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TO:	Health Alert Network
FROM:	Rachel Levine, MD, Secretary of Health
SUBJECT:	Severe Pulmonary Disease Associated with Using E-Cigarette Products
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This transmission is a “Health Advisory” provides important information for a specific incident or situation; may not require immediate action.

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The Pennsylvania Department of Health (DOH) is forwarding the following advisory to healthcare providers, “**Severe Pulmonary Disease Associated with Using E-Cigarette Products**” from the Centers for Disease Control and Prevention (CDC).

This is an official
CDC HEALTH ADVISORY

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Severe Pulmonary Disease Associated with Using E-Cigarette Products

Summary

The Centers for Disease Control and Prevention (CDC) is providing: 1) background information on the forms of e-cigarette products, 2) information on the multistate outbreak of severe pulmonary disease associated with using e-cigarette products (devices, liquids, refill pods, and cartridges), and 3) clinical features of patients with severe pulmonary disease. This health advisory also provides recommendations for clinicians, public health officials, and the public based on currently available information.

General Background

E-cigarettes typically contain nicotine, most also contain flavorings and other chemicals, and some may contain marijuana or other substances. They are known by many different names and come in many shapes, sizes and device types. Devices may be referred to as “e-cigs,” “vapes,” “e-hookahs,” “vape pens,” “mods,” tanks, or electronic nicotine delivery systems (ENDS). Some e-cigarette devices resemble other tobacco products such as cigarettes; some resemble ordinary household items such as USB flash drives, pens, and flashlights; and others have unique shapes. Use of e-cigarettes is sometimes referred to as “vaping” or “juuling.” E-cigarettes used for dabbing are sometimes called “dab” pens.

E-cigarettes can contain harmful or potentially harmful substances, including nicotine, heavy metals (e.g., lead), volatile organic compounds, and cancer-causing chemicals. Additionally, some e-cigarette products are used to deliver illicit substances; may be acquired from unknown or unauthorized (i.e., “street”) sources; and may be modified for uses that could increase their potential for harm to the user. For example, some e-cigarette pods or cartridges marketed for single use can be refilled with illicit or unknown substances. In addition, some e-cigarette products are used for “dripping” or “dabbing.” Dripping involves dropping e-cigarette liquid directly onto the hot coils of an e-cigarette which can result in high concentrations of compounds (e.g., tetrahydrocannabinol [THC] and cannabinoid compounds). Dabbing involves superheating substances such as “budder”, butane hash oil (BHO), and “710” that contain high concentrations of THC and other plant compounds (e.g., cannabidiol [CBD]).

Youth, young adults, pregnant women, as well as adults who do not currently use tobacco products should not use e-cigarettes. E-cigarettes containing nicotine have the potential to help some individual adult smokers reduce their use of and transition away from cigarettes. However, e-cigarettes are not currently approved by the Food and Drug Administration (FDA) as a quit smoking aid, and the available science is inconclusive on whether e-cigarettes are effective for quitting smoking.

Outbreak Background

As of August 27, 2019, 215 possible cases have been reported from 25 states and additional reports of pulmonary illness are under investigation. One patient (in Illinois) with a history of recent e-cigarette use was hospitalized on July 29, 2019 with severe pulmonary disease and died on August 20, 2019. Although the etiology of e-cigarette-associated pulmonary disease is undetermined, epidemiologic investigations in affected states are ongoing to better characterize the exposures, demographic, clinical, and laboratory features and behaviors of patients. All patients have reported using e-cigarette products. The exact number is currently unknown, but many patients have reported using e-cigarettes containing cannabinoid products such as THC or CBD.

Based on reports from several states, patients have experienced respiratory symptoms (cough, shortness of breath, or chest pain), and some have also experienced gastrointestinal symptoms (nausea, vomiting, or diarrhea) or non-specific constitutional symptoms (fatigue, fever, or weight loss). Symptoms typically develop over a period of days but sometimes can manifest over several weeks. Gastrointestinal symptoms sometimes preceded respiratory symptoms. Fever, tachycardia, and elevated white blood cell count have been reported in the absence of an identifiable infectious disease. Many patients have sought initial care in ambulatory settings, some with several visits, before hospital admission.

Radiologic findings have varied and are not present in all patients upon initial presentation.

Bilateral pulmonary infiltrates and diffuse ground-glass opacities have been reported. Many patients required supplemental oxygen, some required assisted ventilation and oxygenation, and some were intubated. Some patients have been treated with corticosteroids with demonstrated improvement. Antimicrobial therapy alone has not consistently been associated with clinical improvement. Assessment for infectious etiologies has been completed in many patients without an identified infectious cause. Several patients from one state have been diagnosed with lipoid pneumonia based on clinical presentation and detection of lipids within bronchoalveolar lavage samples stained specifically to detect oil.

