ABSTRACTS IN URGENT CARE

- The FDA on Cannabidiol
- Improving Diagnosis of Cluster Headache
- Making Tympanostomy Tube Placement Office-Friendly
- Nothing to Fear from NDMA?
- Counseling Patients on Preventing Cardiovascular Disease

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FDA Delves Deeper into Use of CBD Products

Key point: *The FDA is working to answer questions about the science, safety, and quality of products containing cannabis and cannabis-derived compounds, particularly CBD.*

Citation: U.S. Food & Drug Administration. What you need to know (and what we're working to find out) about products containing cannabis or cannabis-derived compounds, including cannabidiol (CBD). Available at: https://www.fda.gov/consumers/consumer-updates/what-you-need-know-and-what-were-working-find-out-about-products-containing-cannabis-or-cannabis. Accessed December 9, 2019.

Aware there is a common belief among cannabidiol (CBD) users that trying the compound "can't hurt," the FDA has evaluated (and seeks to educate the public on) potential dangers associated with its use. The likelihood of experimenting with CBD may be enhanced by seeing celebrities promote or support its use. This is especially relevant in the urgent care setting, where patients may have suggested to you that CBD is "the only thing that works" for their pain. Now the FDA has published information for both physicians and the public to understand the risks, as well as the benefits, of cannabis and cannabis-derived compounds, including CBD.

The FDA states they have only approved one CBD product, Epidiolex, to treat two rare forms of epilepsy. It is illegal for companies to market CBD by adding CBD to food or labeling it as a "dietary supplement."

At this point, there are limited data on CBD and its safety when being taken for any reason. The FDA published the following information for the public with regard to CBD:

1. CBD has the potential to harm you, and harm can happen to you before you are aware of it.
   a. CBD can cause liver injury (as identified by the FDA when studying Epidiolex for rare forms of epilepsy).
   b. CBD can affect the metabolism of other drugs, causing serious side effects.
   c. Use of CBD with alcohol or other CNS depressants increases the risk of sedation or drowsiness, which can lead to injuries.
   d. CBD may cause male reproductive toxicity. The FDA identified possible changes in male reproductive fertility during animal studies while developing Epidiolex, including effects in the male offspring of females exposed to CBD. These findings were only in animals, but affected testicular size and sperm count and the public should be aware this is a possible side effect.
2. CBD can cause side effects that you do notice. These side effects should improve if one stops using CBD, or the amount of CBD ingested or used is decreased. Such side effects include:
   a. Changes in alertness (most commonly experienced as somnolence)
   b. Gastrointestinal distress (most commonly experienced as diarrhea and/or decreased appetite)
   c. Changes in mood (irritability or agitation)

The FDA also warns that there are many important aspects of CBD use that have not been studied at this point. These include the effects of long-term use, or the effects on the developing brain if used during pregnancy or breastfeeding, or when children take CBD. Further, we do not know how or if CBD interacts with herbs/botanicals or prescription medications, but there is an inherent risk of interactions.

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The FDA continues its efforts to block unproven claims made by CBD companies and to determine unknown risks to the public. ■

Moving Toward More Efficient Diagnosis of Cluster Headaches

Key point: Cluster headaches are as hard for the clinician to diagnose as they are unpleasant for the patient to experience. Improving both the quality and timeliness of care hinges on making earlier, and more distinct, diagnosis.

Citation: Martin V. Making the diagnosis of cluster headache. *J Fam Pract*. 2019;68(8):S39-S42.

The very nature of cluster headaches, and the diverse ways in which patients experience them, make timely, precise diagnosis (and subsequent treatment) challenging. Studies show an average delay in diagnosis of 6 to 8 *years*. In this article published in the *Journal of Family Practice*, the author notes that cluster headaches tend to occur in a "cluster period" or "bout" that can last from weeks to months. Further, patients with cluster headaches may experience periods of remission lasting from months to years; 25% of patients are thought to have only one cluster period in their lifetime.

The author also notes, however, that cluster headaches tend to follow a circadian as well as a circannual pattern (meaning they tend to occur at the same time of year, particularly during spring and fall).

The *International Classification of Headache Disorders*, 3rd edition (ICHD-3), describes cluster headache attacks of severe, strictly unilateral pain which is:

- Orbital, supraorbital, temporal, or any combination of these sites
- Lasting 15 to 180 minutes
- Occurring from daily up to eight times per day
- Associated with one or more autonomic signs or symptoms ipsilateral to the headache
- Described as excruciating in intensity, to the extent that patients are usually unable to to lie down and relax, and characteristically pace the floor

Cluster periods or bouts may be precipitated by alcohol, histamine, nitroglycerin, changes in weather, odors, and bright or flashing lights.

