ABSTRACTS IN URGENT CARE

- The Flu–MI Connection
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- One Cigarette a Day Is Too Many

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Each month the College of Urgent Care Medicine (CUCM) provides a handful of abstracts from or related to urgent care practices or practitioners. Glenn Harnett, MD leads this effort.

Confirmed Flu Ups Short-Term Risk for MI

***Key point:** Patients with laboratory-confirmed influenza are almost six times more likely to be admitted for acute myocardial infarction (MI) in the following 7 days.*

Citation: Kwong JC, Schwartz KL, Campitelli MA, et al. Acute myocardial infarction after laboratory-confirmed influenza infection. *N Engl J Med*. 2018;378(4):345-353.

Results of a cohort study published in the *New England Journal of Medicine* revealed that patients with laboratory-confirmed influenza were almost six times as likely to be admitted for acute myocardial infarction in the subsequent 7 days. They defined the risk interval as the first 7 days after respiratory specimen collection and the control interval as 1 year before and 1 year after the risk interval. They identified 364 hospitalizations for acute myocardial infarction that occurred within 1 year before and 1 year after a positive test result for influenza. Of these, 20 occurred during the risk interval and 344 occurred during the control interval. The incidence ratio of an admission for acute MI during the risk interval as compared with the control interval was 6.05 (95% CI, 3.86 to 9.50). No increased incidence was observed after day 7. Incidence ratios for acute myocardial infarction within 7 days after detection of influenza B, influenza A, respiratory syncytial virus, and other viruses were 10.11, 5.17, 3.51, and 2.77, respectively. This risk was even greater in older patients and was independent of flu vaccination status or prior history of MI hospitalization. The authors noted that the increased MI risk regardless of vaccination status should not be seen as evidence that influenza vaccinations are ineffective, because the study wasn't designed to explore that issue. The study also revealed that other forms of respiratory infection can raise the risk for MI admission. Urgent care providers must be aware that when a patient has laboratory-confirmed influenza, they are at much greater risk for an MI in the week following the diagnosis. ■

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Data Confirm Airborne Flu Transmission

***Key point:** Fine aerosol specimens from exhaled breath can carry influenza virus.*

Citation: Yan J, Grantham M, Pantelic J, et al. Infectious virus in exhaled breath of symptomatic seasonal influenza cases from a college community. *Proc Natl Acad Sci*. 2018115(5)1081-1086.

Lack of human data on influenza virus aerosol shedding has previously fueled debate over the likelihood of its airborne transmission. This study enrolled 140 patients with a positive rapid flu test who presented within 3 days of symptom onset and provided 30-minute breath samples and nasopharyngeal swab specimens. Viral cultures were positive for infectious flu virus in 39% of breath samples and 89% of nasal swab specimens. Results revealed that coughing was common but not necessary for generating infectious virus in aerosols, sneezing rarely occurred during the breath-sample collection, and viral shedding in aerosols decreased as days since symptom onset increased. Surprisingly, sneezing did not appear to make an important contribution to influenza virus shedding in aerosols; rather, it was coughing that was determined to be the main culprit. The

"[The FDA] suggests that Medicare Part D prescription drug plans monitor patients who take medications considered to be 'potentiators' of opioid misuse."

researchers stated that their study "clearly establishes that a significant fraction of influenza cases routinely shed infectious virus, not merely detectable RNA, into aerosol particles small enough to remain suspended in air and present a risk for airborne transmission." ■

CMS Looks Hard at Curbing Opioid Use

Key point: CMS proposes 7-day limit on initial opioid prescriptions.

Citation: Centers for Medicare & Medicaid Services. 2019 Medicare Advantage and Part D Advance Notice Part II and Draft Call Letter. Available at: https://www.cms.gov/ Medicare/Health-Plans/MedicareAdvtgSpecRateStats/ Announcements-and-Documents.html. Accessed February 11, 2018.

