Think 'Bronchiectasis' in Frequent Antibiotic Users

BY BRUCE JANCIN
Denver Bureau

KEYSTONE, COLO. — Anybody who needs two or more courses of antibiotics within a year for respiratory tract infections deserves to be evaluated for bronchiectasis, Dr. Gwen A. Huitt asserted at a meeting sponsored by the National Jewish Medical and Research Center.

"It's not normal for anyone to need any antibiotics during the year. By the time you get to somebody who needs two, three, or four courses of antibiotics for, say, a bronchitis or sinusitis—and remember, it's called the sinopulmonary tree—we need to think about underlying predisposing conditions," according to Dr. Huitt, director of the adult infectious disease care unit at the Denver center.

She believes that bronchiectasis is far more common in primary care settings than most physicians realize. This conviction is based in part on the large number of telephone and e-mail consults she handles through National Jewish's "Lung Line" (800-222-5864 or lungline@njc.org) that turn out to involve patients with previously undiagnosed bronchiectasis.

High-resolution chest CT is the diagnostic cornerstone. It will readily show the permanently dilated, grossly distorted bronchi and bronchioles that define bronchiectasis anatomically. The pathogenesis involves some sort of initial inflammatory process leading to a cytokine cascade, including tumor necrosis factor, interleukins, and elastases, along with accumulation of white blood cells. This inflammatory gunk predisposes to bacterial infection, which in turn damages mucociliary function. This process leads to a vicious cycle in which stagnant mucus attracts bacterial pathogens—*Pseudomonas aeruginosa* is the No. 1 infectious agent—further impairing the lungs' ability to clear mucus, resulting in more infections.

Although bronchiectasis is often thought of as a "wet" condition in which patients constantly hack up purulent phlegm, patients can in fact be "dry" and yet still have severe bronchiectasis, Dr. Huitt stressed.

Once it's determined that a patient has bronchiectasis, it's important to try to identify the etiology. Although bronchiectasis is the disease that defines cystic fibrosis, it has numerous other potential causes. These include α_1-antitrypsin (A1A) deficiency, Young's syndrome, allergic bronchopulmonary aspergillosis, autoimmune diseases, a severe pneumonia, and even gastroesophageal reflux disease (GERD).

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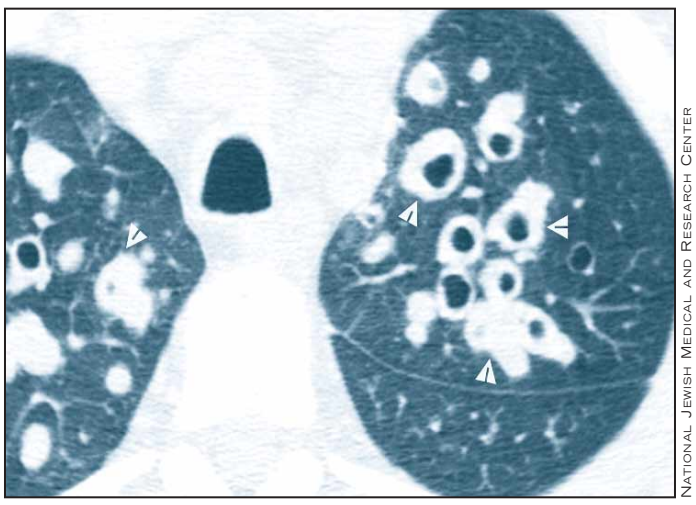
DR. HUITT

Dr. Huitt routinely orders sputum cultures, a genetic screen for cystic fibrosis, an α_1-antitrypsin level and phenotype, an antinuclear antibody test, quantitative immunoglobulins, an esophagram, and pulmonary function tests to sift through the following potential causes of bronchiectasis:

► **Cystic fibrosis.** At last count, roughly 1,300 genetic mutations have been identified that can contribute to the widely varied presentations of this disease. In patients with bronchiectasis, National Jewish physicians routinely order the Genzyme test that covers 97 of the most common ones. The traditional sweat chloride test is not worth ordering in adults where cystic fibrosis is a possibility; the results are generally normal even in affected patients. "Go straight to genotyping, and I believe you'll get a lot better data," Dr. Huitt said.

► **Infection.** Worldwide, the No. 1 cause of bronchiectasis is undoubtedly tuberculosis. But other severe pulmonary infections—for example, pertussis or measles pneumonia—can also damage the mucociliary clearance mechanism and trigger the bronchiectatic process.

► **A1A deficiency.** Although it's classically an emphysematous condition, some affected patients instead present chiefly with recurrent pulmonary infections and bronchiectasis. Dr. Huitt orders both the A1A level and phenotype for screening because of recent data indicating not just homozygotes but phenotypic MZ heterozygotes may benefit from augmentation therapy.



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High-resolution chest CT, the diagnostic cornerstone, shows permanently dilated, grossly distorted bronchi and bronchioles.

