Lenart, Brett

From: Walkovich, Kelly <kwalkovi@med.umich.edu>
Sent: Wednesday, May 16, 2018 8:34 AM
To: Planning
Cc: Lumm, Jane; ryanwoodz@hotmail.com
Subject: Concern regarding proposal to permit 3152 Packard Rd to operate as a medical marijuana provisioning center
Attachments: City Planning Marijuana Notice.jpg; Pediatric Marijuana Exposures in a Medical Marijuana State JAMA 2013.pdf; Unintentional Cannabis Intoxication in Toddlers Pediatrics 2017.pdf; Effects of Cannabis Use on Human Behavior, Including Cognition, Motivation and Psychosis A Review JAMA Pyschiartry 2016.pdf

Dear Planning Commission -

I am writing to you with concerns regarding a notice (see attached) that my daughter's daycare provider, May's Bilingual Preschool, received indicating that a special exception use permit is under consideration to allow 3152 Packard Rd to operate as a Medical Marijuana Provisioning Center. I have previously contact my City Council representatives and they recommended that I forward my concerns onto you directly. I am strongly opposed to the special exception permit being granted. Of note, although my family lives within Ward 2, May's Bilingual Preschool is located at 3181 Packard Rd in Ward 3 and is within 300 feet of the proposed Medical Marijuana Provisioning Center.

Upon review of the city's ordinances, it appears that section 5:50.1(3)(c) provides protection to children in both private and public K-12 elementary and secondary school by requiring medical marijuana provisioning centers, growers and processors be located a minimum of 1000 feet away from the parcel of land supporting the schools. However, daycare sites and preschools are not specifically addressed in the ordinance. May's Bilingual Preschool is licensed for children 0-12 years of age and I was hoping you could clarify whether the school would fall within the requirements of the ordinance for the 1000 feet separation as it currently is written? Or, if an amendment to the ordinance or alternate strategy would be required to protect daycares/preschools in the same fashion as K-12 schools?

Given that marijuana remains a schedule I drug under the federal Controlled Substance Act due to the extremely high risk for addiction (cocaine and heroin are also included in the schedule I drug designation), that medical marijuana is not regulated by the FDA and is therefore not mandated to have child-safe packaging, that ingestion and inhalation, including second-hand inhalation, of marijuana is documented to have both negative immediate impacts on child health and longer-term impacts on brain development (see attached) and that the American Academy of Pediatrics has raised significant concerns related to "normalization" of marijuana use secondary to adult modeling, I suspect that the main driver of the 5:50.1(3)(c) ordinance was to protect the health and development of the children and adolescents in our community. As a pediatric oncologist providing care in this community and particularly as a mother of toddler in Ann Arbor, I kindly request your help in extending the protection provided to K-12 kids, to our youngest and in many ways, most vulnerable children. If an amendment to the ordinance or other change is required, I would appreciate your help in directing me as to the next steps needed to move forward.

My prior understanding is that there was potentially a meeting to be held tonight with the Planning Commission to discuss the 3152 Packard Rd Special Exemption permit request specifically. Neither May's

Bilingual Preschool nor I have received any updated information regarding whether this meeting is still scheduled for today or if it has been moved. I'd very much appreciate it if you can confirm the date/time/location of the public meeting so that I can plan to be in attendance.

Thank you,
Kelly Walkovich, MD
734 476 5964
****
Electronic Mail is not secure, may not be read every day, and should not be used for urgent or sensitive issues

Original Investigation

Pediatric Marijuana Exposures in a Medical Marijuana State

George Sam Wang, MD; Genie Roosevelt, MD, MPH; Kennon Heard, MD

Editorial pages 600 and 602

IMPORTANCE An increasing number of states are decriminalizing the use of medical marijuana, and the effect on the pediatric population has not been evaluated.

OBJECTIVE To compare the proportion of marijuana ingestions by young children who sought care at a children's hospital in Colorado before and after modification of drug enforcement laws in October 2009 regarding medical marijuana possession.

DESIGN Retrospective cohort study from January 1, 2005, through December 31, 2011.

SETTING Tertiary-care children's hospital emergency department in Colorado.

PARTICIPANTS A total of 1378 patients younger than 12 years evaluated for unintentional ingestions: 790 patients before September 30, 2009, and 588 patients after October 1, 2009.

MAIN EXPOSURE Marijuana ingestion.

MAIN OUTCOMES AND MEASURES Marijuana exposure visits, marijuana source, symptoms, and patient disposition.

RESULTS The proportion of ingestion visits in patients younger than 12 years (age range, 8 months to 12 years)that were related to marijuana exposure increased after September 30, 2009, from 0 of 790 (0%; 95% CI, 0%-0.6%) to 14 of 588 (2.4%; 95% CI, 1.4%-4.0%) ($P < .001$). Nine patients had lethargy, 1 had ataxia, and 1 had respiratory insufficiency. Eight patients were admitted, 2 to the intensive care unit. Eight of the 14 cases involved medical marijuana, and 7 of these exposures were from food products.

CONCLUSIONS AND RELEVANCE We found a new appearance of unintentional marijuana ingestions by young children after modification of drug enforcement laws for marijuana possession in Colorado. The consequences of unintentional marijuana exposure in children should be part of the ongoing debate on legalizing marijuana.

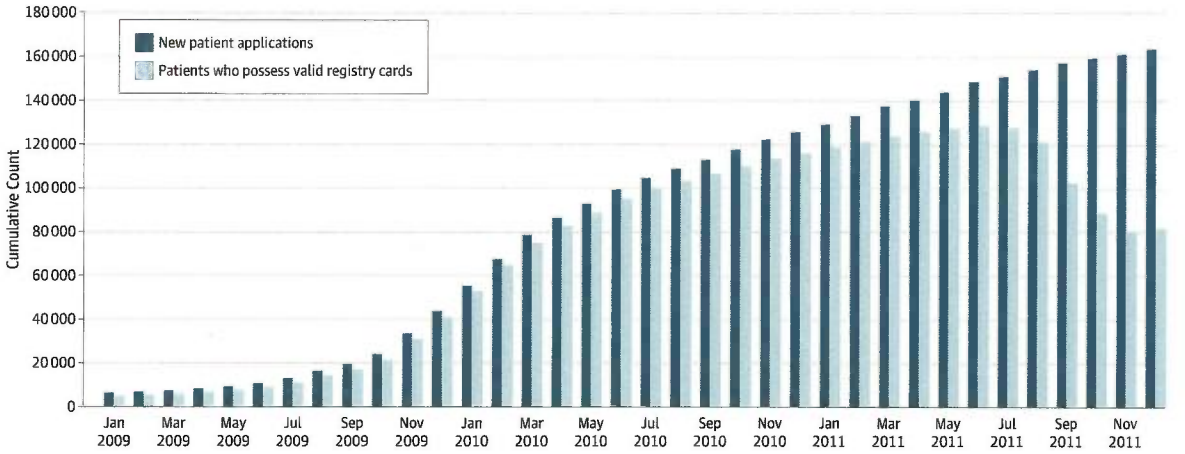
JAMA Pediatr. 2013;167(7):630-633. doi:10.1001/jamapediatrics.2013.140
Published online May 27, 2013.

Author Affiliations: Rocky Mountain Poison and Drug Center, Denver Health, Denver, Colorado (Wang, Heard); Department of Pediatrics, Section of Emergency Medicine, University of Colorado School of Medicine, Aurora (Roosevelt).

Corresponding Author: George Sam Wang, MD, Rocky Mountain Poison and Drug Center, 777 Bannock St, Office Box 0180, Denver, CO 80204 (george.wang@childrenscolorado.org).

The vigorous debate on legalizing marijuana in the United States has received significant media attention, as evidenced by the *60 Minutes* segment, "Medical Marijuana: Will Colorado's 'Green Rush' Last?" that aired on October 21, 2012.[1] Currently, 17 states and Washington, DC, have enacted laws to decriminalize medical marijuana at the state level despite being a Schedule 1 drug under the Controlled Substances Act. Most recently, in November 2012, Colorado and Washington passed amendments legalizing the recreational use of marijuana. In November 2000, Coloradoans passed Amendment 20, establishing the Medical Marijuana Registry, which opened in June 2001 under the auspices of the Colorado Department of Public Health and Environment. Since June 2001, there have been almost 160 000 total patient applications, and almost 89 000 patients currently possess valid registry ID cards (**Figure**). In October 2009, a new Justice Department policy instructed federal prosecutors not to seek arrest of medical marijuana users and suppliers as long as they conform to state laws.[2] In Colorado, this resulted in a sharp increase in the number of medical marijuana cards, with 60 000 cards issued in 2009 compared with 2000 in the 8 years prior.[3] The mean age of a person with a medical marijuana card is 42 years, and 68% are male; 41 patients are younger than 18 years.[2] Reported conditions in patients using medical marijuana include cachexia, cancer, glaucoma, human immunodeficiency virus or AIDS, muscle spasms, seizures, severe pain, and severe nausea.[1] According to the Colorado Medical Marijuana Enforcement Division, as of October 2012, there are 204 medical marijuana dis-

Figure. Colorado Department of Public Health and Environment's Marijuana Registry



New patient applications for medical marijuana cards and patients who possessed valid registry cards in Colorado, from January 1, 2009, through December 31, 2011.

pensaries in the Denver metropolitan area (J. Postlethwait, BA, BS, oral communication, October 2012). The impact that decriminalizing medical marijuana has had on the use of marijuana is unclear. Although one study found higher adolescent marijuana use in medical marijuana states, a second study found no effect.[4,5] Neither study included younger pediatric exposures.

Historically, significant effects following unintentional pediatric marijuana ingestions were very rare, probably due to the poor palatability of the marijuana plant and the enforcement of existing drug laws. Previous literature consists of single case reports and a small case series.[6-10] However, tetrahydrocannabinol, the active chemical in marijuana, is incorporated into medical marijuana products in higher concentrations than typically found in the marijuana bud, the most potent part of the plant. In addition, medical marijuana is sold in baked goods, soft drinks, and candies. Therefore, we conducted a study to compare the number of marijuana exposures in a pediatric emergency department (ED) before and after the federal policy change in October 2009. On the basis of our clinical observation, we hypothesized that there would be a significant increase in pediatric marijuana exposures after October 2009.

Methods

This was a retrospective cohort study at a tertiary-care, freestanding children's hospital with an annual ED census of 65 000 visits. Inclusion criteria included patients younger than 12 years evaluated for ingestion from January 1, 2005, through December 31, 2011. Cases were identified by the following *International Classification of Diseases, Ninth Revision* codes: 930 to 939 (Effects of Foreign Body), 960 to 979 (Poisoning by Drugs, Medicinals, and Biological Substances), 980 to 989 (Toxic Effects of Substances Chiefly Nonmedicinal as to Source), E850 to E858 (Accidental Poisoning by Drugs, Medicinal Substances, and Biologics), E860 to E869 (Accidental Poisoning by Other Solid and Liquid Substances, Gases, and Vapors), and E910 to E915 (Accidents Caused by Submersion, Suffocation, and Foreign Bodies). All marijuana exposures were confirmed by a urine toxicology screen.

Cases were reviewed by a single investigator (G.S.W.), and variables were abstracted onto a standardized data collection form. Abstracted variables included age, sex, date of visit, presenting chief complaint, laboratory work obtained, reported source of marijuana, and patient disposition. The proportion of poisoning cases related to marijuana between January 1, 2005, and September 30, 2009 (57 months), was compared with the proportion of cases between October 1, 2009, and December 31, 2011 (27 months).

Data were analyzed using SPSS, version 16.0 (SPSS, Inc) and SAS, version 9.2 (SAS Institute, Inc). Descriptive statistics were calculated. Medians with interquartile ranges were reported. Proportions were analyzed by the Fisher exact test. This study was approved by the Colorado Institutional Review Board, which granted a waiver of informed consent.

Results

From January 1, 2005, through September 30, 2009, 790 patients younger than 12 years were evaluated in the ED for suspected unintentional ingestions. The median age was 2.6 years (interquartile range, 1.6-3.0), and 449 (56.8%) were male. From October 1, 2009, through December 31, 2011, 588 patients younger than 12 years were evaluated in the ED for suspected unintentional ingestions. The median age was 2.3 years (interquartile range, 1.5-3.6), and 334 (56.8%) were male. The types of ingestions were similar between the 2 periods (Table 1).

Between January 1, 2005, and September 30, 2009, no patients younger than 12 years sought care at the ED for marijuana ingestions. Between October 1, 2009, and December 31, 2011, 14 patients younger than 12 years had confirmed marijuana ingestion by urine toxicology screen (Table 2). The pro-

portion of exposure visits related to marijuana increased from 0 of 790 (0%; 95% CI, 0%-0.6%) to 14 of 588 (2.4%; 95% CI, 1.4%-4.0%) after September 2009 ($P < .001$).

The age of the patients exposed to marijuana ranged from 8 months to 12 years, and 64.2% were male. The majority of patients had central nervous system effects such as lethargy or somnolence with respiratory insufficiency as the most serious symptom. Most patients received an extensive workup, including blood work, radiographs, and lumbar punctures (Table 2). Only 2 patients had a history of marijuana ingestion, and they were the only patients who had minimal ancillary tests performed (urine toxicology screen). One patient was discharged from the ED, 5 patients were observed in the ED and eventually discharged, and 8 were admitted, with 2 admitted to the pediatric intensive care unit. Eight patients were exposed to medical marijuana. In 3 patients, the source of the marijuana was never identified despite investigation. Seven of the medical marijuana exposures and 1 nonmedical marijuana exposure were from food products.

Table 1. Demographics of Patients Seen in the Children's Hospital Emergency Department for Ingestions[a]

Characteristic	January 1, 2005, Through September 30, 2009	October 1, 2009, Through December 31, 2011
No. of patients	790	588
Age, median (IQR), y	2.6 (1.6-3.0)	2.3 (1.5-3.6)
Male sex	449 (56.8)	334 (56.8)
Types of ingestions		
Acetaminophen	90 (11.3)	48 (8.2)
Antihistamine	43 (5.4)	32 (5.4)
Antidepressant	23 (2.9)	14 (2.3)
Antitussive	18 (2.2)	14 (2.3)
Marijuana exposures	0	14 (2.3)

Abbreviation: IQR, interquartile range.

[a] Values are given as number (percentage) unless otherwise noted.

Discussion

We found a new increase in unintentional marijuana ingestions by young children after modification of drug enforcement laws for marijuana possession in Colorado. Most patients (92.8%) were admitted to or observed in the ED. In comparison, there were 1 207 575 exposures reported to US poison centers in 2010 in children younger than 5 years.[11,12] Of those patients, 109 611 (9.1%) were evaluated and discharged by a health care facility, and only 15 941 (1.3%) required admission.[11,12] This suggests that recent marijuana exposures are associated with more significant clinical effects than are typically reported with poisoning exposures in young children.

The increase in marijuana exposures in young children in Colorado is most likely due to the decriminalization of medical marijuana, which has resulted in an explosion of medical marijuana dispensaries and an increase in medical marijuana cards (Figure). Medical marijuana solicitation and advertising are ubiquitous throughout the state, with dispensaries throughout the Denver metropolitan area. In 2010, Denver issued more than 300 sales tax licenses for dispensaries, roughly twice the number of the city's public schools.[13]

Table 2. Pediatric Patients With Marijuana Exposures

Case No./ Sex/Age	Symptoms	Ancillary Tests	Disposition	Source of Marijuana
1/M/8 mo	Lethargy, rigidity	CMP, CBC, UA, Utox	Observation	Unknown
2/M/10 mo	Fussiness, somnolence	CMP, CBC, UA, amylase/lipase, Utox, CT head, c-spine x-rays, abdominal x-rays	Observation	POC medical marijuana
3/F/10 mo	Lethargy, hypoxic	CMP, CBC, UA, RSV, Utox, CT head, CXR, IV antibiotics	Admission	Unknown
4/M/1 y	Lethargy	BMP, CBC, Utox, CT head	Admission	POC with medical marijuana cigarette
5/M/2 y	Lethargy	UA, CMP, CBC, APAP/ASA levels, EKG, Utox, CT head, CXR	Admission	Babysitter with marijuana
6/M/2 y	Ataxia	CMP, CBC, UA, Utox, CT head, LP	Admission	Unknown
7/F/3 y	Lethargy	APAP/ASA levels, Utox, charcoal	Admission	FOC medical marijuana cookie
8/F/3 y	Lethargy	BMP, CBC, UA, Utox, CT head, CXR, LP	Admission	Family friend's medical marijuana cookie
9/M/3 y	Lethargy	BMP, CBC, APAP/ASA levels, valproic acid levels, Utox, CTH, VBG	Admission to PICU	GFOC medical marijuana cookie
10/F/3 y	Lethargy	Utox	Observation	FOC medical marijuana candy
11/M/4 y	Lethargy	UA, BMP, CBC, APAP/ASA levels, EKG, Utox	Observation	GMOC medical marijuana cookie
12/M/5 y	Respiratory insufficiency	CMP, CBC, APAP/ASA levels, EKG, Utox, CT head, VBG	Admission to PICU	GFOC marijuana
13/F/7 y	Asymptomatic	Utox	Discharge	GFOC medical marijuana cookie
14/M/12 y	Dizziness	BMP, CBC, EKG, Utox, rapid strep test	Observation	Marijuana cake

Abbreviations: APAP, acetaminophen; ASA, salicylate; BMP, basic metabolic panel; CBC, complete blood count; CMP, complete metabolic panel; c-spine, cervical spine; CT, computed tomography; CTH, head computed tomography; CXR, chest x-ray; EKG, electrocardiogram; FOC, father of child; GFOC, grandfather of child; GMOC, grandmother of child; IV, intravenous; LP, lumbar puncture; PICU, pediatric intensive care unit; POC, parents of child; RSV, respiratory syncytial virus; UA, urine analysis; Utox, urine toxicology screen; VBG, venous blood gas.