The Centers for Medicare & Medicaid Services (CMS) has proposed that beginning in 2019, initial opioid prescriptions for acute pain should be limited to 7 days. They noted that the growth of Medicare Part D spending on opioids increased 165% from 2006 to 2015. The agency has also suggested in the 2018 Draft Call Letter that Medicare Part D prescription drug plans monitor patients who take medications considered to be "potentiators" of opioid misuse (specifically relating to gabapentin and pregabalin). CMS is asking for public comment on whether it should more closely monitor patients who receive these prescriptions. The agency stated that "given the urgency and scope of the continuing national prescription opioid epidemic, we will propose new strategies to more effectively address this issue for patients in Part D." Those strategies will include:

- Identifying high-risk patients who use gabapentin and pregabalin in combination with prescription opioids to ensure that plans provide appropriate case management
- Creating a new quality measure that would track how well Part D plans flag concurrent use of opioids and benzodiazepines
- Developing a pharmacy point-of-sale edit that prohibits dispensing of any prescription that is more than a 90 morphine mg equivalent, or a 7-day supply
- Implementing point-of-sale edits that flags duplicative therapy of multiple long-acting opioids

The proposal would exempt patients with cancer, in hospice, or in long-term care facilities from much of the strict oversight.

FDA: Kratom is an Opioid

Key point: The most common compounds in kratom share structural characteristics with opioids.

Citation: U.S. Food & Drug Administration. Statement from FDA Commissioner Scott Gottlieb, MD, on the agency's scientific evidence on the presence of opioid compounds in kratom, underscoring its potential for abuse (February 6, 2018). Available at: https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm595622.htm. Accessed February 11, 2018.

FDA scientists analyzed the chemical structures of the 25 most common compounds in kratom and concluded that all the compounds share structural characteristics with controlled opioid analgesics, such as morphine derivatives. They also found that compounds in kratom bind strongly to mu-opioid receptors, comparable to opioid drugs, and reported that kratom has now been linked to 44 deaths, up from 36 in November. FDA Commissioner Scott Gottlieb, MD, stated that the scientific data and adverse event reports have "clearly revealed" that the compounds in kratom make it "not just a plant—it's an opioid…associated with novel risks because of the variability in how it's being formulated, sold, and used recreationally by those who are seeking to self-medicate for pain or who use kratom to treat opioid withdrawal symptoms." He said the claim that kratom is benign "because it's 'just a plant' is shortsighted and dangerous." The FDA also expressed concern about a number of other deaths in which kratom was combined with other drugs such as illicit drugs, prescription opioids, benzodiazepines, and over-the-counter medications, such as loperamide. Gottlieb concluded that "kratom should not be used to treat medical conditions, nor should it be used as an alternative to prescription opioids. There is no evidence to indicate that kratom is safe or effective for any medical use." ■

More Clues When Looking at Bruising in Children

Key point: Key bruising distributions and characteristics can help clinicians distinguish between true and fabricated histories of injury in children.

Citation: Hibberd O, Nuttall D, Watson RE, et al. Childhood bruising distribution observed from eight mechanisms of unintentional injury. *Arch Dis Child*. 2017;102(12):1103-1109.

This prospective cross-sectional study summarized key bruising distributions and characteristics from 559 incidents involving eight specific unintentional injuries in children age ≤13 years. The study was undertaken to enhance understanding of detailed bruising characteristics associated with true accidental injury, to help clinicians better assess injury plausibility, and to identify false or fabricated trauma histories. It provides new, detailed

evidence of bruising characteristics in the context of the child's age and developmental capabilities. Previously published red flags regarding bruising characteristics from physical abuse were further validated by the absence or extremely low frequency of these type of findings in this cohort of patients with unintentional injuries. Among the 372 children examined who had bruising, all but seven were mobile, none had more than five bruises from a single incident, and the majority had only one bruise. Other important points regarding bruise counts included:

- Occurrence of three or more bruises from a single incident is uncommon. When present, the most common mechanisms were a stair fall involving multiple stairs, sports injury, or motor vehicle crash.
- More than five bruises from any stated cause brings into question the plausibility and veracity of the history for children who are otherwise healthy.
- When two or more bruises occurred, they were in the same body region or on the same side of the body.
- Bruises most often occurred to the front of the body over a bony area, such as the forehead or shin.
- There were only two incidents where bruising occurred to both the front and the back of the body from the same event.
- Patterned bruising was uncommon, as was petechial or clustered bruising.

Urgent care providers are encouraged to review this article in order to improve their recognition of bruising patterns from both unintentional and intentional injuries in children. ■

FDA Cites Safety Concerns in Ordering New Packaging for Loperamide

Key point: FDA changes loperamide packaging due to continued reports of misuse and cardiac effects.

