variceal bleeding in patients with liver cirrhosis. It is known that the size and pressure of esophageal varices, which correlate with risk of hemorrhage, parallel azygos blood flow. The volume of a compliant vessel increases more easily, according to the formula of elastic pressure:

\[
\frac{C}{H} = \frac{\Delta V}{\Delta P},
\]

where \(C\) = compliance, \(\Delta V\) = volume change, and \(\Delta P\) = pressure change. According to the Hagen-Poiseuille equation in hydrokinetics (\(Q = \frac{\pi r^4}{8} \ell \Delta P\)), when there is constant pressure in the portoesophageoazygos venous system, an increase in the cross-sectional area contributed by the azygos vein dilation decreases flow within the system. This in turn reduces the risk of variceal bleeding.

In addition to reducing the flow in the system overall, another factor may also be significant in preventing bleeding. In general, portal flow varies diurnally, with peak flow occurring at midnight. The azygos varix increases in size when the patient is recumbent, further reducing flow in the system. This phenomenon, as with the administration of propranolol at night, may play an important role in preventing variceal bleeding. The azygos varix thus may be present on chest radiograph before varices are diagnosed. In our patient, the mediastinal mass was seen 2 years before her first episode of variceal bleeding.

In summary, a mediastinal mass in a patient with cirrhosis of the liver may be a giant azygos vein varix. An awareness of this possible diagnosis should perform non-invasive imaging procedures prior to invasive tests. A comparison between supine and standing chest radiographs is useful in differential diagnosis. However, a chest CT if necessary may be adequate to make the diagnosis.

ACKNOWLEDGMENT: We thank Dr. Mary Jeanne Buttrey, Consulting Physician, Department of Internal Medicine, Mackay Memorial Hospital, for review and revision of the manuscript.

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Hypersensitivity Pneumonitis Reaction to Mycobacterium avium in Household Water*

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Background: Hypersensitivity pneumonitis has been described with exposure to aerosolized Mycobacterium avium complex (MAC) in indoor hot tubs (hot tub lung).

Objectives: To describe a case of MAC-associated hypersensitivity pneumonitis-like reaction possibly from showering and review previous hot tub lung reports.

Methods: For the case report, we investigated a patient with histologically diagnosed hypersensitivity pneumonitis and MAC-positive sputum culture findings. Mycobacterial cultures were obtained from his home and workplace. Isolates were typed using pulsed-field gel electrophoresis. For the review, MEDLINE and EMBASE were searched for hot tub lung reports, which were reviewed and summarized.

Results: A 50-year-old man had progressive dyspnea and episodic fever and myalgias. Pulmonary function testing results revealed obstruction and impaired diffusion; a chest CT scan found diffuse, centrilobular, ground-glass nodules, and air trapping, and a lymphocytic alveolitis with an elevated CD4/CD8 ratio. Transbronchial biopsy showed multiple well-formed noncrotizing granulomas. Multiple respiratory samples and shower and bathtub specimens

Figure 5. Reconstructive two-dimensional CT, sagittal (left) and coronal (right), views showing the mass connected the azygos vein and the superior vena cava (arrow).
grew MAC, with matching pulsed-field gel electrophoresis patterns. The patient changed from showering to tub bathing. Prednisone and antimycobacterial drugs were administered for approximately 1 year. His symptoms, pulmonary function abnormalities, and CT scan findings resolved. The literature review yielded 36 cases of hot tub lung. Clinical features included dyspnea (97%), cough (78%), and fever (58%). Pulmonary function testing showed obstruction (67%), restriction (53%), and impaired diffusion (75%). A chest CT scan showed ground-glass opacification (95%) and nodules (67%). Granulomas were well-formed in 95%. Treatments included discontinuation of hot tub use and prednisone, antimycobacterial drugs, or both. Outcomes were favorable.

Conclusions: A hypersensitivity pneumonitis-like reaction to mycobacteria can occur from exposures other than hot tubs. There are key differences between classic hypersensitivity pneumonitis and MAC-associated hypersensitivity pneumonitis. Anti-mycobacterial therapy may be required. The possibility of MAC hypersensitivity pneumonitis from showering raises potential implications in the investigation of patients with hypersensitivity pneumonitis.

