Case Management Study
Walter Reed Army Medical Center

Fatigue, Sore Throat, and Cough in a 24-Year-Old Active Duty Man

Guarantor: CPT Joshua D. Hartzell, MC
Contributors: CPT Joshua D. Hartzell, MC*; LTC Michael J. Roy, MC†

A 24-year-old active duty male smoker presented with 3 days of fatigue, rhinorrhea, and sore throat. The diagnosis and management of pharyngitis, including a field friendly approach, are reviewed. The impact of the discontinuation of the adenovirus vaccine to military recruits is highlighted. The effects of smoking among military personnel are discussed, and smoking cessation measures are reviewed.

Introduction

A 24-year-old active duty E-3 Caucasian male presented to the General Internal Medicine Clinic at Walter Reed Army Medical Center (WRAMC). Three days previous, the patient noticed rhinorrhea, a sore throat, and a nonproductive cough, but denied shortness of breath, headache, rash, fever, or chills. The symptoms continued for the next 2 days with little improvement. The patient had not tried any over-the-counter cold relief agents or analgesics.

1. Based on the given information, what is the most likely etiology of this patient’s symptomatology?
   a. Viral upper respiratory infection (URI)
   b. Group A β-hemolytic streptococcus (GABHS)
   c. Infectious mononucleosis (Epstein-Barr virus)
   d. Human immunodeficiency virus (HIV)
   e. Neisseria gonorrhoea

Young active duty soldiers with nasal congestion, sore throat, and cough are most likely to be suffering from a viral URI.1 This is especially true in new recruits where adenovirus can be responsible for up to 70% of patients with this set of symptoms. The U.S. military previously vaccinated new recruits against adenovirus, until 1999, when Wyeth Lederle stopped producing the vaccine.2 After the discontinuation of immunization, adenovirus has rapidly reemerged as the leading cause of febrile respiratory illnesses among recruits, and further epidemics are anticipated.2 Consequently, physicians will encounter a higher prevalence of adenovirus infections, making the correct diagnosis of streptococcal pharyngitis, and the decision of when to prescribe antibiotics, more challenging. In addition to adenovirus, there are numerous other viruses that can cause URIs, including scores of strains of rhinovirus, although the symptoms tend to be more mild and self-limiting.

Although viral URI is the most likely diagnosis, it is imperative to consider other potential pathogens. GABHS is an important diagnostic consideration because failure to treat risks the development of sequelae such as acute rheumatic fever. Infectious mononucleosis caused by Epstein-Barr virus warrants consideration in young patients presenting with sore throat, fever, malaise, and cervical adenopathy on physical examination, particularly if symptoms are persistent, or if hepatomegaly, splenomegaly, and/or elevated liver function tests are present.

Sexually transmitted diseases, including gonorrhea, chlamydia, and HIV, should not be overlooked in the differential diagnosis of pharyngitis in soldiers. A sexual history, with particular attention to oral-genital and oral-anal contact, should be taken in all soldiers presenting with pharyngitis. HIV seroconversion illness can mimic mononucleosis. A screening HIV enzyme-linked immunosorbent assay should be performed if HIV is suspected. If it is negative and suspicion is high, an HIV RNA polymerase chain reaction (viral load) should be performed.

The patient was afebrile and had stable vital signs. Physical examination revealed mild pharyngeal erythema without exudates. He had no palpable lymphadenopathy, rash, hepatomegaly, or splenomegaly.

2. Which of the following would you do next in this patient?
   a. Throat culture
   b. Rapid antigen detection test (RADT)
   c. RADT, then throat culture if RADT is negative
   d. Treat patient with antibiotics empirically
   e. Treat patient symptomatically without ordering tests

Streptococcal pharyngitis typically presents with sudden onset of sore throat, pain on swallowing, and fever. The Centor Criteria (Table I) are useful in the process of deciding when a patient with pharyngitis should be treated with antibiotics.3 The criteria include tonsilar exudates, fever by history or at time of visit, tender anterior cervical adenopathy, and absence of cough. The presence of three or four of these criteria has a positive predictive value of only 40 to 60%. The lack of three or four criteria may be more useful and has a negative predictive value of 80%.3 Unfortunately, clinical criteria alone are often unreliable in establishing a diagnosis of streptococcal pharyngitis.