Citation: FDA Drug Safety Communication: FDA limits packaging for anti-diarrhea medicine loperamide (Imodium) to encourage safe use. U.S. Food & Drug Administration. Available at: https://www.fda.gov/Drugs/DrugSafety/ucm594232.htm. Accessed February 11, 2018.

The FDA is working with drug manufacturers to change the packaging for the antidiarrheal loperamide (Imodium), as the agency continues to receive reports of cardiac problems and death in people using higher-than-recommended doses. The new packaging, which will consist of blister packs and other single-dose packaging, as well as limited number of doses in a package, aims to stem such misuse. In 2016, the FDA warned that high doses of loperamide can result in serious cardiac events, including QT interval prolongation, torsades de pointes, other ventricular arrhythmias, syncope, and cardiac arrest. The reported events tend to occur among people who are misusing the drug for its opioid effects. The FDA continues to advise clinicians to stop loperamide immediately if toxicity is suspected, counsel patients to use the drug only as directed, and note that interactions with common medications (such as clarithromycin) can increase the likelihood of adverse cardiac outcomes. This is despite the addition of a black box warning to the medicine label and a previous FDA communication. The agency noted that loperamide is a safe drug when used as directed. The maximum approved dose of loperamide for adults is 8 mg/day for over-the-counter loperamide and 16 mg/day for prescription use. ■

"Recognizing when a tonic-clonic seizure is occurring may allow prompter medical attention during or shortly after the event."

A New Way to Detect Seizures

Key point: FDA clears first smart watch to detect seizures.

Citation: Brooks M. FDA Clears First Smart Watch to Detect Seizures, Manage Epilepsy. Medscape. Available at: https://www.medscape.com/viewarticle/892329. Accessed February 11, 2018.

The Centers for Disease Control and Prevention estimates that about 3.4 million people in the United States have epilepsy, including 470,000 children. Recently, the Food and Drug Administration provided 510(k) clearance to market a smart watch designed for seizure tracking and epilepsy management. The smart watch manufactured by Empatica, called the Embrace, uses advanced machine learning to identify convulsive seizures and can send an alert via text and phone message to caregivers. It was tested in a clinical study involving 135 patients with epilepsy who were admitted to epilepsy monitoring units for continuous monitoring with video electroencephalography, while simultaneously wearing the device. Researchers collected 6,530 hours of data over 272 days, including 40 generalized tonic-clonic seizures. The device's algorithm detected 100% of the seizures, which were then confirmed by independent epilepsy experts. The device can also record sleep, rest, and physical activity data. The lead researcher noted that more than 3,000 Americans die each year from sudden unexpected death in epilepsy. By alerting family members and caretakers that a tonic-clonic seizure is occurring, the watch may allow prompter medical attention during or shortly after the event. ■

'Cutting Back' on Cigarettes Will Not Eliminate Risk

Key point: Smoking just one cigarette a day carries substantial risks for stroke and coronary heart disease (CHD).

Citation: Johnson KC. Just one cigarette a day seriously elevates cardiovascular risk. *BMJ*. 2018;360:k167.

The *British Medical Journal* published a meta-analysis in which researchers reviewed 141 prospective studies to analyze the association between smoking and coronary heart disease or stroke in millions of generally healthy people. Results revealed that smoking just one cigarette daily is associated with a "much greater than expected" increase in risk for CHD and stroke. Overall, as compared with never-smoking, smoking one cigarette daily conferred significantly increased risks for both CHD or stroke. Smoking just one cigarette a day was associated with a 48% to 74% increase in the risk of CHD in men, and a 57% to 119% increase in CHD risk for women. They also revealed an approximate 30% increase in the risk of stroke for both men and women. One cigarette a day accounted for 50% of the excess CHD risk in men compared with smoking 20 cigarettes (one pack) per day. In stroke, one cigarette a day accounted for about one third of the risk associated with smoking a pack a day.

"Data for counseling patients who smoke: Just one cigarette a day was associated with increased risk for CHD of up to 74% in men and up to 119% for women."

Results based on the subset of studies that adjusted for multiple confounders such as hyperlipidemia and hypertension revealed that women who smoked one cigarette daily had a 119% increased risk for CHD and a 46% increased risk for stroke. Men who smoked one cigarette daily had a 74% increased risk for CHD and a 30% increased risk for stroke. In an editorial accompanying the article, the authors stated, "Only total cessation will protect people and populations from tobacco's toxic legacy.... Any assumption that smoking less protects against heart disease or stroke has been dispelled this week." ■