ABSTRACTS IN URGENT CARE

- Guidance on Management of Patients with E-cigarette, or Vaping, Product Use-Associated Lung Injury
- One More Option to Stem Consequences of Flu
- CDC warns STD Rates Skyrocketing
- FDA Update on NDMA-Containing Medications
- Management of Patients Presenting with Acute Upper GI Bleed

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More Advice on Inquiring About—and Assessing—Vaping and EVALI

Key point: Physicians should inquire about e-cig or vaping use in a nonjudgemental but thorough manner. Ask about specific products, frequency, and associated drug use.

Citation: Siegel DA, Jatlaoui TC, Koumans EH, et al. Update: Interim Guidance for Health Care Providers Evaluating and Caring for Patients with Suspected E-cigarette, or Vaping, Product Use Associated Lung Injury—United States, October 2019. *MMWR Morb Mortal Wkly Rep*. 2019;68:919–927.

The Centers for Disease Control and Prevention, Food and Drug Administration, and local health departments continue to investigate multistate outbreaks of pulmonary injury associated with use of e-cigarettes or vaping of cannabis, nicotine, or home brew associated products. Prompt recognition of warning signs and transfer of patients for admission or observation may save lives. Patients suspected to have e-cigarette, or vaping, product use-associated lung injury (EVALI) should have a chest radiograph.

Criteria for admission to the hospital may include patients who have a pulse ox of less than 95% on room air, or who are in respiratory distress. Providers should consider the empiric use of a combination of antivirals, antibiotics, or steroids as clinically appropriate and based on clinical context.

As of October 2019, 1,300 cases of EVALI have been reported in the U.S. with 26 deaths; 70% were male; median age was 24; 80% were less than 35 years old and 15% less than 18 years of age.

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The CDC notes that "EVALI is considered a diagnosis of exclusion because, at present, no specific test or marker exists for its diagnosis. Healthcare providers should consider multiple etiologies, including the possibility of EVALI and concomitant infection. In addition, healthcare providers should evaluate alternative diagnoses as suggested by clinical findings and medical history (eg, cardiac, gastrointestinal, rheumatologic, and neoplastic processes; environmental or occupational exposures; or causes of acute respiratory distress syndrome).

Management of Patients with EVALI

Admit to the hospital if patients have a pulse oximetry of less than 95%, if they have respiratory distress, or if they have comorbidities that decrease pulmonary reserve, such as COPD and asthma.

Outpatient treatment can be considered for patients who are clinically stable, and for whom follow-up within 23-48 hours can be assured. Healthcare providers should specifically counsel patients that symptoms can rapidly worsen within 48 hours and that they should call 911 and go to the nearest emergency room if symptoms worsen. Any worsening of symptoms or respiratory distress in the setting of possible EVALI should be referred to the ED.

Community-acquired pneumonia and influenza should be considered for all patients who complain of symptoms related to e-cigarettes due to symptom overlap. Recent guidelines advocate dual antiviral (within 48 hours) and antibiotic therapy for patients with CAP who test positive for influenza.

The CDC noted that empiric evidence points to a potential for clinical improvement with corticosteroids. With one subset of patients reported to the CDC, over 80% showed clinical improvement with glucocorticoids. Treatment should be tailored based on clinical risks/rewards on a case by case basis.

Follow-up

Patients treated for possible EVALI should have a follow-up visit that includes pulse oximetry within 1-2 weeks, and clinicians should consider repeating the chest radiograph. These guidelines contrast with recent updates in guidelines for CAP that do not recommend follow-up chest radiographs. Repeat CXR may be helpful for the continued evaluation of patients with EVALI. Spirometry should be performed within 1-2 months after initial concern for EVALI.

Smoking and e-cigarette/vaping cessation should be emphasized for patients. The CDC urges providers to consider whether the patient has had exposure to vaping during follow-up. Patients who stop vaping may have a more rapid resolution of clinical symptoms, while those who continue to vape, especially in the setting of comorbidities such as cardiopulmonary disease, may experience repeat symptoms or progression of clinical disease requiring admission or intubation.