The increase in pediatric medical marijuana exposures may also be related to the improved palatability. Besides the plant and cigarette form, medical marijuana is sold in many products, including edibles such as candies, baked goods, and soft drinks, which presumably increases attractiveness to young children. In our study, most exposures were due to ingestion of medical marijuana in a food product. Many of these products contain higher concentrations of tetrahydrocannabinol than typically found in marijuana buds, resulting in symptomatic exposures despite small ingestions. Currently, there are no regulations on storing medical marijuana products in child-resistant containers, including labels with warnings or precautions, or providing counseling on safe storage practices.

While none of these exposures resulted in permanent morbidity or mortality, they caused significant clinical effects. Furthermore, when the diagnosis was unclear or the use of marijuana was not initially provided, children underwent multiple tests, procedures, and imaging during their ED evaluation. Because of a perceived stigma associated with medical marijuana, families may be reluctant to report its use to health care providers. Similar to many accidental medicinal pediatric exposures, the source of the marijuana in most cases was the grandparents, who may not have been available during data collection. Alternatively, the treatment team may fail to ask specifically about medical marijuana in the home.

Proponents of marijuana suggest that it is safer than ethanol. After September 2009, only 2 patients younger than 12 years were evaluated in the ED of the children's hospital for ethanol ingestion. One patient, an 11-year-old who intentionally ingested ethanol, was described as intoxicated; the other patient, a 2-year old who accidentally drank a household product that contained ethanol, was asymptomatic. During the study period, marijuana exposures resulted in more ED evaluations, hospital admissions, and clinical symptoms than did ethanol exposures.

There are some limitations to this study. This was a retrospective medical record review at a single tertiary-care children's hospital, so our findings may not be generalizable to other institutions. The data are from Colorado, and medical marijuana state laws vary, so our findings may not apply to other states. The abstractor of the medical records was not masked to the study question, which may have threatened the internal validity of the study. The abstracted data on the patients exposed to marijuana relied on previously collected medical record data and may have had missing information or details, including follow-up social work visits or police investigation. Patients may have been missed by our electronic medical record search.

In Colorado, the combination of decriminalizing medical marijuana and declining federal prosecution was associated with a significant increase in the exposure of young children to marijuana. Physicians, especially in states that have decriminalized medical marijuana, need to be cognizant of the potential for marijuana exposures and be familiar with the symptoms of marijuana ingestion. This unintended outcome may suggest a role for public health interventions in this emerging industry, such as child-resistant containers and warning labels for medical marijuana. The consequences of marijuana exposure in children should be part of the ongoing debate on legalizing marijuana.

ARTICLE INFORMATION

Accepted for Publication: December 12, 2012.

Published Online: May 27, 2013. doi:10.1001/jamapediatrics.2013.140.

Author Contributions: All authors had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.
Study concept and design: All authors.
Acquisition of data: Wang.
Analysis and interpretation of data: All authors.
Drafting of the manuscript: All authors.
Critical revision of the manuscript for important intellectual content: All authors.
Statistical analysis: Wang.
Administrative, technical, and material support: Wang, Roosevelt.
Study supervision: Roosevelt, Heard.

Conflict of Interest Disclosures: None reported.

REFERENCES

1. Medical marijuana: will Colorado's "green rush" last? *60 Minutes*. CBS television. October 21, 2012. http://www.cbsnews.com/8301-18560_162-57536827/medical-marijuana-will-colorados-green-rush-last/?tag=contentMain;contentBody. Accessed October 26, 2012.

2. Colorado Department of Public Health and Environment. Colorado Medical Marijuana Registry website. http://www.cdphe.state.co.us/hs/medicalmarijuana/. Accessed September 5, 2012.

3. Warner J. Medical marijuana timeline: what a long, strange trip it's been. *Westword*. May 28, 2010. http://blogs.westword.com/latestword/2010/05/medical_marijuana_timeline_wha.php?page=3. Accessed September 5, 2012.

4. Wall MM, Poh E, Cerdá M, Keyes KM, Galea S, Hasin DS. Adolescent marijuana use from 2002 to 2008: higher in states with medical marijuana laws, cause still unclear. *Ann Epidemiol*. 2011;21(9):714-716.

5. Harper S, Strumpf EC, Kaufman JS. Do medical marijuana laws increase marijuana use? replication study and extension. *Ann Epidemiol*. 2012;22(3):207-212.

6. Appelboam A, Oades PJ. Coma due to cannabis toxicity in an infant. *Eur J Emerg Med*. 2006;13(3):177-179.

7. Bonkowsky JL, Sarco D, Pomeroy SL. Ataxia and shaking in a 2-year-old girl: acute marijuana intoxication presenting as seizure. *Pediatr Emerg Care*. 2005;21(8):527-528.

8. Carstairs SD, Fujinaka MK, Keeney GE, Ly BT. Prolonged coma in a child due to hashish ingestion with quantitation of THC metabolites in urine. *J Emerg Med*. 2011;41(3):e69-e71.

9. Macnab A, Anderson E, Susak L. Ingestion of cannabis: a cause of coma in children. *Pediatr Emerg Care*. 1989;5(4):238-239.

10. Weinberg D, Lande A, Hilton N, Kerns DL. Intoxication from accidental marijuana ingestion. *Pediatrics*. 1983;71(5):848-850.

11. Bronstein AC, Spyker DA, Cantilena LR Jr, Green JL, Rumack BH, Dart RC. 2010 Annual report of the American Association of Poison Control Centers' National Poison Data System (NPDS): 28th annual report. *Clin Toxicol (Phila)*. 2011;49(10):910-941.

12. National Poison Data System website. https://www.npds.us/. Accessed May 30, 2012.

13. Osher CN. As dispensaries pop up, Denver may be Pot Capital, U.S.A. *Denver Post*. January 21, 2011. http://www.denverpost.com/ci_14112792. Accessed September 5, 2012.

Review

Effects of Cannabis Use on Human Behavior, Including Cognition, Motivation, and Psychosis: A Review

Nora D. Volkow, MD; James M. Swanson, PhD; A. Eden Evins, MD; Lynn E. DeLisi, MD; Madeline H. Meier, PhD; Raul Gonzalez, PhD; Michael A. P. Bloomfield, MRCPsych; H. Valerie Curran, PhD; Ruben Baler, PhD

With a political debate about the potential risks and benefits of cannabis use as a backdrop, the wave of legalization and liberalization initiatives continues to spread. Four states (Colorado, Washington, Oregon, and Alaska) and the District of Columbia have passed laws that legalized cannabis for recreational use by adults, and 23 others plus the District of Columbia now regulate cannabis use for medical purposes. These policy changes could trigger a broad range of unintended consequences, with profound and lasting implications for the health and social systems in our country. Cannabis use is emerging as one among many interacting factors that can affect brain development and mental function. To inform the political discourse with scientific evidence, the literature was reviewed to identify what is known and not known about the effects of cannabis use on human behavior, including cognition, motivation, and psychosis.

JAMA Psychiatry. 2016;73(3):292-297. doi:10.1001/jamapsychiatry.2015.3278
Published online February 3, 2016.

Author Affiliations: Author affiliations are listed at the end of this article.

Corresponding Author: Nora D. Volkow, MD, National Institute on Drug Abuse, National Institutes of Health, 6001 Executive Blvd, Bethesda, MD 20892 (nvolkow@nida.nih.gov).

It is well established that cannabis use causes acute impairment in the ability of the brain to hold information (ie, cognitive capacity). Hence, temporary deficits occur in learning and memory, attention, and working memory.

Does Cannabis Use Affect Cognitive Capacity?

Cannabis use causes acute impairment of learning and memory, attention, and working memory,[1-3] but it is less clear if cannabis use is associated with enduring neuropsychological impairment. Case-control studies comparing nonintoxicated heavy cannabis users with nonusers have fairly consistently shown that heavy cannabis users perform worse on neuropsychological tests. For example, the results from 2 separate meta-analyses[4,5] showed that compared with nonusers, nonintoxicated cannabis users perform worse on measures of global neuropsychological function, with effect sizes for specific neuropsychological domains (executive functions, attention, learning and memory, motor skills, and verbal abilities) of approximately one-third of a standard deviation or less. When analyses in the second meta-analysis[5] were limited to 13 studies of cannabis users with at least 1 month of abstinence, there was no discernible difference between cannabis users and nonusers on neuropsychological test performance, suggesting that neuropsychological functions might recover with prolonged abstinence. Evidence suggests that the magnitude of neuropsychological impairment and the extent to which it persists after abstinence may depend on the frequency and duration of cannabis use, length of abstinence, and age at onset of use.[6]

Emerging evidence suggests that adolescents may be particularly vulnerable to the adverse effects of cannabis use. Adolescence represents a critical neurodevelopmental period characterized by marked synaptic pruning and increased myelination.[7] Moreover, the endocannabinoid system appears to be involved in the regulation of key neurodevelopmental processes,[7] suggesting that the introduction of exogenous cannabinoids during adolescence could disrupt normal brain development. Animal research supports the possibility that adolescence represents a period of heightened vulnerability to cannabis exposure.[7] For example, pubertal rats treated with a cannabinoid agonist showed persistent deficits on object recognition tasks, whereas adult rats did not.[8,9] Accumulating evidence in humans parallels the animal findings.[6] For example, several studies have shown that earlier age at onset of cannabis use is associated with greater neuropsychological impairment,[10,11] and a 2012 population-representative longitudinal study[12] documented that adolescent-onset (but not adult-onset) persistent cannabis users showed neuropsychological decline from ages 13 to 38 years.

Neuroimaging investigations of adolescent and adult cannabis users have yielded somewhat inconsistent findings. Recent reviews have demonstrated that there is fairly clear evidence of structural alterations in medial temporal (amygdala and hippocampus), frontal, and cerebellar regions associated with cannabis exposure.[13,14] However, another recent study[15] that carefully matched participants on alcohol intake reported no evidence of morphological brain alteration among adolescent or adult cannabis abusers, suggesting the possibility that comorbid alcohol use could explain some of the morphological alterations observed in prior research. There is also some evidence that cannabis users have impaired neural connectivity. For example, a study[16] of adults with long histories of heavy cannabis use showed evidence of decreased connectivity in the right fimbria of the hippocampus (fornix) and the splenium of the corpus callosum and the commissural fibers. Finally, functional magnetic resonance imaging investigations have suggested that cannabis users show altered neural activity both in the resting state and during cognitive testing.[14] For example, male adolescent cannabis

users showed increased blood oxygen level–dependent functional magnetic resonance imaging activity in the prefrontal cortex during a novel working memory task, which was interpreted to reflect inefficient processing.[17] This observation is consistent with studies measuring resting functional connectivity in adolescent cannabis users that have documented altered patterns of connectivity affecting interhemispheric traffic[18] and the frontotemporal network.[19,20] Some evidence suggests that cannabidiol, another cannabinoid found in the cannabis plant (although usually at very low concentrations), may protect against some of the harmful effects of tetrahydrocannabinol (THC) on cognition.[21,22]

There are areas that require further research. First, observed differences in neuropsychological test performance, as well as in brain structure and function, might reflect individual differences that precede cannabis use. Progress has been limited by reliance on cross-sectional investigations comparing cannabis users and nonusers. Two longitudinal studies[12,23] with before-and-after neuropsychological testing have shown evidence of within-individual decline in neuropsychological function associated with cannabis use. The findings could not be explained by alcohol and other drug use, psychiatric disorders, low socioeconomic status, or a host of other potential confounds. However, the number of cannabis users in these cohorts was small, and brain imaging was not performed. Yet, neuroimaging findings raise the possibility that smaller regional brain volumes among cannabis users could be partially accounted for by preexisting differences. For example, one prospective longitudinal study[24] showed that smaller orbitofrontal cortex volumes increased risk for adolescent cannabis use initiation, while a study[25] of twins and siblings found that reduced amygdala volumes among cannabis users could be explained by familial factors. Taken together, these findings highlight the need for longitudinal studies that follow up adolescents from before to after initiation of cannabis use and combine neuropsychological testing with neuroimaging. The Adolescent Brain Cognitive Development Study,[26] a large prospective National Institutes of Health–funded investigation of children ages 9 to 10 years who will be followed up for at least 10 years, is being launched to in part meet this need.

A second area that is ripe for further research pertains to the need to reconcile neuroimaging findings with neuropsychological test performance. Current neuroimaging evidence is inconsistent, and alterations in brain structure and function tend not to correlate with decrements in neuropsychological test performance.[27] Larger samples are needed for imaging along with careful consideration of participant characteristics, including comorbid use of alcohol and other drugs and length of abstinence from cannabis.

Third, more work is needed to answer the question "How much cannabis use is too much?" Because many study samples include a large portion of individuals with cannabis dependence (as defined by the *DSM-IV*), it is unclear if the effects generalize to individuals with less severe cannabis use disorders and to more casual recreational users.

Fourth, because of the potential effect of exogenous cannabinoids on brain development, more work is needed to answer the question "At what age is cannabis use most harmful?" In addition to studying the effects of cannabis use on adolescents, research is also needed to understand older adults' susceptibility to cannabis-related neuropsychological impairment. This population experiences changes in brain plasticity and age-related cognitive decline that may make them more vulnerable to the effects of cannabis use.

Fifth, recent evidence suggests sex differences in neuropsychological deficits associated with cannabis use.[1,28] Hence, future work should help clarify mechanisms underlying these potential sex differences.

Sixth, genetic factors such as polymorphisms in the *COMT* (OMIM 116790) and *AKT1* (OMIM 164730) genes may also increase susceptibility to cannabis-related neuropsychological impairment.[29] Other examples include a recent study[30] that showed that THC caused acute impairment of working memory for *COMT* Val/Val carriers (but not Met carriers), as well as another study[31] of 3 population-based cohorts that showed that cannabis use was associated with decreased cortical thickness among male individuals at high (but not low) genetic risk for schizophrenia as indexed by a polygenic risk score. The possibility that individual differences among cannabis users may have significant effects and be predictive of the extent of adverse consequences suggests that recent approaches to leveraging genetic information to create polygenic risk scores might be useful toward advancing the study of cannabis use and neuropsychological function.

Does Cannabis Use Decrease Motivation?

As early as the late 19th century, the Indian Hemp Drugs Commission[32] reported that heavy cannabis use was associated with apathy, defined as reduced motivation for goal-directed behavior.[33] However, it was only after the marked increase in cannabis use of the 1960s that the amotivational effects of chronic cannabis use were linked to impairments in learning and sustained attention. The term *cannabis amotivational syndrome* was proposed by McGlothlin and West,[34] who characterized it as apathy and diminished ability to concentrate, follow routines, or successfully master new material. While there has always been some controversy around the need for defining such a distinct phenotype, there is evidence that long-term heavy cannabis use is associated with educational underachievement and impaired motivation, which have been proposed to be potential mediators of poorer functional outcomes.[35]

There is both preclinical and clinical evidence supporting the view that cannabis use is associated with an amotivational state. In rhesus monkeys, heavy chronic cannabis use or administration has been found to dampen motivation, as measured on progressive ratio and conditioned position responding operant tests.[36] There is preliminary laboratory evidence supporting an association between reduced motivation for reward-related behavior in cannabis users compared with control individuals.[37] Because these findings appear to be related to repeated doses of THC, it is likely that reduced motivation is one pathway to impaired learning, as THC can disrupt reward-based learning.[38] In support of this theory, cannabis users exhibit reduced striatal dopamine synthesis capacity,[39] with an inverse relationship to amotivation. Inasmuch as dopamine signaling sustains motivation,[40] impaired dopamine synthesis could underlie the amotivational state in cannabis users. Similarly, imaging investigations documented decreased reactivity to dopamine stimulation in cannabis users that was associated with negative emotionality and that would also contribute to reduce engagement in non–drug-related activities.[41]

Amotivation in chronic heavy users may also reflect the fact that cannabis itself has become a major motivator, so other activities (eg,

schoolwork) become demoted in the individual's reward hierarchy. Indeed, addiction to the drug occurs in about 9% of users[42] who appear more vulnerable than other users because of a multiplicity of variables, including age at onset, level of use, and environmental and genetic factors.

What remains to be seen is whether changes in the concentration of the active ingredients of cannabis could affect the risk of amotivation or addiction. The cannabis plant contains approximately 100 unique cannabinoid ingredients, with the most researched being THC and cannabidiol. Over the last 30 years, levels of THC in street cannabis have increased.[43] Of these 2 compounds, only THC determines the level of the subjective high. Alongside a blunted dopamine system,[41] chronic heavy use of cannabis is associated with changes in the endocannabinoid system, including reduced levels of anandamide (an endogenous ligand for the cannabinoid receptors) in human cerebrospinal fluid[44] and reduced levels of cannabinoid 1 receptors.[45] Indeed, a growing preclinical literature implicates cannabinoid 1 receptors and their endogenous ligands in the motivational effects of cannabis use.[46] Similar to the association of cannabis use with cognitive impairment, it is impossible to unambiguously establish whether cannabis use is a cause, consequence, or correlate of altered motivation. Further work is needed to distinguish whether the potential amotivational effects are related to cannabis use disorders rather than cannabis use per se.

Does Cannabis Use Increase the Risk for Psychosis?

One of the most persistent controversies vis-à-vis cannabis use pertains to its effect on the risk of psychiatric disorders, particularly psychotic disorders and full-blown schizophrenia. Longitudinal investigations show a consistent association between adolescent cannabis use and psychosis. Cannabis use is considered a preventable risk factor for psychosis.[47] The link between cannabis use and schizophrenia could stem from direct causality, gene-environment interactions, shared etiology, or self-medication for premorbid symptoms, although some researchers have suggested that only the first 3 hypotheses remain open questions.[48-50] The sporadic emergence of conflicting data should not be surprising given the nature of this particular biological problem. For example, the effects of cannabis exposure may be modest in the total population and contingent on the presence of multiple genetic and environmental variables. On the other hand, there remains a lingering and legitimate controversy over what proportion of psychosis risk can be attributed to cannabis use and the extent to which individuals without genetic predisposition can be precipitated into the illness.

