



# Respiratory Exchange

## The Heat is On for Severe Asthma

### Bronchial Thermoplasty Provides New Relief

By Thomas R. Gildea, MD, and Serpil Erzurum, MD

Bronchial thermoplasty can improve the quality of life, and significantly reduce emergency department visits in adults with severe asthma.

The results of the Asthma Intervention Research 2 (AIR2) trial recently were released at the American Thoracic Society International Conference in San Diego in May 2009. The AIR2 trial was a randomized, prospective, blinded trial comparing the Alair System (Asthmatx), the device used in the bronchial thermoplasty (BT) procedure, to sham bronchoscopy.

The multi-center study enrolled 297 patients at 30 centers in six countries. Cleveland Clinic was a high-enrolling center in this trial, which was conducted as a follow-up to the AIR trial published in the *New England Journal of Medicine* in March 2007 that showed improvements of asthma control in individuals with moderate or severe disease. The AIR2 trial served as a pivotal study that included a sham procedure arm, an unprecedented recommendation, whose results and application for approval are now before the U.S. Food and Drug Administration under a rare expedited review process.

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## Dear Colleagues:

At Cleveland Clinic, patients with respiratory disease benefit from the expertise of a multidisciplinary team consisting of clinicians specializing in pulmonary and critical care medicine, allergy and clinical immunology and thoracic surgery, all working in close collaboration with thoracic radiologists and pulmonary pathologists.

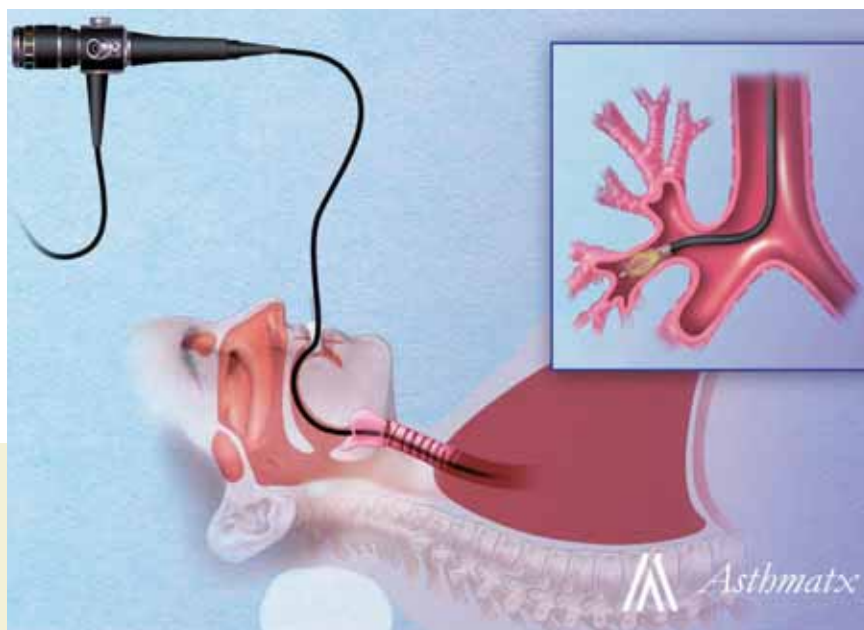
In 2008, we experienced continued growth in our clinical programs, research funding and application of innovative technologies. In this issue of *Respiratory Exchange*, you will find articles illustrating much of this work, particularly in the areas of asthma, lung transplantation, breath analysis and interstitial lung disease.

For more information about our ongoing clinical and research activities in respiratory disorders, please visit [clevelandclinic.org/pulmonary](http://clevelandclinic.org/pulmonary) (current and archived issues of *Respiratory Exchange* are available here) and [clevelandclinic.org/thoracic](http://clevelandclinic.org/thoracic).

I hope that you are able to spend some time reviewing *Respiratory Exchange* and find it valuable and helpful in your practice. Please feel free to contact us at our toll-free number for physicians, 866.CCF.LUNG (866.223.5864), if you have any questions or would like to refer a patient. As always, we welcome the opportunity to work with you.

