Marijuana and the Pediatric Population

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abstract

Cannabinoids, the psychoactive compounds in marijuana, are one of the most commonly used substances in the United States. In this review, we summarize the impact of marijuana on child and adolescent health and discuss the implications of marijuana use for pediatric practice. We review the changing epidemiology of cannabis use and provide an update on medical use, routes of administration, synthetic marijuana and other novel products, the effect of cannabis on the developing brain, other health and social consequences of use, and issues related to marijuana legalization.

EPIDEMIOLOGY

Cannabis is one of the most commonly used psychoactive substances in the United States.

In recent years, the increase in potency of cannabis (which includes a sixfold to sevenfold increase in tetrahydrocannabinol [THC] content), the proliferation of alternative forms of cannabis for consumption, and electronic vapor device use pose challenges to both public health and clinical practice.[1] In 2017, the Centers for Disease Control and Prevention Youth Risk Behavior Survey found that 19.8% of youth of high school age reported past-month marijuana use, and 35.6% had ever tried marijuana,[2] down from a peak rate of 47.1% in 1997. Synthetic marijuana use also declined, from 9% in 2015 to 6% in 2017. Although use has declined, youth who use marijuana often engage in other risk-taking behaviors that impact their overall well-being; for example, 13% of youth reported driving after using marijuana.[2] In 2017, ever use of marijuana among Black or African American (42.8%) and Hispanic (42.2%) students was higher than among white (32.0%) students. The prevalence of current marijuana use was also higher among gay, lesbian, and bisexual (30.6%) students compared with heterosexual (19.1%) and "not sure" (18.9%) students. Older students had a higher prevalence of current marijuana use, with 13.1% of ninth-grade students, 18.7% of 10th-grade students, 22.6% of 11th-grade students, and 25.7% of 12th-grade students reporting current use. With legalization, marijuana use during pregnancy has become more common, with 7.1% of pregnant women reporting marijuana use in the past month and 3.1% reporting daily use.[3]

Only one recent study has examined the relationship between the availability of legal medical marijuana and use in adolescents. This cross-sectional survey of students whose school was within a 5-mile radius from a medical dispensary did not find increased use of marijuana among these youth.[4] More studies are needed to determine the effect of proximity to medical dispensaries on marijuana use.

National surveys have found that youth who engaged in marijuana use in later teen-aged years (>17) were less likely to develop substance use disorders compared with those who started earlier. Positive attitudes toward school, parental monitoring, and strong disapproval of peer's substance abuse were found to be protective factors against substance use disorder.[3]

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Drs Dharmapuri and Klein drafted the initial manuscript and reviewed and revised the manuscript; Dr Miller reviewed and revised the manuscript; and all authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

DOI: https://doi.org/10.1542/peds.2019-2629

Accepted for publication Feb 27, 2020

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PEDIATRICS (ISSN Numbers: Print, 0031-4005; Online, 1098-4275).

FINANCIAL DISCLOSURE: The authors have indicated they have no financial relationships relevant to this article to disclose.

FUNDING: No external funding.

POTENTIAL CONFLICT OF INTEREST: The authors have indicated they have no potential conflicts of interest to disclose.

To cite: Dharmapuri S, Miller K, Klein JD. Marijuana and the Pediatric Population. *Pediatrics.* 2020; 146(2):e20192629

PHARMACOLOGY

Although a comprehensive review of pharmacokinetics and pharmacodynamics is beyond the scope of this review, it is helpful to summarize the kinetics of cannabis and common cannabis extracts and concentrates to aid clinicians in better understand the effects of various forms of cannabis on youth.

Cannabis occurs naturally as a plant, leading to production of cannabis products made of dried leaves, oils, and concentrates. Many cannabis products contain numerous substances, including terpenes, flavonoids, alkaloids, and >100 cannabinoids. There is no standardized form of cannabis; the presence and relative amount of various substances may differ between cannabis extracts as well as between products designed to be smoked or vaporized.[5]

The endocannabinoid system, composed of endocannabinoids and cannabinoid receptors, is widely distributed in the brain and spinal cord. This system has a regulatory role in many physiologic processes, including inflammation, appetite regulation, immune function, cardiovascular function, neural development, pain, the sleep and wake cycle, psychiatric disease, and others. Endocannabinoids, endogenous lipids with precursors that are present in lipid membranes, interact with endocannabinoid receptors CB1 and CB2.[6] Being lipophilic, cannabinoids are rapidly absorbed.