Despite this ambiguity, there is strong physiological and epidemiological evidence supporting a mechanistic link between cannabis use and schizophrenia. Tetrahydrocannabinol (particularly at high doses) can cause acute, transient, dose-dependent psychosis (schizophrenia-like positive and negative symptoms).[51] In addition, prospective, longitudinal, epidemiological studies consistently report an association between cannabis use and schizophrenia in which cannabis use precedes psychosis[52] independent of alcohol consumption[53] and even after removing[52,54] or controlling for[55,56] those individuals who had used other drugs. Although the prodromal period before full-blown illness complicates determining whether or not cannabis use precedes symptoms or reflects an attempt to treat them, cannabis use preceded psychosis in these studies.[52,54,57] Moreover, persistent cannabis use after a first episode is associated with poorer prognosis[58] even after controlling for other substance use.[59]

Although cannabis use may have long been discontinued before the onset of psychosis, the age at which cannabis use begins appears to correlate with the age at onset of psychosis, suggesting a causal relationship to initiating psychosis that is independent of actual use.[49,60,61] The association between cannabis use and chronic psychosis (including a schizophrenia diagnosis) is stronger in those individuals who have had heavy or frequent cannabis use during adolescence,[53,54,60,62,63] earlier use,[52] or use of cannabis with high THC potency.[60,62] From these studies, ever use of cannabis is estimated to increase the risk of schizophrenia by approximately 2-fold, accounting for 8% to 14% of cases,[55] with frequent use or use of cannabis with high THC potency increasing the risk of schizophrenia 6-fold.[53] Consistent with this notion, the greater cannabinoid receptor type 1 availability that has been reported in some patients with schizophrenia,[64,65] and which correlates with negative symptoms,[66] may also contribute to an enhanced sensitivity to the psychotogenic effects of cannabis use. It is important to highlight in this context that most individuals who use cannabis do not develop schizophrenia. Therefore, while cannabis use is neither necessary nor sufficient for the development of schizophrenia, available evidence suggests that cannabis use may initiate the emergence of a lasting psychotic illness in some persons (most likely those individuals with a genetic vulnerability),[67] and this finding warrants serious consideration from the point of view of public health policy.

It is becoming increasingly clear that acute psychosis, schizophreniform disorder, and schizophrenia are the result of interactions among many different factors operating at various levels. For example, having a close family member with schizophrenia is the strongest known risk factor for schizophrenia, yet few investigations linking cannabis use and schizophrenia have controlled specifically for familial schizophrenia risk. The results of one study[68] suggested that cannabis use may lead to schizophrenia in individuals with a family history of the disease compared with those individuals without a family history. However, controlling for familial risk in one large epidemiological study[69] considerably attenuated but did not completely eliminate the association of cannabis use with schizophrenia, with odds ratios of 3.3 and 1.6 with 3-year and 7-year temporal delays, respectively.

Possible 3-way interactions among genotype, cannabis use, and psychosis have also been explored. The *DRD2* genotype (OMIM 126450) influenced the likelihood of a psychotic disorder in individuals who used cannabis.[70] Among occasional cannabis users and daily cannabis users, carriers of the *DRD2*, rs1076560, *T* allele had 3-fold and 5-fold higher likelihoods of a psychotic disorder, respectively.[70] The functional *COMT* Val-158 polymorphism has also been reported to moderate the effect of adolescent cannabis use on adult psychosis, such that carriers of this allele were more likely to develop schizophreniform disorder if they used cannabis than noncarriers of the allele.[67] In an experimental THC study,[71] *COMT* Val carriers had greater cognitive impairment after THC exposure and more psychotic symptoms than *COMT* Met/Met carriers. An *AKT1* genotype by cannabis use interaction has also been reported, with those individuals having C/C rs2494732 genotypes and also using cannabis having a 2-fold higher chance of experiencing a psychotic

disorder.[72] In another study,[73] those participants who were carriers of the *AKT1* C/C genotype with ever use of cannabis and daily use showed 2-fold and 7-fold increased likelihoods of a psychotic disorder, respectively, compared with users and daily users who were T/T carriers.

The results supporting the hypothesis that some gene variants influence the likelihood of developing schizophrenia contingent on certain environmental exposure (eg, cannabis use) reflect tentative findings among small numbers of individuals that require replication.[74] An alternative explanation is that individuals at genetic high risk for schizophrenia may be more likely to use cannabis through a shared genetic risk for schizophrenia and cannabis use disorder. Indeed, the recent report from a large genome-wide association study[75] of an association between schizophrenia risk alleles and cannabis use suggests that part of the association between schizophrenia and cannabis use may be because of a shared genetic etiology. However, the use of cannabis with high THC potency was strongly associated with later development of schizophrenia in one study,[63] while the recently reported polygenic risk score for schizophrenia[76] was unrelated to cannabis use or the potency of cannabis used.[77]

Finally, as in chronic or heavy cannabis users,[78] patients with schizophrenia also show reduced volumes in the amygdala and hippocampus.[79] This observation could help explain the worse clinical outcomes in individuals with schizophrenia who use cannabis because those morphological changes are likely to underlie or contribute to the cannabis-associated exacerbation of symptoms seen in schizophrenia.[80]

Conclusions

Decades of ill-informed and porous legal and illegal drug regulations have exacted a devastating public health toll from our society. It is clear that the cumulative effect of nicotine exposure and alcohol use on morbidity and mortality has been staggering, as has the disproportionate criminal justice influence of the "war on drugs" on minority and disadvantaged populations. Current efforts to normalize cannabis use are being driven largely by a combination of grassroots activism, pharmacological ingenuity, and private profiteering, with a worrisome disregard for scientific evidence, gaps in our knowledge, or the possibility of unintended consequences. Given the critical and wide-ranging role of the endocannabinoid system in the brain,[81-83] the increasing prevalence of cannabis use and use disorders over the last decade and the increased THC concentration in cannabis plants, there is a need to clarify which aspects of cannabis exposure (eg, age at initiation, quantity used, frequency of use, duration of use, and potency of cannabis used) confer the greatest risk for the development of cannabis use disorder or for other adverse consequences (ie, cognitive deficits, lack of motivation, or psychosis). In addition, there are many unanswered questions more directly linked to the soundness of hastily implemented policies. For example, will advertising be permitted? What patterns of use and associated toxic effects will emerge if and when "e-joints" become widespread or even the norm among adolescents? How will expanding the pool of pregnant cannabis users affect the developmental trajectories of exposed fetuses? Finally, what are the consequences of secondhand cannabis smoke?

If we stay the current course, we are likely to uncover effects that were rare in the past only because the use was not as widespread as that of legal drugs. Vulnerable populations such as children, adolescents, the elderly, or individuals with other disorders may experience novel toxic effects (as well as the potential benefits). The changing landscape of cannabis use (eg, strains with higher THC potency, new routes of administration ["vaping" and edibles], and novel drug combinations) and a culture of rapidly changing norms and perceptions raise the possibility that our current, limited knowledge may only apply to the ways in which the drug was used in the past.

The areas explored in this article, which reflect only a subset of the multiple effects of cannabis use on the brain and body, belie the ubiquity of the cannabinoid signaling system. Therefore, in addition to expanding our basic research efforts, we should try to learn as much and as rapidly as we can from the ongoing changes in local policies to minimize the harms and maximize the potential benefits.

ARTICLE INFORMATION

Submitted for Publication: October 9, 2015; final revision received December 8, 2015; accepted December 10, 2015.

Published Online: February 3, 2016. doi:10.1001/jamapsychiatry.2015.3278.

Author Affiliations: National Institute on Drug Abuse, National Institutes of Health, Bethesda, Maryland (Volkow, Baler); Child Development Center, University of California, Irvine (Swanson); Center for Addiction Medicine, Department of Psychiatry, Massachusetts General Hospital, Boston (Evins); Harvard Medical School, Boston, Massachusetts (Evins); Veterans Affairs Boston Healthcare System, Harvard Medical School, Brockton, Massachusetts (DeLisi); Department of Psychology, Arizona State University, Tempe (Meier); Center for Children and Families, Department of Psychology, Florida International University, Miami (Gonzalez); Division of Psychiatry, University College London, London, England (Bloomfield); Psychiatric Imaging Group, Medical Research Council Clinical Sciences Centre, Hammersmith Hospital, London, England (Bloomfield); Clinical Psychopharmacology Unit, Clinical Health Psychology, University College London, London, England (Curran).

Author Contributions: Dr Volkow had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.
Study concept and design: All authors.
Acquisition, analysis, or interpretation of data: Volkow, Swanson, Evins, DeLisi, Meier, Gonzalez, Bloomfield, Curran.
Drafting of the manuscript: All authors.
Critical revision of the manuscript for important intellectual content: All authors.
Statistical analysis: Swanson, Evins, DeLisi, Meier, Gonzalez, Bloomfield, Curran.
Obtained funding: Volkow, Swanson, Evins, DeLisi, Meier, Gonzalez, Bloomfield, Curran.
Administrative, technical, or material support: Volkow, Baler.

Conflict of Interest Disclosures: Dr Swanson reported receiving support from Alza, Richwood, Shire, Celgene, Novartis, Celltech, Gliatech, Cephalon, Watson, CIBA, Janssen, and McNeil; reported serving on advisory boards of Alza, Richwood, Shire, Celgene, Novartis, Celltech, UCB, Gliatech, Cephalon, McNeil, and Eli Lilly; reported serving on speakers bureaus of Alza, Shire, Novartis, Celltech, UCB, Cephalon, CIBA, Janssen, and McNeil; and reported being a consultant to Alza, Richwood, Shire, Celgene, Novartis, Celltech, UCB, Gliatech, Cephalon, Watson, CIBA, Jansen, McNeil, and Eli Lilly. Dr Evins reported serving as an advisor and paid grant reviewer for the Pfizer Global Research Awards for Nicotine Dependence (GRAND) Grants Program. No other disclosures were reported.

Funding/Support: This work was financed in part by support from the following: Forum Pharmaceuticals to support grant R01 DA030992 from the National Institute of Drug Abuse and Pfizer to support grant R01 DA021245 from the National Institute of Drug Abuse (Dr Evins); National Institutes of Health Intramural Research Program (National Institute on Alcohol Abuse and Alcoholism) using the infrastructure of the Brookhaven National Laboratory under contract

DE-AC02-98CH10886 (Dr Volkow); grant R01 DA021576 from the National Institute of Drug Abuse (Dr DeLisi); United Kingdom Medical Research Council, National Institute of Health Research, and British Medical Association (Dr Bloomfield); and a grant from the United Kingdom National Institute of Health Research Biomedical Research Council to King's College London and a United Kingdom Medical Research Council grant (Dr Curran).

Role of the Funder/Sponsor: The funding agencies did not participate in the design and conduct of the study; collection, management, analysis, and interpretation of the data; and preparation, review, or approval of the manuscript.

REFERENCES

1. Crane NA, Schuster RM, Fusar-Poli P, Gonzalez R. Effects of cannabis on neurocognitive functioning: recent advances, neurodevelopmental influences, and sex differences. *Neuropsychol Rev*. 2013;23(2):117-137.

2. Crean RD, Crane NA, Mason BJ. An evidence based review of acute and long-term effects of cannabis use on executive cognitive functions. *J Addict Med*. 2011;5(1):1-8.

3. Ranganathan M, D'Souza DC. The acute effects of cannabinoids on memory in humans: a review. *Psychopharmacology (Berl)*. 2006;188(4):425-444.

4. Grant I, Gonzalez R, Carey CL, Natarajan L, Wolfson T. Non-acute (residual) neurocognitive effects of cannabis use: a meta-analytic study. *J Int Neuropsychol Soc*. 2003;9(5):679-689.

5. Schreiner AM, Dunn ME. Residual effects of cannabis use on neurocognitive performance after prolonged abstinence: a meta-analysis. *Exp Clin Psychopharmacol*. 2012;20(5):420-429.

6. Solowij N, Pesa N. Cannabis and cognition: short and long term effects. In: Castle DMR, D'Souza DC, eds. *Marijuana and Madness*. 2nd ed. New York, NY: Cambridge University Press; 2012:91-102.

7. Lubman DI, Cheetham A, Yücel M. Cannabis and adolescent brain development. *Pharmacol Ther*. 2015;148:1-16.

8. O'Shea M, Singh ME, McGregor IS, Mallet PE. Chronic cannabinoid exposure produces lasting memory impairment and increased anxiety in adolescent but not adult rats. *J Psychopharmacol*. 2004;18(4):502-508.

9. Schneider M, Schömig E, Leweke FM. Acute and chronic cannabinoid treatment differentially affects recognition memory and social behavior in pubertal and adult rats. *Addict Biol*. 2008;13(3-4):345-357.

10. Fontes MA, Bolla KI, Cunha PJ, et al. Cannabis use before age 15 and subsequent executive functioning. *Br J Psychiatry*. 2011;198(6):442-447.

11. Gruber SA, Sagar KA, Dahlgren MK, Racine M, Lukas SE. Age of onset of marijuana use and executive function. *Psychol Addict Behav*. 2012;26(3):496-506.

12. Meier MH, Caspi A, Ambler A, et al. Persistent cannabis users show neuropsychological decline from childhood to midlife. *Proc Natl Acad Sci U S A*. 2012;109(40):E2657-E2664. doi:10.1073/pnas.1206820109.

13. Lorenzetti V, Solowij N, Fornito A, Lubman DI, Yucel M. The association between regular cannabis exposure and alterations of human brain morphology: an updated review of the literature. *Curr Pharm Des*. 2014;20(13):2138-2167.

14. Batalla A, Crippa JA, Busatto GF, et al. Neuroimaging studies of acute effects of THC and CBD in humans and animals: a systematic review. *Curr Pharm Des*. 2014;20(13):2168-2185.

15. Weiland BJ, Thayer RE, Depue BE, Sabbineni A, Bryan AD, Hutchison KE. Daily marijuana use is not associated with brain morphometric measures in adolescents or adults. *J Neurosci*. 2015;35(4):1505-1512.

16. Zalesky A, Solowij N, Yücel M, et al. Effect of long-term cannabis use on axonal fibre connectivity. *Brain*. 2012;135(pt 7):2245-2255.

17. Jager G, Block RI, Luijten M, Ramsey NF. Cannabis use and memory brain function in adolescent boys: a cross-sectional multicenter functional magnetic resonance imaging study. *J Am Acad Child Adolesc Psychiatry*. 2010;49(6):561-572, 572.e1-572.e3. doi:10.1016/j.jaac.2010.02.001.

18. Orr C, Morioka R, Behan B, et al. Altered resting-state connectivity in adolescent cannabis users. *Am J Drug Alcohol Abuse*. 2013;39(6):372-381.

19. Houck JM, Bryan AD, Feldstein Ewing SW. Functional connectivity and cannabis use in high-risk adolescents. *Am J Drug Alcohol Abuse*. 2013;39(6):414-423.

20. Jacobsen LK, Pugh KR, Constable RT, Westerveld M, Mencl WE. Functional correlates of verbal memory deficits emerging during nicotine withdrawal in abstinent adolescent cannabis users. *Biol Psychiatry*. 2007;61(1):31-40.

21. Morgan CJ, Schafer G, Freeman TP, Curran HV. Impact of cannabidiol on the acute memory and psychotomimetic effects of smoked cannabis: naturalistic study [published correction appears in *Br J Psychiatry*. 2010;197:416]. *Br J Psychiatry*. 2010;197(4):285-290.

22. Englund A, Morrison PD, Nottage J, et al. Cannabidiol inhibits THC-elicited paranoid symptoms and hippocampal-dependent memory impairment. *J Psychopharmacol*. 2013;27(1):19-27.

23. Fried PA, Watkinson B, Gray R. Neurocognitive consequences of marihuana: a comparison with pre-drug performance. *Neurotoxicol Teratol*. 2005;27(2):231-239.

24. Cheetham A, Allen NB, Whittle S, Simmons JG, Yücel M, Lubman DI. Orbitofrontal volumes in early adolescence predict initiation of cannabis use: a 4-year longitudinal and prospective study. *Biol Psychiatry*. 2012;71(8):684-692.

25. Pagliaccio D, Barch DM, Bogdan R, et al. Shared predisposition in the association between cannabis use and subcortical brain structure. *JAMA Psychiatry*. 2015;72(10):994-1001.

26. National Institutes of Health. Adolescent Brain Cognitive Development Study. http://addictionresearch.nih.gov/adolescent-brain-cognitive-development-study. Published 2015. Accessed December 17, 2015.

27. Batalla A, Bhattacharyya S, Yücel M, et al. Structural and functional imaging studies in chronic cannabis users: a systematic review of adolescent and adult findings. *PLoS One*. 2013;8(2):e55821. doi:10.1371/journal.pone.0055821.

28. Crane NA, Schuster RM, Mermelstein RJ, Gonzalez R. Neuropsychological sex differences associated with age of initiated use among young adult cannabis users. *J Clin Exp Neuropsychol*. 2015;37(4):389-401.

29. Radhakrishnan R, Wilkinson ST, D'Souza DC. Gone to pot: a review of the association between cannabis and psychosis. *Front Psychiatry*. 2014;5:54.

30. Tunbridge EM, Dunn G, Murray RM, et al. Genetic moderation of the effects of cannabis: catechol-O-methyltransferase (COMT) affects the impact of Δ^9-tetrahydrocannabinol (THC) on working memory performance but not on the occurrence of psychotic experiences. *J Psychopharmacol*. 2015;29(11):1146-1151.

31. French L, Gray C, Leonard G, et al. Early cannabis use, polygenic risk score for schizophrenia and brain maturation in adolescence. *JAMA Psychiatry*. 2015;72(10):1002-1011.

32. Kalant OJ. Report of the Indian Hemp Drugs Commission, 1893-94: a critical review. *Int J Addict*. 1972;7(1):77-96.

33. Marin RS. Apathy: a neuropsychiatric syndrome. *J Neuropsychiatry Clin Neurosci*. 1991;3(3):243-254.

34. McGlothlin WH, West LJ. The marihuana problem: an overview. *Am J Psychiatry*. 1968;125(3):126-134.

35. Silins E, Horwood LJ, Patton GC, et al; Cannabis Cohorts Research Consortium. Young adult sequelae of adolescent cannabis use: an integrative analysis. *Lancet Psychiatry*. 2014;1(4):286-293.

36. Paule MG, Allen RR, Bailey JR, et al. Chronic marijuana smoke exposure in the rhesus monkey, II: effects on progressive ratio and conditioned position responding. *J Pharmacol Exp Ther*. 1992;260(1):210-222.