Sincerely,

**Herbert P. Wiedemann, MD, MBA**  
Chairman, Cleveland Clinic  
Respiratory Institute



## The Heat is On for Severe Asthma continued

If approved, it would become the first non-pharmaceutical therapy to effectively treat severe asthma. The Alair System has a CE mark, which certifies that a product has met EU consumer safety, health or environmental requirements.

The main findings of the AIR2 trial<sup>1,2</sup> were:

- Improvement in the average Asthma Quality of Life Questionnaire (AQLQ) score at 6-, 9-, and 12 months over sham control
- 80 percent of BT-treated patients noted a clinically significant improvement in AQLQ compared to 64 percent of sham controls
- 32 percent reduction in asthma attacks
- 84 percent reduction in emergency room visits for respiratory symptoms
- 36 percent reduction in patients reporting episodes of asthma (multiple symptoms) adverse events
- 66 percent reduction in days lost from work/school or other activities due to respiratory symptoms

Bronchial thermoplasty is a minimally invasive treatment regimen. A complete treatment includes three separate bronchoscopic procedures performed in an outpatient suite under conscious sedation, with no hospitalization required. In each procedure, which takes about one hour, a catheter within an expandable wire basket makes contact with airway walls and delivers about 10 seconds of thermal energy per actuation. The number of regions treated varies depending on the patient's lung size, but the intent is to treat every visible airway of 3 mm size or greater. We start treatment at the farthest distal region of the airway and work backwards (proximal) to the main bronchi.

## Bronchial Thermoplasty Being Performed at Cleveland Clinic



Catheter deployed through bronchoscope into airway to be treated.



Basket deployed making contact and delivering energy (note blanching).

Each lower lobe is treated in its own session and then both upper lobes are treated in a third session to complete the treatment.

Respiratory adverse events were more common during the treatment phase for BT-treated subjects, 161 (85 percent) vs. sham bronchoscopy 74 (76 percent), but this trend reversed in the 12 to 52 weeks after treatment in which 130 (70 percent) respiratory adverse events were noted in the BT group and 78 (80 percent) in the sham bronchoscopy group. The most common adverse events were upper respiratory tract infections, asthma exacerbations and chest pain. Severe adverse events occurred in 3 percent of treated patients, the most significant of which was hemoptysis treated with embolization. There were no reports of episodes of pneumothorax, respiratory failure, airway stenosis or death.

In anticipation of FDA-approval later this year, we are building a clinical program in the Respiratory Institute that incorporates bronchial thermoplasty into our existing comprehensive Asthma Center as a treatment option for individuals who would likely benefit from the treatment.

**Dr. Thomas Gildea, MD, is the Head of the Section of Bronchoscopy in the Respiratory Institute. He can be contacted at 216.444.6490 or [gildeat@ccf.org](mailto:gildeat@ccf.org). Dr. Serpil Erzurum is the Chairman of the Department of Pathobiology and Co-Director of the Asthma Center. She can be reached at 216.445.7191 or [erzurum@ccf.org](mailto:erzurum@ccf.org). For patient referrals, please call Michelle Koo at 216.445.1756.**

<sup>1</sup> <http://www.asthmatx.com/united-states/about-us/asthma-information.html>

<sup>2</sup> <http://www.thoracic.org/sections/publications/press-releases/conference/articles/2009/abstracts-and-press-releases/castro.pdf>

### Recommended Reading

Cox G, Thompson N, Rubin A, et al. Asthma control during the year after bronchial thermoplasty. *N Engl J Med* 2007; 356:1327-1337.

M Wechsler, R Olivenstein, R Niven, and I Pavord. Asthma-related ER visits and hospitalizations following bronchial thermoplasty (BT) in patients with severe, symptomatic asthma. *Am. J. Respir. Crit. Care Med.*, Apr 2009; 179: A2779.

P Shah, J Fiterman, C McEvoy, and S Erzurum. Safety of bronchial thermoplasty (BT) in patients with severe, symptomatic asthma: positive safety profile in the AIR2 trial. *Am. J. Respir. Crit. Care Med.*, Apr 2009; 179: A2814.