At this point, the CDC has not identified a common cause of EVALI. It is important for clinicians to know that it is not only THC but possibly nicotine-containing products that cause EVALI, and the safest recommendation is for patients to stop all e-cigarette, vaping, and cigarette use. ■

Another Weapon in Preventing and Minimizing Risk for Influenza

Key point: As flu season intensifies, the FDA has expanded the indication of one medication beyond patients with influenza infection, to include those merely at high risk for infection.

Citation: FDA Approval of Xofluza (Baloxavir Marboxil) for People at High Risk of Developing Influenza-Related Complications. Available at: https://www.gene.com/media/press-releases/14817/2019-10-17/genentech-announces-fda-approval-of-xofl. Accessed October 31, 2019.

The FDA has expanded the indications of Xofluza (baloxavir marboxil) to include patients at high risk of complications from influenza. The initial indication was for the treatment of patients with influenza within the first 48 hours of symptoms. Single-dose Xofluza is the sole antiviral medication indicated for patients at high risk of developing serious complications from flu.

The Centers for Disease Control and Prevention defines people at a high risk of serious flu complications as those with:

- Asthma
- Chronic lung disease
- Heart disease
- Diabetes
- Morbid obesity
- Age 65 years or older

The authors note that the expanded indication for baloxavir follows the CAPSTONE-2 a Phase III multicenter randomized double-blinded trial which evaluated single-dose Xofluza (40 or 80 mg based on weight in kg) in patients 12 and older who have developed symptoms of influenza in the previous 48 hours. The study compared single-dose baloxavir with placebo and with oseltamivir.

"There was an alarming increase in congenital syphilis (22% from 2017 to 2018), resulting in between 77 and 94 deaths, between 2017 and 2018. Incidence of all gonorrhea and chlamydia rose, as well, during that period (though not as dramatically as syphilis did)."

Baloxavir significantly reduced the time to resolution of symptoms in patients at high risk of significant complications from the flu from 102 to about 73 hours ($p<0.001\%$). It is a first-in-class antiviral medication which affects a cap endonuclease and inhibits viral replication. Baloxavir has shown efficacy in oseltamivir-resistant strains and avian strains in nonclinical laboratory studies. Baloxavir is currently being studied in children less than 1 year of age and severely ill hospitalized patients. The ability of baloxavir to reduce the transmission of flu from infected to healthy people is also being assessed. There may be more indications in the future.

Side effects were mild and baloxavir was well tolerated with the main side effects being diarrhea, bronchitis, sinusitis, nausea, and headache. Serious side effects and allergic reactions have occurred, so urgent care providers should advise patients to seek medical attention if serious side effects are noticed; these include:

- Dizziness or lightheadedness
- Throat swelling
- Trouble breathing
- Skin rash or hives

Baloxavir is not indicated for children under 12 or women who are pregnant or breastfeeding. Inform patients that baloxavir can be taken without respect to meals, but should not be taken with dairy products, laxatives, antacids, or foods or beverages containing calcium, iron, selenium, zinc, or magnesium. ■

STDs Continue to Rise, Led by Record Syphilis Infections

Key point: The CDC warns that combined cases of the three most frequently reported sexually transmitted diseases reached an all-time high in the U.S., according to its annual Sexually Transmitted Disease Surveillance Report.

Citation: Centers for Disease Control and Prevention. New

CDC Report: STDs continue to Rise in the U.S. October 8, 2019. Available at: https://www.cdc.gov/nchhstp/newsroom/2019/2018-STD-surveillance-report-press-release.html. Accessed November 8, 2019.

The Centers for Disease Control and Prevention warns that there was an alarming increase in congenital syphilis (22% from 2017 to 2018), resulting in between 77 and 94 deaths, between 2017 and 2018. Incidence of all gonorrhea and chlamydia rose, as well, during that period (though not as dramatically as syphilis did).