37. Lane SD, Cherek DR, Pietras CJ, Steinberg JL. Performance of heavy marijuana-smoking adolescents on a laboratory measure of motivation. *Addict Behav*. 2005;30(4):815-828.

38. Lane SD, Cherek DR. Marijuana effects on sensitivity to reinforcement in humans. *Neuropsychopharmacology*. 2002;26(4):520-529.

39. Bloomfield MA, Morgan CJ, Egerton A, Kapur S, Curran HV, Howes OD. Dopaminergic function in cannabis users and its relationship to cannabis-induced psychotic symptoms. *Biol Psychiatry*. 2014;75(6):470-478.

40. Berridge KC, Robinson TE. What is the role of dopamine in reward: hedonic impact, reward learning, or incentive salience? *Brain Res Brain Res Rev*. 1998;28(3):309-369.

41. Volkow ND, Wang GJ, Telang F, et al. Decreased dopamine brain reactivity in marijuana abusers is associated with negative emotionality and addiction severity. *Proc Natl Acad Sci U S A*. 2014;111(30):E3149-E3156. doi:10.1073/pnas.1411228111.

42. Garner EL. Cannabinoids and addiction. In: Pertwee R, ed. *Handbook of Cannabis*. Oxford, England: Oxford University Press; 2014.

43. ElSohly MA. *Potency Monitoring Program Quarterly Report No. 123*. Oxford: National Center for Natural Products Research, University of Mississippi; 2014.

44. Morgan CJ, Page E, Schaefer C, et al. Cerebrospinal fluid anandamide levels, cannabis use and psychotic-like symptoms. *Br J Psychiatry*. 2013;202(5):381-382.

45. Hirvonen J, Goodwin RS, Li CT, et al. Reversible and regionally selective downregulation of brain

cannabinoid CB_1 receptors in chronic daily cannabis smokers. *Mol Psychiatry*. 2012;17(6):642-649.

46. Serrano A, Parsons LH. Endocannabinoid influence in drug reinforcement, dependence and addiction-related behaviors. *Pharmacol Ther*. 2011; 132(3):215-241.

47. Schizophrenia Commission. *The Abandoned Illness: A Report by the Schizophrenia Commission*. London, England: Rethink Mental Illness; November 2012.

48. Ferraro L, Russo M, O'Connor J, et al. Cannabis users have higher premorbid IQ than other patients with first onset psychosis. *Schizophr Res*. 2013;150 (1):129-135.

49. Large M, Sharma S, Compton MT, Slade T, Nielssen O. Cannabis use and earlier onset of psychosis: a systematic meta-analysis. *Arch Gen Psychiatry*. 2011;68(6):555-561.

50. Miettunen J, Törmänen S, Murray GK, et al. Association of cannabis use with prodromal symptoms of psychosis in adolescence. *Br J Psychiatry*. 2008;192(6):470-471.

51. D'Souza DC, Perry E, MacDougall L, et al. The psychotomimetic effects of intravenous delta-9-tetrahydrocannabinol in healthy individuals: implications for psychosis. *Neuropsychopharmacology*. 2004;29(8):1558-1572.

52. Arseneault L, Cannon M, Poulton R, Murray R, Caspi A, Moffitt TE. Cannabis use in adolescence and risk for adult psychosis: longitudinal prospective study. *BMJ*. 2002;325(7374):1212-1213.

53. Andréasson S, Allebeck P, Engström A, Rydberg U. Cannabis and schizophrenia: a longitudinal study of Swedish conscripts. *Lancet*. 1987;2(8574):1483-1486.

54. Zammit S, Allebeck P, Andreasson S, Lundberg I, Lewis G. Self reported cannabis use as a risk factor for schizophrenia in Swedish conscripts of 1969: historical cohort study. *BMJ*. 2002;325(7374):1199.

55. van Os J, Bak M, Hanssen M, Bijl RV, de Graaf R, Verdoux H. Cannabis use and psychosis: a longitudinal population-based study. *Am J Epidemiol*. 2002;156(4):319-327.

56. Fergusson DM, Horwood LJ, Swain-Campbell NR. Cannabis dependence and psychotic symptoms in young people. *Psychol Med*. 2003;33(1):15-21.

57. Weiser M, Knobler HY, Noy S, Kaplan Z. Clinical characteristics of adolescents later hospitalized for schizophrenia. *Am J Med Genet*. 2002;114(8):949-955.

58. Alvarez-Jimenez M, Priede A, Hetrick SE, et al. Risk factors for relapse following treatment for first episode psychosis: a systematic review and meta-analysis of longitudinal studies. *Schizophr Res*. 2012;139(1-3):116-128.

59. Foti DJ, Kotov R, Guey LT, Bromet EJ. Cannabis use and the course of schizophrenia: 10-year follow-up after first hospitalization. *Am J Psychiatry*. 2010;167(8):987-993.

60. Di Forti M, Sallis H, Allegri F, et al. Daily use, especially of high-potency cannabis, drives the earlier onset of psychosis in cannabis users. *Schizophr Bull*. 2014;40(6):1509-1517.

61. Galvez-Buccollini JA, Proal AC, Tomaselli V, et al. Association between age at onset of psychosis and age at onset of cannabis use in non-affective psychosis. *Schizophr Res*. 2012;139(1-3):157-160.

62. Di Forti M, Morgan C, Dazzan P, et al. High-potency cannabis and the risk of psychosis. *Br J Psychiatry*. 2009;195(6):488-491.

63. Di Forti M, Marconi A, Carra E, et al. Proportion of patients in south London with first-episode psychosis attributable to use of high potency cannabis: a case-control study. *Lancet Psychiatry*. 2015;2(3):233-238.

64. Volk DW, Eggan SM, Horti AG, Wong DF, Lewis DA. Reciprocal alterations in cortical cannabinoid receptor 1 binding relative to protein immunoreactivity and transcript levels in schizophrenia. *Schizophr Res*. 2014;159(1):124-129.

65. Wong DF, Kuwabara H, Horti AG, et al. Quantification of cerebral cannabinoid receptors subtype 1 (CB1) in healthy subjects and schizophrenia by the novel PET radioligand [^{11}C]OMAR. *Neuroimage*. 2010;52(4):1505-1513.

66. Wong DF, Kuwabara H, Horti AG, et al. Cannabinoid receptor subtype 1 (CB1) distribution correlates with neuropsychiatric ratings. In: Proceedings from the Society of Biological Psychiatry; May 20-22, 2010; New Orleans, Louisiana.

67. Caspi A, Moffitt TE, Cannon M, et al. Moderation of the effect of adolescent-onset cannabis use on adult psychosis by a functional polymorphism in the catechol-O-methyltransferase gene: longitudinal evidence of a gene × environment interaction. *Biol Psychiatry*. 2005;57 (10):1117-1127.

68. Proal AC, Fleming J, Galvez-Buccollini JA, Delisi LE. A controlled family study of cannabis users with and without psychosis. *Schizophr Res*. 2014;152(1): 283-288.

69. Giordano GN, Ohlsson H, Sundquist K, Sundquist J, Kendler KS. The association between cannabis abuse and subsequent schizophrenia: a Swedish national co-relative control study. *Psychol Med*. 2015;45(2):407-414.

70. Colizzi M, Iyegbe C, Powell J, et al. Interaction between functional genetic variation of *DRD2* and cannabis use on risk of psychosis. *Schizophr Bull*. 2015;41(5):1171-1182.

71. Henquet C, Rosa A, Krabbendam L, et al. An experimental study of *catechol-O-methyltransferase* Val^{158}Met moderation of |[Delta]|-9-tetrahydrocannabinol-induced effects on psychosis and cognition. *Neuropsychopharmacology*. 2006;31(12):2748-2757.

72. van Winkel R, van Beveren NJ, Simons C; Genetic Risk and Outcome of Psychosis (GROUP) Investigators. AKT1 moderation of cannabis-induced cognitive alterations in psychotic disorder. *Neuropsychopharmacology*. 2011;36(12): 2529-2537.

73. Di Forti M, Iyegbe C, Sallis H, et al. Confirmation that the *AKT1* (rs2494732) genotype influences the risk of psychosis in cannabis users. *Biol Psychiatry*. 2012;72(10):811-816.

74. Decoster J, van Os J, Myin-Germeys I, De Hert M, van Winkel R. Genetic variation underlying psychosis-inducing effects of cannabis: critical review and future directions. *Curr Pharm Des*. 2012; 18(32):5015-5023.

75. Power RA, Verweij KJ, Zuhair M, et al. Genetic predisposition to schizophrenia associated with increased use of cannabis. *Mol Psychiatry*. 2014;19 (11):1201-1204.

76. Schizophrenia Working Group of the Psychiatric Genomics Consortium. Biological insights from 108 schizophrenia-associated genetic loci. *Nature*. 2014;511(7510):421-427.

77. Di Forti M, Vassos E, Lynskey M, Craig M, Murray R. Data vs speculation concerning the greater risk of psychosis associated with the use of high potency cannabis [letter]. *Lancet Psychiatry*. 2015;2(5):382.

78. Yücel M, Solowij N, Respondek C, et al. Regional brain abnormalities associated with long-term heavy cannabis use. *Arch Gen Psychiatry*. 2008;65(6):694-701.

79. van Erp TG, Hibar DP, Rasmussen JM, et al. Subcortical brain volume abnormalities in 2028 individuals with schizophrenia and 2540 healthy controls via the ENIGMA consortium [published online August 18, 2015]. *Mol Psychiatry*.

80. D'Souza DC. Cannabinoids and psychosis. *Int Rev Neurobiol*. 2007;78:289-326.

81. Kano M, Ohno-Shosaku T, Hashimotodani Y, Uchigashima M, Watanabe M. Endocannabinoid-mediated control of synaptic transmission. *Physiol Rev*. 2009;89(1):309-380.

82. Morena M, Patel S, Bains JS, Hill MN. Neurobiological interactions between stress and the endocannabinoid system. *Neuropsychopharmacology*. 2016;41(1):80-102.

83. Woodhams SG, Sagar DR, Burston JJ, Chapman V. The role of the endocannabinoid system in pain. *Handb Exp Pharmacol*. 2015;227:119-143.

Unintentional Cannabis Intoxication in Toddlers

Isabelle Claudet, MD, MSc,[a] Sébastien Mouvier, MD,[b] Magali Labadie, MD,[c] Cécile Manin, MD,[d] Anne-Pascale Michard-Lenoir, MD,[e] Didier Eyer, MD,[f] Damien Dufour, MD,[g] for the Marie-Jeanne Study Group

abstract

BACKGROUND AND OBJECTIVES: In France, cannabis consumption is illegal. The health impact of its increasing use and higher tetrahydrocannabinol (THC) concentrations is still poorly documented, particularly that of unintentional pediatric intoxications. We sought to evaluate the French national trend of admissions for unintentional cannabis intoxication in children over an 11-year period (2004–2014).

METHODS: A retrospective, national, multicenter, observational study of a pediatric cohort. All children aged <6 years admitted to a tertiary-level pediatric emergency department (PED) for proven cannabis intoxication (compatible symptoms and positive toxicological screening results) during the reference period were included.

RESULTS: Twenty-four PEDs participated in our study; 235 children were included, and 71% of the patients were 18 months old or younger. Annual admissions increased by a factor of 13. Hashish resin was the main form ingested (72%). During the study period, the evolution was characterized by a national increase in intoxications, younger intoxicated children (1.28 ± 0.4 vs 1.7 ± 0.7 years, $P = .005$), and more comas ($n = 38$) ($P = .05$, odds ratio 3.5 [1.02–11.8]). Compared with other intoxications, other PED admissions, and the same age population, cannabis-related admissions were greater. There was a potential link between the increased incidence of comas and increased THC concentration in resin seized in France over the period.

CONCLUSIONS: Children are collateral victims of changing trends in cannabis use and a prevailing THC concentration. Intoxicated children are more frequent, are younger, and have intoxications that are more severe. This raises a real issue of public health.

FREE

[a]*Service d'Accueil des Urgences Pédiatriques, Hôpital des Enfants, Centre Hospitalier Universitaire de Toulouse and Inserm, UMR 1027, Université Paul Sabatier Toulouse III, Toulouse, France;* [b]*Urgences Enfants, Hôpital Nord, Assistance Publique Hôpitaux de Marseille, Marseille, France;* [c]*Centre Antipoison et de Toxicovigilance, Groupe Hospitalier Pellegrin, Centre Hospitalier Universitaire de Bordeaux, Bordeaux, France;* [d]*Service de Pédiatrie, Centre Hospitalier de Perpignan, Perpignan, France;* [e]*Urgences Pédiatriques, Hôpital Couple Enfant, Centre Hospitalier Universitaire de Grenoble Alpes, La Tronche, France;* [f]*Urgences Pédiatriques, Hôpitaux Universitaires de Strasbourg, Strasbourg, France; and* [g]*Urgences Pédiatriques, Hôpital Jacques Monod, Groupe Hospitalier du Havre, Le Havre, France*

Dr Claudet conceived the project and the study design, analyzed results, interpreted data, and drafted the initial manuscript; Dr Labadie performed all the data extraction and analysis from the national database of French poison control centers; Drs Mouvier, Manin, Michard-Lenoir, Eyer, and Dufour collected data and critically reviewed and revised the manuscript; all authors contributed to data collection and substantially participated in data analysis; 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.2017-0017

Accepted for publication Jun 26, 2017

WHAT'S KNOWN ON THIS SUBJECT: The outbreak of pediatric cannabis intoxication has been recently published in relation to decriminalization in several states in the United States. In France, consumption is illegal. Unintentional pediatric intoxications related to increasing use are poorly documented.

WHAT THIS STUDY ADDS: In this national, retrospective, multicenter study, we included 235 intoxications. During the 11-year period, the evolution of intoxications was significant for younger children, and an increase in severe presentations potentially correlated to the increase in cannabis resin potency.

To cite: Claudet I, Mouvier S, Labadie M, et al. Unintentional Cannabis Intoxication in Toddlers. *Pediatrics.* 2017; 140(3):e20170017

France, where cannabis is illegal, is the highest drug-consuming country in Europe.[1] Users are mainly young adults and teenagers aged 15 to 16 years old with rates of 22% and 39%, respectively. Among ninth graders, this rate was 24% among girls and 28% among boys in 2014.[2,3] Whereas the herbal cannabis market changes with increased French production, most cannabis resin is imported from Morocco via Spain by air or sea and moves through France toward the Netherlands and Northern Europe by road using "go fast or go slow" vehicles. The resin form has changed to smaller, olive-shaped pellets rather than traditional 250 g bars.[1] Another major change is increased Δ9-tetrahydrocannabinol (THC) concentrations in both marijuana and hashish (9.3% in 2004 and 20.7% in 2014 in France).[4] The health impact of these trends remains poorly documented, particularly that of the evolution of unintentional intoxication in young children.

The primary objective was to analyze the national evolution of pediatric admissions for unintentional cannabis intoxication in the main French pediatric emergency departments (PEDs) over an 11-year period (2004–2014). The secondary objectives were to detail clinical presentations and analyze the evolution of severe intoxications (coma, respiratory depression, and apnea) and the resulting social and legal measures.

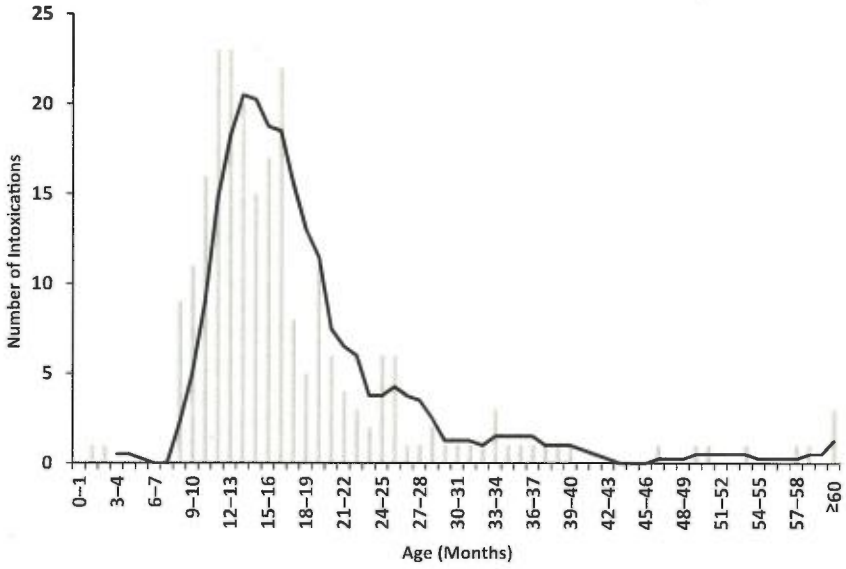


FIGURE 1
Pediatric cannabis intoxication distribution by age.

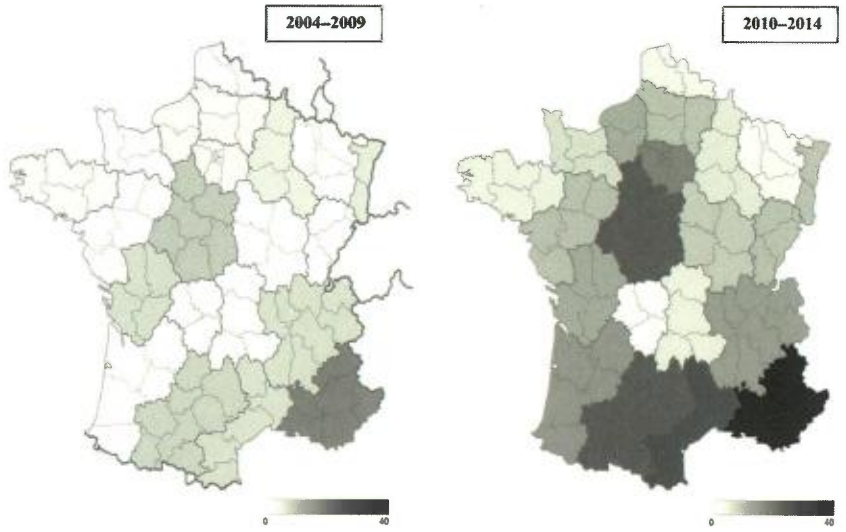


FIGURE 2
French geographical distribution of cannabis unintentional intoxication from 2004 to 2009 and 2010 to 2014 in children aged <6 years (number of cases).