► **Autoimmune diseases.** Rheumatoid arthritis, scleroderma, Sjögren's syndrome, vasculitis, and mixed connective tissue diseases are very common in patients with bronchiectasis, and it's not at all unusual for the pulmonary manifestations to precede diagnosis of the autoimmune disease. Indeed, it's for this reason Dr. Huitt advocates screening all bronchiectatic patients with an antinuclear antibody test. In addition, she routinely orders separate serologies for anti-SSA and anti-SSB because she finds a large number of bronchiectatic patients have previously undiagnosed Sjögren's syndrome.

► **HIV.** Although highly active antiretroviral therapy (HAART) effectively controls viral replication, there remains an ongoing inflammatory state affecting the pulmonary system. Expect to encounter a lot more cases of bronchiectasis due to underlying HIV in coming years as HAART-treated patients survive far longer than in the epidemic's early years.

► **GERD.** Although it is considered controversial as a cause of bronchiectasis, Dr. Huitt believes that GERD is actually an important cause, and that the controversy exists only because of limitations in current methods of evaluating reflux. GERD can be clinically silent. Radiologists have taught Dr. Huitt two CT pearls that are indicators of esophageal hypertrophy secondary to reflux: an esophageal wall thickness in excess of 3 mm, or more than 15 mm of retained air in the esophageal lumen.

Sputum cultures should be obtained at baseline and every 6 months. Knowledge of the predominant chronic lung pathogen guides maintenance antimicrobial therapy aimed at preventing acute exacerbations of bronchiectasis that will require hospitalization and several weeks of intravenous antibiotics.

In the event sputum microbiology shows *P. aeruginosa*, it's essential that the laboratory describe whether the strain is mucoid or nonmucoid—something many large national laboratories are reluctant to do. "As soon as a patient acquires a mucoid strain as the predominant organism, the time to mortality definitely quickens," she said.

Periodic sputum analyses are also done to survey for the presence of a chronic nontuberculous mycobacterial infection. Antimicrobial susceptibility testing has been a controversial issue. New American Thoracic Society guidelines to come out later this year will for the first time call for routine susceptibility testing in individuals with nontuberculous mycobacterial lung infection, said Dr. Huitt. ■

Ralstonia Found in More Vapotherm Devices, Recall Launched

BY MARY ANN MOON
Contributing Writer

Vapotherm respiratory gas administration devices are being voluntarily recalled, following federal government reports that twenty-nine hospitals in 16 states found *Ralstonia* organisms colonizing the devices, and cultures from approximately 40 pediatric patients also yielded the bacteria.

The Centers for Disease Control and Prevention and the Food and Drug Administration late last year had advised clinicians to use alternative devices to provide humidified oxygen therapy until the source of contamination has been identified and removed. They also recommended that any patients who have been exposed to the Vapotherm system be monitored for signs and symptoms suggesting infection, including fever, poor feeding, irritability, and changes in hematologic indices.

In addition, "clinicians may want to consider *Ralstonia* species infection in the differential diagnosis of symptomatic patients even if the organism has not been isolated," the FDA said in a public health notification (www.fda.gov/cdrh/safety/122005-vapotherm.html).

In response, the device manufacturer, Vapotherm, announced last month that it would recall and disinfect Vapotherm 2000i and 2000h devices. Units will then be returned to the owners with updated disinfection and usage recommendations.

Contamination of the Vapotherm system was first reported by the CDC and the FDA in October 2005, after a Pennsylvania hospital isolated *Ralstonia* in several patients who had used the device. The Vapotherm system is used "to add moisture to and to warm breathing gases for administration to patients," according to its manufacturer, Vapotherm Inc. (Stevensville, Md.).

Since the October reports, the CDC and FDA have found additional cases of *Ralstonia* contamination. Cultures of unused Vapotherm cartridges at two hospitals yielded *Ralstonia*, but cultures of other unused cartridges from the same lot did not grow the organism.

After the procedures for disinfecting the device that were listed in its original instructions were found to be inadequate, the manufacturer issued new instructions for chloride dioxide disinfection. However this method also "may not achieve sustained bacterial control," according to the FDA.

"Infections caused by *Ralstonia* should be treated on the basis of results of susceptibility testing of the patient's isolate," according to the CDC (MMWR 2005;54:1-2).

"Clinicians who elect to use Vapotherm are encouraged to weigh the risk of potential bacterial contamination of the device against the benefits Vapotherm might provide patients who require humidified oxygen therapy," the CDC said.

For more information, visit www.vtherm.com/recall. Cases of colonization or infection with *Ralstonia* or related bacteria (gram-negative rods) in patients exposed to Vapotherm should be reported to the manufacturer, to local or state health departments, and to the CDC at 800-893-0485. Adverse events associated with medical devices should be reported to the FDA's MedWatch program at www.fda.gov/Medwatch or by calling 800-332-1088 or faxing 800-332-0178. ■