(CHEST 2005; 127:664–671)

Key words: alveolitis, extrinsic allergic; Mycobacterium avium-intracellulare infection; Mycobacterium infections, atypical; water microbiology

Abbreviations: BCG = bacille Calmette-Guérin; MAC = Mycobacterium avium complex; NTM = nontuberculous mycobacteria

Pulmonary nontuberculous mycobacteria (NTM) infection is an increasingly common problem,1 usually associated with structural lung disease such as bronchiectasis or cystic fibrosis, but often also in otherwise apparently normal hosts. The classic response to pulmonary NTM includes both signs and symptoms of infection and necrotizing granulomas with acid-fast bacilli on histopathologic examination.2,3 However, NTM can incite a range of histopathologic changes in the lung.4 In particular, a hypersensitivity pneumonitis-like syndrome in patients exposed primarily to aerosolized Mycobacterium avium complex (MAC) has recently been described by a number of investigators.5–14 The term hot tub lung has been used to describe these hypersensitivity pneumonitis-like cases because they have generally been associated with hot tub use, a situation thought to lead to particularly high levels of infectious aerosols containing organisms found in the water.6 Whether this pulmonary response to MAC represents true infection or “classic” hypersensitivity pneumonitis is controversial, as some patients improve only after antimycobacterial drug therapy, while other patients improve after corticosteroids or the removal of the exposure. The classification of this pulmonary response to MAC is further complicated by the increasing observations of histopathologic and bronchoscopic differences between “classic” hypersensitivity pneumonitis and MAC-associated hypersensitivity pneumonitis.6,9,14

We present the first reported case of MAC hypersensitivity pneumonitis associated with exposure to MAC in the routine use of household water. Water samples from the patient’s shower and bathtub faucets and his sputum all yielded the same strain of MAC, as defined by pulsed-field gel electrophoresis. A review of the details of this case and other cases of MAC- and NTM-associated hypersensitivity pneumonitis highlights the clinical differences between “classic” hypersensitivity pneumonitis and MAC hypersensitivity pneumonitis, which we propose may have implications for classification and treatment. Further, our report stresses the clinical importance of alternative sources of aerosolized MAC that can lead to MAC hypersensitivity pneumonitis.

CASE REPORT

A 50-year-old man had progressive exertional dyspnea and chest tightness for 3 months. He noted two or three previous discrete self-limited episodes characterized by malaise, subjective fever, and myalgias, each lasting 24 to 72 h, the first of which predated his pulmonary symptoms by 1 week. His medical history was noncontributory, he took no medications, never smoked, used no illicit substances, and had no significant risk factors for HIV infection. He drank one to two glasses of wine on weekends. He had always been extremely active and regularly completed a demanding mountain bicycling course until pulmonary limitations developed. He had worked as a dentist for 23 years, performing routine examinations and procedures and producing oral appliances with dimethacrylates, but there was no history of exposure to beryllium. He wore a paper ear-loop mask when fabricating appliances and working with patients. His symptoms were not clearly associated with work, and there was no change on the weekends. He lived with his wife in the same house for 16 years. The structure was 65 years old, and had been renovated before they moved in. Minor remodeling, involving removal of some drywall and subsequent plastering, was performed around the time his symptoms began. He intermittently used his outdoor hot tub, which filtered through an adjacent swimming pool, but not for several weeks before symptom onset. He kept no pets.

Physical examination was unremarkable. The chest examina-
tion was normal. In addition, there were no obvious skin or ocular lesions, organomegaly, or other features suggestive of sarcoidosis. His pulmonary function testing showed mild obstruction (FEV$_1$/FVC = 0.67, FEV$_1$ = 80% of predicted) and impaired diffusing capacity (62% of predicted). High-resolution CT of the lungs showed small, bilateral, diffuse, centrilobular, ground-glass nodules (Fig 1, top, A) and extensive mosaic attenuation consistent with air trapping on expiratory images, all thought to be most consistent with hypersensitivity pneumonitis. Of note, there was no adenopathy, no large nodules or consolidation, and no peribronchovascular or pleural thickening or nodularity. A CBC count with differential leukocyte count, serum creatinine, and liver enzymes and ECG were normal. An HIV test was negative. A serologic hypersensitivity pneumonitis panel comprising A. fumigatus, Micropolyspora faeni, Thymus vulgaris, and pigeon breeder’s serology was negative. Fiberoptic bronchoscopy was performed. Cellular analysis of the BAL revealed 53% lymphocytes, with an elevated CD4/CD8 ratio of 15. Transbronchial biopsies showed multiple well-formed nonnecrotizing granulomas, with an elevated CD4/CD8 ratio of 15. Transbronchial biopsies showed multiple well-formed nonnecrotizing granulomas (Fig 2). Special stains for acid-fast bacilli were negative. Cultures from the BAL and two induced-sputum specimens grew MAC.

