ABSTRACTS IN URGENT CARE

- Possible Links Between E-cigarettes and Pulmonary Disease, Neurological Complaints
- Migraine in Pediatric Patients
- HPV Catchup: Now Good Until 2026
- Consider JHR for Symptoms Post Lyme Disease, Syphilis Treatment
- New Lyme Guidelines

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Report Pulmonary Illness Possibly Involving Vaping to State, Local Health Departments

Key point: *The CDC is working with state health departments to characterize severe pulmonary disease in patients who use e-cigarettes, also known as vaping.*

Citations: Centers for Disease Control and Prevention. CDC urges clinicians to report possible cases of unexplained vaping-associated pulmonary illness to their state/local health department. Available at: https://emergency.cdc.gov/newsletters/coca/081619.htm. Accessed September 6, 2019. Caporale A, Langham MC, Wensheng G, et al. Acute effects of electronic cigarette aerosol inhalation on vascular function detected at quantitative MRI. *Radiology*. August 20, 2019. [Epub ahead of print]

The Centers for Disease Control and Prevention is exploring possible links between sudden pulmonary disease and use of e-cigarettes, also known as "vaping," in patients of all ages. Patients in whom vaping should be probed may present with:

- Cough
- Shortness of breath
- Fatigue
- Chest pain
- Fever
- Weight loss
- Diarrhea
- Nausea

The symptoms worsen over a period of days to weeks and have led to admission to the hospital in several cases. No vital sign data were given, but several patients had progressive respiratory compromise leading to mechanical ventilation. No data indicated CPAP/BIPAP were used. Chest radiographs showed bilateral opacities; CT showed ground glass opacities, often with subpleural sparing. No infectious etiologies were noted in almost every case. All patients reported vaping, with several admitting use of THC-containing products. However, no single product was identified as being involved in all cases.

The CDC asks that healthcare providers evaluate cases of pulmonary illness and make sure to ask about a history of vaping. With regard to questions to ask in the history, include:

- Type of products used (commercially available bottles, cartridges, or pods)
- Any illegal drugs used?
- What is the frequency of use?
- What is the exact device used to vape/inhale/smoke?
- Are the products shared with other people?
- Are cartridges reused?
- Are the products heated to concentrate then inhaled (aka "dabbing")?
- Refer *all* patients for tobacco cessation assistance.

The authors note the importance of a full clinical workup (infectious vs other) as indicated per the patient clinical history. Keep a high index of suspicion in cases where vaping is part of the social history. Consider transfer for a higher level of care if concerning symptoms are present, such as shortness of breath, tachypnea, seizures, muscular pain. In severe cases, transfer/admission to the hospital and consultation with pulmonology, infectious disease, and critical care may be indicated.

A report published recently in the journal *Radiology* noted that previous studies have already proven that vaping was related to systemic oxidative stress and inflammation, but no effects on endothelial function were noted prior to their study.

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The authors stated that after only one dose of vaping without nicotine, endothelial function in nonsmokers was affected, including changes in the resistivity index, luminal flow, and other parameters showing immediate early effects on blood vessels. The authors note further studies are needed to understand the physiologic stress induced by vaping.

News surrounding use of e-cigarettes continues to evolve, with hundreds of cases across the country. Fatalities have been reported.

Finally, pass along to patients that the FDA advises not to vape at all—especially, products with THC oil and vitamin E ecetate (though no one common ingredient has been identified across case reports). ■

FDA Alert: Seizures and Respiratory Distress from Vaping

Key point: The FDA is seeking help from clinicians in evaluating whether there is a link between e-cigarette use and seizures.

Citation: FDA In Brief: FDA encourages continued submission of reports related to seizures following e-cigarette use as part of agency's ongoing scientific investigation of potential safety issue. August 7, 2019. Available at: https://www.fda.gov/news-events/fda-brief/fda-brief-fda-encourages-continued-submission-reports-related-seizures-following-e-cigarette-use. Accessed September 5, 2019.

Patients who use e-cigarettes ("vaping") are presenting to urgent care centers and emergency departments with neurological symptoms and seizures. The FDA encourages submission of case reports from providers who see patients with these symptoms, and recommends that healthcare providers ask patients presenting with neurological symptoms about e-cigarette use.

To date, the agency has received 127 reports of serious neurological symptoms related to vaping going back to 2010. The data do not necessarily indicate such symptoms are increasing in prevalence or frequency compared with the population at large, though the FDA is investigating the issue.

Reported neurological symptoms after vaping include tremors or syncope not related to epileptiform activity. Most such reports have been in younger patients.

