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# Cannabinoid Hyperemesis Syndrome: An Update for Primary Care Providers

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**ABSTRACT**

Cannabis is the most commonly used recreational drug worldwide. Crossbreeding and genetic modification techniques have dramatically increased the delta-9-tetrahydrocannabinol content, with resultant increased rates of cannabis use disorders and other toxic effects among users. Cannabinoid hyperemesis syndrome (CHS) is a recently identified disorder and should be considered as a differential diagnosis in patients exhibiting recurrent symptoms of abdominal pain, weight loss, intractable vomiting, and compulsive bathing. Treatment includes vigorous rehydration with intravenous fluids, antiemetics, proton pump inhibitor administration, weight monitoring, and cannabis use cessation. Awareness of CHS symptomology and clinical management strategies can prevent extensive diagnostic workups and unnecessary hospitalizations.

**Keywords:** cannabinoid hyperemesis syndrome, delta-9-tetrahydrocannabinol, diagnosis, symptoms, treatment



Worldwide, cannabis is the most commonly used psychoactive drug. According to the World Health Organization,[1] cannabis is used for nonmedical purposes by an estimated 182 million people, or 2.5% of the world's population, annually. In the United States, more than 2.6 million Americans become new recreational users each year, and with more states sanctioning legalized usage, this number is increasing multifold.[2]

Cannabis comes from the female *Cannabis sativa* plant, which contains over 750 chemicals and over 100 different cannabinoids. The primary cannabinoids in the cannabis plant include delta-9-tetrahydrocannabinol (THC), cannabidiol (CBD), and cannabinol. Cannabinoids are used medicinally as antiemetics (THC and CBD), for seizure prevention (CBD), as a sedative (cannabinol), and for pain control (THC and CBD). Cannabis can be smoked, vaporized, and consumed whole or in oil extract form.[1]

## PHARMACOKINETICS AND PHARMACODYNAMICS OF THE CANNABINOIDS

THC is the most psychoactive component of cannabis, causing euphoria, increased appetite, drowsiness, analgesia, and short-term memory loss. THC activates 2 receptors within the central nervous system, cannabinoid receptors type 1 (CB1) and type 2, which are located primarily in the dorsal ganglia, hypothalamus, hippocampus, cerebellum, and frontal limbic system of the brain. CB1 receptors are also found in the enteric plexus.[3]

The metabolism of THC occurs principally in the liver and is carried out by the CYP2C isoenzyme, which is a subtype of the cytochrome P450 complex. THC has a prolonged half-life of 20 to 30 hours; it is accumulated and stored largely in body fat. During times of lipolysis, which occurs during increased stress or food deprivation, the plasma levels rise and can cause reintoxication symptoms and toxic effects.[3]

## PHYSIOLOGIC EFFECTS OF CANNABIS USE

Over the past decade, crossbreeding and genetic modification techniques have dramatically increased the THC content of different cannabis strains, yielding plants with much higher cannabinoid content. For example, the THC content may be increased from 3% content to upwards of 30%. This increased potency contributes to the increased rates of cannabis-related

**Box 1. 3 Phases of Cannabinoid Hyperemesis Syndrome[2,6]**

Prodromal phase
Recurrent/persistent symptoms for months or years
Early morning nausea
Fear of vomiting
Abdominal discomfort
Normal eating pattern
May increase cannabis use to relieve nausea

Hyperemetic phase
Bouts of intense, persistent vomiting that is debilitating
Weight loss up to 14 kg
Compulsive warm bathing relieves nausea and

Recovery phase
Follows complete cessation of cannabis use*
Total resolution of symptoms within 12 hours to 3 weeks
Return of normal eating patterns
Weight gain
Regular bathing habits

*May require ongoing therapy/support for withdrawal and psychological dependence.

**Box 2. Treatment for Cannabinoid Hyperemesis Syndrome**

Vigorous rehydration and supportive therapy
Immediate and continued abstinence from cannabis in any form
Possible hospitalization during hyperemetic phase
Treatment with Haldol during hyperemetic phase
Administration of a proton pump inhibitor
Weight monitoring

adverse effects, such as cannabis use disorder and acute intoxication, and toxic effects, such as cannabinoid hyperemesis syndrome (CHS).[1]

With the current trend of increased legal access to cannabis and the increased potency, it is necessary for the primary care provider to recognize and investigate cannabis usage patterns and related adverse side effects. For example, cannabis use disorder, occurring in 10% of regular cannabis users, is associated with cognitive impairment, poor school or work performance, episodic or chronic mood changes, and thought disturbances that may resemble non–drug-related psychiatric disorders.[4]

## ACUTE CANNABIS INTOXICATION

The clinical manifestations of acute cannabis intoxication vary with age. In children, cannabis intoxication can produce neurologic abnormalities such as ataxia, hyperkinesia, lethargy, and coma.[5] After limited exposure, children may exhibit symptoms such as sleepiness, euphoria, nausea, vomiting, conjunctival injection, ataxia, or slurred speech. In large doses, coma with depressed respirations can occur, which may be life-threatening. Toxicity in children is usually from ingesting highly concentrated cannabinoid food products. In adolescents and adults, the signs of cannabis intoxication include tachycardia, hypertension, increased respiratory rate, conjunctival injection, dry mouth, increased appetite, nystagmus, ataxia, and slurred speech.[6]

## CHS

A relatively new clinical diagnosis, CHS, has emerged over the past 2 decades. In 2004, Allen first coined the term *cannabis hyperemesis syndrome* in a published case series of 9 patients in Australia.[7] In the US, primary care providers are just becoming aware of this disorder and its management. The Mayo Clinic study in 2012, the largest study to date with 98 patient case studies, has also contributed to the diagnostic criteria of CHS.[7]

## CLINICAL PRESENTATION

The knowledge and awareness of CHS symptomology can promote quick diagnosis and treatment of this condition and prevent unnecessary emergency department visits, hospitalizations, diagnostic testing, and treatment trials.[7,8] The clinical presentation of CHS includes a health history of long-term, regular cannabis use with severe cyclic episodes of nausea,