Based on a diagnosis of hypersensitivity pneumonitis, the professional and home exposures, and positive sputum culture findings, the patient stopped work, completely discontinued use of his hot tub, and changed from showering to taking tub baths. Treatment was started: prednisone, 60 mg/d; and antituberculosis therapy: clarithromycin, 1,000 mg/d; rifabutin, 300 mg/d; and ethambutol, 25 mg/kg/d. An industrial hygienist visited his home and workplace. Home sampling comprised water specimens from his hot tub and swimming pool (both outdoor) and his bathroom (shower and bathtub). Faucets and water nozzle covers were inspected for biofilm formation, identified only in a bathtub fitting, which was also sampled for culture. Three of four specimens from his bathroom water (from both shower and bathtub) were positive for MAC, while all specimens from the hot tub and swimming pool were negative. The biofilm culture yielded no mycobacteria. Inspection failed to identify any areas suspicious for mold contamination and yielded equivalent indoor and outdoor airborne mold counts in the home. Workplace sampling comprised four water samples from each of two dental units (two specimens collected through the air-water syringe and high-speed hand piece from each unit), with one of eight specimens positive for MAC. Inspection of pieces of water tubing revealed no evidence of gross biofilm formation. Isolates from two respiratory specimen cultures, the three positive bathroom water samples, and the single positive workplace sample were typed by pulsed-field gel electrophoresis, with restriction fragment length polymorphism analysis following digestion with DraI and XbaI. We found near-identical restriction patterns (0–1 band differences) for all isolates, suggesting the strains were clonal (Fig 3). We reasoned that the single positive workplace culture finding was either mislabeled or contaminated from a home sample. This conclusion is supported by the recovery of MAC from three of four bathroom samples but only one of eight workplace samples and clonal strains by molecular typing despite geographically distinct water sources served by different counties’ municipal water supplies. We therefore think that the source of the patient’s MAC was his home bathroom.

Sputum culture findings became negative after approximately 6 months of therapy (after three additional sets of positive sputum culture findings). Currently, the patient is receiving prednisone, 5 mg/d, and antituberculosis therapy described above. It is planned to continue antituberculosis drugs for at least 18 months, 12 months after culture findings became negative, and discontinue prednisone after discontinuation of antituberculosis therapy. The patient’s symptoms, pulmonary function testing abnormalities, and high-resolution CT all returned to near normal (Fig 1, bottom, B).

**FIGURE 1.** High-resolution CT images (window width, 1,000 Hounsfield units; level, −700 Hounsfield units). Top, A: Diffuse bilateral nonhomogenous lung opacification comprising reticulation, numerous small bilateral nodules, and foci of ground-glass opacity. Bottom, B: Near resolution of the abnormalities after 7 months of treatment.

**LITERATURE REVIEW**

We sought to identify all reports of hot tub lung. MEDLINE (1966 onwards) and EMBASE (1980 onwards) were searched using three sets. The first set used the terms and medical subject headings Mycobacterium (as a genus, including all catalogued species except tuberculosis complex) or mycobacterium infections, atypical combined with hypersensitivity pneumonitis; alveolitis, extrinsic allergic; or allergic pneumonitis. The second set used the terms and medical subject headings Mycobacterium (as a genus, including all catalogued species except tuberculosis complex) or mycobacterium infections, atypical combined with hot tub. The third set used the term hot tub lung. The ISI Web of Science was also searched using the term hot tub lung. Abstracts of resulting citations were reviewed, and selected citations were retrieved for full review. Reference lists of all retrieved articles were searched for additional reports. All reports of cases of hypersensitivity pneumonitis-like syndromes proposed to be secondary to exposure to aerosolized MAC from hot tub use were included.