Over the past few years, debate has surfaced over how to best...
use the Centor Criteria in directing therapy. Snow et al.4 have proposed a decision tree based on the Centor Criteria that has been accepted by the American College of Physicians-American Society of Internal Medicine (ACP-ASIM) as a guideline for treating potential GABHS pharyngitis.5 They recommended two different treatment algorithms. The first recommends testing everyone who meets two or three Centor criteria using a RADT, and then treating patients with positive tests or those who meet all four criteria with antibiotics. The second method is based solely on clinical criteria and treats all patients who meet three or four Centor criteria. The ACP-ASIM only advises using throat cultures when RADT sensitivity at your laboratory is less than 80% (sensitivity ranges from 70 to 90%, depending on population studied), during outbreaks, if tracking antibiotic resistance, or when gonococcus is a potential diagnosis.4–6

The Infectious Disease Society of America (IDSA) believes that this method overtreats patients who may have nonstreptococcal pharyngitis.7 They recommend that all adults suspected of having acute GABHS pharyngitis have the diagnosis confirmed by RADT before antibiotic treatment, unless the diagnosis can be excluded on clinical (Centor Criteria) or epidemiological grounds. The IDSA recommends using a throat culture or an RADT to confirm the diagnosis before treating with antibiotics. There is no need to confirm a negative RADT with culture in adults; however, the IDSA does recommend throat cultures in children and adolescents when the RADT is negative, given the higher prevalence in this age group.7

The IDSA guidelines may not be practical in some military settings where diagnostic tests are not available. The approach offered by Snow et al.4 and the ACP-ASIM provides a useful clinical pathway for providers in this environment. The best approach would be to follow the IDSA guidelines if the RADT or throat culture is available because this would limit unnecessary antibiotic usage.

The patient in this case did not meet any of the Centor Criteria. Therefore, he was not tested for streptococcal pharyngitis and he was treated conservatively.

The patient admitted to smoking one pack of cigarettes per day for the previous 3 years. He attributed his smoking to peer group influences, stating he had not smoked before joining the military.

3. All of the following are true regarding cigarette use in this patient EXCEPT?
   a. Increased risk of myocardial infarction
   b. Decreased level of physical fitness
   c. Higher risk of viral infections
   d. Higher risk of asthma and infections in his children
   e. Smoking cessation typically results in greater than 10-lb weight gain

Smoking is known to contribute to a myriad of health problems and it is estimated that more than 430,000 U.S. citizens die from smoking in the United States each year.8,9 Smoking is associated with four of the top five causes of death in America: myocardial infarction, lung cancer, chronic obstructive pulmonary disease, and stroke. Although some risks of smoking are well publicized, there remain many impacts of smoking on health that are often not considered by smokers.

Many young smokers ignore the health risks associated with tobacco, thinking that they will quit before they develop adverse affects from smoking. They fail to realize that smoking has many effects even with short-term usage. One such effect with military relevance is that smoking decreases levels of physical activity and results in decreased endurance.10

Smoking increases the risk of infections—especially respiratory infections—not only in smokers, but also in children living in the same home.10 Children of smokers have significantly increased rates of otitis media and asthma. Although this patient does not have a history of recurrent infections or a prolonged illness with this episode, he is at risk in the future if he continues to smoke.

Some smokers use cigarette smoking as a form of diet control, and smokers use the fear of gaining weight as a reason not to stop. Most smokers will gain weight after stopping, but approximately 80 to 85% of smokers gain less than 10 lbs when quitting.8,9 Smoking cessation by itself does not cause weight gain; instead, it is the adoption of unhealthy dietary practices, in lieu of cigarettes, that sometimes leads to weight gain. Physicians can help their patients avoid this by encouraging exercise, nicotine supplements, and bupropion.8,10

After further questioning, the patient reported that he had attempted to quit smoking in the past, but was unsuccessful. He had attempted to quit using the “cold turkey” method, but found it to difficult because he was constantly around other smokers, felt irritable, had decreased concentration, and craved “a smoke.” The patient would like to try to quit smoking again, but is frustrated with his past failure.