Phytocannabinoids, plant-derived cannabinoids, can be categorized into several classes; δ-9 tetrahydrocannabinol (generally known as THC) and cannabidiol (generally known as CBD) are the most abundant and studied forms. THC is considered the main psychoactive component of the plant.

Phytocannabinoids affect users through their interactions with endocannabinoid receptors CB1 and CB2 and related binding proteins in the nervous system. CB1 receptors are found in the central nervous system on neurons in the prefrontal cortex, basal ganglia, hippocampus, amygdala, hypothalamus, and cerebellum. CB1 receptors are also found in smooth muscle, myocardium, adipocytes, and preganglionic sympathetic neurons. The CB2 receptor is expressed in peripheral blood mononuclear cells as well as in the smooth muscle, myocardium, and vascular endothelium.

THC acts as an agonist at CB1 and CB2 receptor sites. Binding the receptor site reduces neurotransmission, producing effects such as impairments in learning, memory, spatial orientation, and attention and physiologic effects such as tachycardia. THC also has analgesic and antiinflammatory effects.[7] CBD has weak affinity for CB1 receptors, does not interact directly with CB2 receptors, and does not produce the intoxicating effects of THC ingestion.

There is considerable variation in the pharmacokinetic profiles of THC and CBD between users, by cannabis dosages and forms, with acute and chronic use, and by route of administration. Smoked and/or vaporized cannabis has a rapid onset of action, with peak levels achieved within 10 minutes and greater bioavailability compared with oral ingestion. Bioavailability of THC ranges from 2% to 56% with smoked or vaporized cannabis and from 11% to 45% with smoked CBD. Oral absorption has more variability and lower bioavailability. The acute effects of ingested cannabis may last for several hours, depending on concentration, formulation of the product, and gastrointestinal motility, vascularity, and blood flow.[5] Distribution of THC is time dependent and is immediate with absorption into fat tissue and highly perfused organs. Elimination half-life also varies. THC has a fast initial half-life (6 minutes) and a longer terminal half-life (22 hours). Chronic users have longer elimination times, with THC present for >24 hours. CBD has a long terminal half-life, from 33 hours to 5 days, depending on the amount used.

Metabolism of THC occurs mainly in the liver by the cytochrome P450 system. CBD inhibits cytochrome oxidases; thus, it may interfere with other commonly used medications. CBD has a regulatory effect on THC, with the potential to decrease some adverse effects (ie, tachycardia, anxiety, and sedation).[5]

Drug interactions have been noted with the use of cannabis. For example, cannabis containing THC has been associated with increased rates of psychotic relapse and treatment failure.[8] In an animal study, THC had a negative effect on the efficacy of risperidone.[9] Drug interactions noted for CBD included increases in serum levels of antiepileptic drugs, resulting in sedation.[8]

Synthetic cannabinoids (SCs) are biochemically similar to THC and are used for both medicinal purposes and recreational purposes. Dronabinol is a schedule III drug and is approved for the treatment of nausea and vomiting associated with chemotherapy and for the treatment of anorexia and weight loss due to AIDS. Dronabinol typically comes in 2.5-, 5-, and 10-mg tablets and is taken 1 or 2 times a day in doses of up to 40 mg/day. Nabilone, a schedule II SC, comes in 0.25-, 0.5-, and 1-mg tablets, is prescribed up to 3 times a day, and is approved for chemotherapy associated nausea and vomiting.[8]