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Syphilis

There were 115,000 cases of syphilis reported during the period covered by the report. Primary syphilis presents with a painless sore (a chancre) between 3 weeks and 3 months post infection. This chancre lasts 3 weeks to 6 weeks. The patient still has syphilis if not treated, however. Secondary syphilis presents with fever, lymphadenopathy, joint pain, and a rash involving the palms of the hands and soles of the feet. This has historically been called a "nickel and dime rash." Primary and secondary infections increased by 14%, to over 35,000 cases. This represents the largest number of cases in the U.S. since 1991.

Be prepared to recognize signs and symptoms of syphilis in your clinic. Syphilis has traditionally been called *the great masquerador* due to the nature of the symptoms. Many patients deny any sexual activity and may even refuse testing. In addition, the *Morbidity and Mortality Weekly Report* has reported an increase in methamphetamine, heroin, fentanyl, and other hard drug use in heterosexual patients with syphilis and men-who-have-sex-with-men and have syphilis.

Of paramount importance for physicians, the CDC reports that the number of congenital syphilis cases rose more than 40% to over 1,300 cases. Given that these are confirmed reports, the actual number of cases may be much higher.

The authors note that the national rise in syphilis cases mirrors the national rise in syphilis among women of childbearing age. "The national rise in congenital syphilis parallels increases in syphilis among women of reproductive age. From 2017 to 2018, syphilis cases increased 36% among women of childbearing age. Addressing rising syphilis incidence is critical to prevent congenital syphilis. Women can protect themselves by practicing safer sex, being tested for syphilis by a health care provider, and if infected, seeking treatment immediately and asking her partner to get tested and treated to avoid reinfection."

The World Health Organization states: "Congenital syphilis is the second leading cause of preventable stillbirth globally, preceded only by malaria."

Gonorrhea

Gonorrhea cases grew 5% to more than 580,000 from 2017 to 2018. This is also a record high in the U.S., and the highest number of cases since 1991.

Chlamydia

Chlamydia cases increased 3% to over 1.7 million cases—the most ever reported to the CDC.

Chlamydia can be cured in most cases with a single 1 g oral dose of azithromycin. Many young women are asymptomatic carriers of this infection.

The CDC reminds clinicians that "antibiotics can cure syphilis, gonorrhea, and chlamydia. However, left untreated, STDs can be transmitted to others and produce adverse health outcomes such as infertility, ectopic pregnancy, and increased HIV risk."

General Considerations

The CDC reports that it is essential that women who present to a physicain for the first time about their pregnancy be tested for STDs, including syphilis. Education about STDs, prevention, testing, and treatment are important. The authors note that women who are at high risk should be tested early during the third trimester and at delivery. A simple discussion about the dangers of STDs during pregnancy can be helpful.

Urgent care providers should consider ordering a full STD panel when testing patients for STDs (as opposed to testing only for a specific infection).

The CDC notes that factors behind the increase in STDs include decreased condom use, testing, high risk behaviors, and socioeconomic issues. The CDC encourages all stakeholders to increase testing, treatment, partner treatment, and education of patients to decrease the prevalence of STDs. ■

FDA Reaffirms Stance on NDMA-Containing Products

Key points: The FDA says its recommendations for patients remain unchanged: Patients using OTC ranitidine or nizatidine "can consider" using OTC alternatives, like famotidine or omeprazole. Those using prescription ranitidine or nizatidine should talk with their clinicians about other options.

Citation: Food and Drug Administration. FDA updates and press announcement on NDMA in Zantac (ranitidine). Available at: https://www.fda.gov/drugs/drug-safety-and-avail-

ability/fda-updates-and-press-announcements-ndma-zantac-ranitidine. Accessed November 8, 2019.

The FDA reports that over-the-counter alternatives to ranitidine do not contain traces of N-nitrosdimethylamine (NDMA), a potentially carcinogenic substance. Further, the FDA states that both brand name Zantac and generic products carried by several stores had trace amounts of NDMA and were recalled.

