NewYork-Presbyterian

ADVANCES IN RHEUMATOLOGY

Affiliated with Columbia University College of Physicians and Surgeons and Weill Cornell Medical College

JUNE/JULY 2014

The rheumatology program at NewYork-Presbyterian Hospital is comprised of faculty affiliated with Weill Cornell Medical College and Hospital for Special Surgery, and Columbia University College of Physicians and Surgeons. The program provides state-of-the-art care to patients with the broad range of inflammatory and autoimmune diseases, pursues groundbreaking research at both the laboratory level and through clinical studies, and offers comprehensive training to medical residents and fellows.

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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.

> **"We emphasize the importance of proper diagnosis and initial optimal therapy, particularly in the early stages of inflammatory arthritis."**
> — Vivian P. Bykerk, MD

"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

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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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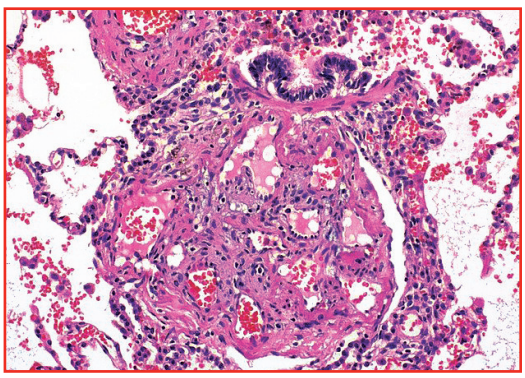

Micrograph showing a plexiform lesion of the lung, as seen in irreversible pulmonary hypertension

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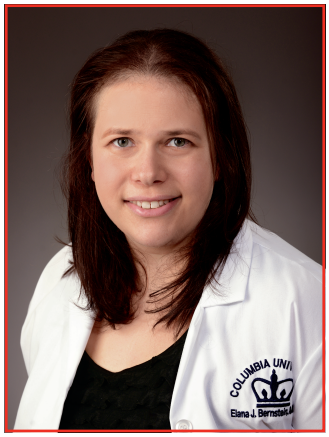
NewYork-Presbyterian/Columbia Welcomes Rheumatologist with Expertise in Systemic Sclerosis *(continued from page 1)*

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."



Dr. Elana J. Bernstein

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."

> **"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."**
>
> **— Dr. Elana J. Bernstein**

Dr. Bernstein collaborated with Evelyn M. Horn, MD, Director of Heart Failure and Pulmonary Hypertension at the Perkin Heart Failure Center at NewYork-Presbyterian/Weill Cornell Medical Center, as well as rheumatologists at Hospital for Special Surgery. Their study sought to determine if the submaximal heart and pulmonary evaluation (step test) could be used to identify patients with PH and to assess the correlation between change in end-tidal carbon dioxide from rest to end-exercise on the step test and mean pulmonary artery pressure (mPAP) on right-sided heart catheterization (RHC) in scleroderma patients.

"Although right-sided heart catheterization is the gold standard for diagnosing pulmonary hypertension, it is an invasive test with associated risks," says Dr. Bernstein. The retrospective cohort study examined the charts of 19 patients with limited or diffuse cutaneous system sclerosis who were evaluated in an academic cardiology practice over a four-year period and who underwent a step test and RHC. The researchers concluded that the step test has a strong, statistically significant negative correlation with mPAP on RHC. Dr. Bernstein presented the results of this study at a recent American College of Rheumatology Annual Meeting.

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."

Reference Articles

Bernstein EJ, Isakova T, Sullivan ME, Chibnik LB, Wolf M, Kay J. Nephrogenic systemic fibrosis is associated with hypophosphataemia: a case-control study. *Rheumatology* (Oxford). 2014 Apr 4. [Epub ahead of print]

Bernstein EJ, Mandl LA, Gordon JK, Spiera RF, Horn EM. Submaximal heart and pulmonary evaluation: a novel noninvasive test to identify pulmonary hypertension in patients with systemic sclerosis. *Arthritis Care & Research* (Hoboken). 2013 Oct;65(10):1713-18.