MEDICAL USES OF CANNABIS

The Drug Enforcement Agency has classified cannabis as a schedule I drug. This precludes cannabis being considered for legal medical uses, and therefore it is also not regulated,

except for dronabinol, nabilone, and CBD. Dronabinol and nabilone are SCs. CBD is a plant-derived product approved for use in children as a second-line treatment of 2 conditions: Lennox-Gastaut syndrome and Dravet syndrome.[10]

The medical conditions that CBD can be legally used for vary by state. Most studies examining CBD treatment of various conditions (cachexia or wasting, AIDS, cancer pain, etc) have been on adults. According to a National Academy of Sciences review, cannabis and cannabinoids are effective for the treatment of chronic pain in adults, are effective as antiemetics for the treatment of chemotherapy-induced nausea and vomiting, and are effective for improving spasticity in adults with multiple sclerosis.[11]

Although some benefits of marijuana for treatment of behavioral conditions have been reported in animal studies, there are few studies in humans. In 2 case reports, authors noted benefits from dronabinol in children: one report of a 6-year-old boy with autism and the other of an adolescent with self-injurious behaviors.[12,13]

The use of medical cannabis for treatment of inflammatory bowel disease (IBD) has increased in recent years. There is some evidence that cannabis may have antiinflammatory properties, improve IBD symptoms, and improve quality of life. However, in adults, CBD did not improve IBD pathology, and use of cannabis in pediatric IBD is not recommended.[14]

In a systematic review of cannabis for treatment of seizures, 4 high-quality randomized controlled studies found a reduction in seizures with the use of Epidiolex, a CBD product US Food Drug Administration (FDA) approved for treatment of Dravet syndrome and Lennox-Gastaut syndrome. Outcomes using other cannabis preparations were inconclusive.[15] A few small, nonrandomized studies have suggested benefits from CBD use in other seizure disorders, including Sturge-Weber epilepsy and febrile infection–related epilepsy; however, there is limited evidence for use in these disorders.[16,17] Limitations of these studies include the following: use of other CBD products were not compared with use of Epidiolex, treatment time was short, studies had small samples, and CBD was added as an adjunct rather than as a first-line treatment.[15] CBD was noted to provide seizure-free activity in a small proportion of children with Dravet syndrome. However, the authors suggest that a reduction in seizures may be a more realistic expectation with use of CBD rather than seizure-free activity.[15]

Parents and providers should be aware that there are limited studies addressing CBD use in children or adolescents and that there often is cross-contamination of CBD products with THC. Thus, CBD products may lead to positive urine drug test results for THC. This is especially important for adolescents required to take drug tests for sports or employment. Additionally, CBD products are unregulated, except for those drugs that are FDA approved.

DUAL USE OF CANNABIS AND TOBACCO

Population-based surveys from the 1990s revealed that most cannabis users were co-users of tobacco. Until the recent electronic cigarette (e-cigarette) or JUUL epidemic, there had been a steady decrease in self-report of tobacco use in youth. However, youth who smoke tobacco remain more likely to report marijuana use.[18,19] Co-users in this study had lower academic performance compared with cannabis-only users and were more likely to be male than female. In this study, the authors speculated that the increased use of cannabis was associated with normative behavior, whereas tobacco use was perceived as riskier behavior. Another study examining the co-use of tobacco and marijuana found that marijuana use was associated with greater nicotine addiction among adolescent smokers and that compulsion to smoke and preference to smoke were associated with marijuana use.[20] These authors hypothesized that smoking cues for one substance may trigger cravings for the other substance and lead to increased use in adulthood.[20,21] They suggest that the association of marijuana use with tobacco use should be considered when developing prevention programs for both substances. Alcohol co-use with marijuana has also been identified in several studies. Alcohol has adverse effects on the developing adolescent brain similar to those for marijuana, such as poorer attention and executive functioning, heightened emotional reactivity, and poorer distress tolerance.[22] A longitudinal study examining the effect of alcohol use on marijuana use found that alcohol was a significant predictor of cannabis initiation within a year. In their study, Terry-McElrath et al[23] found that co-use of marijuana and alcohol was associated with unsafe driving. They suggested that co-use of alcohol and marijuana in the context of driving should be explored when providing preventive care.