Patients may ask the urgent care provider questions regarding alternatives and FDA claims that no traces of NDMA were found in several alternatives, including:

- Famotadine (Pepcid)
- Cimetidine (Tagamet)
- Esomeprazole (Nexium)
- Omeprazole (Prilosec)
- Lansoprazole (Prevacid)

The FDA submitted an additional news release on November 4, 2019 stating that the amount of NDMA seen in ranitidine products is similar to the amount of NDMA in "common foods like grilled or smoked meats."

An Update on Managing Patients with Nonvariceal UGIB

Key points: Patients with an acute upper gastrointestinal bleed should be transferred to the ED immediately. Patients with hemodynamic instability should receive resuscitation with IV fluids, stat labs, IV proton pump inhibitors and upper endocscopy within 24 hours. Specialist treatment of bleeding foci is described. The group recommends proton pump inhibitors for patients with history of a bleeding ulcer who require antiplatelet therapy or anticoagulation for cardiovascualr disease.

Citation: Barkum AN, Almadi M, Kuipers EJ, et al. Management of nonvariceal upper gastrointestinal bleeding: guideline recommendations from the International Consensus Group. *Ann Intern Med*. October 29, 2019. [Epub ahead of print]

This article represents an update of the 2010 International Consensus Recommendations on the Management of Patients with Nonvariceal Upper Gastrointestinal Bleeding (UGIB). As such, its content is important when evaluating a patient who may not be compliant with follow-up after emergency care for an acute UGIB or with a history of acute UGIB. The expert panel used an iterative approach with regard to the expert panel examining existing guidelines and the analysis of systematic reviews to construct a GRADE (Grading of Recommendations Assessment, Development and Evaluation) based set of guidelines based on PICO (patient population, intervention, comparator, and outcome).

The authors note that, similar to the 2003 and 2010 guidelines, this update focuses on resuscitation and risk assessment; preendoscopic, endoscopic, and pharmacologic management; and secondary prophylaxis for recurrent UGIB.

- For patients with acute UGIB, the group suggests using a Glasgow Blatchford Bleeding Score of 1 or less to identify patients who are at very low risk for rebleeding or mortality and thus may not require hospitalization or inpatient endoscopy.

"The goals of fluid resuscitation are to restore end-organ perfusion and tissue oxygenation while steps are taken to control bleeding."

The Glasgow–Blachford can be utilized on smartphone apps such as MDCALC and involves the systolic blood pressure, tachycardia, factors such as melena, syncope, and CBC/BUN. This score should be calculated using labs; only one or two factors (since some are worth +2 points) are needed to ensure the patient should be hospitalized. If all risk factors are ruled out, the thinking is that the bleed may have spontaneously resolved, however direct visualization with endoscopy is certainly safer for the patient. This system espouses fluid rescuscitation prior to any stratification. The guidelines go on to recommend against using the AIM65B score.

- For patients with acute UGIB and hemodynamic instability, resuscitation should be initiated.
- For the urgent care clinician, the most important guideline is the initiation of IV fluid resuscitation in patients with or who may be developing hemodynamic compromise.

  The authors further note that hemorrhagic shock may lead to multiorgan failure and death. The goals of fluid resuscitation are to restore end-organ perfusion and tissue oxygenation while steps are taken to control bleeding.

  The guidelines go on to recommend a threshold of 8g/dL for transfusions of patient without significant cardiovascular disease but recommend a higher threshold for patients with significant CV disease. They recommend upper endoscopy is not delayed for patients taking anticoagulation.
- The committee recommends upper endoscopy within 24 hours for patients with acute UGIB. The guidelines continue to discuss specialty endocscopy hemostatic recommendations, outside of the scope of the urgent care provider.

  The committee recommends that patients with a previous UGIB taking antiplatelet therapy or anticoagulation receive proton pump inhibitor therapy vs no therapy. ■