### Respiratory Exchange

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## What is the Role of TNF Inhibitors in Sarcoidosis?

By Daniel A. Culver, DO, and Joseph Parambil, MD

Management of severe or multi-organ sarcoidosis poses a challenge for pulmonologists, who are often called upon to plan and coordinate the overall treatment approach. Biologic therapies targeting tumor necrosis factor now offer a powerful therapeutic option for selected individuals with serious disease. Some manifestations, especially cutaneous and central nervous system sarcoidosis, may respond dramatically.

Tumor necrosis factor (TNF) is a pivotal mediator of granuloma formation. TNF also modulates cell activation, recruitment, endothelial permeability and apoptosis. At Cleveland Clinic, we have used monoclonal antibodies that block TNF, mainly infliximab infusions, for a wide variety of sarcoidosis manifestations over the past seven years. Adalimumab, which has the advantages of lower immunogenicity and subcutaneous administration, also has efficacy for some patients; however, in our experience infliximab is a more reliably effective agent for severe disease. There have been no head-to-head comparisons of these agents in sarcoidosis. Similar to inflammatory bowel disease, the soluble receptor antagonist etanercept does

not appear to be effective for sarcoidosis. We are also participating in a new study to evaluate the effects of a novel subcutaneous TNF inhibitor (golimumab) and an IL-12/IL-23 inhibitor (ustekinumab) (see sidebar).

We participated in a three-arm randomized, double-blind placebo controlled trial of infliximab (3 mg/kg and 5 mg/kg) vs. placebo for pulmonary sarcoidosis, published in 2006. The overall results of the trial were a disappointment in some quarters: although the primary end-point, FVC, was improved (2.5 percent increase from baseline,  $p < 0.04$ ), the effect size was deemed small. However, it appears that patients with more dyspnea, worse baseline vital capacity and disease duration

more than two years can derive more substantial benefits. In our experience, moderate or marked benefit from the addition of infliximab has been seen in 79 percent of patients with pulmonary disease as the index lesion (see graph at left).

Infliximab appears to be most effective for treatment of some extrapulmonary manifestations. Central

nervous system and cutaneous involvement often respond dramatically. We recently reported overwhelming benefits from switching to infliximab in patients with refractory severe central nervous system sarcoidosis, all of whom were actively progressing on moderate- to high-dose corticosteroids and IV cyclophosphamide. As a result, we generally add infliximab early in the disease course for patients with organ-threatening, severe disease, if corticosteroids are ineffective (see typical MRI response to IFX at right).

As a result of our approach, we have been able to reduce the prednisone dose to less than 10 mg/d in over 90 percent of patients treated with infliximab. Since corticosteroid toxicities are a substantial burden in the chronic sarcoidosis population, quality of life is typically enhanced with this approach. Similar to other investigators, we have found that more than half of patients experience a relapse of their disease if the infusions are stopped.

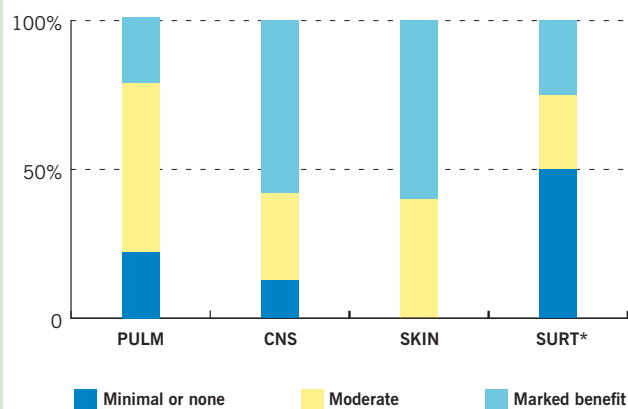
Important issues for consideration prior to starting TNF antagonists for sarcoidosis include:

- Screening for latent tuberculosis is mandatory. Since sarcoidosis patients are typically anergic, the history is the most important screening tool. Interestingly, however, to our knowledge there have not been any cases of tuberculosis among sarcoidosis patients treated with TNF antagonists. But, other granulomatous and non-granulomatous infections, especially endemic fungi, have occurred.