The *Bright Futures: Guidelines for Health Supervision of Infants, Children and Adolescents, Fourth Edition*[24] highlights health issues to be screened for at health maintenance visits. Tobacco, alcohol, and drug risk assessment is recommended throughout the adolescent years.[24] The American Academy of Pediatrics (AAP) policy statement on substance abuse and prevention suggests that pediatricians become familiar with substance abuse screening.[25] The AAP recommends using short validated screeners to determine youth at risk.[25] One validated screener is the CRAFFT (car, relax, alone, forget, family or friends, and trouble), which screens to identify

youth aged 12 to 21 years old at risk for alcohol or substance use, driving or riding risk, and substance use disorder. CRAFFT 2.1 is an updated version of that incorporates opening questions that quantify the amount of use within the past 12 months, and CRAFFT + N includes an opening question on tobacco, including smoking and/or vaping use.[26] The tool is scored as low, medium, and high risk. CRAFFT 2.1 includes recommendations on how to discuss risk and how to contract for safe rides, which has been shown to decrease the risk of adolescents riding in a car with someone who has been drinking or using drugs.[26]

MARIJUANA AND PREGNANCY

Marijuana is one of the most commonly used illicit substances in women, and the estimated prevalence of use among pregnant women in the United States ranges between 3% and 16%.[27] From 2002 to 2014 past-month marijuana use among pregnant women increased by 62%.[28] Legalization has increased accessibility and strengthened advocacy for its use, which may contribute to the increased use and perceived safety for pregnant women. Pregnant women are using marijuana for several reasons. In a Canadian survey, researchers found that 77% of medicinal cannabis use was for treatment of nausea. Half of the women surveyed reported using marijuana to treat poor appetite, pain, insomnia, or mood disorders (depression and anxiety).[28] Use of cannabinoids during pregnancy has led to health concerns related to fetal development because exogenous cannabinoids containing THC cross the fetal-placental barrier in humans.[29–31]

The endocannabinoid system plays a major role in fetal development, and the concentration of CB1 receptors is higher in fetal brains than in adults.[32] THC binds to the CB1 receptor instead of endocannabinoids, leading to various neurodevelopmental changes. Animal studies of prenatal THC exposure provide strong evidence for these adverse effects.[33] In a review of several studies on prenatal marijuana use, investigators found a dose-response effect on fetal growth; increased use was associated with decreased growth.[34] It was unclear whether prenatal exposure had an effect on preterm births. In a meta-analysis of 31 studies on marijuana use during pregnancy, investigators found that maternal marijuana use and concomitant tobacco exposure contributed to adverse neonatal outcome.[34–36] Marijuana exposure has also been associated with NICU admissions as well as with increased respiratory and neurologic infections and hematologic morbidity.[34]

Animal studies revealed that even low levels of exposure to marijuana have adverse neurologic effects.[37] In a recent systematic review examining 7 longitudinal studies on the effects of prenatal exposure on neuropsychological function in children, investigators found varied results between the association of prenatal exposure to marijuana and a child's neuropsychological development at ages 1 to 11 years. The majority of studies demonstrated a negative impact of marijuana during pregnancy, including deficits in neuropsychological functioning, decreased attention, memory problems, and poor impulse control.[37] However, there were mixed results between studies, and the authors acknowledged that there may be confounding biases.

Another area of interest has been the relationship between breastfeeding and maternal marijuana use. Cannabis concentration in breast milk is related to the maternal dose ingested and frequency of ingestion.[38–40] In 2 studies, authors investigated outcomes for infants exposed to cannabis from breastfeeding. In 1 study, the authors found an association between marijuana detected in breast milk and decreased motor development at 1 year; however, the authors noted that this result could have been confounded by the use of marijuana during pregnancy. In the other study, authors compared breastfed infants exposed to marijuana and those not exposed to marijuana; these authors noted no differences in motor or cognitive skills at 1 year.[38,39]

Human studies on maternal marijuana use have been limited, and most have been observational or retrospective, relying on patient self-report. These studies have been confounded by polysubstance abuse and had small sample sizes. At this time, a causal relationship cannot be established. However, because of the paucity of research, it is recommended that women refrain from marijuana use during pregnancy and breastfeeding. The American College of Obstetrics and Gynecology and the AAP recommend that breastfeeding mothers refrain from marijuana use.[41,42] Standard of care for prenatal and postnatal visits should include screening for drug use, including marijuana use. Clinicians should be aware that women may also seek information on marijuana use in pregnancy and breastfeeding from other sources. Clinicians should try to ensure that patients have access to current evidence-based information about marijuana use.