4. All of the following interventions would be appropriate at this time EXCEPT?
   a. Smoking cessation counseling and classes
   b. Nicotine replacement therapy (gum, patch, inhaler, and/or spray)
   c. Bupropion
   d. A combination of nicotine replacement and bupropion
   e. Clonidine or nortriptyline

Only approximately 7% of smokers are able to successfully quit smoking after one attempt without the aid of their physician.8,10 Classes and counseling are effective in improving the smoking cessation success rates, yet they are not as effective as pharmacological therapy. The current recommendations by the U.S. Public Health Service for smoking cessation suggest that anyone attempting to quit smoking should be provided with pharmacological therapy along with smoking cessation classes and counseling.10 The two Food and Drug Administration-ap-
proved pharmacological therapies that have shown to increase smoking cessation rates are nicotine replacement and bupropion SR (Table II). 10

Nicotine gum is an easily titratable form of nicotine replacement. The success rate in a meta-analysis was 24%, and it appears that it is best used in combination with counseling and smoking cessation classes. 10 The nicotine transdermal patch has an efficacy rate of approximately 30% and is easier to use than nicotine gum. Nicotine inhalers and nasal sprays have abstinence rates of 23 and 30%, respectively. 10 These two methods are more cumbersome to use given their frequent dosing, but they do provide the habit component of taking a spray or puff. The nasal spray has rapid absorption that some patients find beneficial. Nicotine preparations can be used in combination with each other and have efficacy rates higher than single-agent regimens. The patch is typically combined with gum or nasal spray. 10

Bupropion SR (Zyban) is an antidepressant that has proven efficacy in smoking cessation, with abstinence rates of 31%. 10 The mechanism of action is thought to be blockade of neuronal reuptake of dopamine and/or norepinephrine. The medicine should be started 1 week before the quit date and continued for 8 weeks after stopping smoking. Bupropion combined with a nicotine patch appears to have an additive effect. 10

Clonidine and nortriptyline have abstinence rates of 25 and 30%, respectively. 10 Although successful, their side effect profiles and lack of Food and Drug Administration approval make them second-line agents.

After discussing the treatment options with the patient, he agreed to attempt to quit smoking. The patient was concerned about whether or not the medicine was safe for him to take.

<table>
<thead>
<tr>
<th>Name</th>
<th>Dosage</th>
<th>Duration of Treatment</th>
<th>Side Effects</th>
<th>Odds Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nicotine patch</td>
<td>7-, 14-, or 21-mg patch worn for 24 hours 10; 15-mg patch worn for 16 hours 10</td>
<td>8–12 weeks</td>
<td>Skin irritation and insomnia 10</td>
<td>2.7 (1.8–4.1)</td>
</tr>
<tr>
<td>Nicotrol 25 mg</td>
<td>75 mg/day for 3 days 10</td>
<td>8–12 weeks</td>
<td>Mouth irritation, sore jaw, dyspepsia, hiccups 10</td>
<td>1.5 (1.3–1.8)</td>
</tr>
<tr>
<td>Habitrol</td>
<td>750 mg/day for 3 days 10</td>
<td>8–12 weeks</td>
<td>Local irritation, cough, rhinitis 10</td>
<td>2.5 (1.7–3.6)</td>
</tr>
<tr>
<td>Nicotine inhaler</td>
<td>6–16 cartridges/day 10</td>
<td>3–6 months</td>
<td>Nasal irritation and congestion 10</td>
<td>2.7 (1.8–4.1)</td>
</tr>
<tr>
<td>Nicotine nasal spray</td>
<td>0.5 mg/nostril, 8–40 doses a day (5 doses/hour)</td>
<td>3–6 months</td>
<td>Insomnia, dry mouth, agitation 10</td>
<td>2.1 (1.5–3.0)</td>
</tr>
<tr>
<td>Clonidine</td>
<td>0.1 mg orally twice a day 10</td>
<td>3–10 weeks</td>
<td>Sedation, dry mouth, blurred vision, urinary retention, light-headedness, shaky hands 10</td>
<td>3.1 (1.8–5.7)</td>
</tr>
<tr>
<td>Nortriptyline</td>
<td>750 mg/day for 3 days 10</td>
<td>12 weeks</td>
<td>Dry mouth, drowsiness, sedation 10</td>
<td>2.1 (1.4–3.2)</td>
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<tr>
<td>Bupropion (Zyban or Wellbutrin SR)</td>
<td>150 mg twice a day 10</td>
<td>3–10 weeks</td>
<td>Hypotension, constipation 10</td>
<td>2.1 (1.4–3.2)</td>
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5. Which of the following is NOT a contraindication to nicotine replacement and bupropion?
   a. Eating disorders
   b. History of seizures
   c. Use of monoamine oxidase inhibitor
   d. Coronary artery disease
   e. Pregnancy

Patients with eating disorders, who are at increased risk of seizures, and those with a history of seizures should not be prescribed bupropion because it lowers the seizure threshold. In addition, patients who are being treated with or have been treated with a monoamine oxidase inhibitor in the past 14 days should not be prescribed bupropion. The combination of the two drugs can lead to a serotonin syndrome characterized by agitation, fever, tachycardia, and neuromuscular rigidity.