Urgent care providers are urged to file a report when they encounter such presentations. Go to www.fda.gov and enter "safety portal" in the search engine in the upper right corner of the screen. The FDA is specifically interested in the brand name and how the product (eg, for what purpose) was used. It is important to include the patient's past medical history, medications, other risk factors. In addition, the agency suggests that you consider testing for levels of cotinine, a nicotine metabolite, in addition to typical urine toxicology screening tests.

It is important for the urgent care provider to synthesize knowledge of the recent reports of potential neurological side effects of vaping to recent reports of respiratory distress and pulmonary complications, and updates on nicotine overdose. Vaping additives have come under scrutiny. ■

"Serologic testing for Lyme disease is often negative when a patient presents with erythema migrans tested before seroconversion. Seroconversion can be tested after antibiotic treatment."

Weighing the Available Options for Pediatric Patients with Migraine

Key point: Migraine is a chronic disorder with spontaneous remissions and relapses.

Citation: Oskoui M, Pringsheim T, Billinghurst L, et al. Practice guideline update summary: pharmacologic treatment for pediatric migraine prevention. *Neurology*. 2019;93(11):500-509.

This practice guideline update by the journal *Neurology* examines a plethora of clinical trials studying migraine prevention in children ages 3-18. The incidence of migraines in children 1-7 years of age is around 1% to 11% and rises up to the range of 8% to 23% by age 15. Many of the studies fail to show noninferiority of preventative treatment to placebo in clinical trials. The study systematically examines whether preventative pharmacologic treatments with and without cognitive behavioral therapy (CBT) show efficacy in reduction in headache frequency compared with placebo.

Methods involved applying the American Academy of Neurology's 2011 evidence-based methodology to determine risk ratios (RR) of >1.25% compared with placebo to be significant. Interventions with a RR of 1.10 or less were seen as insignificant.

Most children with a diagnosis of migraine disorder benefit from acute treatments and behavioral/lifestyle modification and do not require more robust preventative methods.

When headache frequency does not improve, or other red flags are present, the Pediatric Migraine Disability Assessment (PedMIDAS) is a validated six-question test examining disability related to migraines over a 3-month period.

Ibuprofen is the preferred treatment in the pediatric population with migraines. Treatment given earlier in the episode has higher efficacy. Pediatric patients with migraines can also take triptans. Amitriptyline (Elavil) and CBT were superior to amitriptyline and headache education in adolescents (high confidence in data 4 Class I studies). Topiramate (Topamax) is the only FDA-indicated drug for migraine prevention in kids 13 to 17 years of age. There is concern it may be no better than placebo

in achieving a 50% reduction, although there is moderate confidence it can decrease the frequency of migraines overall. The study notes that patients should be counseled on the teratogenic effects of topiramate. Also teach patients about limits of drug use—ibuprofen no more than 14 days in a month, triptans no more than 9 days per month, etc. Taking medications over these limits can lead to medication overuse headache. ■

More Evidence Supporting Wider HPV Immunization

Key point: The authors note that vaccination against HPV is given to prevent HPV infection and associated conditions, including some cancers.

Citation: Meites E, Szilagyi PG, Chesson HW, et al. Human papillomavirus vaccination for adults: updated recommendations of the Advisory Committee on Immunization Practices. *MMWR Morb Mortal Wkly Rep*. 2018;68(32):698-702.

Routine vaccination against human papillomavirus (HPV) is given at 11 to 12 years of age, but may begin at age 9. Patients less than 15 years of age require 2 vaccinations (0, 6-12 mo). Patients over 15 years of age need 3 vaccinations (0, 1-2, 6-month schedule). New evidence prompted the Advisory Committee on Immunization Practices to recommend HPV vaccine catchup until age 26 in both women, men, and special populations.

Urgent care providers commonly screen and treat patients for STDs. HPV is a common sexually transmitted disease which is frequently asked about by patients in the urgent care center. Infection is usually acquired during first sexual activity. HPV infection is usually brief and asymptomatic. Most young sexually active people and most sexually active adults have been exposed and infected with HPV.

It is important to counsel patients that they can get a new infection with HPV with each sexual partner.

The authors note that If a patient is infected with an oncogenic strain of HPV, it can lead to several types of cancer including cervical, vaginal, vulvar, oropharyngeal, anal and penile cancers usually decades after infection.

Gardasil 9, 9vHPV is the only HPV vaccine currently distributed in the United States.

This updated set of recommendations reminds healthcare providers that vaccination will be most effective in young patients under age 15 and most effective before sexual activity, but you can protect your patients from acquiring new, potential oncogenic strain infections safely and effectively with this vaccine. ■

Symptoms After Treatment for Syphilis or Lyme Disease? Consider Jarish-Herxheimer Reaction

Key point: Jarish-Herxheimer Reaction should be suspected in patients treated for syphilis or Lyme disease who return to clinic or call complaining of fever, shaking chills, myalgias, dizziness, facial flushing. It is not an antibiotic allergy.