ADVERSE EFFECTS FROM CANNABIS USE

The adverse effects of cannabis use are well documented. Adverse effects include distorted perception, poor concentration, psychosis, excessive vomiting, and addiction.

Endogenous cannabinoids have an important role in the control of neural circuits and structures in the prefrontal cortex and the hippocampus. During adolescence,

these circuits mature and regulate attention, executive functioning, and memory. Studies have revealed that the development and maturation of these circuits can be affected by cannabis, causing impairment in neurocognitive functioning.[43,44] THC is a lipophilic substance with a long half-life that becomes distributed in various tissue, including the brain's myelin. It is released back into the bloodstream over the course of 5 to 95 days in individuals with heavy, regular use, meaning that neurodevelopmental changes can continue to occur for weeks to months after consumption.[45,46] Of note, manufactured and synthetic marijuana products may have higher THC concentrations than naturally occurring products, which can lead to more intense and longer-lasting effects.

In a longitudinal study by Meier et al,[45] cannabis use >20 years was associated with neuropsychological decline, with worsening effects for long-term users. In another study, authors explored neurocognitive measures in adolescents with recent cannabis use disorder who were now abstaining and also found that younger onset was associated with lower overall neurocognitive function. Similarly, Meier et al[45] found persistent neurocognitive changes 1 year after cessation of cannabis use.

In a recent longitudinal study on marijuana use and adolescent brain development, researchers found that cannabis use had adverse effects on IQ and executive functioning.[46] This cross-sectional longitudinal study revealed differences in resting-state networks known to mediate executive functioning (left dorsolateral prefrontal cortex) and regulatory control (anterior cingulate cortex). Marijuana use was associated with declines in neural connectivity over time, especially in adolescents with cannabis use disorder.[46] In an Australian longitudinal study, authors found that individuals who used before age 17 years old had a reduced odds of high school graduation and degree completion compared with nonusers. These individuals were more likely to have cannabis use disorder, were more likely to use other illicit substances, and had more suicide attempts.[47]

Animal studies of cannabis use and psychosis have suggested a remodeling of brain structure due to effects on the endocannabinoid system. These changes are similar to changes seen in schizophrenia.[48] In a recent study by Di Forti et al,[49] the authors found that daily marijuana use and high-potency marijuana (THC content >10%) are the strongest independent predictors of whether an individual will have a psychotic episode. Initiation of marijuana use by age 15 years slightly increased the odds of having a psychotic episode, but this was not independent of potency and frequency of use. Individuals with daily use had a 3.2 times higher likelihood of developing psychosis compared with nonusers. Individuals who used high-potency marijuana were 1.6 times more likely to develop psychosis compared with nonusers.[49] Individuals who had both daily use and high-potency use were almost 5 times as likely to develop psychosis compared with nonusers. Further studies exploring frequency and potency of use and gene expression may help elucidate the neurobiology behind the development of psychosis due to cannabis. Physicians should be aware of the increasing potency of legal marijuana products; for example, the average THC content of marijuana sold legally in Colorado is ~18%.

Marijuana use has also been found to be linked to an increase in use of prescription pain medication (opioids). Individuals who used marijuana had a 2.78 increase risk of having an opioid use disorder.[50] Other drugs associated with marijuana use include stimulants, cocaine, and injection drugs.[51] In 2018, the Insurance Institute for Highway Safety and the Highway Loss Data Institute reported an increase in motor vehicle crashes in states that had legalized marijuana use. In one study comparing perceptions of impaired driving after alcohol use, young adults felt that marijuana use was safer than alcohol use for driving.[52] However, study participants did not feel as knowledgeable about the effects of marijuana on driving.