All patients have reported using e-cigarette products and the symptom onset has ranged from a few days to several weeks after e-cigarette use. Within two states, recent inhalation of cannabinoid products, THC or cannabidiol, have been reported in many of the patients. To date, no single substance or e-cigarette product has been consistently associated with illness. CDC is working closely with state health departments to facilitate collecting product specimens for testing at the U.S. FDA Forensic Chemistry Center.

Recommendations for Clinicians

1. Report cases of severe pulmonary disease of unclear etiology and a history of e-cigarette product use within the past 90 days to your state or local health department. Reporting of cases may help CDC and state health departments determine the cause or causes of these pulmonary illnesses.
2. Ask all patients who report e-cigarette product use within the last 90 days about signs and symptoms of pulmonary illness.
3. If e-cigarette product use is suspected as a possible etiology of a patient's severe pulmonary disease, obtain detailed history regarding:
 - Substance(s) used: nicotine, cannabinoids (e.g., marijuana, THC, THC concentrates, CBD, CBD oil, synthetic cannabinoids [e.g., K2 or spice], hash oil, Dank vapes), flavors, or other substances
 - Substance source(s): commercially available liquids (i.e., bottles, cartridges, or pods), homemade liquids, and re-use of old cartridges or pods with homemade or commercially bought liquids
 - Device(s) used: manufacturer; brand name; product name; model; serial number of the product, device, or e-liquid; if the device can be customized by the user; and any product modifications by the user (e.g., exposure of the atomizer or heating coil)
 - Where the product(s) were purchased
 - Method of substance use: aerosolization, dabbing, or dripping
 - Other potential cases: sharing e-cigarette products (devices, liquids, refill pods, or cartridges) with others
4. Determine if any remaining product, including devices and liquids, are available for testing. Testing can be coordinated with the local or state health departments.
5. Consider all possible causes of illness in patients reporting respiratory and gastrointestinal symptoms and of e-cigarette product use. Evaluate and treat for other possible causes of illness (e.g., infectious, rheumatologic, neoplastic) as clinically indicated. Consider consultation with specialists (pulmonary, infectious disease, critical care, medical toxicology) as appropriate.
6. Clinical improvement of patients with severe pulmonary disease associated with e-cigarette use has been reported with the use of corticosteroids. The decision to use corticosteroids

should be made on a case-by-case basis based on risks and benefits and the likelihood of other etiologies.

7. Lipoid pneumonia associated with inhalation of lipids in aerosols generated by e-cigarettes has been reported based on the detection of lipid-laden alveolar macrophages obtained by bronchoalveolar lavage (BAL) and lipid staining (e.g., oil red O). The decision about whether to perform a BAL should be based on individual clinical circumstances.
8. Lung biopsies have been performed on some patients. If a lung biopsy is obtained, lipid staining may be considered during pathologic examination, and is best performed on fresh tissue. Routine pathology tissue processing (including formalin-fixation and paraffin-embedding) can remove lipids. Conducting routine tissue processing and histopathologic evaluation is still important. Consider consultation with specialists in pulmonary medicine and pathology to help inform any evaluation plan.
9. Patients who have received treatment for severe pulmonary disease related to e-cigarette product use should undergo follow-up evaluation as clinically indicated to monitor pulmonary function.

Recommendations for Public Health Officials

1. State public health officials should promptly notify CDC about possible cases via VapingAssocIllness@cdc.gov.
2. Contact CDC at VapingAssocIllness@cdc.gov for case classification criteria, reporting guidelines, case investigation forms, and questions about this outbreak.
3. Consider conducting case-finding activities that use existing data sources (e.g., local poison control center, coroner and medical examiner's office, and other applicable surveillance systems including syndromic surveillance). CDC has developed two working syndromic surveillance definitions (one version with specific symptoms and a second focused on e-cigarette product use). CDC will be programming these definitions in CDC's National Syndromic Surveillance Program's BioSense/ESSENCE platform for case-finding within the platform.
4. Consider asking the medical examiner or coroner's office and other pathologists to report possible cases, especially those without an alternative, likely diagnosis. If individuals are identified after death or at autopsy who showed signs of severe pulmonary disease as described above, medical examiners and coroners are encouraged to report the cases to their local or state health department. Thorough sampling of trachea, bronchi, and lung parenchyma with collection of fresh lung tissue for staining of lipids (e.g., oil red O) and submission of formalin-fixed, paraffin-embedded tissues for routine histopathology are recommended. For further consultation, public health officials can contact CDC's Infectious Diseases Pathology Branch at pathology@cdc.gov.
5. State health department officials seeking technical assistance with an epidemiologic investigation can contact CDC at VapingAssocIllness@cdc.gov. State health department officials seeking technical assistance with laboratory testing can discuss with their state health department laboratories or contact CDC at VapingAssocIllness@cdc.gov.

