

Letters to the Editor

Differential Diagnosis of Muscle Weakness in Adults

Original Article: Muscle Weakness in Adults: Evaluation and Differential Diagnosis

Issue Date: January 15, 2020

Available online at: <https://www.aafp.org/afp/2020/0115/p95.html>

To the Editor: We read this article with interest. The authors concluded that if the cause of muscle weakness remains elusive, a muscle biopsy or consultation with a specialist may be necessary to reach the correct diagnosis. However, other possible etiologies should be added to the differential diagnosis.

Because lactic acidosis can cause muscle weakness, we recommend obtaining serum or cerebrospinal fluid lactate levels. If resting lactate is normal but lactic acidosis is still suspected, a lactate stress test should be performed.¹ In patients with a subclinical or mildly manifesting mitochondrial disorder, the lactate stress test may reveal lactate elevations with mild exercise that are below the normal lactate threshold.

Pituitary insufficiency is another cause of muscle weakness.² Thus, it is important to determine hormone levels, particularly those produced in the pituitary gland. Reduced production of pituitary hormones may lead not only to short stature or hypothyroidism but also to hypogonadism or hypocorticism. Low levels of gonadotropic hormones, glucocorticoids, or mineralocorticoids may lead to severe muscle weakness with or without hypotonia.

Muscle weakness in adults may also be caused by reduced extraction of oxygen from the arterial blood.³ To assess if the muscle weakness is from hypooxygenation of the skeletal muscle, it is crucial to determine the oxygen concentration in the venous blood or measure the oxygen extraction fraction using magnetic resonance imaging. The

muscle will be unable to use arterial oxygen properly if functions of respiratory chain complexes are impaired or if the oxidative phosphorylation is disrupted.

In patients with subclinical myopathy, general or local anesthetics or muscle relaxants may trigger muscle weakness postintervention.⁴ Obstructive or restrictive sleep apnea syndrome may be associated with severe daytime fatigue and muscle weakness. Thus, all patients with undiagnosed muscle weakness and fatigue should undergo testing for sleep apnea syndrome. Wilson disease is another rare cause of muscle weakness, which can be diagnosed with serum copper levels.⁵

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In Reply: We appreciate Dr. Finsterer's close reading of our manuscript and his attention to detail. Although we wish that we could have written an article on the diagnostic evaluation of muscle weakness that was all-inclusive, our perspective was that of the family physician and the

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This series is coordinated by Kenny Lin, MD, MPH, deputy editor.

typical office evaluation for this presentation. We certainly considered discussing invasive and specialized testing methods for the evaluation of weakness, but most family physicians would not have access to or familiarity with some of the tests Dr. Finsterer suggests. For this reason, we recommend specialty referral after completing a reasonably thorough primary care evaluation.

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Skin Disorders in Patients with Skin of Color

Original Article: Erythema Multiforme: Recognition and Management

Issue Date: July 15, 2019

See additional reader comments at: <https://www.aafp.org/afp/2019/0715/p82.html>

To the Editor: The article by Drs. Trayer, Love, and Studdiford was informative and well written. However, it was unclear from the article if erythema multiforme presents differently in patients with skin of color. Are the lesions erythematous, hyper-, or hypopigmented? I needed to search my *Atlas of African Dermatology* to find that one presentation of erythema multiforme was target lesions composed of different shades of brown.¹ This information gap highlights a broader issue in medical education. A 2006 analysis found limited and inconsistent coverage of skin conditions in skin of color in textbooks and at national dermatology meetings.² This disparity applies to most dermatologic conditions, including skin cancer. A recent article about the disparities in outcomes of patients with melanoma suggested that the “disproportionately high melanoma mortality rates in patients with skin of color may be driven by a lack of representation and data in awareness campaigns, in clinical research, and in the field of dermatology itself.”³ By 2060, more than one-half of the population is projected to belong to a minority group.⁴ Family physicians must learn how dermatologic conditions present in skin of color to serve our increasingly diverse patient population better and to avoid incorrect or delayed diagnoses. Any article about dermatologic disorders in *American Family Physician (AFP)* must include how the skin disorder presents in skin of color. If there is no available information about the presentation, then that should be noted.