Toxicity from consumption of marijuana has been documented in several case studies. Most individuals who experience toxicity have been exposed to high concentrations of cannabinoids. These individuals can experience adverse health effects, including sedation, respiratory depression, hyperemesis, and cardiotoxicity.

Marijuana use has also been associated with the positive health effect of decreasing nausea. However, chronic use can cause a paradoxical effect, leading to hyperemesis. Patients typically present with cyclic vomiting, nausea, and epigastric pain. Interestingly, these symptoms are often reported to be relieved by hot showers.[53–55] Capsaicin has also been a successful treatment of hyperemesis.[55]

A systematic review of unintentional cannabis ingestion in children and adolescents revealed rates increasing in states that had legalized marijuana.[56] The most common form of ingestion were cannabis resin, followed by cookies and joints.[57] Other exposures to cannabis included passive smoke, candies, beverages, and hemp oil. The most common sign of cannabis ingestion was lethargy. Ataxia, mydriasis, hypotonia, and tachycardia were also common presenting signs.[57]

NEW WAYS TO USE

The traditional method of marijuana consumption has been to smoke the dry leaves of the plant. A joint is dried marijuana leaves rolled in cigarette paper. Blunts are marijuana leaves rolled in a hollowed-out cigar. Adolescent users may prefer blunts to joints because blunts hold a larger quantity of marijuana and burn slower. However, use of blunts is a health concern because of the co-use of cannabis and tobacco. In a study by Fairman,[58] the author found that blunt users had higher severity of current cannabis use–related problems, reporting more tolerance as well as spending more time getting, using, and getting over the effects of cannabis. Because of dual use of tobacco and cannabis in blunts, there is concern that those trying to quit smoking blunts could be at greater risk for relapse because of nicotine withdrawal symptoms.[58]

Other forms of marijuana available for consumption include hashish (a plant extract containing psychoactive resins), hash oil (cannabis concentrate extracted from hashish), and dabs (also cannabis concentrate). THC content varies but is generally much higher than concentrations found in the plant. Typical THC content of the marijuana plant ranges from 12% to 20%. Products produced by using solvents (butane hash oil and dabs) have THC content ranging from 39% to 80%.[59] Nonsolvent-produced concentrates have THC concentrations between 39% and 60%.

Marijuana is also available as vaporizable cannabis concentrates, as edibles, or as liquids. Vaporizable concentrates include "shatter" (a brittle, translucent material made from marijuana plant materials and solvents), "oil," wax," and "butane hash." Vaporizable cannabis concentrates contain 60% to 85% THC, contain higher concentrations (compared with dried-leaf products), and can be consumed through vape pens, e-cigarettes, and dabs.[60] Dabs are concentrated butane hash oil consumed when the concentrate is heated to high temperatures and the user inhales the resulting vapor. In one study by Loflin and Earleywine,[61] the authors examined why users preferred dabs and examined whether dab use was associated with more problems than traditional cannabis use. Study participants reported that dabs required fewer hits to achieve desired effects. Study participants did not feel that their use was associated with more problems, but dab use was more likely to lead to dependence and withdrawal.[61]

E-cigarettes have been advertised as safe and healthier than traditional cigarettes; sales of these devices have targeted adolescents. The 2011–2018 National Youth Tobacco Survey and the Monitoring the Future survey both identified increases in e-cigarette use in middle and high school students compared with other tobacco products.[62,63] Eggers et al[64] explored use of cannabis through e-cigarette systems; cannabis use through e-cigarettes was higher among 11th-graders than ninth-graders and among youth with worse grades. In this study, the authors also found that use of cannabis through e-cigarettes (versus smoking blunts) had similar adverse effects on school performance. Both e-cigarette delivery of cannabis and blunt use were associated with greater tobacco use.[64] Physicians should consider methods of delivery when discussing cannabis use because e-cigarettes are a novel route of administration and appeal to youth who are not otherwise susceptible to cannabis via blunts or joints. The AAP 2015 policy statement on electronic nicotine delivery systems strongly recommends that pediatricians screen for and discourage vaping device use.[65]

