nicotine addiction, quitting resources include:
    - Minnesota Department of Health free Quit Support
    - https://truthinitiative.org/
    - https://teen.smokefree.gov/
    - Mylifemyquit.com
    - Texting 36072 to take the first step towards quitting

Note 10. Discharge Medications may include:

Medication	Dose	Notes
Capsaicin	0.075% TID prn	Use gloves for application to back of arms or abdomen. Thoroughly wash hands after application. Avoid face and eyes. Discontinue if any skin irritation/burning.
Aprepitant	125 mg day 1, then 80 mg days 2 and 3, after that 2x/week until symptoms cease	
Famotidine	0.5 mg/kg PO BID (max 20 mg/dose) x 2 weeks	
Olanzapine	5-10 mg PO BID prn	If found to be beneficial, may discharge with a few doses
Hydroxyzine*	25-50 mg q6h PO prn (max 100mg/dose)	May be useful for concurrent anxiety
Ondansetron*	0.15 mg/kg PO Q6H (max 8 mg)	Only if found to be beneficial
N-acetylcysteine	1,200 mg PO BID	If recommended by Toxicology Specialist to treat patient's substance use disorder in the outpatient setting
Naloxone Intranasal	Use once prn if concern for possible opioid overdose	Strongly consider as a discharge prescription, even if patients do not have an opioid use disorder. Note that some street drugs may be laced with opioids, unbeknownst to the user.

***Avoid in patients with prolonged QTc. See Note 12.*

Note. 11. Dosing for Nicotine Replacement Therapy

If concurrent nicotine addiction, consider prescribing nicotine replacement therapy

Suggested Dosing:

- If >10 cigarettes per day OR 1+ pods per day of e-cigarettes: 21 mg x 4-6 weeks, then 14 mg/day x 2 weeks → 7 mg/day x 2 weeks
- If <10 cigarettes per day OR 0.5-1 pod per day of e-cigarettes: 14 mg/day x 6 weeks → 7 mg/day x 2 weeks
- If a "few hits" per day: 7 mg patch x 2 weeks
- Nicotine lozenge (2 mg Q2H prn, max 8 mg/day)

Note 12. Patients with QTc prolongation (Males >460, females >480 for the purpose of this guideline and proper medication administration per cardiology)

- Correct any electrolyte derangements that may be contributing to QTc prolongation (e.g. hypokalemia, hypomagnesemia, hypocalcemia)
- If QTc is above normal but <500 and patient is meeting discharge criteria: EKG should be repeated as an outpatient within 2 weeks
    - If QTc remains prolonged at follow-up, patient should be referred to outpatient Cardiology Clinic.
- If QTc >500 even after electrolyte derangements are corrected and QTc-prolonging medications are held, consult Cardiology.

Note 13. IV fluids for Hyperemesis Cannabinoid Syndrome

THC is stored in adipocytes, so fasting-induced lipolysis is thought to exacerbate the hyperemetic phase of CHS. Dextrose-containing maintenance fluids are important to minimize ongoing lipolysis. D10 should be considered in patients presenting with prolonged vomiting (e.g. >3 days) or ketonemia.

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