Citations: Roberts JR. An unusual reaction to antibiotic treatment of spirochetal infections. Roberts JR. *Emerg Med News*. 2019;41(8):16-17.

Butler T. The Jarisch-Herxheimer reaction after antibiotic treatment of spirochetal Infections: A Review of Recent Cases and Our Understanding of the Pathogenesis. *Am J Trop Med Hyg*. 2017;96(1):46.

Jarish-Herxheimer Reaction (JHR) should be suspected in patients treated for syphilis or Lyme disease who return to clinic or call complaining of fever, shaking chills, myalgias, dizziness, or facial flushing. It is *not* an antibiotic allergy. Patients appear very toxic. The reaction is short-lived but mimics more serious conditions, so be careful not to overreact. The JHR reaction is indicative of successful antibiotic treatment.

Treatment of syphilis with penicillin G now the most common cause of a JHR (50%-90% of patients). Patients with Lyme treated with doxycycline may also develop JHR (15-20%).

The author of the *Emergency Medicine News* article notes that that physicians tend to see nowhere near this rate of JHR, so the epidemiology may be questionable; still, the ability and concern to suspect this reaction needs to be reinforced as infections with syphilis are on the rise, as are tick-borne diseases, according to the CDC.

The urgent care clinician may also benefit from reading the 2017 article in the *American Journal of Tropical Medicine and Hygiene*, which discusses JHR in the context of antibiotic treatment for spirochetal infections such as syphilis, Lyme disease, leptospirosis, and relapsing fever.

The exact pathogenesis of the JHR is unknown. As the immune system responds to the spirochetal infection and increases phagocytosis of the spirochetes, spirochetal lipoprotein and non-endotoxin pyrogens are released. Pro-inflammatory cytokines are also released from leukocytes during the JHR.

JHR develops 2-6 hours after antibiotic treatment and may mimic antibiotic allergy or sepsis, so observation for 12-24 hours is not unreasonable. The article mentions that patients with mild symptoms can be sent home, however. Patients may experience a transient worsening of the rash. At the other end of the spectrum, patients with severe reactions have rarely required intubation and mechanical ventilation but the incidence of this is rare and may be due to underlying pathology. ■

Updated Lyme Disease Guidelines Shed More Light on Prevention, Testing, and Treatment

Key point: Nonspecific symptoms that persist after the recommended course of treatment has concluded do not necessarily warrant additional antibiotics.

Citation: Lantos P, Rumbaugh J, Bockenstedt L, et al. Draft Clinical Guidelines by the Infectious Diseases Society of America (IDSA), American Academy of Neurology (AAN), and American College of Rheumatology (ACR): 2019 Guidelines for the Prevention, Diagnosis and Treatment of Lyme Disease. Available at: https://view.protectedpdf.com/ad6GFZ. Accessed September 4, 2019.

In 2017, the last year for which the Centers for Disease Control and Prevention has published data, a total of 42,743 confirmed and probable cases of Lyme disease were reported—an increase of 17% from 2016. This rate of growth speaks to the need not just for current recommendations on treating patients with confirmed Lyme disease, but also on testing patients who *may* have Lyme disease, as well as prevention.

Given the fact that many patients may experience a tick bite while on vacation—and far away from their primary care provider—it is likely that urgent care providers will see a growing number of affected patients. Of particular note for this audience is that serologic testing for Lyme disease is often negative when a patient presents with erythema migrans tested before seroconversion. Seroconversion can be tested after antibiotic treatment using tiered immunoassays and does not require Immunoblot.

The use of a second immunoassay is a new feature of the guidelines. For prevention, the guidelines suggest that doxycycline (200 mg for adults, 4.4 mg/kg for children up to a maximum of 200 mg) be administered within 72 hours of a tick bite, provided that the tick is of the Ixodes variety; is found in an area endemic for Lyme disease; is engorged; and has been attached for 36 hours. For patients with early localized disease, a 10-day course of doxycycline, a 14-day course of amoxicillin or cefuroxime, or a 7-day course of azithromycin is recommended.

Pregnant patients should have a risk/benefit discussion with their physician with regard to treatment.

Of particular note for urgent care providers is that additional antibiotics are not recommended for patients who follow up after the recommended course of treatment with nonspecific persistent symptoms such as pain or fatigue without evidence of reinfection or treatment failure. Routine testing is not indicated for patients with mental illness. ■