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In Reply: We thank Drs. Irwin and Crawford-Faucher for pointing out that the lesions of erythema multiforme present differently in skin of color. We agree that, whenever possible, review articles about skin conditions should include examples of the condition in skin of color. Unfortunately, suitable, noncopyrighted photos of sufficient resolution for publication are not always available. For further information, readers may wish to consult *AFP's* previous two-part article on dermatologic conditions in skin of color.^{1,2}

Kenny Lin, MD, MPH

Deputy Editor

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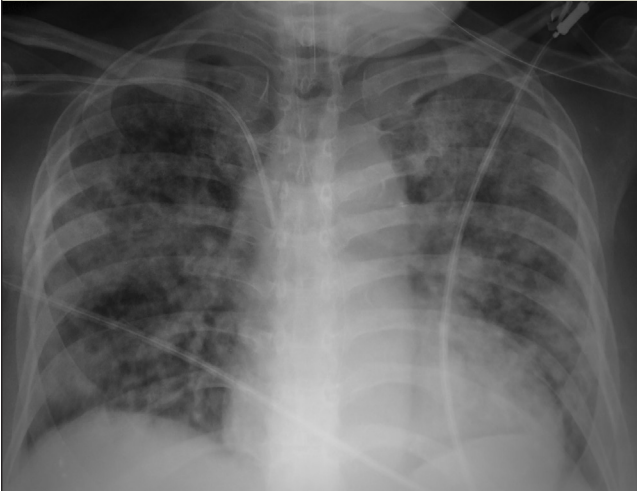
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Case Report: Flavored Vaping–Associated Hypokalemia

To the Editor: Electronic cigarette (e-cigarette) or vaping product use–associated lung injury (EVALI) is an emerging public health epidemic.¹ The pathogenesis and natural history are still unknown despite a series of cases that have been reported in the United States.² Vitamin E acetate and tetrahydrocannabinol (THC) have been proposed as the cause of the lung injury.³ Deaths have been reported; however, extrapulmonary manifestations and the degree of residual lung damage in survivors is still unclear.

A 51-year-old woman who was vaping flavored nicotine e-cigarettes for 18 months for smoking cessation presented with acute breathlessness, bilateral diffuse alveolar opacities on chest radiography (*Figure 1*), and a partial pressure of arterial oxygen to fraction of inspired oxygen of 48. Her history of vaping, acute respiratory distress syndrome (ARDS), negative septic and autoimmune profiles, and normal cardiac and renal functions satisfied current diagnostic criteria for EVALI.² Her serum potassium level was 2.2 mEq per L (2.2 mmol per L). Plasma renin and aldosterone levels

FIGURE 1



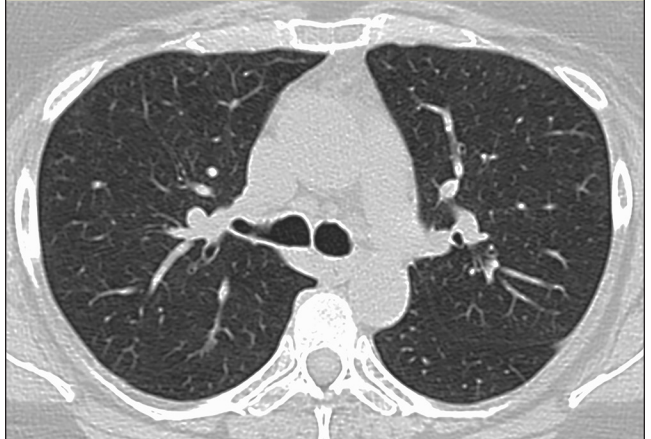
Bilateral alveolar opacities on chest radiography at initial presentation.

