A Multipronged Approach to Inflammatory Disorders

An estimated 50 million U.S. adults have physician-diagnosed arthritis, and as the country’s population ages, the number of adults with arthritis is expected to increase sharply to 67 million by 2030. To help address the needs of this growing patient population, Hospital for Special Surgery established the Center for Inflammatory Arthritis in 2008 to provide comprehensive and optimal care for patients with rheumatoid arthritis (RA), psoriatic arthritis, spondyloarthropathies, and other inflammatory disorders. Today, under the direction of Vivian P. Bykerk, MD, the Center’s rheumatologists pursue advances in clinical care, facilitate translational research by enhancing communication between basic scientists and clinicians, participate in the development of novel therapeutics for patients, and take an active role in the education and training of residents and fellows.

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“The Center for Inflammatory Arthritis includes a dedicated inflammatory arthritis clinic, extensive arthritis registries, scientific studies focused on musculoskeletal and autoimmune diseases, and a physician education program,” says Dr. Bykerk. “Most importantly, we emphasize the importance of proper diagnosis and initial optimal therapy, particularly in the early stages of inflammatory arthritis, when one has the best chance to prevent serious, lifelong complications.”

The message of early diagnosis and treatment is one the Center stresses repeatedly – to patients as well as clinicians. “As rheumatologists, we want to see patients with new onset rheumatoid arthritis ideally as soon as possible,” says Dr. Bykerk. “Patients often don’t get to us for four to six months after their symptoms have appeared.”

NewYork-Presbyterian/Columbia Welcomes Rheumatologist with Expertise in Systemic Sclerosis

In 2014 Elana J. Bernstein, MD, MSc, joined the Division of Rheumatology at NewYork-Presbyterian/ Columbia University Medical Center, further expanding the Division’s expertise in fibrosing disorders. Dr. Bernstein’s clinical and research interests focus on scleroderma, as well as on the treatment of pulmonary hypertension and interstitial lung disease in patients with autoimmune diseases.

It was during her residency at Massachusetts General Hospital that Dr. Bernstein first became interested in fibrosing disorders. “My research there focused on nephrogenic systemic fibrosis, a condition that results from exposure to gadolinium contrast during MRI,” says Dr. Bernstein. “I think scleroderma was a natural transition for me during my fellowship in rheumatology at Hospital for Special Surgery.”

Dr. Bernstein joined Columbia in 2014 following her fellowship, during which time she received the American College of Rheumatology Distinguished Fellow Award and the Hospital for Special Surgery Charles L. Christian Award for Excellence in Musculoskeletal Research.

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Most recently Dr. Bernstein’s research on the use of a novel non-invasive test to identify pulmonary hypertension (PH) in patients with systemic sclerosis was published in the October 2013 issue of *Arthritis Care & Research*.

“Pulmonary hypertension is a serious complication of scleroderma, and a leading cause of death. Unfortunately, it happens all too often that by the time patients present with symptoms of pulmonary hypertension, they already have significant hemodynamic compromise,” says Dr. Bernstein. “One of my goals is to be able to identify pulmonary hypertension early, before patients become symptomatic, so that we can treat them early and, hopefully, improve outcomes.”

Traditionally, screening methods for pulmonary hypertension in people with scleroderma have included an echocardiogram and pulmonary function tests. “These tests do give us important information, but unfortunately they do not identify everyone with pulmonary hypertension,” says Dr. Bernstein. “The echocardiogram can actually be quite inaccurate in its estimation of pulmonary artery pressure. The research that I began at Hospital for Special Surgery is investigating a submaximal stress test as a way to identify scleroderma patients with pulmonary hypertension.”

In other research at Columbia, Dr. Bernstein is looking at outcomes in scleroderma patients who undergo lung transplantation. “Lung transplantation is a potentially lifesaving procedure for scleroderma patients who develop end-stage lung disease due to pulmonary hypertension or interstitial lung disease,” says Dr. Bernstein. “However, some transplant centers hesitate to transplant these patients for fear that they might not do as well compared to people who are transplanted for interstitial lung disease or pulmonary hypertension not due to scleroderma. This hesitancy stems from the extra-pulmonary manifestations that scleroderma patients often have, such as gastroesophageal reflux disease, that can go on to injure the transplanted lung.

The goal of this research is to determine how scleroderma patients actually fare following lung transplantation, to identify risk factors for outcome, and to modify those that are modifiable.”

In this research endeavor, Dr. Bernstein is working with Columbia colleagues David J. Lederer, MD, MS, Associate Medical Director of the Lung Transplant Program and Co-Director of the Interstitial Lung Disease Program, and Nina Patel, MD, Associate Director of the Interstitial Lung Disease Program, to study and treat patients with autoimmune disease-related interstitial lung disease.

**On the Horizon**

NewYork-Presbyterian/Columbia will be taking part in a National Institutes of Health-sponsored multicenter trial of rituximab for the treatment of scleroderma-associated pulmonary arterial hypertension. “Scleroderma is a complex disease with many manifestations that requires a multidisciplinary approach not only for the care and management of patients, but also to study the disease and all of its components,” says Dr. Bernstein. “We are committed to taking care of the medical and psychosocial needs of patients with complex autoimmune disorders, and are also furthering a very rigorous research program that we hope will benefit patients in the future.”