METHODS

Study Design

This was a national, multicenter, retrospective, observational study of a pediatric cohort.

Setting and Study Participants

All children <6 years of age who were admitted with proven cannabis intoxication (compatible clinical symptoms and positive toxicological screening results) in a tertiary-level PED during the reference period were eligible. Compatible clinical symptoms that defined "intoxicated" children were any acute neurologic symptom(s) (eg, drowsiness, ataxia, hypo- or hypertonia, seizures, comatose status, altered consciousness, agitation, euphoria, and/or mydriasis) occurring in a previously healthy, afebrile toddler with no antecedents. Patients >6 years of age, asymptomatic patients (those who were exposed but not intoxicated), and those with suspected but unproven cannabis intoxications were not included. Since 2000, French hospital medical records have progressively switched from paper charts to electronic records. Two-thirds of French hospitals have electronic medical records. Laboratory results are also electronically linked to medical

TABLE 1 Comparison of Demographic Characteristics Between the 2010–2014 and 2004–2009 Periods

Characteristics	Total, *n* (%)	2010–2014, *n* (%)	2004–2009, *n* (%)	*P*	OR (95% CI)
Number of admissions	235	187	48	—	—
Male sex	127 (54)	101 (54)	26 (55)	.98	1.0 (0.6–1.9)
Seasonal distribution					
Summer (June to August)	55 (23)	44 (24)	11 (23)	.93	1.0 (0.5–2.2)
Spring (March to May)	29 (12)	18 (9)	11 (23)	.015	0.4 (0.2–0.8)
Autumn (September to November)	93 (40)	82 (44)	11 (23)	.009	2.6 (1.3–5.5)
Winter (December to February)	58 (25)	43 (23)	15 (29)	.24	0.7 (0.3–1.9)
Weekly distribution					
Weekend admission	61 (26)	48 (26)	13 (27)	.84	0.9 (0.5–1.9)
Mode of admission					
Family	165 (70)	128 (68)	37 (77)	—	—
Sanitary (ambulance, firefighters) and medicalized transport	44 (19)	39 (21)	5 (10)	.11	2.3 (0.8–6.1)
NS	26 (11)	20 (11)	6 (13)	.86	—
Time of admission					
8:00 AM–11:00 AM	28 (12)	24 (13)	4 (8)	.39	1.6 (0.5–4.9)
12:00 AM–5:00 PM	88 (37)	72 (39)	16 (34)	.51	1.3 (0.6–2.4)
6:00 PM–11:00 PM	103 (44)	79 (42)	24 (50)	.34	0.7 (0.4–1.4)
12:00 PM–7:00 AM	16 (7)	12 (6)	4 (8)	.67	0.7 (0.2–2.5)
Mean delay of admission, min (SD)	270 (190)	293 (209)	176 (99)	.08	—
Age, mo					
0–11	61 (26)	51 (27)	10 (21)	.36	1.4 (0.7–3.1)
12–23	136 (58)	109 (59)	27 (56)	.79	1.1 (0.6–2.1)
24–35	25 (11)	19 (10)	6 (13)	.55	0.7 (0.3–1.9)
≥36	13 (5)	8 (4)	5 (10)	.11	0.4 (0.1–1.2)
Mean age, y (SD) [range]	1.5 (0.6) [0.1–5.8]	1.4 (0.5) [0.1–5.3]	1.7 (0.7) [0.2–5.8]	.17	—
Location of intoxication					
Home	156 (66)	127 (68)	29 (60)	.33	1.4 (0.7–2.7)
Public area	28 (12)	23 (12)	5 (10)	.72	1.2 (0.4–3.4)
With friends	24 (10)	13 (7)	11 (33)	.002	0.3 (0.1–0.6)
Others[a]	7 (3)	7 (4)	0 (0)	—	—
NS	20 (9)	17 (9)	3 (7)	.53	1.5 (0.4–5.3)
Cannabis type					
Resin (hashish)	169 (72)	136 (73)	33 (69)	.82	1.1 (0.5–2.1)
Marijuana (herbal)	16 (7)	14 (7)	2 (4)	.54	1.9 (0.4–17.4)
NS	50 (21)	37 (20)	13 (27)	.27	0.7 (0.3–1.4)
Severity of intoxication					
PSS 1	170 (72)	130 (70)	40 (83)	.06	0.5 (0.2–1.0)
PSS 2	25 (11)	20 (11)	5 (10)	.96	1.0 (0.4–2.9)
PSS 3	40 (17)	37 (19)	3 (7)	.03	3.7 (1.1–11.8)
Parental consumption					
Yes	105 (45)	89 (48)	16 (33)	.08	1.8 (0.9–3.5)
No	41 (17)	32 (11)	9 (20)	—	—
NS	89 (38)	77 (41)	12 (25)	.04	2.1 (1.0–4.3)
Social measures					
No report	54 (23)	41 (22)	13 (27)	.45	0.7 (0.4–1.6)
Simple referral to CPS	162 (69)	132 (71)	30 (63)	.28	1.4 (0.7–2.8)
Report for special concern to CPS	39 (17)	31 (17)	8 (17)	.98	1.0 (0.4–2.3)
Foster care placement	5 (0)	4 (2)	1 (2)	—	—
Complaint to the police department	4 (0)	3 (2)	1 (2)	—	—
NS	10 (4)	9 (5)	1 (2)	—	—

NS, nonspecified. —, not applicable.
[a] Others = grandparent, uncle, aunt, or nanny.

files. For each hospitalized patient, the diagnostic code is electronically assigned through the medical information system program by using the *International Classification of Diseases, 10th Revision*. The medical files were selected by cross referencing the associated *International Classification of Diseases, 10th Revision* diagnostic codes (T407 and F120-F122) and positive cannabis screening results in urine and/or blood at the toxicology laboratories affiliated with each hospital.

The data collected per patient were as follows: demographic data (age, sex, weight, date and time of admission, and mode of transportation); clinical data (vital parameters on admission, Glasgow Coma Score, heart rate, blood pressure, respiration rate, and body temperature); neurologic symptoms (dizziness, coma, convulsions, agitation, and euphoria); respiratory symptoms (bradypnea and apnea); ophthalmologic symptoms (mydriasis and conjunctival hyperemia); cardiovascular symptoms (hypotension, hypertension, and tachycardia); intoxication-related data (time and mode of exposure, estimated ingested amount, place of intoxication, form of cannabis [resin, joint, edible products ("space cakes" or "space cookies," candies, and chocolate bars), or liquid (e-cigarettes)]); data related to examinations (blood tests, lumbar puncture, head computed tomography scans, electrocardiograms, EEGs, toxicological tests [blood, urine, and hair]); disposition (home, general pediatric ward, intensive care or resuscitation unit [mechanical ventilation required]); and a notion of parental consumption and evolution (date and time of discharge from the emergency unit, total hospitalization duration, social measures [Child Protective Services (CPS), alert information, reporting to the judge of juvenile or family

TABLE 2 Clinical Manifestations of Cannabis-Intoxicated Patients Aged <6 Years Admitted Between 2004 and 2014 in French PEDs and Compared With Published Series (Percentage in Columns)

	Present Study			*P*[a]	Spadari et al[6]	Onders et al[7]	Cao et al[8]
Type of unit, location	PEDs, France				PCC, France	PCC, United States	PCC, United States
Study design	Retrospective, multicenter				Retrospective, single center	Retrospective, multicenter	Retrospective, multicenter
Years	2004–2009	2010–2014	2004–2014	—	1993–2008	2000–2013	2013–2015
Patients,[b] *n*	46	183	229	—	93	1969[c]	92
Symptoms, % (*n*)							
Neurologic	80.4 (37)	87.4 (160)	86.0 (197)	.22	57.0 (53)	45.5	85.8 (79)
Drowsiness	63.0 (29)	60.1 (110)	60.7 (139)	.72	48.4 (41)	29.5	66.3 (61)
Hypotonia	34.8 (16)	35.5 (65)	35.4 (81)	.93	10.7 (10)	0.7	—
Coma	4.35 (2)	16.9 (31)	14.4 (33)	.03	<1 (1)	0.9	—
Agitation	6.52 (3)	10.9 (20)	10.0 (23)	.58	8.6 (8)	3.3	5.4 (5)
Ataxia	17.4 (8)	7.10 (13)	9.17 (21)	.04	3.2 (3)	5.4	14.1 (13)
Convulsions	6.52 (3)	5.46 (10)	5.24 (12)	.77	2.2 (2)	0.5	—
Euphoria	6.52 (3)	4.37 (8)	4.80 (11)	.46	3.2 (3)	NS	NS
Cardiovascular	30.4 (14)	29.5 (54)	29.7 (68)	.90	6.5 (6)	4.1	—
Hypertension	17.4 (8)	9.28 (17)	10.9 (25)	.12	—	0.3	—
Tachycardia	6.52 (3)	14.2 (26)	13.5 (31)	.22	5.4 (5)	3.1	9.8 (9)
Hypotension	2.17 (1)	1.09 (2)	1.31 (3)	.49	<1 (1)	0.3	—
Ophthalmologic	45.6 (21)	52.4 (98)	51.1 (117)	.34	10.7 (10)	5.9	—
Mydriasis	41.3 (19)	46.9 (88)	45.8 (105)	.41	8.6 (8)	3.4	9.8 (9)
Conjunctival hyperemia	2.17 (1)	12.0 (22)	10.0 (23)	.05	2.2 (2)	1.2	8.7 (8)
Respiratory	4.35 (2)	10.4 (19)	9.17 (21)	.26	5.4 (5)	1.2	—
Hypoventilation	6.52 (3)	6.01 (11)	6.11 (14)	.89	5.4 (5)	—	—
Apnea	0.00 (0)	3.27 (6)	2.62 (6)	.60	—	0.7	3.3 (3)
Assisted ventilation	0.00 (0)	4.37 (8)	3.49 (8)	.36	—	NS	2.2 (2)
Temperature							
Hyperthermia (≥38.5°C)	4.34 (2)	2.73 (5)	3.06 (7)	.57	<1 (1)	0.3	—
Hypothermia (<36°C)	2.17 (1)	2.73 (5)	2.62 (6)	.83	<1 (1)	—	—
Disposition					—	—	—
Hospitalization, % (*n*)	86.9 (40)	88.5 (162)	88.2 (202)	.77			
ICU, % (*n*)	4.34 (2)	14.7 (25)	12.1 (27)	.08			

NS, nonspecified. —, not applicable.

[a] Compare years 2010–2014 and 2004–2009.

[b] Exclusion of patients with cointoxications.

[c] Percentages have been calculated out of the number of exposures (symptomatic and asymptomatic patients) and not out of the number of symptomatic patients (intoxicated).

court, and foster care]). Each center sent its confidential database to the study coordinator. The severity criteria were as follows: coma status (unarousable or unresponsive), seizures, respiratory failure (apneas and/or respiratory rate <10th percentile for age and/or tracheal intubation), hypotension (systolic blood pressure <fifth percentile for age), hypertension (systolic blood pressure >95th percentile for age), bradycardia (pulse rate <80 beats per minute [age ≤1 year]), pulse rate <60 beats per minute [1–6 years]), and a Poisoning Severity Score (PSS) value of 3.[5] To depict the evolution of unintentional pediatric cannabis intoxication, our data were compared with French poison control centers (PCCs) data concerning calls for cannabis exposure or intoxications (in symptomatic patients) and calls for other intoxications in the same age group.

Statistical Analysis

For statistical analysis, data were entered in Microsoft Excel tables (Microsoft Corporation, Redmond, WA). Analysis was performed with StatView 5.1 (SAS Institute Inc, Cary, NC) and EpiInfo 6.04fr (VF, ENSP-Epiconcept, Paris, France). In the descriptive analysis, data are presented as a mean ± SD, a median with extreme values, or with 95% confidence intervals (CIs) when appropriate unless otherwise indicated. To compare qualitative variables, a χ^2 test (Cochran-Mantel-Haenszel) was used, and a 2-tailed Fisher's exact test was used if the expected value was <5. For quantitative independent variables, a paired Student's *t* test was applied. A nonparametric Kruskal-Wallis test was performed in cases of non-normal distribution. Statistical significance was considered at $P < .05$.

Ethical and Regulatory Considerations

The data recorded during this research were subject to electronic processing at the Toulouse University Hospital PED in accordance with law

TABLE 3 Comparison of Comatose and Noncomatose Intoxicated Children (Percentage in Columns)

	Comatose[a] *n* (%), (*n* = 32)	Noncomatose, *n* (%), (*n* = 197)	*P*	OR (95% CI)
Mean age, y	1.5 ± 0.4	1.5 ± 0.6	.24	—
Age group, mo				
0–5	0 (0)	2 (1)	.99	1.02 (0.05–21.6)
6–11	7 (18)	52 (26)	.59	0.78 (0.32–1.91)
12–17	12 (37)	89 (45)	.42	0.73 (0.34–1.57)
18–23	8 (25)	21 (11)	.03	2.79 (1.11–7.00)
≥24	5 (16)	33 (17)	.87	0.92 (0.33–2.56)
Autumn admission	14 (44)	93 (47)	.72	0.87 (0.41–1.35)
Weekend admission	7 (22)	61 (26)	.30	0.62 (0.26–1.52)
Nonreferred by a physician	20 (63)	141 (82)	.30	0.66 (0.30–1.44)
Time of admission				
8:00 AM–11:00 AM	6 (19)	21 (11)	.19	1.93 (0.71–5.23)
12:00 AM–5:00 PM	8 (25)	79 (40)	.11	0.49 (0.21–1.16)
6:00 PM–11:00 PM	14 (44)	85 (43)	.95	1.02 (0.48–2.17)
12:00 PM–7:00 AM	4 (11)	12 (6)	.25	2.19 (0.48–7.91)
Tachycardia	5 (16)	24 (12)	.57	1.33 (0.37–3.99)
Hypertension	5 (16)	84 (43)	.004	0.27 (0.10–0.67)
Hypotension	7 (22)	14 (7)	.01	3.66 (1.35–9.93)
Hypoventilation	22 (69)	87 (44)	.01	2.78 (1.25–6.18)
Mydriasis	24 (75)	82 (42)	.001	4.20 (1.80–9.83)
High glycemia	3 (9)	8 (6)	.19	2.43 (0.39–10.9)
Hyponatremia	3 (9)	3 (12)	.04	6.59 (1.28–34.7)

—, not applicable.

[a] Cointoxications with molecules of neurologic effects are excluded (*n* = 6).

number 78-17 of January 6, 1978, regarding information technology, files, and liberties amended by law 2004-801 of August 6, 2004. The research protocol (number 15.1019a) received a favorable opinion of the National French Institutional Board (Advisory Committee on Health Research Information Processing).

RESULTS

Descriptive Analysis

Twenty-four PEDs (80% of national PEDs) in 20 French districts and 21 regions took part in the study. During the study period, 235 children matching the inclusion criteria were admitted. Seventy-one percent were aged 18 months old or younger (Fig 1). Figure 2 illustrates the national geographical distribution of these admissions from 2004 to 2009 and 2010 to 2014. The main demographic characteristics are summarized in Table 1 and compared between the 2 periods. Annual admissions increased by a factor of 13 over 11 years (+133%). Between 2004 and 2014, the number of severe cases increased by a factor of 20 and by a factor of 4 between 2013 and 2014. The estimated time of ingestion had a bimodal distribution with 2 peaks (10:00 AM–1:00 PM and 06:00 PM–10:00 PM). The average delay between ingestion and admission was 4 hours 24 minutes ± 3 hours 6 minutes. The main place of intoxication was the parental home (72%). Ingestion was the main route of intoxication (75%). Resin sticks, balls, and cones were the principal form ingested (72%), and the most frequent amount (80%) was 1 stick (average weight of 2–3 g) (data came from the French Office for Drugs and Drug Addiction) or 1 ball (average weight of 2–4 g). The clinical signs at admission are shown in Tables 2 and 3 and were predominantly neurologic symptoms (86%). Eighty-three (35%) children had at least 1 severity criteria. Fifty-three percent of all children with comas were admitted during 2014 (Fig 3). Fourteen patients were diagnosed with respiratory failure, and 8 required assisted ventilation for 24 hours or less. Basic metabolic panel blood tests that were performed on 178 patients (76%) revealed abnormalities (*n* = 40). These included high blood sugar levels (*n* = 14), hyponatremia (≤130 mmol/L) (*n* = 8), metabolic acidosis (*n* = 5), and functional kidney failure (*n* = 5). Additional procedures included the following: electrocardiograms (*n* = 63), head computed tomography scans (*n* = 39), abdominal ultrasounds (*n* = 39), lumbar puncture (*n* = 24), and EEGs (*n* = 24). In addition to cannabis detection, blood and/or urine toxicological screenings (for benzodiazepines, barbiturates, opiates, amphetamines, methamphetamine, cocaine, buprenorphine, norbuprenorphine, methadone, codeine, lysergic acid diethylamide, ethanol, tricyclic antidepressants, paracetamol, and tramadol) were performed in 205 cases. Eight other molecules were isolated in 8 children (4%) (Table 4). None of these patients required assisted ventilation. Paracetamol was allegedly being given to treat hyperthermia (*n* = 2). Benzodiazepines were detected in children who had received diazepam to stop seizures. Most of the children were hospitalized (88%), of whom 27 were in a resuscitation unit or ICU. Parental cannabis consumption was indicated in 146 cases (62%), and 72% declared to be regular users. Social or legal measures included a referral to CPS for 162 cases, a written report for special concern for 39 children, 5 children were placed in foster care by court order, and 4 families were subject to a complaint filed with a police department.