Bernstein EJ, Schmidt-Lauber C, Kay J. Nephrogenic systemic fibrosis: a systemic fibrosing disease resulting from gadolinium exposure. *Best Practice & Research Clinical Rheumatology.* 2012 Aug;26(4):489-503.

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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."

Dr. Vivian P. Bykerk

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 OMERACT RA Flare Group 11

RA Core Set[1]	New Domains[2]	Additional Domains[3]
1) Pain	6) Fatigue	Sleep
2) Function	7) Stiffness	Emotional distress
3) Tender joints	8) Participation	Systemic features
4) Swollen joints	9) Self-management	
5) Patient global assessment		

[1] *American College of Rheumatology preliminary core set of disease activity measures for rheumatoid arthritis clinical trials (1993)*
[2] *New domains added by OMERACT RA Flare Group 11*
[3] *Met lower rates of consensus (> 50% but < 70%) but would form part of the research agenda*
Source: *Journal of Rheumatology*, April 2014

Developing Guidelines for Perioperative Management

In collaboration with the Hospital's orthopedic surgeons, the Center for Inflammatory Arthritis also has a number of research projects underway to improve perioperative outcomes of patients with rheumatic disease. In particular, Dr. Bykerk works in close collaboration with Susan M. Goodman, MD, and her colleagues as a team to develop new recommendations for perioperative management of patients with inflammatory arthritis in terms of medication use.

"We're following all of our patients with inflammatory arthritis who undergo hip and knee arthroplasties and examining their outcomes in relation to flares of RA," says Dr. Bykerk. "We're posing a number of questions that will enable us to inform clinicians on how to best advise their patients when they're going for surgery if they're on biologics, methotrexate, or steroids to best navigate through the perioperative course. We're looking at predictors of infection, impact of flare at the time of arthroplasty, and how the flare will affect the patient's ability to undergo rehabilitation and subsequently its bearing on the success of a joint arthroplasty one year later. We want to be able to establish perioperative guidelines for patients with inflammatory arthritis that are evidence-based and lead to better outcomes."

The researchers are also studying predictors of response to therapy to see if they can identify any molecular signatures to help

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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

Bykerk VP, Lie E, Bartlett SJ, Alten R, Boonen A, Christensen R, Furst DE, Hewlett S, Leong AL, Lyddiatt A, March L, May JE, Montie P, Orbai AM, Pohl C, Scholte Voshaar M, Woodworth T, Bingham CO 3rd, Choy EH. Establishing a core domain set to measure rheumatoid arthritis flares: report of the OMERACT 11 RA Flare Workshop. *Journal of Rheumatology.* 2014 Apr;41(4):799-809.

Choy T, Bykerk VP, Boire G, Haraoui BP, Hitchon C, Thorne C, Keystone EC, Pope JE; CATCH Investigators. Physician global assessment at 3 months is strongly predictive of remission at 12 months in early rheumatoid arthritis: results from the CATCH cohort. *Rheumatology* (Oxford). 2014 Mar;53(3):482-90.

Arnold MB, Bykerk VP, Boire G, Haraoui BP, Hitchon C, Thorne C, Keystone EC, Pope JE; on behalf of CATCH Investigators. Are there differences between young- and older-onset early inflammatory arthritis and do these impact outcomes? An analysis from the CATCH cohort. *Rheumatology* (Oxford). 2014 Feb 5. [Epub ahead of print]

Bykerk VP, Shadick N, Frits M, Bingham CO 3rd, Jeffery I, Iannaccone C, Weinblatt M, Solomon DH. Flares in rheumatoid arthritis: frequency and management. A report from the BRASS registry. *Journal of Rheumatology.* 2014 Feb;41(2):227-34.

For More Information

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