First- and second-line relatives of patients with cluster headaches are more likely to be similarly afflicted than the general population. Further, the U.S. Cluster Headache Survey showed a history of head trauma in 18% of patients who subsequently developed cluster headaches. In over 75% of male patients with head trauma preceding CH, the average time interval between head trauma and CH was 10.1 years, suggesting the possibility that there was no causal association, only correlation.

ICHD-3 diagnostic criteria for cluster headaches are outlined in **Table 1**. ■

Table 1. ICHD-3 Diagnostic Criteria for Cluster Headaches

A. At least five attacks fulfilling criteria B–D
B. Severe or very severe unilateral orbital, supraorbital and/or temporal pain lasting 15-180 minutes when untreated
C. Either or both of the following:
  1. At least one of the following symptoms or signs, ipsilateral to the headache:
    a. Conjunctival injection or lacrimation
    b. Nasal congestion or rhinorrhea
    c. Eyelid edema
    d. Forehead and facial sweating
    e. Miosis and /or ptosis
  2. A sense of restlessness or agitation
D. Occurring with a frequency between one every other day and eight per day
E. Not better accounted for by another ICHD-3 diagnosis

Diagnosis of cluster headache is clinical, based on a detailed history and neurological examination. Laboratory tests are usually not useful. MRI can be useful to rule out other disorders. In cluster headaches, MRI tends to show enlargement of anterior hypothalamic gray matter ipsilateral to the headache side compared with controls. Functional MRI has shown cerebral activation in ipsilateral hypothalamic gray matter during an attack.

Cluster headache attacks are unilateral, affecting peri- and retro-orbital regions and the temple, sometimes involving the teeth. Some patients have compared the sensation, per the author, with being poked in the eye with a hot needle or knife. During an attack, patients experience one or more cranial autonomic symptoms ipsilateral to the pain. These include:

- Lacrimation
- Eye redness
- Eye discomfort
- Nasal congestion
- Rhinorrhea
- Aural fullness
- Throat swelling
- Flushing ■

General Anesthesia No Longer a Necessity for Placement of Ear Tubes

Key point: A new "breakthrough device" facilitates placement of ear tubes under local anesthesia.

Citation: U.S. Food and Drug Administration. News release. FDA approves system for the delivery of ear tubes under local anesthesia to treat ear infection. November 25, 2019. Available at: https://www.fda.gov/news-events/press-announcements/fda-approves-system-delivery-ear-tubes-under-local-anesthesia-treat-ear-infection. Accessed December 9, 2019.

The U.S. Food and Drug Administration has approved use of a new system for delivering local anesthesia in children undergoing placement of tympanostomy tubes. The Tubes Under Local Anesthesia system (Tula) consists of the anesthetic Tymbion, Tusker Medical Tympanostomy Tubes, and several devices needed for delivery of the anesthetic and ear tubes into the eardrum. The benefit to the patient—and, potentially, to the urgent care provider—is that tubes will be able to be placed in a physician's office with minimal discomfort to the patient, according to the FDA. According to the National Institute of Deafness and Other Communication Disorders, five out of every six children will have at least one ear infection before the age of 3 years. The Tula system uses an electric current to deliver a local anesthetic to the patient prior to the placement of tympanostomy tubes, thus avoiding the use of general anesthesia. This system can be used in infants as young as 6 months of age, as well as in adults. Tula is not for use in patients with allergies to local anesthetics or preexisting problems with their eardrums, such as a perforated eardrum. The most common problem was lack of adequate anesthesia during the procedure. The FDA also granted Breakthrough Device status to Tula; that designation is reserved for devices that treat a life-threatening or permanently debilitating condition and meets one of the following criteria: the device is in the best interest of patients; there are no cleared or approved alternatives; or the device shows significant advantage over cleared and approved alternatives. ■

Deflating Fear of Products Containing NDMA

***Key point:** Some mainstream media reports have created warrantless uneasiness among patients who take certain medications falsely perceived to be unsafe due to the presence of the substance NDMA.*

Citation: U.S. Food and Drug Administration. Statement from Janet Woodcock, MD, director of FDA's Center for Drug Evaluation and Research, on impurities found in diabetes drugs outside the U.S. December 05, 2019. Available at: https://www.fda.gov/news-events/press-announcements/statement-janet-woodcock-md-director-fdas-center-drug-evaluation-and-research-impurities-found. Accessed December 9, 2019.