Recommendations for the Public

1. While this investigation is ongoing, if you are concerned about these specific health risks, consider refraining from using e-cigarette products.
2. Regardless of the ongoing investigation, anyone who uses e-cigarette products should not buy these products off the street (e.g., e-cigarette products with THC, other cannabinoids)

and should not modify e-cigarette products or add any substances to these products that are not intended by the manufacturer.

3. Regardless of the ongoing investigation, e-cigarette products should not be used by youth, young adults, pregnant women, as well as adults who do not currently use tobacco products. If you use e-cigarette products, monitor yourself for symptoms (e.g., cough, shortness of breath, chest pain) and promptly seek medical attention if you have concerns about your health. CDC and FDA will continue to advise and alert the public as more information becomes available.
4. Adult smokers who are attempting to quit should use evidence-based treatments, including counseling and FDA-approved medications. If you need help quitting tobacco products, including e-cigarettes, contact your doctor.
5. If you are concerned about harmful effects from e-cigarette products, call your local poison control center at: 1-800-222-1222.
6. We encourage the public to submit detailed reports of any unexpected tobacco or e-cigarette-related health or product issues to the FDA via the online Safety Reporting Portal: <https://www.safetyreporting.hhs.gov>.

For More Information

- For assistance with managing patients suspected of illness related to recreational, illicit, or other drugs, call your local poison control center at: 1-800-222-1222.
- Information on electronic cigarettes and similar devices: <https://www.cdc.gov/e-cigarettes>
- CDC Press Statement: <https://www.cdc.gov/media/releases/2019/s0821-cdc-fda-states-e-cigarettes.html>
- CDC Clinical Outreach and Communication Activity announcement: <https://emergency.cdc.gov/newsletters/coca/081619.htm>
- CDC's National Syndromic Surveillance Program's BioSense/ESSENCE: <https://www.cdc.gov/nssp/index.html>
- For more information, visit CDC Info: <https://www.cdc.gov/cdc-info/index.html>

References

- Barrington-Trimis JL, Samet JM, McConnell R. Flavorings in electronic cigarettes: an unrecognized respiratory health hazard? *JAMA*. 2014;312(23):2493-4. <https://jamanetwork.com/journals/jama/fullarticle/1935097>
- Behar RZ, Davis B, Wang Y, Bahl V, Lin S, Talbot P. Identification of toxicants in cinnamon-flavored electronic cigarette refill fluids. *Toxicol In Vitro*. 2014;28(2):198-208. <https://www.ncbi.nlm.nih.gov/pubmed/24516877>
- Flower M, Nandakumar L, Singh M, Wyld D, Windsor M, Fielding D. Respiratory bronchiolitis-associated interstitial lung disease secondary to electronic nicotine delivery system use confirmed with open lung biopsy. *Respirol Case Rep*. 2017;5(3):e00230. <https://onlinelibrary.wiley.com/doi/full/10.1002/rcr2.230>
- Gerloff J, Sundar IK, Freter R, Sekera ER, Friedman AE, Robinson R, et al. Inflammatory Response and Barrier Dysfunction by Different e-Cigarette Flavoring Chemicals Identified by Gas Chromatography-Mass Spectrometry in e-Liquids and e-Vapors on Human Lung

Epithelial Cells and Fibroblasts. Appl In Vitro Toxicol. 2017;3(1):28-40.
<https://www.liebertpub.com/doi/10.1089/aivt.2016.0030>

He T, Oks M, Esposito M, Steinberg H, Makaryus M. "Tree-in-Bloom": Severe Acute Lung Injury Induced by Vaping Cannabis Oil. Ann Am Thorac Soc. 2017;14(3):468-70.
<https://www.atsjournals.org/doi/10.1513/AnnalsATS.201612-974LE>

Khan MS, Khateeb F, Akhtar J, Khan Z, Lal A, Kholodovych V, et al. Organizing pneumonia related to electronic cigarette use: A case report and review of literature. Clin Respir J. 2018;12(3):1295-9. <https://onlinelibrary.wiley.com/doi/abs/10.1111/crj.12775>

Kosmider L, Sobczak A, Prokopowicz A, Kurek J, Zaciera M, Knysak J, et al. Cherry-flavoured electronic cigarettes expose users to the inhalation irritant, benzaldehyde. Thorax. 2016;71(4):376-7. <https://thorax.bmj.com/content/71/4/376>

The Centers for Disease Control and Prevention (CDC) protects people's health and safety by preventing and controlling diseases and injuries; enhances health decisions by providing credible information on critical health issues; and promotes healthy living through strong partnerships with local, national, and international organizations.

Categories of Health Alert messages:

Health Alert: conveys the highest level of importance; warrants immediate action or attention.

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Health Update: provides updated information regarding an incident or situation; unlikely to require immediate action.

This information is current as of September 3, 2019 but may be modified in the future.