SCS

SCs, (eg, Spice and K2) have become popular recreational substances among young adults. These substances are plant-derived material adulterated with substances similar to synthetic THC. These are readily available for purchase online or in shops specializing in marijuana and tobacco paraphernalia. SCs are often marketed as safe, natural, herbal blends not intended for human consumption in attractive packaging. However, these products are not naturally produced. They are typically mass produced outside of the United States. They are typically dissolved and mixed with dried vegetation in an imprecise process. The dosing of one product batch can vary greatly from that of another batch. These products can also be contaminated with heavy metals, bacteria, and chemicals. For example, in 2018, 70 individuals experienced serious drug overdose in Connecticut from using synthetic cannabis that was contaminated with rat poison. Unlike THC, which is a partial agonist at CB1 and CB2 receptors, SCs are full agonists at CB1 and CB2 sites, increasing the potency of SCs.[66] This may account for the increased morbidity and mortality seen with the use of SCs compared with marijuana.[67]

Serious adverse health effects have been documented with the use of SCs. Adverse effects include cardiac abnormalities, coagulopathies, and neurologic and psychiatric abnormalities.[68] Cardiac effects include tachycardia and acute myocardial infarction.[69,70] A cardiac fatality was reported in a young adult after smoking SCs.[71] Hematologic abnormalities due to long-acting vitamin K–dependent antagonist contamination of SCs have been reported.[71] In a review of SC use, reports of acute kidney injury were noted. All individuals required hospitalization, and one individual required dialysis.[72] Neurologic abnormalities are also well

documented. SCs have been linked to strokes, seizures, and psychiatric effects, including anxiety, agitation, suicidal ideation, and psychosis. The neuropsychologic effects of SCs, compared with marijuana, are enhanced because of the difference in SC action at CB1 and CB2 sites.

There can be significant variation in SC potency, which can lead to serious adverse health events. These compounds can be mixed with other psychoactive substances, (eg, ecstasy, bath salts, and others). SC detection is often difficult in medical settings, and typical drug screening is often not helpful. Providers should be aware of possible adverse side effects of SC and should have a high index of suspicion when patients present with symptoms that could be due to consumption of SCs.

MARIJUANA AND THE MEDIA

In 2019, marijuana was legal in 33 states for medical use and in 11 states for recreational use by adults. As legalization has increased, more and more information has appeared in mainstream press and social media discussing the benefits and risks of marijuana. Reports include discussion of different strains of marijuana plants, health benefit claims, adverse effects, where to purchase marijuana, how to obtain medical certification, where to use marijuana, and other topics. Thus, pediatricians should be aware of the information about marijuana use being disseminated through the media. Marijuana can be obtained through dispensaries for medicinal purposes with appropriate certification. Generally, patients need to consult with a physician and need to have a qualifying condition (which varies in different states). Depending on the state, they may be given an identification card, which allows them to purchase marijuana at a medical dispensary. The amount an individual may possess or purchase also varies by state. Medicaid and Medicare will not pay for medicinal marijuana because the federal government prohibits the sale of schedule I drugs.

In general, consumers aged 21 years or older can purchase marijuana legally from recreational dispensaries. Although many cannabis purchases occur through traditional illegal face-to-face sales, cannabis products can also be purchased online, both through legal recreational use sales and illegal drug markets on the dark Web. Recreational sales are cash only in most states. Prices vary by product type, weight, and location of the sale. For example, a sativa-hybrid dried plant bought online costs $60 per 3.5 g, and indica dried leaf bought from a recreational dispensary costs $18 per gram.