The search strategy yielded 164 hits of published articles. Eight citations were selected for retrieval and full review. Review of the reference lists identified two additional citations. A summary of the clinical presentation and investigations reported in the...
identified studies is presented in Table 1. All cases involved exposures from indoor hot tubs and the majority of patients had dyspnea, cough, and fever. CT scanning was performed in 23 patients, while high-resolution CT was performed in at least 16 patients. In addition to the common findings of ground-glass opacities and nodules, “nonspecific alveolitis” and findings “compatible with hypersensitivity pneumonitis” were also described. Pulmonary function was discussed in only 12 cases, and there was no predominant abnormality, with obstruction, restriction, and impaired diffusion all present in the majority of patients. Cytologic BAL data were reviewed in only three cases; there was a lymphocytic alveolitis (mean, 67% lymphocytes) with elevated CD4/CD8 ratios of 12, 6, 49, and 6. Tissue biopsies were reported in 26 cases, from at least one patient in all of the reviewed articles. Surgical lung biopsies were performed in 23 cases, and transbronchial biopsies were the only source of tissue in 3 cases. In addition to the characteristically described well-formed granulomas, a peribronchial distribution of the granulomas was present in four studies (14 patients), absent in two studies (2 patients), and not commented on in the remaining four reports (11 patients).

Table 2 presents a summary of treatments and outcomes. All patients either recovered or improved. A higher fraction of patients who received antimycobacterial drugs, either alone or combined with corticosteroids, were reported to have clinical resolution compared with patients who received corticosteroids alone: 11 of 13 patients (85%) vs 1 of 6 patients (17%) [p < 0.01, Fisher exact test]. This comparison is limited, however, by a lack of data on the definitions of clinical outcomes and possible selection bias for using specific therapeutic regimens.

**Discussion**

We present a case of hypersensitivity pneumonitis-like reaction to inhaled MAC from a previously unreported source, a household shower. Although causality is difficult to establish with certainty, previously reported studies have often relied on simply recovering the organism from the patients’ environment. Molecular typing was described in three reports, all studying *M avium*. Two studies used restriction fragment length polymorphism analysis with IS1245 hybridization: one study found a three-band difference, and another study found identical banding patterns. A third report found environ-
‡Clinical pulmonary specimens included sputum, bronchoscopic and surgical biopsy specimens. Information regarding acid-fast bacillus stain results were not consistently reported. No negative hot tub water in the patient’s area,17 the multiple positive home specimens, and the clonality of the isolates as determined by pulsed-field gel electrophoresis.

A controversial issue in patients with hypersensitivity pneumonitis-like reactions to inhaled MAC is whether the syndrome represents classic hypersensitivity pneumonitis, infection, or both. Support for the hypothesis that antigens from MAC organisms can cause pulmonary hypersensitivity reactions comes from case series of intravesical instillation of bacille Calmette-Guérin (BCG) for carcinoma of the bladder,18,19 and exposure to metal working fluids in machinists.20–22 Israel-Biet et al 18 reported a series of three patients who acquired systemic illness after intravesical BCG instillations, two of whom had diffuse interstitial changes on chest radiography. Respiratory culture and biopsy results were negative for mycobacteria, but BAL revealed a lymphocytic alveolitis with CD4/CD8 ratios ranging from 3 to 7.5. Two patients were treated with corticosteroids, the third patient was treated simply with discontinuation of BCG instillations, and all recovered. The authors concluded that interstitial pneumonitis during BCG therapy was explained by a hypersensitivity phenomenon in response to mycobacterial antigens. Exposure to Mycobacterium immunogenum in metal-working fluids has also been proposed as a cause of an hypersensitivity pneumonitis-like reaction in machinists.20–22 The recently proposed species was recovered from metal-working fluids in all cases, and serum precipitins to the organism were sought and identified in two reports.20,22 Affected patients have been treated with corticosteroids and removal from the work environment.22 Although we did not observe acid-fast bacilli in our patient’s transbronchial lung biopsy, or process the biopsy for mycobacterial culture, we are confident that MAC was the cause for his pulmonary syndrome. Acid-fast stains of granulomas from patients with hot tub lung in previous reports9–11,13,14 were negative in 19 of 26 cases (73%). In addition, in miliary tuberculosis, a mycobacterial infection with a diffuse pulmonary granulomatous reaction, acid-fast

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Table 1—Features of Previously Reported Cases (n = 36) of MAC-Associated Hypersensitivity Pneumonitis*