FIGURE 2



Interlobular and intralobular septal thickening with architectural distortion on computed tomography three weeks after initial presentation.

FIGURE 3



Normal lung parenchyma on computed tomography four years after initial presentation.

were within normal limits. Hypokalemia was refractory for seven days despite potassium supplementation. After seven days of mechanical ventilation and empiric broad-spectrum antibiotic therapy, the patient was successfully weaned off ventilatory support. High-resolution computed tomography of the chest three weeks later showed interlobular and intralobular septal thickening with architectural distortion consistent with a late or fibrotic phase of ARDS (*Figure 2*), which subsequently normalized (*Figure 3*). Clinical normalization occurred at 12 weeks, and further progress was

uneventful. The patient stopped vaping, and subsequent serum potassium levels remained normal for four years after her acute presentation of EVALI.

Persistent profound hypokalemia without any other distinct risk factors suggests a link to the licorice flavoring in vaping. Ingestion of glycyrrhizic acid, the active ingredient in licorice, is known to cause hypokalemia through a mineralocorticoid effect by inhibition of renal 11 beta-hydroxysteroid dehydrogenase.⁴ Hypokalemia caused by inhalation has been reported in a single study.⁵ Flavoring chemicals such as methyl and ethyl salicylates have been shown to cause hypokalemia when ingested. Hypokalemia caused by vaping has not been previously reported. More research on flavors in tobacco products and e-liquids is needed.

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Importance of Appropriate Diagnosis Before Prescribing Corticosteroids

Original Article: Short-Term Systemic Corticosteroids: Appropriate Use in Primary Care

Issue Date: January 15, 2020

See additional reader comments at: <https://www.aafp.org/afp/2020/0115/p89.html>

To the Editor: As a researcher and family physician, I was pleased to see the article by Drs. Dvorin and Ebell reminding physicians of the importance of weighing the risks and benefits of prescribing short-term systemic corticosteroids. In the article, the authors suggest that there may be evidence for treating acute bronchitis with short-term systemic corticosteroids in the context of asthma or chronic obstructive pulmonary disease (COPD). I would like to elaborate on that statement.

In the context of asthma or COPD, acute bronchitis is likely to represent an exacerbation of asthma or COPD, which is indeed an indication for a short course of oral corticosteroids.^{1,2} Acute bronchitis is not an indication and is likely not the correct diagnosis when a patient has been correctly diagnosed with asthma or COPD. Some may say this is simply a difference in terminology, but it is not. The frequency and severity of asthma or COPD exacerbations are important when selecting appropriate maintenance treatment for those conditions,^{1,2} and calling the events acute bronchitis may lead to failure to recognize the importance of recurrent events in the context of chronic obstructive lung diseases.

In addition to correct diagnostic labeling, asthma and COPD exacerbations are often recurrent and therefore may require multiple short courses of systemic corticosteroids over one or more years, elevating the patient's risks above those experienced from a single short course. Therefore, in addition to thinking about the risks of prescribing one

short-term course, consider the risks of prescribing recurrent short-term courses and periodically reevaluate the adequacy of the underlying disease treatment.

Thank you for the reminder to physicians to use systemic corticosteroids appropriately, and please use appropriate diagnostic labels when prescribing those corticosteroids.

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In Reply: Thank you for your thoughtful response. In our review, we chose to focus on conditions in which a clear consensus for the role of systemic corticosteroids has not been achieved (unlike asthma, COPD, and other chronic inflammatory conditions in which a clear role for steroids occurs). One of our recent publications showed a high level of inappropriate systemic steroid use for patients with acute respiratory tract infections, even after excluding patients with asthma, COPD, and other inflammatory conditions in which steroids may be indicated,¹ which further highlights the importance of quality improvement in appropriate steroid use.

We agree with you that for a patient with asthma and/or COPD who presents with symptoms consistent with an exacerbation of their underlying disease process, it would be more appropriate to diagnose an exacerbation of that process as opposed to bronchitis.

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