Comparative Analysis

Table 2 shows the comparison of clinical manifestations between the 2004–2009 and 2010–2014 periods. The most recent period was marked by the number of comas (excluding patients with cointoxications) (16.9% vs 4.4%, *P* = .03, odds ratio 4.9,

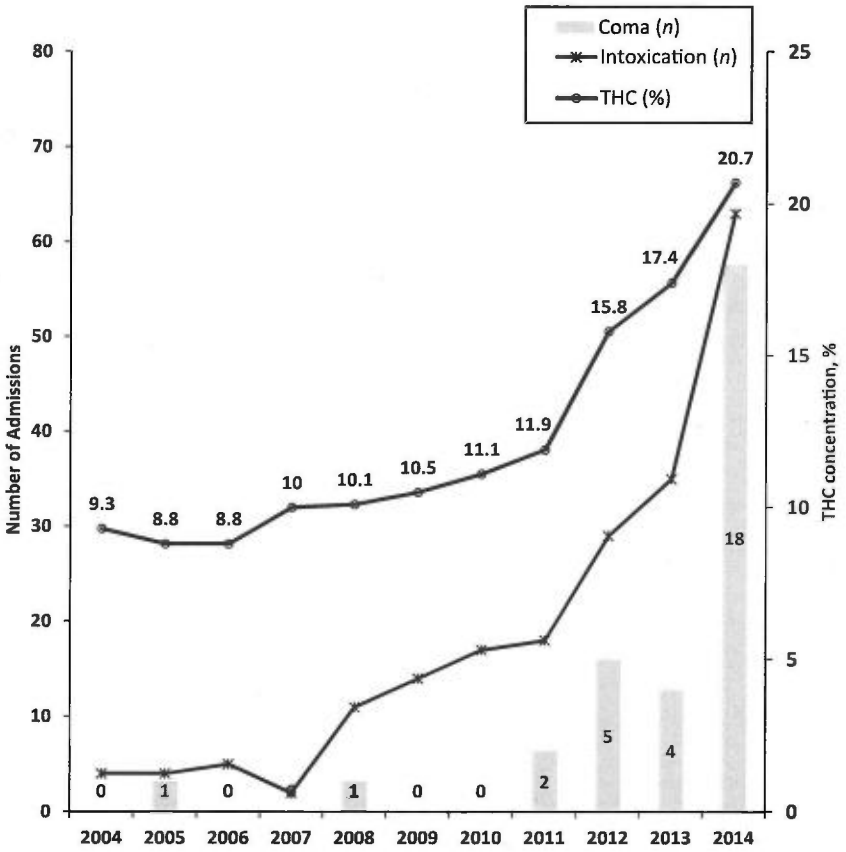


FIGURE 3

Distribution of pediatric cannabis intoxications and comatose presentations and THC concentration in hashish resin (results obtained from the analysis of products seized by French customs) during the study period (2004–2014).

95% CI 1.03–19.5). The comparison of PSS distribution (excluding patients with cointoxications) indicated more severe presentations (PSS 3) (18.5% vs 4.3%, OR 5.0, 95% CI 1.2–21.7, $P = .02$). When 2004 was compared with 2014, the average age of intoxicated patients revealed younger children ($P = .005$) (Table 1). The increase in intoxications and comas was compared with the concentration of THC in resin seized by French customs over the same period (Fig 3). Data were compared with cannabis-related calls and other toxic exposure-related calls (in symptomatic and nonsymptomatic patients) received by French PCCs during the same period. Patients included in this study represented 84% of national cannabis-related calls for symptomatic children.

Between 2004 and 2014, the rate for cannabis exposures in children aged <6 years progressed from 5.4 to 15.4 per 10 000 toxic exposures. The number of cannabis-related calls to French PCCs increased by 312%, 8.3% for noncannabis exposures and 3.3% for the pediatric population younger than 6 years old between 2004 and 2014 in the same geographical areas (data came from the French National Institute of Statistics and Economic Studies). Compared with the French population of children <6 years old in 2004 and 2014, the overall national rate per capita for cannabis-related calls progressed from 0.7 to 3.6 per 100 000. Compared with PED admissions for children aged <6 years between 2004 and 2014, cannabis-related PED visits increased from 1.7 to 16.1 per 100 000 admissions per year.

DISCUSSION

The evolution of unintentional pediatric cannabis intoxications is remarkable because of increased admissions throughout the country and an increase in severe presentations (Fig 3). Between 2004 and 2014, the evolution of PED visits for cannabis intoxication in toddlers increased 133%, and cannabis exposure-related calls to French PCCs increased 312%. Calls for other toxic exposures increased by only 45%. The phenomenon was not related to an equivalent increase in the French pediatric population for the same age group. Between 2000 and 2013, the evolution of similar calls to American PCCs showed a variation of 147% for pediatric exposure to cannabis.[7] In France, Spadari et al[6] of the Marseille PCC raised an initial alert in 2009 when they reported 93 calls for pediatric intoxications. They suspected a link between higher THC concentrations in cannabis products and more severe cases. Since this warning, 1 French series of 8 pediatric intoxications was reported in 2015.[9] Contrary to other European countries, hashish (resin) is the most popular cannabis form in France. Increased THC concentration in resin has been demonstrated and is related to a change in production. Cannabis hybrids that allow higher resin yields and THC content[10,11] have replaced the traditional Moroccan plants. In France, Dujourdy and Besacier recently published that almost three-quarters of records corresponded to a mean THC content >20% per gram (cannabis potency).[12] European data on cannabis potency are based on forensic analysis of seized materials. This is not necessarily representative of the market, especially in countries with significant domestic cultivation (eg, the Netherlands).[13] Detailed data on cannabis product potency have been studied in the Netherlands,

TABLE 4 Characteristics of Pediatric Patients With Cointoxications

Patients	1	2	3	4
Year	2005	2007	2010	2011
Age, mo	10	19	13	22
Symptoms	Hypotension, tachycardia, agitation, seizures, and altered consciousness	Tachycardia, comatose, apneas, and hypoventilation	Hypertension, comatose, and hypothermia	Tachycardia and ataxia
Mydriasis	No	No	Yes	Yes
GCS	10	6	6	14
Cointoxicants	Cocaine	Buprenorphine	Cocaine and tramadol	Levorphanol
LOS, d	7	1	3	NS
PICU	No	No	Yes	Yes
Social measures	Foster care placement	Simple CPS report	Special concern CPS report	None
Patients	5	6	7	8
Year	2013	2013	2014	2014
Age, mo	13	9	17	14
Symptoms	Tachycardia, hypothermia, hyperventilation, hypertonia, and hyponatremia	Tachycardia, hypotonia, and altered consciousness	Comatose, nystagmus, and hyponatremia	Tachycardia, hypoventilation, altered consciousness, and hyperthermia
Mydriasis	Yes	No	Yes	No
GCS	7	13	6	12
Cointoxicants	Benzodiazepines	Paracetamol	Benzodiazepines	Paracetamol
LOS, d	2	2	2	1
PICU	Yes	No	Yes	No
Social measures	Simple CPS report	Simple CPS report	Simple CPS report	Special concern CPS report

GCS, Glasgow Coma Scale; LOS, length of stay; NS, nonspecified.

the United Kingdom, France, the United States,[14] and Australia.[15] In the Netherlands, the THC content of resin is higher than herbal products of the same origin (local or imported), and Dutch products are more potent than imported ones (local resin 29.6% vs 14.3%).[13,16] In the United Kingdom, cannabis seized by law enforcement showed no change in the mean potency of resin (5.9%) or imported herbs (8.5%) in 2008.[17] In the United States, ElSohly et al,[14] focusing on seized products, published a mean cannabis potency of 12%. In Australia, Swift et al[15] found the same evolution toward a higher potency of herbal cannabis (a mean THC content of 14.9%). Cannabis decriminalization also seems to contribute to the progression of moderate to severe pediatric intoxications. In the United States, these clinical forms are significantly more represented in states where cannabis has been decriminalized.[18–21] In these states, the ingestion of food products containing cannabis is of concern.[22] The risk of exposure is high because of attractive packaging and naming that is phonetically similar to the original candy (eg, "Beef-Kat" or "Oeo").[10,22–24] In France, the ingestion of resin sticks or balls is the main source of intoxication.[6,8,9,25–29] Intoxication in infants through passive inhalation has also been described.[30] The main compounds in cannabis have a plasma peak between 1 hour for inhalation and 3 to 4 hours for ingestion. The effects last between 6 and 24 hours.[30] More prolonged neurologic effects have been published.[31] The comparison of the evolution of clinical manifestations of pediatric intoxications presented by Spadari et al[6] or Cao et al[8] to the current study indicates a higher proportion of neurologic and cardiovascular symptoms in our cohort (Table 2). We believe this difference could be related to an elevated resin potency. The occurrence of seizures was described by several authors.[6–8,25] The proconvulsive effect of cannabis is not unanimous. Some authors advocate the opposite effect because of the physiopathology of cannabinoids and the capacity to reduce the release of neurotransmitters, such as γ-aminobutyric acid or glutamate, and therefore neuronal excitability.[31,32] Seizures would be related to possible adulterants of the resin (eg, anticholinergic substances, cocaine, or methamphetamine) or a concomitant ingestion of another toxin instead.[33] The adulteration of cannabis resin was previously alleged. Moroccan hashish is cut mainly with a range of inert or active substances (eg, soil, henna, paraffin or bee wax, glue, licorice, or coffee).[34] There is little data on adulterants in cannabis resin, and the existing data are controversial. The presence of adulterants in cannabis resin could not been confirmed by studies conducted in France by the French Office for Drugs and Drug Addiction (2007) or the French Reitox focal point.[34] Therefore, positive results for cannabis and other drugs or molecules through a blood and/or urine screening are more likely because of separate poisonings. Because other drugs or toxic molecules may not be detected by classic enzyme immunoassays, more sophisticated techniques (such as gas chromatography and mass spectrometry) should be requested for their isolation, especially when clinical presentation is unusual or severe. The existence of mydriasis associated with other neurologic signs is a decisive element suggesting cannabis intoxication in children, but

its presence is inconsistent (Table 2). This inconsistency explains the diagnostic uncertainty in cases of coma and the use of additional tests (eg, head computed tomography scans, lumbar puncture, EEGs, and metabolic tests).[35] Cardiovascular symptoms are the result of the stimulation of type 1 cannabinoid receptors located in the heart. This stimulation generates an orthostatic and parasympathetic imbalance and the activation of the sympathetic system and potential blockage of the parasympathetic system.[36–38] These transitory manifestations, which are dominated by sinus tachycardia, do not usually require any specific therapy.[38,39] Adulterants should also be considered in the presence of severe cardiovascular manifestations (eg, myocardial infarction, coronary syndrome, and rhythm disorder). Hyponatremia may be explained by the direct effect of THC on the hypothalamic-pituitary axis (the release of vasopressin)[23] or the effects of an adulterant, such as methamphetamine.[40] In our cohort, 6 of 8 patients with hyponatremia were screened. Results were negative for methamphetamine.

The increase in severe pediatric patients admitted to a pediatric intensive care or resuscitation unit was identified in France by Le Garrec et al.[35] Because of the current prevalence of cannabis intoxication in young children, this diagnosis should be considered when an afebrile comatose child is admitted to a French emergency unit.[29,35] Given the increased frequency, it could also be assumed that physicians investigated cannabis intoxication more often, and this may have contributed to the increase in prevalence in the last 2 years.

No pediatric deaths because of cannabis intoxication have been reported. The systematic postmortem toxicological detection in a pediatric cohort of 730 children <19 years of age showed that 38% tested positive for toxic drugs or medications, but none of them were for cannabis.[41]

The variation in social measures accounts for the difficulty (in legal terms) of such cases in which the intoxicated person is not the user of the illicit drug but is vulnerable and subjected to the environment and parental or caregiver supervision.[42]

Because of the retrospective character of the study, some data available were insufficient (eg, parental cannabis consumption). Some children could have been admitted to non-PEDs, but usually (because of the alarming clinical presentation), they are transferred to the nearest regional PED. Extensive toxicological screening was not performed for all children. Cointoxications could have been underestimated for 30 patients. Cointoxication was detected in 4% (n = 8) of the screened patients (n = 205), making the risk of underestimation low for the unscreened patients. Most molecules known to produce false-positives for THC in urinalysis were not taken by our pediatric population (eg, dronabinol, efavirenz, naproxen, pantoprazole, and tolmetin). Concerning ibuprofen, a false-positive result for cannabinoids in urine tests has been shown only in 2 of 24 adult patients with chronic treatment.[43] Niflumic acid can cause false-positive urine test results in some commercial immunoassays for cannabinoids,[44] but it is not recommended in France for fever management. The risk of false-positive urine detection because of niflumic acid use was therefore limited in nonscreened patients.

CONCLUSIONS

In France, the increase of cannabis-related PED admissions seems obviously linked to changing consumption trends and a higher potency of the predominant form on the market (hashish). In countries where marijuana has been decriminalized, this increase is related to greater availability and the growing lucrative market of edible products containing marijuana. In countries where cannabis potency has remained low, this pediatric health issue has not been reported. In the Netherlands, cannabis has been culturally smoked in coffee shops for some time. This could explain the absence of published pediatric intoxication. The most recent trends (2015–2016) provided by French PCCs confirm our results, showing an increase in the phenomenon and raising a real public health issue. Unintentional intoxication should be tightly monitored, and it should be mandatory to report such cases. Our data demonstrate incomplete reporting to CPS, especially when clinical presentation is not severe. Intervention by social services must also be mandatory and homogeneous across the country.

ACKNOWLEDGMENTS

We thank the following members of the Marie-Jeanne Study Group for sharing and collecting data: Nicolas Franchitto, MD, PhD; Camille Bréhin MD, MSc (Centre Antipoison et Toxicovigilance, Urgences Pédiatriques, CHU Toulouse); Philippe Minodier, MD, PhD (Urgences pédiatriques, Hopital Nord, AP-HM, CHU Marseille); Luigi Titomanlio, MD, PhD; Simon Rivière, MD (Urgences Pédiatriques, Robert-Debré, Paris); Gaël Guyon, MD (Urgences Pédiatriques, CHU Montpellier); Marion Favier, MD; Olivier Richer, MD; Magali Labadie (Urgences Pédiatriques et Centre Antipoison, CHU Bordeaux); Christèle Gras-Le Guen, MD, PhD; Bénédicte Vrignaud, MD (Urgences Pédiatriques, CHU Nantes); Delphine Minette-Brunel, MD (Urgences Pédiatriques, CHU Reims); Marie Bournez, MD; Louise Hautin, MD

(Urgences Pédiatriques, CHU Dijon); Gérard Chéron, MD, PhD; Anne-Laure Tarbé de Saint Hardouin, MD (Urgences Pédiatriques, Necker-Enfants Malades, Paris); Tiphaine Hervé (Urgences Pédiatriques, CHU Rennes); Hervé Haas, MD (Urgences Pédiatriques, CHU Nice); Alexandra David, MD (Urgences Pédiatriques, CH Pau); Olivier Mory, MD; Aymeric Cantais, MD (Urgences Pédiatriques, CHU Saint-Etienne); François Dubos, MD, PhD (Urgences Pédiatriques, CHU Lille); Christine Laguille, MD (Urgences Pédiatriques, CHU Limoges); Anne Borsa-Dorion, MD; Maud André, MD (Urgences Pédiatriques, CHU Nancy); and Emmanuel Cixous, MD (Urgences Pédiatriques, CH Roubaix). We thank Jacques Manel, MD (Centre Antipoison et Toxicovigilance, CHU Nancy) for giving the authorization to extract data from French PCCs to depict the evolution of cannabis intoxication as accurately as possible. We also thank Mrs Vanessa Houzé-Cerfon for her help in the management of mandatory declarations for ethical and regulatory considerations. We gratefully acknowledge Mrs Claire Walker for her help with translating the article.

ABBREVIATIONS

CI: confidence interval
CPS: Child Protective Services
PCC: poison control center
PED: pediatric emergency department
PSS: Poisoning Severity Score
THC: tetrahydrocannabinol

Address correspondence to Isabelle Claudet, MD, MSc, Urgences Pédiatriques, Hôpital des Enfants, 330 Avenue de Grande-Bretagne, TSA 70034, 31059 Toulouse Cedex 9, France. E-mail: claudet.i@chu-toulouse.fr

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.

