

## ASK THE EXPERT

## Lung Disease in Rheumatoid Arthritis

**P**ulmonary involvement occurs frequently in patients who have rheumatoid arthritis.

Additionally, as one of the most common extra-articular manifestations of the autoimmune condition, pulmonary involvement contributes substantially to the morbidity and premature mortality that are associated with rheumatoid arthritis, according to Dr. Eric L. Matteson, who is the chair of the rheumatology department at the Mayo Clinic in Rochester, Minn.

In addition to lung disease that is secondary to treatment with certain drugs, such as methotrexate, and lung infection secondary to immunosuppression—the latter of which is relatively common in rheumatoid arthritis (RA)—pulmonary involvement is often directly associated with the underlying RA disease process itself, Dr. Matteson and his colleagues explained in a paper that was published earlier this year.

Indeed, pleural disease, rheumatoid nodules, interstitial lung disease, airway involvement, and pulmonary hypertension are among the lung disease manifestations in this patient population, the researchers wrote (*Curr. Opin. Rheumatol.* 2008;20:340-6).

In this month's column, Dr. Matteson discusses the epidemiology of pulmonary involvement in rheumatoid arthritis patients and provides recommendations and

insight into its diagnosis and management.

**Rheumatology News:** How common is pulmonary disease among rheumatoid arthritis patients?

**Dr. Matteson:** About 8% of patients who have rheumatoid arthritis will also develop clinically important lung disease, although estimates of the prevalence of lung disease vary widely among studies, depending on the method of detection, the criteria used to define the disease, and the study population. However, when it does occur, lung disease has an important effect on reducing the life expectancy of patients who have rheumatoid arthritis.



ERIC L. MATTESON, M.D.

**RN:** What exactly should rheumatologists be looking for?

**Dr. Matteson:** The two major forms of pulmonary disease in RA are forms of interstitial lung disease and obstructive lung disease. The former is related to inflammation in the lung tissue and subsequent scarring. The latter condition is related to diseases of the airways, for example, asthma or emphysema. The most common clinical presentations are shortness of breath and coughing.

The physical examination of the patient may yield some clues about the presence of lung disease, and if there is a suspicion of lung disease, the relevant diagnostic tests include a chest radiograph, pulmonary function tests, and of-

ten a computed tomography examination of the lungs.

High resolution computed tomography (HRCT) in particular is highly sensitive for detecting the presence of interstitial lung disease. Recent advances in HRCT reveal basilar ground glass and reticulonodular opacities, which, along with supporting clinical and physiologic data in asymptomatic patients with rheumatoid arthritis, can lead to earlier diagnosis.

Of course, it is very important to separate the lung disease of rheumatoid arthritis from medication effects on the lung and pulmonary infections as part of this evaluation.

**RN:** What is the presumed mechanism for pulmonary involvement in this group of patients?

**Dr. Matteson:** Unfortunately, so far, this is not very well understood. One thought is that the systemic inflammatory disease that causes the arthritis in the first place may also affect the lung in certain susceptible individuals. Some recently completed studies suggest that T-cell, mast cells, and the CD20+ B cell play a central role in the pathogenesis of interstitial lung disease.

Genetic predisposition and aberrant tissue repair have also been implicated, and obviously there is a certain environmental component to the pathogenetic mechanism, in that people with rheumatoid arthritis who also smoke, for example, are at greater risk of developing lung disease above and beyond those patients who have arthritis but who don't smoke,

and smokers who don't have arthritis.

**RN:** Is it known whether the treatment of RA has any impact on pulmonary involvement in these patients?

**Dr. Matteson:** This is uncertain. It is very likely that early and appropriate treatment may reduce the occurrence of lung disease, and some treatments may conceivably help the lung disease once it is present, but this has not yet been established. The scarring from restrictive lung disease is, as far as we know, not reversible, while obstructive lung disease often responds well to appropriate therapy.

Additionally, there is some evidence linking treatment with anti-CD20 therapy in patients with connective tissue disease with good outcomes in lung disease. Randomized clinical trials are needed to better understand the pathophysiology of lung disease in RA as well as therapeutic response.