A variety of marijuana products are available in recreational and medical dispensaries. Retail shops may display menus listing THC content, cannabis strain, and the mood or symptom relief it may provide. For example, Afgooey (indica strain), has 22.9% THC and is advertised as "manageable psychoactivity and a wide range of applications, including pain relief and sedation."[73] Although different strains may be advertised as sedating or invigorating, there is no scientific evidence to support these claims. These aspects of a product may be due to other components of the plant, such as terpene content.[74,75] Further research is needed to accurately describe the effects of specific products.

Many people purchase medical and recreational marijuana online. In a 2017 *JAMA* study, authors found that nearly 70% of CBD products sold online contained higher or lower concentrations of the drug than was on their label. Some CBD products contained significant amounts of THC. CBD products sold for vaping were mislabeled 88% of the time, and THC was detected in 18 of 84 samples, some with enough to produce intoxication.[76] It is important to counsel patients and parents about the THC content in CBD products and to note that they lack regulation by the FDA. Pediatricians should also refer to individual state laws for further information concerning purchasing, use, and possession of marijuana.

CANNABIS USE DISORDER

Monitoring the Future survey data suggest that most adolescents do not perceive marijuana use as harmful, addictive, or associated with withdrawal.[77,78] However, 8% to 12% of marijuana users will develop moderate to severe cannabis use disorders. Additionally, animal studies reveal that marijuana can prime the brain to the effects of other illicit substances. Although less clearly delineated in humans, according to the Substance Abuse and Mental Health Services Administration, 4.2 million people in the United States had cannabis use disorder in 2017. The *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition* defines cannabis use disorder as use of cannabis for at least 1 year with the presence of 1 or 2 other findings consistent with addiction and significant impairment of functioning and distress.[79] Although cannabis use can negatively impact the user's health, to date it has not been linked to fatal overdoses.[80–82] In addition, individuals can experience cannabis withdrawal. The *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition* describes cannabis withdrawal as having ≥3 of the following signs and symptoms within the 1 week of discontinuing use: (1) irritability, anger, or aggression; (2) nervousness or anxiety; (3) sleep difficulty or insomnia; (4) decreased appetite or weight loss; (5) restlessness; (6) depressed mood; and (7) at least 1 of the following: abdominal pain, shakiness or tremors, sweating, fever, chills, or headache.[79]

Being young, having a lower socioeconomic status, male sex, and being a minority increases the risk of developing cannabis use disorder.[83]

Several treatments have been investigated for treatment of cannabis use disorder. In a review by Brezing and Levin,[84] the authors found several medication treatments that may be of benefit. Only one study was focused on treating adolescents: topiramate reduced marijuana use in adolescents but was not well tolerated.[85] In adult studies, gabapentin has been found to reduce withdrawal, reduce cravings, and improve cognitive functioning. Dronabinol and nabilone were also found to improve withdrawal symptoms and reduce cannabis use.[86,87] Nabilone plus zolpidem also improved withdrawal symptoms and reduced cannabis use.[88] Limitations to the current studies include inclusion of individuals with severe cannabis use disorder and high attrition rates. Brezing and Levin[84] note that reduction in use, rather than abstinence, may be an appropriate goal for treatment of cannabis use disorder. However, there is no consensus in the literature defining a meaningful reduction in use. Although research on medications for cannabis use disorder continues; motivational and cognitive behavioral therapies continue to be the mainstays of treatment at this time.

CONCLUSIONS

Marijuana is one of the most commonly used psychoactive substances. The literature reveals a number of health concerns associated with marijuana use, from physical health effects to mental health effects, that can occur over the course of development and social consequences associated with use. It is important for providers to be aware of policies and laws around marijuana in their states to provide appropriate and evidenced-based recommendations and to counsel appropriately to prevent exposure and thus harm to developing brains. The health and well-being of children and adolescents should be prioritized when providing this information. More research is needed on the long-term effects of marijuana and should also be focused on prevention of use in adolescents.

ABBREVIATIONS

AAP: American Academy of Pediatrics
CBD: cannabidiol
e-cigarette: electronic cigarette
FDA: US Food and Drug Administration
IBD: inflammatory bowel disease
SC: synthetic cannabinoid
THC: tetrahydrocannabinol

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