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Data</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female sex, No. (%)</td>
<td>20 (56)</td>
</tr>
<tr>
<td>Mean age, yr (SD)</td>
<td>45 (16)</td>
</tr>
<tr>
<td>Exposure (indoor hot tub), No. (%)</td>
<td>36 (100)</td>
</tr>
<tr>
<td>Signs and symptoms</td>
<td></td>
</tr>
<tr>
<td>Dyspnea</td>
<td>35/36 (97)</td>
</tr>
<tr>
<td>Cough</td>
<td>28/36 (78)</td>
</tr>
<tr>
<td>Fever</td>
<td>21/36 (58)</td>
</tr>
<tr>
<td>Weight loss</td>
<td>8/36 (22)</td>
</tr>
<tr>
<td>Pulmonary function studies†</td>
<td></td>
</tr>
<tr>
<td>Obstruction</td>
<td>8/12 (67)</td>
</tr>
<tr>
<td>Restriction</td>
<td>6/11 (55)</td>
</tr>
<tr>
<td>Low diffusion capacity</td>
<td>6/8 (75)</td>
</tr>
<tr>
<td>Chest CT</td>
<td></td>
</tr>
<tr>
<td>Ground-glass opacification</td>
<td>20/21 (95)</td>
</tr>
<tr>
<td>Nodules</td>
<td>14/21 (67)</td>
</tr>
<tr>
<td>Histopathology of granulomas</td>
<td></td>
</tr>
<tr>
<td>Present</td>
<td>26/26 (100)</td>
</tr>
<tr>
<td>Well formed</td>
<td>24/25 (96)</td>
</tr>
<tr>
<td>Necrosis</td>
<td>5/26 (19)</td>
</tr>
<tr>
<td>Acid-fast stain positive</td>
<td>7/20 (35)</td>
</tr>
<tr>
<td>Isolation of MAC‡</td>
<td></td>
</tr>
<tr>
<td>Clinical pulmonary specimens</td>
<td>29/34 (85)</td>
</tr>
<tr>
<td>Hot tub</td>
<td>21/21 (100)</td>
</tr>
</tbody>
</table>

*Data are presented as No./total cases (%) unless otherwise indicated.
†The specific definition of individual pulmonary function abnormalities was generally not provided in previous reports.
‡Clinical pulmonary specimens included sputum, bronchoscopic and surgical biopsy specimens. Information regarding acid-fast bacillus stain results were not consistently reported. No negative hot tub specimens were reported.

Table 2—Treatment and Outcomes in Previously Reported Cases of MAC-Associated Hypersensitivity Pneumonitis*

<table>
<thead>
<tr>
<th>Treatment†</th>
<th>Outcome†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antimycobacterial drugs only</td>
<td></td>
</tr>
<tr>
<td>(9 of 35 cases, 26%)</td>
<td>8/9 (89)</td>
</tr>
<tr>
<td>Systemic corticosteroids only</td>
<td></td>
</tr>
<tr>
<td>(12 of 35 cases, 34%)</td>
<td>1/6 (17)</td>
</tr>
<tr>
<td>Antimycobacterial drugs plus systemic</td>
<td></td>
</tr>
<tr>
<td>corticosteroids (7 of 35 cases, 20%)</td>
<td>3/4 (75)</td>
</tr>
<tr>
<td>No antimycobacterial or systemic</td>
<td></td>
</tr>
<tr>
<td>corticosteroid therapy (6 of 35 cases,</td>
<td>6/6 (100)</td>
</tr>
<tr>
<td>17%)</td>
<td></td>
</tr>
</tbody>
</table>

*Data are presented as No./No. of cases (%).
†All patients discontinued exposure.
‡All patients had either improvement or resolution; one study did not report outcome by treatment regimen.

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stains are generally negative. Data in pulmonary NTM are less readily available, but the lack of acid-fast organisms in granulomas is well recognized. In fact, finding granulomas in a lung biopsy, without coexisting acid-fast bacilli, fulfills a component of the diagnostic criteria for pulmonary NTM disease.