The FDA has investigated several drugs for genotoxic impurities including the substance NDMA over the past few years. Certain

drugs, including angiotensin II receptor blockers (ARBs) and ranitidine, have been found to have small amounts of the substance, sometimes compared with amounts that may be found in charred beef. Consequently, the FDA has announced efforts to ensure that U.S. drug supply meets strict quality standards. One example: There are some reports that metformin has been found to have low levels of NDMA or other nitrosamines in other countries. Again, these levels are tantamount to those contained in food and water naturally.

NDMA is found in dairy products, seafood, cured and grilled meats, and even vegetables. Everyone is exposed to some level of NDMA. It may be most helpful to counsel your patients on these facts. The international scientific community and FDA do not expect NDMA or nitrosamines to cause damage when ingested at low levels. ■

Counseling Patients on Reducing Risk for Cardiovascular Disease

Key points: The AHA and ACC have boiled down their latest guidelines update into a "Top 10" list to facilitate discussion with patients.

Citation: Arnett DK, Blumenthal RS, Albert MA, et al. 2019 ACC/AHA Guideline on the Primary Prevention of Cardiovascular Disease: A report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *Circulation*. 2019;140(11):e596-e646.

The latest guidelines update issued by the American Heart Association and American College of Cardiology features a list of the Top 10 Take-Home Messages for the Primary Prevention of Cardiovascular Disease. Given that patients may present to urgent care centers with questions on reducing their own risk for CVD, this is of great relevance to the urgent care provider. The top 10 topics urgent care clinicians should consider discussing with patients include:

1. Prevention of atherosclerotic vascular disease (ASCVD), heart failure, and atrial fibrillation through healthy lifestyle
2. A team-based care approach that evaluates social determinants of health that affect individuals to inform treatment decisions.
3. A 10-year ASCVD risk estimation for patients between 40 and 75 years of age, including a clinician-patient risk discussion before starting on pharmacological therapy (eg, antihypertensive therapy, a statin, or aspirin). In addition, assessing for other risk enhancing factors can help guide decisions about preventative interventions in select individuals, as can coronary artery calcium scanning.
4. All adults should consume a healthy diet that emphasizes the intake of vegetables, fruits, nuts, whole grains, lean vegetable or animal protein, and fish and minimizes the intake of trans fats, red meat and processed meats, refined carbohydrates, and sugar-sweetened beverages. For adults with overweight/obesity, counseling and caloric restriction are recommended for achieving and maintaining weight loss.

"Nonpharmacological interventions are recommended for adults with elevated blood pressure or hypertension. For those requiring pharmacological therapy, the target blood pressure should generally be <130/80 mmHg."

5. Engaging in at least 150 minutes per week of accumulated moderate-intensity physical activity or 75 minutes per week of vigorous-intensity physical activity.
6. For adults with type 2 diabetes mellitus, lifestyle changes, such as improving dietary habits and achieving exercise recommendations. If medication is indicated, metformin is a first-line therapy, followed by consideration of a sodium-glucose cotransporter 2 inhibitor (SGLT2 inhibitor) or a glucagon-like peptide-1 receptor agonist (GLP-1 receptor agonist).
7. Assessment of tobacco use at every visit; those who use tobacco should be assisted and strongly advised to quit.
8. Advice that aspirin should be used infrequently in the routine primary prevention of ASCVD because of lack of net benefit.
9. Statin therapy is first-line treatment for primary prevention of ASCVD in patient with elevated low-density lipoprotein cholesterol levels (>190 mg/dL); those with diabetes mellitus; who are 40 to 75 years of age; and those determined to be at sufficient ASCVD risk after a clinician-patient risk discussion.
10. Nonpharmacological interventions are recommended for all adults with elevated blood pressure or hypertension. For those requiring pharmacological therapy, the target blood pressure should generally be <130/80 mmHg.

In addition to the top 10 take-home messages, the ACC/AHA highlight additional risk factors that are key points for clinician-patient risk discussions and high-complexity clinical decision-making. Among the "risk-enhancing factors" recommended for discussion with patients are family history of premature ASCVD (males, age <55; females, age <65); primary hypercholesterolemia (LDL-C, 160-189 mg/dL [4.1-4.8 mmol/L]); non-HDL 190-219 mg/dL [4.9-5.6 mmol/L]; metabolic syndrome; chronic kidney disease; chronic inflammatory conditions (eg, psoriasis, rheumatoid arthritis, systemic lupus erythematosus); history of premature menopause (prior to age 40); being of a high-risk face (eg, South Asian ancestry); lipids/biomarkers associated with ASCVD risk. ■