**RN:** What are the most important management considerations?

**Dr. Matteson:** Having the underlying arthritis and systemic inflammation under control is very important, and stopping smoking! Assessment for obstructive lung disease and treatment with inhalers is also very important, as is assessment for the present of heart disease associated with lung involvement. ■

DR. MATTESON is a professor of medicine and chair of the department of rheumatology at the Mayo Clinic in Rochester, Minn.

By Diana Mahoney, New England Bureau

## Rheumatologists Spot Overlooked Interstitial Pulmonary Disease

BY SHERRY BOSCHERT  
San Francisco Bureau

SAN FRANCISCO — Clinicians detected underlying rheumatic disease in 17 of 28 patients referred to a multidisciplinary clinic for interstitial lung disease.

The evaluations changed the diagnosis in 11 of the 28 patients, including 4 of 15 patients who had been referred for idiopathic interstitial lung disease and 7 of 13 who had been referred for rheumatic disease related to interstitial lung disease.

As a result, clinicians changed therapy for 14 (50%) of the patients, Dr. Flavia V. Castelino and her associates reported at the annual meeting of the American College of Rheumatology.

The results emphasize that all patients with interstitial lung disease should be evaluated by a rheumatologist, concluded Dr. Castelino of Massachusetts General Hospital, Boston.

Distinguishing between interstitial lung disease that is idiopathic versus related to rheumatic disease is important because the former carries a worse prognosis, and the response to treatment may differ, she said.

A separate retrospective study of 362 cases of interstitial lung disease found 5-year survival rates of approximately 40% with idiopathic disease and approximately 70% with cases that were associated with rheumatic disease (*Am. J. Resp. Crit. Care Med.* 2007;175:705-11).

The difference in prognosis is thought to be related to the major lung histopathology, previously published studies suggest.

For example, nonspecific interstitial pneumonia was present in 4 (9%) of 47 patients with idiopathic interstitial lung disease and in 23 (83%) of 28 patients with undifferentiated connective tissue disease and interstitial lung disease in one study (*Am. J. Resp. Crit. Care Med.* 2007;176:691-7).

A separate, recently published study of 39 cases of interstitial lung disease found that community physicians were more likely to diagnose the condition as idiopathic disease, compared with retrospective diagnoses from a multidisciplinary academic team review conducted by a group of pulmonologists, radiologists, and pathologists (*Am. J. Resp. Crit. Care Med.* 2007;175:1054-60).

In the current prospective study of patients referred by pulmonologists over an 8-month period to a new multidisciplinary clinic at Brigham and Women's Hospital, Boston, all patients were evaluated by a pulmonologist and a rheumatologist, who took a complete history and physical examination (including capillary microscopy) and reviewed laboratory and serologic data.

The physicians also reviewed available imaging and pathologic specimens in consultation with a dedicated radiologist and a pathologist experienced in interstitial lung disease.

Additional serologic tests, imaging, or biopsies were performed at the discretion of the clinic physicians.

They initiated or changed therapy in collaboration with the referring physician.

Evaluations by a rheumatologist significantly affected diagnoses because of additional serologic testing (such as a myositis panel) and because the rheumatologist was able to elicit subtle clues suggestive of a rheumatologic diagnosis.

Recognition of "mechanic's hands," periungual erythema, abnormal capillary microscopy and inflammatory arthritis led to new diagnoses including antisynthetase syndrome, systemic sclerosis, rheumatoid arthritis-associated interstitial lung disease, mixed connective tissue disease, dermatomyositis, and also undifferentiated connective tissue disease.

The patient cohort was half female, with a median age of 63 years and a history of smoking in 23 (82%) of patients.

The multidisciplinary interstitial lung disease clinic now meets weekly and has evaluated an additional 28 patients.

In this group, diagnoses were changed in eight patients, including five patients referred for idiopathic disease who were ultimately found to have rheumatic disease-related interstitial lung disease, Dr. Castelino commented.

The investigators reported having no potential conflicts of interest related to this study. ■



**Rheumatologists' recognition of rheumatic lung disease changed therapy in 50% of cases.**

DR. CASTELINO