Despite the radiographic and clinical evidence suggesting that MAC hypersensitivity pneumonitis may be a form of classic hypersensitivity pneumonitis, data from our case and previous reports (Tables 1, 2) highlight some key differences between classic hypersensitivity pneumonitis and hypersensitivity pneumonitis-like reaction to MAC and other NTM infections. Although all 17 reported patients with MAC-associated hot tub lung who underwent biopsies had granulomas identified, in all 15 reports containing detailed descriptions, granulomas were described as “well-formed,” and in 3 of 17 cases (19%) some were necrotic, findings not typical for classic hypersensitivity pneumonitis. In the three previous cases reported with BAL data, and our patient, the CD4/CD8 ratios were elevated at 12.6, 49 and 6.12,15 and 15, respectively. These findings are consistent with BAL reports in patients with hypersensitivity to intravesical BCG18,19 and sarcoidosis,20 rather than classic hypersensitivity pneumonitis, where the CD4/CD8 ratio is expected to be < 1.2 In addition, BAL CD4/CD8 ratios are increased in patients with classic pulmonary MAC infection, with a mean ratio of 6 reported in one study.20 The elevated CD4/CD8 ratio reported in our patient and previous patients with MAC hypersensitivity pneumonitis suggests that the pulmonary response to MAC may be immunologically different than in patients with classic hypersensitivity pneumonitis in response to other antigens. However, whether this immune response reflects an infectious reaction is not clear, as some patients with hot tub lung have been reported to improve with simple avoidance of the hot tub. However, the elevated CD4/CD8 ratio is consistent with reports of variable29 or increased30 ratios in patients with farmer’s lung and CD4/CD8 ratios that increased over time in a group of patients with hypersensitivity pneumonitis of mixed etiology.31 Finally, the finding of airflow limitation in our case and in those previously reported differs from classic hypersensitivity pneumonitis, where restriction is the dominant spirometric abnormality. The finding of airflow limitation is likely secondary to a bronchiolitis, which has been shown to correlate with obstruction in hypersensitivity pneumonitis,32 and likely dominates the determinants of physiologic manifestations of MAC hypersensitivity pneumonitis.

Support for the hypothesis that MAC hypersensitivity pneumonitis is a form of infection is found in two previous reports. Kahana et al3 described a patient with hot tub lung who progressed despite discontinuing exposure, and improved only after the institution of antimycobacterial therapy. Khoor et al5 described a patient with an indoor hot tub who acquired MAC bacteremia after an initial diagnosis of sarcoidosis and initiation of corticosteroid therapy. The patient improved after discontinuation of corticosteroids and treatment with antimycobacterial drugs. It was only later that the patient was thought to have hot tub lung. Details regarding timing of discontinuation of hot tub use were unclear in the latter case. Although discontinuation of exposure is probably the most important treatment measure, the data summarized in Table 2 suggest that antimycobacterial therapy may be more important than systemic corticosteroids. This notion rests on the assumptions that the cases represent a homogeneous group and that outcomes were defined similarly in all studies, which may be incorrect. Data regarding BAL CD4/CD8 ratios are inadequate to aid the decision regarding specific therapy. The presence of necrotic granulomas may intuitively support the use of antimycobacterial drugs, but the available data are inadequate to support this hypothesis. Based on the limited available data, we recommend the combination of antimycobacterial drugs and systemic corticosteroids in moderate to severe cases of MAC hypersensitivity pneumonitis.

Another potentially difficult distinction in our patient’s case is between sarcoidosis and a hypersensitivity pneumonitis-like pattern. The histologic distinction between MAC hypersensitivity pneumonitis and sarcoidosis is ours, and previously reported cases, is difficult. The granulomas in MAC hypersensitivity pneumonitis have been described as well formed, possibly consistent with sarcoidosis. However, granulomas in MAC hypersensitivity pneumonitis tend to be centrilobular in distribution, without pleural or septal involvement, and occasionally necrotic, both of which are unusual for sarcoidosis. The high-resolution CT findings in our case would be very unusual in sarcoidosis. None of the usual high-resolution CT findings were present in our patient, who had neither lymph node enlargement nor peribronchovascular or pleural thickening or nodularity. In addition, we are unaware of a convincing reported case of clinical pulmonary MAC infection with coexisting sarcoidosis. Also, the two cases outlined above, where antimycobacterial therapy was clearly required,5,9 argue against sarcoidosis as the cause of this syndrome. Finally, the development of pulmonary hypersensitivity syndromes in response to other mycobacterial species, including BCG in intravesical therapy for bladder carcinoma and M immunogenenum in metal-working fluids argues further against sarcoidosis. The isolation of mycobacterial nucleic acid from lesions in some patients with sarcoidosis is also an interesting consideration in this context. However, we argue that the case we describe is a hypersensitivity pneumonitis-like reaction, rather than a mycobacterial reaction that is indistinguishable from sarcoidosis.