REFERENCES

1. French Monitoring Center for Drugs and Addiction (OFDT). European Drugs Report [in French]. Available at: www.ofdt.fr/BDD/publications/docs/OEDT2015EDR.pdf. Accessed June 20, 2016
2. Spilka S, Ehlinger V, Le Nézet O, et al; French Monitoring Center for Drugs and Addiction. Alcohol, tobacco and cannabis in 2014, during "high school years" [in French]. Available at: www.ofdt.fr/BDD/publications/docs/eftxssvc.pdf. Accessed June 20, 2016
3. Cadet-Taïrou A, Gandilhon M, Martinez M, Nefau T; French Monitoring Centre for Drugs and Addiction (OFDT). Illicit substances: recent trends (2013–2014) [in French]. 2014. Available at: www.ofdt.fr/BDD/publications/docs/eftxacuc.pdf. Accessed June 20, 2016
4. French Monitoring Centre for Drugs and Addiction (OFDT). Drugs, key figures – 6th edition [in French]. 2015:8. Available at: www.ofdt.fr/BDD/publications/docs/dcc2015.pdf. Accessed June 20, 2016
5. Persson HE, Sjöberg GK, Haines JA, Pronczuk de Garbino J. Poisoning severity score. Grading of acute poisoning. *J Toxicol Clin Toxicol*. 1998;36(3):205–213
6. Spadari M, Glaizal M, Tichadou L, et al. Accidental cannabis poisoning in children: experience of the Marseille poison center [in French]. *Presse Med*. 2009;38(11):1563–1567
7. Onders B, Casavant MJ, Spiller HA, Chounthirath T, Smith GA. Marijuana exposure among children younger than six years in the United States. *Clin Pediatr (Phila)*. 2016;55(5):428–436
8. Cao D, Srisuma S, Bronstein AC, Hoyte CO. Characterization of edible marijuana product exposures reported to United States poison centers. *Clin Toxicol (Phila)*. 2016;54(9):840–846
9. Patissier C, Akdhar M, Manin C, et al. Intoxication from accidental ingestion of cannabis: analysis of eight cases [in French]. *Arch Pediatr*. 2015;22(1):43–46
10. Chouvy PA, Afsahi K. Hashish revival in Morocco. *Int J Drug Policy*. 2014;25(3):416–423
11. Cannabis. In: *2016 EU Drug Markets Report: In-depth Analysis*. Lisbon, Portugal: European Monitoring Centre for Drugs and Drug Addiction (EMCDDA); 2016:55–71. Available at: www.emcdda.europa.eu/system/files/publications/2373/TD0216072ENN.PDF
12. Dujourdy L, Besacier F. A study of cannabis potency in France over a 25 years period (1992-2016). *Forensic Sci Int*. 2017;272:72–80
13. European Monitoring Centre for Drugs and Drug Addiction. *EMCDDA Insights: Cannabis Production and Markets in Europe*. Lisbon, Portugal: European Monitoring Centre for Drugs and Drug Addiction; 2012
14. ElSohly MA, Mehmedic Z, Foster S, Gon C, Chandra S, Church JC. Changes in cannabis potency over the last 2 decades (1995-2014): analysis of current data in the United States. *Biol Psychiatry*. 2016;79(7):613–619
15. Swift W, Wong A, Li KM, Arnold JC, McGregor IS. Analysis of cannabis seizures in NSW, Australia: cannabis potency and cannabinoid profile. *PLoS One*. 2013;8(7):e70052

16. Niesink RJ, Rigter S, Koeter MW, Brunt TM. Potency trends of Δ9-tetrahydrocannabinol, cannabidiol and cannabinol in cannabis in the Netherlands: 2005-15. *Addiction*. 2015;110(12):1941–1950

17. Harwick S, King L. Home office cannabis potency study 2008. 2008. Available at: www.dldocs.stir.ac.uk/documents/potency.pdf. Accessed June 20, 2016

18. Wang GS, Roosevelt G, Heard K. Pediatric marijuana exposures in a medical marijuana state. *JAMA Pediatr*. 2013;167(7):630–633

19. Amirav I, Luder A, Viner Y, Finkel M. Decriminalization of cannabis–potential risks for children? *Acta Paediatr*. 2011;100(4):618–619

20. Wang GS, Roosevelt G, Le Lait MC, et al. Association of unintentional pediatric exposures with decriminalization of marijuana in the United States. *Ann Emerg Med*. 2014;63(6):684–689

21. Wang GS, Narang SK, Wells K, Chuang R. A case series of marijuana exposures in pediatric patients less than 5 years of age. *Child Abuse Negl*. 2011;35(7):563–565

22. MacCoun RJ, Mello MM. Half-baked–the retail promotion of marijuana edibles. *N Engl J Med*. 2015;372(11):989–991

23. Boros CA, Parsons DW, Zoanetti GD, Ketteridge D, Kennedy D. Cannabis cookies: a cause of coma. *J Paediatr Child Health*. 1996;32(2):194–195

24. Wang GS, Le Lait MC, Deakyne SJ, Bronstein AC, Bajaj L, Roosevelt G. Unintentional pediatric exposures to Marijuana in Colorado, 2009-2015. *JAMA Pediatr*. 2016;170(9):e160971

25. Bonkowsky JL, Sarco D, Pomeroy SL. Ataxia and shaking in a 2-year-old girl: acute marijuana intoxication presenting as seizure. *Pediatr Emerg Care*. 2005;21(8):527–528

26. Molly C, Mory O, Basset T, Patural H. Acute cannabis poisoning in a 10-month-old infant [in French]. *Arch Pediatr*. 2012;19(7):729–732

27. Appelboam A, Oades PJ. Coma due to cannabis toxicity in an infant. *Eur J Emerg Med*. 2006;13(3):177–179

28. Macnab A, Anderson E, Susak L. Ingestion of cannabis: a cause of coma in children. *Pediatr Emerg Care*. 1989;5(4):238–239

29. Lavi E, Rekhtman D, Berkun Y, Wexler I. Sudden onset unexplained encephalopathy in infants: think of cannabis intoxication. *Eur J Pediatr*. 2016;175(3):417–420

30. Zarfin Y, Yefet E, Abozaid S, Nasser W, Mor T, Finkelstein Y. Infant with altered consciousness after cannabis passive inhalation. *Child Abuse Negl*. 2012;36(2):81–83

31. Carstairs SD, Fujinaka MK, Keeney GE, Ly BT. Prolonged coma in a child due to hashish ingestion with quantitation of THC metabolites in urine. *J Emerg Med*. 2011;41(3):e69–e71

32. Borgelt LM, Franson KL, Nussbaum AM, Wang GS. The pharmacologic and clinical effects of medical cannabis. *Pharmacotherapy*. 2013;33(2):195–209

33. Tilelli JA, Spack LD. Marijuana intoxication presenting as seizure–comment. *Pediatr Emerg Care*. 2006;22(2):141

34. Chouvy PA. The supply of hashish to Europe. Background paper commissioned by the EMCDDA for the 2016 EU Drug Markets Report. 2016. Available at: http://www.emcdda.europa.eu/system/files/publications/2373/downloads/EDRM2016%20Background%20paper_CHOUVY_The%20Supply%20of%20Hashish%20to%20Europe.pdf. Accessed June 20, 2016

35. Le Garrec S, Dauger S, Sachs P. Cannabis poisoning in children. *Intensive Care Med*. 2014;40(9):1394–1395

36. Derkinderen P, Valjent E, Darcel F, Damier P, Girault JA. Cannabis and cannabinoid receptors: from pathophysiology to therapeutic options. *Rev Neurol (Paris)*. 2004;160(6–7):639–649

37. Thomas G, Kloner RA, Rezkalla S. Adverse cardiovascular, cerebrovascular, and peripheral vascular effects of marijuana inhalation: what cardiologists need to know. *Am J Cardiol*. 2014;113(1):187–190

38. Franz CA, Frishman WH. Marijuana use and cardiovascular disease. *Cardiol Rev*. 2016;24(4):158–162

39. Barber PA, Roberts S, Spriggs DA, Anderson NE. Adverse cardiovascular, cerebrovascular, and peripheral vascular effects of marijuana: what cardiologists need to know. *Am J Cardiol*. 2014;113(6):1086

40. Crippa JA, Derenusson GN, Chagas MH, et al. Pharmacological interventions in the treatment of the acute effects of cannabis: a systematic review of literature. *Harm Reduct J*. 2012;9(1):7

41. Naso C, Jenkins AJ, Younger D III. A study of drug detection in a postmortem pediatric population. *J Forensic Sci*. 2008;53(2):483–490

42. Pélissier F, Claudet I, Pélissier-Alicot AL, Franchitto N. Parental cannabis abuse and accidental intoxications in children: prevention by detecting neglectful situations and at-risk families. *Pediatr Emerg Care*. 2014;30(12):862–866

43. Rollins DE, Jennison TA, Jones G. Investigation of interference by nonsteroidal anti-inflammatory drugs in urine tests for abused drugs. *Clin Chem*. 1990;36(4):602–606

44. Saitman A, Park HD, Fitzgerald RL. False-positive interferences of common urine drug screen immunoassays: a review. *J Anal Toxicol*. 2014;38(7):387–396

Unintentional Cannabis Intoxication in Toddlers

Isabelle Claudet, Sébastien Mouvier, Magali Labadie, Cécile Manin, Anne-Pascale Michard-Lenoir, Didier Eyer, Damien Dufour and for the Marie-Jeanne Study Group

Pediatrics 2017;140;
DOI: 10.1542/peds.2017-0017 originally published online August 14, 2017;

PEDIATRICS®
OFFICIAL JOURNAL OF THE AMERICAN ACADEMY OF PEDIATRICS

Unintentional Cannabis Intoxication in Toddlers

Isabelle Claudet, Sébastien Mouvier, Magali Labadie, Cécile Manin, Anne-Pascale Michard-Lenoir, Didier Eyer, Damien Dufour and for the Marie-Jeanne Study Group

Pediatrics 2017;140;
DOI: 10.1542/peds.2017-0017 originally published online August 14, 2017;

Lenart, Brett

From: beth collins <rdhbeth@gmail.com>
Sent: Monday, May 21, 2018 8:12 AM
To: Kowalski, Matthew; Lenart, Brett; Planning; Ackerman, Zach
Subject: Lockwood having another Weber's meeting

Hello Planning Staff and Planning Commission,

Some of the neighbors received notices of a Lockwood informational meeting on May 31st at Weber's at 7 pm. I had just spoken with Matt last Friday and he did not mention this, so I am assuming you do not know of this meeting. Should a City representative be present ? They have no new plans on the eTrakit, so I am not sure what the meeting is about. I guess we can all go voice our concerns YET again.?

The residents who filled out their information at the PC meeting May 1st, did not get notices of this meeting, only the radius homes ?

I have sent a letter out to our core group of residents opposed to the project, so they all know of the meeting, and I extended the invitation to our 2 Councilmembers, however, we residents would rather have a meeting with Staff and planning about any updates on the concerns from the May 1st meeting. What is the update on the 1,4-dioxane and the enviromental concerns with the First Sister Lake, and a new traffic study. Jackson Rd is so congested and worsens each day, and the project will add all the semi trucks and ambulances. The tot-lot, loading zone placement, and lack of secondary exit concerns. And a PAC person to discuss the parkland and a NAP person to talk about the bird migration.

Why don't we just get this project rejected NOW, and go on with the next plans for this parcel. This project should go up where the Barton Greens project was rejected. If seniors do not drive, it would be the perfect location. They obviously do not need the whole parcel up there, but you are planners, help Lockwood to figure this out.
Should they really waste more time and money, when they do not own the land, it is contingent upon a rezone. We have our supermajority needed for City Council also, with petition signatures.

What good is a Weber's meeting going to accomplish ? So they can tell you they met with us, like the one held 1 1/2 weeks before the May 1st meeting, where NOTHING could be changed. The packet was complete. They have not made any changes to the plans today. They are not going to change our minds about this development encroaching on our homes. This is way too late. We should have been involved in the early planning stages, not in the 11th hour.
THIS LAND IS ZONED SINGLE FAMILY RESIDENTIAL. A 4 1/2 STORY BUILDING WITH COMMERCIAL DUMPSTERS, SEMI-TRUCKS, AND 3O EMPLOYEES SHOULD NOT BE ON THIS PROPERTY AT ALL.

Sincerely,
Elizabeth Collins
Sister Lakes neighborhood representative

Lenart, Brett

From: BARBARA TREVETHAN <bittrev@aol.com>
Sent: Saturday, May 19, 2018 9:14 AM
To: Planning
Subject: On migrating birds and the integrity of Dolph Park
Attachments: Bird Counts May 2018.odt

Dear Members of the Ann Arbor Planning Commission,

We need to think carefully about cause and effect. There is a crisisin migrating bird population that is declining precipitously world-wide. For example, see the New York Times article of April 29, 2018, focusing on long-distance migrators throughout Asia. The sameis true in North America, though perhaps to a lesser extent.Still, it demands our attention.Birds in migration are dependent on stop-over places for rest and refueling. These stop-overs are wetlands, lakes, marshes. Dolph Park and its natural surrounding area is just such a place. Around the globe these natural stop-over placesare being sacrificed to development and to buildings. What is happening world-wide couldhappen in miniature right here because of the proposed development of 3365 Jackson Ave.The potential degradation of the habitat of migrating birds bythe over-large development of this parcel is troubling.

May 4thI had the privilege of going down to Dolph Park in the evening. I asked the first people coming out of the woods, "What have youseen?" They replied, "Well, if you're looking for the Kirtland's Warbler, take this path over the bridge and go as far north as you can and then as far east as you can." I set offeagerly and when I arrived at a point where the path stopped in the far NE of Dolph Parkmany people were there – many had seen the Kirtland's Warbler, avery rare species of warbler.I stood among these people, marveling at how they could rattle off warbler's names, as the birds fed on insects in the trees above. Itturns out that this NE corner is the place where most of the warblers were seen. In fact, one-half of the warblers usually seen in Michigan were seen inthis area of Dolph.Then I turned around from facing the wetland to look directly north. There, just a stone's throw away, were the orange tape markers of the property in question. It was remarked by one of the birders that day that most of all the birds seen were up in the NE corner. And I observed that this is within yards of the proposed property.

In the attachment is a list of birds sighted in the Dolph Nature Area this year, including inthe far north-east corner.There are also two photographs taken by Karen Markey of a Blackburnian Warblerand a Kirtlands Warbler. These photos are of better quality than any we could find in our birding books, and are copy-righted by Karen. You can access these photos at https://ebird.org/view/checklist/S45258901.

Also, we have founda nesting female Mute Swan in the marshy area between the Sister's lakes.

This property is a treasure – a jewel. Little bits of glory touch down in our park every year for those who have eyes to see. We are and need to be stewards of this space for the coming generation. If it were tobecome a park with children's play equipment, picnic tables, and open space, the trees would be spared, the bird's stop-over habitat spared, the monitoring of the dioxsinplume couldcontinue, and theneighborhoodwould be cared for. I can imagine many people, neighbors and those who work in businesses along Jackson nearby, bringing their lunches to relax in this sort of space, much like happens on the Highline linear Park in New York City!

Have you been to this site, to walk around the property, the neighborhood, and bushwack your way out to the bluff overlooking the First Sister Lake? It could be important to do that in order to make an informed decision. Also, if you were to visit at 7:30AM and 5:00PM you would experience what the traffic is like at the proposed entrance.Please consider what is best, good, most important for all concerned. Please, weigh the cause and effect of building on this site over againstattaching the parcel to Dolph Park. We ask you to be vigilant in protecting the park, which belongs to the citizens of Ann Arbor. Please, then, do not rezone this adjacent parcel.

Grateful for your attention and the hard work you do!

Barbara Trevethan
323 Mason Ave.
Ann Arbor, MI 48103
734-769-0710
bittrev@aol.com

BIRD-COUNT LIST FOR DOLPH NATURE AREA

May, 2018

Canada Goose	Hermit Thrush	Barn Swallow
Mute Swan (nesting)	Wood Thrush	Northern Waterthrush
Wood Duck	American Robin	Great Blue Heron
Mallard	Gray Catbird	Lesser Scaup
Green Heron	Black-and-white Warbler	Northern Shoveler
Turkey Vulture	Nashville Warbler	Bufflehead
Cooper's Hawk	Yellow Warbler	Least Flycatcher
Mourning Dove	Palm Warbler	Tufted Titmouse
Red-bellied Woodpecker	Yellow rumped Warbler	Bell's Vireo
Downy Woodpecker	Chipping Sparrow	Kirtland's Warbler (2018)
Hairy Woodpecker	White-throated Sparrow	Orange-Crowned Warbler
Northern Flicker	Song Sparrow	Redstart
Solitary Sandpiper	Swamp Sparrow	Tennessee Warbler
Great Crested Flycatcher	Northern Cardinal	Chestnut-sided Warbler
Blue-headed Vireo	Rose-breasted Grosbeak	Black-throated Green Warbler
Warbling Vireo	Baltimore Oriole	Blue-winged Warbler
Blue Jay	Red-winged Blackbird	Lincoln's Sparrow
American Crow	Brown-headed Cowbird	Black-throated Blue Warbler
Northern Rough-winged Swallow	Common Grackle	Northern Parula
Black-capped Chickadee	House Finch	Magnolia Warbler
White-breasted Nuthatch	Pine Siskin	Blackburnian Warbler
House Wren (winter)	American Goldfinch	Pine Warbler
Carolina Wren	House Sparrow	Killdeer
Blue-gray Gnatcatcher	Common Yellowthroat	
Ruby-crowned Kinglet	Tree Swallow	

Main Ann Arbor Corners

To Ann Arbor City Planners

Re: 702 S Main SEU

This valley on South Main has long been a collection of locally owned and operated businesses serving our community. Before the construction of large condominiums and apartments, the South Main Market, which included Anthony's Gourmet, By the Pound, Copernicus Deli and other locally owned shops catered to the residents of Ann Arbor; neighbors Arcadian Antiques, Washtenaw Dairy, and Japanese Auto carry on that tradition of local entities serving the community. As a member and agent of the property-owning LLC, I was approached by numerous parties proposing to lease the premises for the purpose of a marihuana provisioning center. Mr. Daly expressed genuine concern for helping patients and benefitting the local community. I believe that Mr. Daly will carry on the South Main valley tradition of local entities serving the local community.

Through my own due diligence I was able to discern that Mr. Daly and Mr. Doelle possessed the knowledge and integrity to successfully operate a provisioning center on the premises. During the leasing process, I met with other individuals, toured provisioning centers and was privy to potential lessees' intentions. Mr. Daly's connection and proven track record of service and accountability to the community was unmatched by the other competing groups.

The location will serve Ann Arbor patients and fill a long vacant property. Although I aggressively marketed the property after it was vacated by the prior tenant, there was very little interest from outside parties looking to lease the property until the passage of the Medical Marihuana Ordinance. The accessibility of, ample parking located at, and central location of the facility will make this a model location for serving the needs of Ann Arbor patients.

This commission should vote to approve a medical marihuana provision center at 702 South Main because it meets all the requirements for such as adopted by this and City Council, will be operated with integrity and compassion, and such use is befitting of the location and community.

Sincerely,

Dave Ebner
Main/Ann Arbor Corners LLC
702 S Main St

Lenart, Brett

From: Laura Strowe <leksarts@yahoo.com>
Sent: Thursday, May 31, 2018 11:26 AM
To: Planning
Subject: changes to the conditions of the zoning for 1140 Broadway

To the City of Ann Arbor Planning Commissioners:

I wrote to you before the last scheduled hearing on the changes to the zoning conditions for 1140 Broadway, but it was before the proposal was made public and I was basing my letter on what the developer had told us at the required neighborhood meeting in February. He told us at that meeting that the change to the conditions of the zoning was to align the zoning conditions with the actual proposed height limits. The original zoning conditions that had been approved by the Planning Commission and City Council called for a height limit of 60 feet or 4 stories within 70 feet of the creek and 100 feet or 8 stories for the balance of the property. The new conditions that he is proposing changes the height limits away from the creek to 90 feet or 7 stories. He said that he was revising these conditions in order to tie them to the approved site plan. What many of us did not understand, and he did not make clear (purposefully?) was that the new conditions were to enshrine every aspect of the site plan to the zoning.....not just the height limitations.

We had specifically asked at previous hearings during the approval process that the developer at least cap the heights to match the site plan, but he went one step further by requiring complete adherence to the site plan.