Nicotine replacement therapy was initially thought to cause an increased number of cardiovascular events in patients with coronary artery disease, but studies have dispelled this myth. 10 Nicotine replacement therapy is not an independent risk factor for acute coronary events and is safe even in patients who continue to smoke. Nicotine replacement should be used with caution in patients who are 2 weeks postmyocardial infarction, are having serious arrhythmias, or who have unstable angina. Bupropion has no cardiac side effects and may initially be a better choice in these high-risk patients.

Pregnancy is a relative contraindication to using bupropion or nicotine replacement. Although smoking during pregnancy is associated with spontaneous abortions, premature births, low birth weight babies, placental abruption, and childhood malignancies, pharmacological aids also carry potential risks. 10 Bupropion and nicotine are associated with maternal seizures and

Predicted effects:

a. Eating disorders
b. History of seizures
c. Use of monoamine oxidase inhibitor
d. Coronary artery disease
e. Pregnancy

**TABLE II**

PHARMACOTHERAPY FOR SMOKING CESSATION

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<td>150 mg twice a day</td>
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</tr>
<tr>
<td>Nortriptyline</td>
<td>750 mg/day for 3 days</td>
<td>12 weeks</td>
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a. Twenty-one-mg patch for 4 weeks; 14-mg patch for 2 weeks; 7-mg patch for 2 weeks. Nicotrol 15-mg patch should be worn for 8 weeks.
b. Minimized by rotating the patch placement. Insomnia averted by changing to 16-hour patch or removing before sleep.
c. Recommended starting doses are based upon number of cigarettes smoked: <25 cigarettes/day should use 2-mg dosage; ≥25 cigarettes should use 4-mg dosage.
d. Started 1 week before quit date.
e. Not Food and Drug Administration approved.
f. Most providers start at 25 mg and titrate up to 75–100 mg. Medication should be started 10 to 28 days before to quit date.
g. The doses in cessation trials varied and no dose-response relation was observed. The dose can be increased by 0.1 mg/day per week as needed.

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fetal neurotoxicity, respectively. These agents should only be used as a last resort when the risks of the medications are considered less than the patient continuing smoking.

Discussion

Upper respiratory symptoms are one of the most common presenting complaints in military health care settings. It can place a large burden on health care providers and resources. This is especially true in training environments where troops are in close quarters. The recent loss of the adenovirus vaccine has already proven to have an adverse impact, with the return of adenovirus epidemics. It is unlikely that the vaccine will be available in the immediate future; therefore, the ability to distinguish viral infections from bacterial infections with potential sequelae will be important. The guidelines provided by the ACP-ASIM and the IDSA provide two practical strategies in appropriately diagnosing and treating group A streptococcal infection, which accounts for approximately 10% of patients with acute pharyngitis. The practicing environment of the military physician may dictate which set of guidelines can be used. The standard treatment for those diagnosed with GABHS pharyngitis remains penicillin or erythromycin in patients allergic to penicillin.

Smoking continues to be a huge public health problem despite widespread knowledge of its detrimental effects. Almost one-quarter of the U.S. population still smokes, with the highest rate of smoking among the 18- to 24-year age group. The financial impact of smoking on society is enormous, costing $70 billion in medical expenses and another $50 billion in indirect financial impact of smoking on society is enormous, costing $70 billion in medical expenses and another $50 billion in indirect costs, making smoking cessation of paramount importance to military physicians and health care systems.

Many smokers want to quit, but only 7% are able to accomplish this goal without assistance. With effective treatment options, including nicotine replacement and bupropion now available, physician intervention increases the cessation rates. The "ABCs" of smoking cessation (Fig. 1) is a model providers can use to approach patients about smoking cessation. It stems from the U.S. Preventive Task Force (ask, advise, assist, and arrange) model, but is expanded to provide a more individualized approach. Whether or not this model is used is up to individual providers, but it is imperative that all have an approach that they are comfortable using to maximize the number of patients who successfully quit smoking.

Answers

1. a; 2. e; 3. e; 4. e; 5. d

References