Our findings may have important clinical implications regarding the investigation of patients with hypersensitivity pneumonitis. MAC and other NTM may cause an hypersensitivity pneumonitis-like reaction, and these organisms may be isolated from household water supplies. Showering, which has become the dominant method of bathing in recent decades, has been proposed as an ideal mode of entry of NTM into the lungs, and is strongly supported by our findings. In this context, the routine collection of sputum (and when available bronchoscopic and surgical specimens) and environmental samples for mycobacterial studies may be an important component of patient evaluation in hypersensitivity pneumonitis of un-
known etiology. BAL CD4/CD8 ratios may also be helpful in supporting the diagnosis, but these data are limited.

In summary, we present a case of hypersensitivity pneumonitis-like reaction secondary to exposure to MAC, possibly from showering, a previously unreported source of antigen in this syndrome. Findings suggest that the reaction differs from classic hypersensitivity pneumonitis but remains poorly defined. The potential implications for the clinical assessment of hypersensitivity pneumonitis in general are significant and deserve further investigation.

ACKNOWLEDGMENT: We would like to acknowledge M. Gotway, MD, for interpreting and reproducing radiographic images; T. Colby, MD, and S. Nishimura, MD, for interpreting and photographing biopsy slides; C. Quinlan, MPH, C.I.H., for collecting environmental samples; Y. Zhang, for performing the pulsed-field gel electrophoresis analysis; and T. Elbeik, PhD, and M. Roemer for processing, culturing, and isolating MAC specimens.

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Phrenic Nerve Pacing Via Intramuscular Diaphragm Electrodes in Tetraplegic Subjects*

Anthony F. DiMarco, MD, FCCP; Raymond P. Onders, MD; Anthony Ignagni; Krzysztof E. Kowalski, PhD; and J. Thomas Mortimer, PhD

Context: Diaphragm pacing in ventilator-dependent tetraplegic subjects is usually achieved by the placement of phrenic nerve electrodes via thoracotomy. However, this technique may be accomplished less invasively via laparoscopic placement of IM electrodes, at a lower cost and with less risk of injury to the phrenic nerve. 

Objective: To assess the feasibility of laparoscopic placement of IM diaphragm electrodes to achieve long-term ventilatory support in ventilator-dependent tetraplegic subjects.

Design, setting, and participants: Two IM diaphragm electrodes were placed laparoscopically in each hemidiaphragm in five subjects with ventilator-dependent tetraplegia. Studies were performed either on an outpatient basis or with a single overnight hospitalization. Ventilator-dependent tetraplegic subjects were identified in whom bilateral phrenic nerve function was present, as determined by phrenic nerve conduction studies. Following electrode placement, subjects participated in a conditioning program to improve the strength and endurance of the diaphragm over a period of 15 to 25 weeks. The duration of the study was variable depending on the time necessary to determine the maximum duration that individuals could be maintained without mechanical ventilation support.

Main outcome measures: Magnitude of inspired volume generation and duration of ventilatory support with bilateral diaphragm pacing alone.

Results: In four of the five subjects studied, initial bilateral diaphragm stimulation resulted in inspired volumes between 430 and 1,060 mL. Reconditioning of the diaphragm over several weeks resulted in substantial increases in inspired volumes to 1,100 to 1,240 mL. These subjects were comfortably maintained without mechanical ventilatory support for prolonged time periods by diaphragm pacing, by full-time ventilatory support in three subjects, and 20 h per day, in the fourth subject. No response to stimulation was observed in one subject, most likely secondary to denervation atrophy.

Conclusions: Diaphragm pacing in ventilator-dependent tetraplegic subjects can be successfully achieved via laparoscopic placement of IM electrodes.

*From the Department of Physiology and Biophysics (Drs. DiMarco and Kowalski), and the Department of Biomedical Engineering (Dr. Mortimer), Case Western Reserve University, Cleveland, OH; and the Department of Surgery (Dr. Onders and Mr. Ignagni), University Hospitals of Cleveland, Cleveland, OH. This work was supported by US Food and Drug Administration grant FD-R-001839 and by the Rehabilitation Research Service of the Veterans Affairs.

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Materials and Methods

Subjects

Five subjects with trauma-induced high cervical spinal cord injury who required long-term mechanical ventilatory support were studied. All subjects were in stable condition at the time of...