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**Reference Articles**


**For More Information**

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been identified. The longer they wait, the higher the chance damage will occur. We strive to increase awareness about inflammatory arthritis to ensure that these patients are promptly and appropriately referred.”

According to Dr. Bykerk, patients with early RA need to know that with prompt diagnosis and treatment, they will be functioning better one to two years later, with a greater opportunity for remission and a lower risk for joint damage. “If patients know that these are our goals, then when their doctor recommends treatment, they will be more aligned with and accepting of the plan of care,” says Dr. Bykerk. “I think that’s where we can make a difference.”

From a research perspective, says Dr. Bykerk, the Center for Inflammatory Arthritis is “trying to move the bar in terms of understanding disease mechanisms, finding new treatment targets, and testing new therapies. We want to be able to characterize clinical scenarios that make the benefits of having early therapy clear, as well as clarify the advantages of one strategy versus another – comparative effectiveness-type questions. We also want to translate the knowledge to the patients so that they are more informed when they are under care, which, eventually, will make care easier for the providers.”

**Toward a Better Definition of Flare**

Defining and managing flare is another major topic of interest for Dr. Bykerk and her colleagues. “We have studies that are looking at de-escalating therapies,” says Dr. Bykerk. “It’s partly to save cost, but mostly to avoid therapies with additional risk and save patients the aggravation of having to be on so much medication. So we want to be able to identify patients who could de-escalate therapy safely, but also to teach patients to self-manage their flares, and provide them with guidance on when to contact their physician if they are in flare. However, the overall foremost aim is to keep these diseases under excellent control.”

Dr. Bykerk is quick to point out, however, that there needs to be consensus on the definition of flare and the ability to identify and measure flare in patients. To this end, she and members – including patients from around the world – of the OMERACT (Outcome Measures in Rheumatology) RA Flare Group have been developing a data-driven, patient-inclusive, consensus-based RA flare definition for use in clinical trials, long-term observational studies, and clinical practice.

During the Flare Group’s recent workshop, a core domain set to measure RA flare was ratified and endorsed by those in attendance. According to the OMERACT Flare Group, “A reliable and valid method to identify and quantify significant inflammatory flares in severity and effect is needed given that biological drug tapering and withdrawal trials are now being conducted with ‘time to flare’ and ‘number of flares’ proposed as outcomes.”

**Core Set of Nine Domains to Identify and Measure RA Flare**

<table>
<thead>
<tr>
<th>RA Core Set¹</th>
<th>New Domains²</th>
<th>Additional Domains³</th>
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<tbody>
<tr>
<td>1) Pain</td>
<td>6) Fatigue</td>
<td>Sleep</td>
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<tr>
<td>2) Function</td>
<td>7) Stiffness</td>
<td>Emotional distress</td>
</tr>
<tr>
<td>3) Tender joints</td>
<td>8) Participation</td>
<td>Systemic features</td>
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<tr>
<td>4) Swollen joints</td>
<td>9) Self-management</td>
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<td>5) Patient global assessment</td>
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¹American College of Rheumatology preliminary core set of disease activity measures for rheumatoid arthritis clinical trials (1993)
²New domains added by OMERACT RA Flare Group 11
³Met lower rates of consensus (> 50% but < 70%) but would form part of the research agenda

Source: *Journal of Rheumatology*, April 2014

(continued on page 4)
predict who will be a responder to what strategy from the outset. “We know that 30 to 40 percent of people with early RA will fare very well with methotrexate at effective doses – 25 milligrams; however, the remainder require a more intensive treatment strategy,” says Dr. Bykerk. “It would be very helpful to know in advance how people are going to do so that we’ll be able to inform them. We’re working towards that aim.”

Continuing Studies on a Multicenter Scale

Before relocating to the United States three years ago, Dr. Bykerk initiated the Canadian early ArThritis CoHort (CATCH) multicenter research project in early arthritis, and she is now extending this work by revamping the project to keep its relevance to modern day research questions. This project will now include sites throughout North America, including its American counterpart of CATCH-US. “When we first started CATCH, our core group was interested in the clinical outcomes of our patients with early arthritis to better understand the disparate outcomes. We are now looking to find better ways to predict their outcomes based on certain characteristics and biological features,” says Dr. Bykerk. “It is primarily a mission to continue to ensure best outcomes. Along with that, we wanted to educate patients to the importance of early diagnosis and prevent them from developing deformity, disability, dysfunction, and other related health consequences.”

The research has produced and continues to deliver abundant and important data on outcomes of patients with early RA – defined as having symptoms of joint pain and swelling for one year or less – including patient-reported measures, medication usage, physical findings, and changes noted in imaging studies. “We have shown, for example, that people who have been treated in larger sites tended to have higher rates of remission and are generally prescribed a more intensive treatment regimen,” notes Dr. Bykerk.

In the development of CATCH-US, Dr. Bykerk and her colleagues are using a similar data capture mechanism and are working towards the same goal: that is to understand best practices that can be implemented more widely to enable patients with new onset RA to achieve remission.

Reference Articles


For More Information

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