Thus, all the objectionable things about the site plan will also now be enshrined in the zoning: the lack of sufficient parking, the reduced set-backs, the huge massing and height, the proximity to the creek, the lack of meaningful mixed-use, the lack of reasonable open space consistent with the neighborhood, the paucity of affordable units, the homely and cheap-looking facades, the ridiculously inappropriate traffic circle at the Broadway bend, and a total disregard of the Master Plan.

What this means is that if, perchance, this developer should back out of the plan, or any part of it, a future owner/developer will be obligated to follow all these specifications, even though we all envision a more neighborhood-friendly alternative.

Add to all this is another recent change. The property has undergone an administrative split, at the request of the developer, into two lots, and it is being requested that the property be split again, so that the result is a separate lot for each building. All three will be zoned C1A/R (Campus Business and Residential), and all will be subject to these new zoning conditions when they are approved. We understood that the separation of the condo building's site was because of the legal complications of ownership, but why spilt A and C? We can only guess. Future sale? However, this means that we will have 2 properties that are entirely residential, but zoned C1A/R, which is a mixed-use zoning. Any other---appropriate---zoning for those two residential properties would have required completely different specs on set-backs, density, parking, etc. But because the development had been approved as one property, the small amount of retail on one of those sites counted for all the others. Similarly, the parking allotments will cross property boundaries in order to meet even the approved parking variance which we have argued is insufficient.

This project has run roughshod over the re-zoning process from the very start, and these latest proposed changes are an added insult. We in the neighborhood are still stunned that a project this big, this dense, this inappropriate to the surrounding area is about to engulf us. The recent advertisements for the sale of the condominium units touts the condo as "Downtown Ann Arbor." Since when do we live downtown? We don't. But we are about to have something imitating "downtown" with downtown heights, massing, density and set-backs. The developer talked about "activating the streets" by having small set-backs, as if these were commercial buildings downtown. With the proposed lot-splits, this rhetoric makes even less sense, since two of the lots will have no commercial whatever, and having residential buildings close to the sidewalk is in no one's interest, neither the new residents nor the neighbors.

I beseech the Planning Commission to urge the developer to come back with a different set of changes to the conditions on the zoning, a set that protects the neighborhood rather than imposes on us the worst of this site plan.

Thank you,

Laura Strowe

From: Tom Stulberg
To: DiLeo, Alexis
Cc: Mary Underwood; Laura Strowe; Bannister, Anne; Kailasapathy, Sumi; Lenart, Brett
Subject: Re: Questions re 1140 Broadway and 999 Maiden Lane
Date: Wednesday, May 30, 2018 10:35:18 AM

Alexis,

I have had the opportunity to meet with the neighborhood leadership. We conclude that the possible negative consequences of tying the site plan to the zoning far outweigh any benefit. We don't perceive a benefit because most of our concerns were already disregarded in the existing site plan. Other protections we would like are no more protected by this new condition than they already would be.

One question that I could not answer well for my neighbors is what differences are there in this voluntary zoning condition's protections than the protections in a PUD? Are they precisely the same protections, more than a PUD, or less than a PUD? It seems a pretty close call to me, with maybe a little more protection in a PUD, but it is not clear enough to me to be able to explain to the neighborhood.

Also asked of me was would the lot splits have been able to be approved administratively if it was a PUD? I am guessing no, but I am not sure. It raises additional questions in my mind about protections: Under a PUD, if the development was not constructed before expiration of the site plan, the entire site plan would expire and would need to be extended or changed for the entire project. In the current scenario, there will soon be three separate lots. What if the site plans expire? Can one be extended without extending the others? Would their changes all have to be applied for together after expiration or could they be redesigned separately then? Some of this may seem academic, but that is the care we must take at this moment in time, to evaluate the ramifications of this application.

In my personal opinion, it seems like bad precedence to enshrine in zoning something so complicated and controversial as this development.

Thanks,

Tom

From: DiLeo, Alexis <ADiLeo@a2gov.org>
Sent: Thursday, May 24, 2018 9:48 AM
To: Tom Stulberg
Cc: Mary Underwood; Laura Strowe; Bannister, Anne; Kailasapathy, Sumi; Lenart, Brett

Subject: RE: Questions re 1140 Broadway and 999 Maiden Lane

Tom,

I respectfully disagree, I do think the Planning Commission was comfortable with the offer to tie the zoning designation with the site plan. However, I'll do my best to offer a bit more about what that means.

By city code, site plan approval means that for 3 years "permits may be issued and the land developed consistent with that plan and the regulations, laws and ordinances in effect at the time of approval, unless new regulations, laws and ordinances are made applicable to previously approved developments." See 5:122(7) of the Municode version of City Code or Section 5.29.6.E of the UDC version. The site plans are plans for structures, buildings, hardscapes, landscapes, buffers, and natural features. Uses come into play because some development regulations are use specific, such as off-street parking. The uses themselves are not part of the site plan but the requirements and physical improvement to the land they generate (i.e. parking spaces) are.

Site plans are required in order to issue permits for everything but 4 types of development (from Section 5.29.6.A of the UDC):

Building a single family or two family home
Removing or disturbing a natural feature on lot with a single family or two family home
Construction inside of an existing building that does not increase floor area
Eleven specific accessory structures, such as signs, fences, fire escapes, lights and poles, decks and patios (see 5.29.6.A.4.a-k)

The third type, construction within an existing building, is what allows remodeling of buildings – offices, stores, restaurants, etc. – without site plan approval.

Zoning permits are required to construct anything and to change land use(see Section 5.29.1 of the UDC). When a building permit is submitted, the building permit serves as the zoning permit as well. Even if construction does not require a site plan, a change of use requires approval. Zoning permits, or building permits with change of use, are only issued when the application complies with all development codes (Section 5.29.1.I). Sometimes the change of use still complies with all codes, sometimes more things need to be included as part of the application (more parking spaces?) in order to be approved. If "more things" are needed, and doing those things requires a site plan (see above), then the code also dictates the approving body for the site plan. Most site plans are approved by City Council, the Planning Commission is authorized to approve some site plans (mostly ones that involve landscape plans or parking lots but not ones that involve the buildings), and 17 things may be approved by staff (see below).

Changes allowed administratively include (from 5.29.6.B.3 of the UDC):

Building additions of 10% of the existing floor area up to 10,000 square feet
One accessory building up to 240 square feet
Adding or changing phase lines
Change in building height that does not create new floor area

Relocation of sidewalks
Change to landscape plans
Relocation solid waste/recycling facilities
Rearranging or reconfiguring parking stalls and aisles within the vehicular use area
Decrease in building size
Moving a building 10 feet or 5% of the distance to the closest lot line
Changes to storm water management (up to 50% capacity)
Changes to mitigations plans (with limitations)
Substitutions to natural features protection plans (with limitations)
Removing newly recognized invasive species
Addition of carports
Replacement of wireless communication towers (with limitations)
Adding canopies over vehicular use areas

The additional condition to tie the site plan to the zoning district includes the stipulation that site plans for administrative approval are permitted. If accepted, only the 17 things listed for site plans for administrative approval could be done without going back to City Council to first reconsider the zoning designation and the statement of conditions.

Architecture is not part of a site plan. However, the architecture at 1140 Broadway is already addressed by the 1140 Broadway Development Agreement, approved by City Council on December 4, 2017. Paragraph P-22 requires construction of all buildings consistent with the elevation drawings submitted to City Council with the site plan. Any substantive changes to the approved building elevations, aesthetics, or materials must be brought back to City Council for consideration. You asked specifically about changing the amount of brick, balconies, or windows. Those are substantive changes and, regardless of this additional zoning condition, they need to go back to City Council. So, on the one hand, the additional condition to tie the site plan to the zoning district doesn't change anything about how architecture is regulated. But on the other hand, since the development agreement only provides architectural assurances IF the 1140 Broadway site plan is developed, the additional condition assurances THAT the 1140 Broadway site plan would be developed – and the development agreement for the site plan makes sure that there aren't any substantive changes to the architecture.

The land division does not add any other unknowns. It simply divides up the site into smaller parcels. The extent of the site plan remains the same and the extent of the zoning district remains the same. The C1A/R With Conditions (and C1A/R With More Conditions if they are accepted) applies all land zoned such no matter if there is one, two or 100 lots.

The administrative amendment, or Site Plan for Administrative Approval, also does not add any unknowns. In fact, it removes them. The Site Plan for Administrative Approval demonstrates that Parcel 1 (with Buildings A and C) has enough lot area to support the floor area of those buildings, and that Parcel 2 (with Building B) has enough lot area to support the floor area of that building. The plan also shows that all other development requirements are still met with by the individual lots or by the total development as required.

I hope this information provides the clarity you were looking for.

Sincerely,

Alexis DiLeo, AICP | City Planner
City of Ann Arbor Planning & Development
301 East Huron Street, P.O. Box 8647
Ann Arbor, MI 48107-8647
Direct 734-794-6000 x 42610 | General 734-794-6265

From: Tom Stulberg <tomstulberg@hotmail.com>
Sent: Wednesday, May 23, 2018 8:37 AM
To: DiLeo, Alexis <ADiLeo@a2gov.org>
Cc: Mary Underwood <amoscorey@me.com>; Laura Strowe <leksarts@yahoo.com>; Bannister, Anne <ABannister@a2gov.org>; Kailasapathy, Sumi <SKailasapathy@a2gov.org>; Lenart, Brett <BLenart@a2gov.org>
Subject: Questions re 1140 Broadway and 999 Maiden Lane

Alexis,

I think it was clear from the last Planning Commission meeting that commissioners and citizens alike don't understand what the tying of the site plan to zoning means the developer can or can't do. Further explanation would be helpful. For example, if the developer keeps the same footprint, without having to come back for an additional re-zoning can it reduce or increase the amount of brick, can it remove or add balconies, can it add or remove windows? Clarity on site plan items that can still be altered after tying them to the zoning would be illuminating to all of the interested parties. Other than the obvious height limit being changed from 8 stories to 7, it is not obvious what the rest of the conditions really mean.

The administrative approval of the lot split for the condo building now adds another unknown. Could you update us on what the impact of this lot split is on the application? What will be restricted by the zoning condition changes that are proposed: both 1140 and 999, or just 1140 now that 999 is split off?

Thanks,

Tom

From: DiLeo, Alexis <ADiLeo@a2gov.org>
Sent: Monday, May 14, 2018 12:43 PM
To: Tom Stulberg
Cc: Mary Underwood; Laura Strowe; Bannister, Anne; Kailasapathy, Sumi; Lenart, Brett

Subject: RE: Questions re 1140 Broadway at PC part two

Yes. Any permitted use could be swapped for another permitted use. Swaps are approved with zoning compliance permits if all development requirements are still satisfied, or changes are proposed. Most changes, however, require site plan approval.

Alexis DiLeo, AICP | City Planner
City of Ann Arbor Planning & Development
301 East Huron Street, P.O. Box 8647
Ann Arbor, MI 48107-8647
Direct 734-794-6000 x 42610 | General 734-794-6265

From: Tom Stulberg <tomstulberg@hotmail.com>
Sent: Monday, May 14, 2018 11:52 AM
To: DiLeo, Alexis <ADiLeo@a2gov.org>
Cc: Mary Underwood <amoscorey@me.com>; Laura Strowe <leksarts@yahoo.com>; Bannister, Anne <ABannister@a2gov.org>; Kailasapathy, Sumi <SKailasapathy@a2gov.org>; Lenart, Brett <BLenart@a2gov.org>
Subject: Re: Questions re 1140 Broadway at PC part two

Does that mean the 4600 square feet of commercial could similarly be removed?

Sent from my iPhone

On May 14, 2018, at 11:45 AM, DiLeo, Alexis <ADiLeo@a2gov.org> wrote:

> Tom,
>
> Again, please see below for responses.
>
> **Alexis DiLeo, AICP | City Planner**
> City of Ann Arbor Planning & Development
> 301 East Huron Street, P.O. Box 8647
> Ann Arbor, MI 48107-8647
> Direct 734-794-6000 x 42610 | General 734-794-6265
>
> ---
>
> **From:** Tom Stulberg <tomstulberg@hotmail.com>
> **Sent:** Sunday, May 13, 2018 1:05 PM
> **To:** DiLeo, Alexis <ADiLeo@a2gov.org>
> **Cc:** Mary Underwood <amoscorey@me.com>; Laura Strowe <leksarts@yahoo.com>; Bannister, Anne <ABannister@a2gov.org>; Kailasapathy, Sumi <SKailasapathy@a2gov.org>
> **Subject:** Re: Questions re 1140 Broadway at PC part two

Alexis, I forgot to include a question:

The development was approved with 4600 square feet of commercial use in building C, about one half of one percent of the 825,074 total square feet. The developer offered to "possibly" almost double that, bringing the amount of commercial use to about 1% in my calculation. What would the effect of approving the proposed changes be on this additional possible commercial space above the 4600 square feet?

[DiLeo, Alexis] The two are not related. Site plans approve buildings, structures and site improvements but not use. Zoning designations control use. Changes to sites that do not increase floor area are exempt from site plan review, so the commercial space could be increased to any amount with a zoning permit as long as the site development can still meet requirements. Parking is usually the barrier. The zoning permit will evaluate the reduction in residential space versus the addition in commercial space for off-street parking purposes. If the change still meets zoning and parking, it will be approved. If it does not, the developer will need to decide what to do – perhaps reducing the increase or providing more parking. Those secondary changes might trigger site plan review.

Thanks,

Tom

From: Tom Stulberg <tomstulberg@hotmail.com>
Sent: Sunday, May 13, 2018 12:47 PM
To: DiLeo, Alexis
Cc: Mary Underwood; Laura Strowe; Bannister, Anne; Kailasapathy, Sumi
Subject: Questions re 1140 Broadway at Planning Commission

Alexis,

I have a few questions:

When do citizens need to send emails to the Planning Commission to get into the packet?

The staff report document on Legistar has blank pages for Exhibits B and C. Can you please provide them?

Can you provide any recent examples of voluntary zoning conditions that include tying the site plan to the zoning, as this proposal requests? If there is an example,

can you speak to unanticipated consequences that may or may not have arisen and were they addressed administratively or with a return to Planning Commission and Council for further approval?

The city does not yet have construction drawings for the parking structure surrounded by building A. Thus, the fire department has yet to do the review it needs to do to address the serious concerns it raised about the parking structure. Do we know when these construction drawings will be submitted and reviewed? Should the design of the structure not be approved by the fire department, the structure might not be buildable, yet this structure was a significant driver of the design of the site plan, and soon perhaps locked in by zoning.

Would this proposal lock in the roundabout at Broadway and the entrance to this development between buildings A and C? The residents have raised concerns about the wisdom of this roundabout which will make the residential Broadway hill route more attractive for traffic generated by this development than other traffic flow options. This concern has not been addressed sufficiently to be locking the roundabout into zoning, in the opinion of the neighborhood.

What is the impact of tying the site plan of the entire 6.4 acre parcel to the zoning upon the pending application for a lot split for building B? What is the current status of that administrative lot split application?

I would not be surprised if others have more questions, but we can start with this list of concerns that would benefit from input from the planing department.

Thank you,

Tom Stulberg, on behalf of the Broadway and Traver neighborhoods.

From: DiLeo, Alexis <ADiLeo@a2gov.org>
Sent: Thursday, May 10, 2018 9:30 AM
To: Tom Stulberg
Cc: Mary Underwood; Laura Strowe; Bannister, Anne; Kailasapathy, Sumi
Subject: RE: 1140 Broadway at Planning Commission

Tom,

The meeting packet will be available by late afternoon Friday, May 11 online through the Legistar system. Click on the democracy tab on www.a2gov.org and then click on

meetings and agendas. If you're signed up for the planning updates service, you'll get an email as early as noon-ish Saturday (depending on your subscription preferences) with a list of all agenda items, a link to Legistar and more detailed instructions. Please consider signing yourself up and encourage your neighbors as well.

There is no formal procedure for speaking at a Planning Commission public hearing. Five minutes are offered to the first person who identifies themselves as a representative of a registered group. Just advise the substitute representatives to be sure to say "I am representing the Broadway and Traver Neighborhood Group" – and coordinate with other speaking members so they do not inadvertently claim the 5 minutes if they speak before the substitute.

Alexis DiLeo, AICP | City Planner
City of Ann Arbor Planning & Development
301 East Huron Street, P.O. Box 8647
Ann Arbor, MI 48107-8647
Direct 734-794-6000 x 42610 | General 734-794-6265

From: Tom Stulberg <tomstulberg@hotmail.com>
Sent: Wednesday, May 09, 2018 4:05 PM
To: DiLeo, Alexis <ADiLeo@a2gov.org>
Cc: Mary Underwood <amoscorey@me.com>; Laura Strowe <leksarts@yahoo.com>; Bannister, Anne <ABannister@a2gov.org>; Kailasapathy, Sumi <SKailasapathy@a2gov.org>
Subject: 1140 Broadway at Planning Commission

Alexis,

The official representatives of the Broadway and Traver Neighborhoods, Laura Strowe and Mary Underwood, respectively, will be out of town for next Wednesday's Planning Commission meeting. Many neighbors are highly interested in the planning department's report. Can you send it to me when it is available so that I may distribute it to the neighborhood groups. Also, what is the procedure to allow someone else to have their five minute time slot at the public hearing in their absence?

Thanks,

Tom

Lenart, Brett

From: Tonya Shoults <twoloaf@gmail.com>
Sent: Friday, June 01, 2018 9:39 AM
To: Planning
Subject: 702 S Main St

To whom it may concern at the Ann Arbor Planning Commision,

Thank you so much for taking the time to read my email today. I am writing in support of the new provisioning center being opened at 702 S Main St. Arbors Wellness is an excellent establishment with quality medicine and a professional staff. They always treat me with respect and have a true dedication to helping me manage my pain responsibly. A new shop located on S Main will make it so much easier for me to pick up my medication. I work on the south side of town, live on the west side, and the downtown location can be difficult to access at certain times of day, especially due to all of the wonderful street parties and events that make Ann Arbor great. Having a new location at 702 Main St would allow me much easier access to my medication and would prevent extra driving in a congested area.

Kind Regards,
Tonya Shoults