### Severe Sarcoidosis:

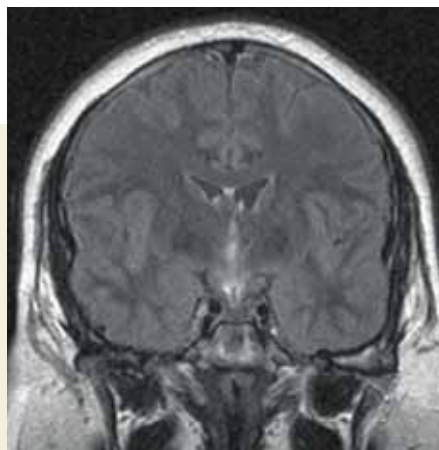
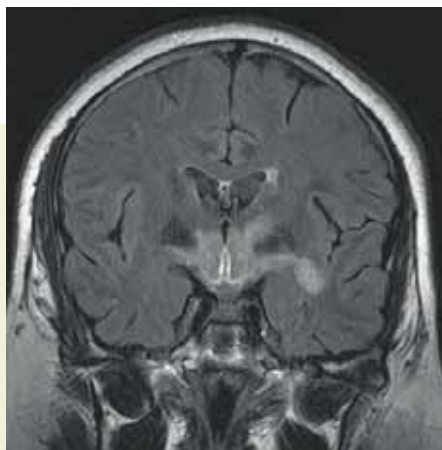
#### Infliximab Response Rates at Cleveland Clinic: Four Most Common Primary Indications

N=50



\*sarcoidosis of the upper respiratory tract

Effects of treatment with infliximab for the four most common index lesions treated at the Cleveland Clinic Sarcoidosis Center of Excellence. Marked response connotes resolution or near-resolution of the disease, and moderate response implies that there was improvement of the index lesion and reduction of corticosteroids to less than 10 mg/day.



Response to infliximab in a 20 year-old male with severe CNS sarcoidosis refractory to high doses of steroids. FLAIR images reveal substantial involvement of the cerebral peduncles at baseline (left), which has resolved after four doses of infliximab (right).

- Infusion reactions are rare in our experience, but more common (up to 10 percent) in the literature, so all infusions should occur in a monitored setting. We typically perform infusions in our outpatient clinic.
- We generally administer a second agent, such as methotrexate or leflunomide, concomitantly to improve effectiveness of the TNF antagonist, perhaps by reducing immunogenicity provoked by the monoclonal antibodies or by synergistic effects.
- Other cautions regarding the use of TNF antagonists include possible increased

risk of malignancy, presence of severe cardiomyopathy, and development of new demyelinating lesions.

Given the expense and potential toxicities associated with their use, TNF antagonists remain third- or fourth-line therapy in most individuals. Tools to predict which patients will benefit most are not available, but the presence of active inflammation, longer disease duration, elevated C-reactive protein, more severe symptoms and certain organ manifestations suggest the highest likelihood of success.

#### Recommended Reading:

Sodhi M, Pearson K, White ES, Culver DA. Infliximab therapy rescues cyclophosphamide failure in severe central nervous system sarcoidosis. *Respir Med* 2009; 103:268-73.

Crouser ED, Culver DA, Knox KS, Julian MW, Shao G, Macre JE, Liyanarachchi S, Abraham S, Wewers MD, Gavrilin M, Ross P, Abbas A, Eng C. Gene expression profiling identifies MMP-12 and ADAMDEC1 as potential pathogenic mediators of pulmonary sarcoidosis. *Am J Respir Crit Care Med* 2009; 179: 929-38.

Diaz-Guzman E, Farver CF, Parambil J, Culver DA. Pulmonary hypertension caused by sarcoidosis. *Clin Chest Med*. 2008; 29:549-63.

Culver DA, Newman LS, Kavuru MS. Gene-environment interactions in sarcoidosis: challenge and opportunity. *Clin Dermatol* 2007; 25:267-75.

Pandya C, Brunken RC, Tchou P, Schoenhagen P, Culver DA. Detecting cardiac involvement in sarcoidosis: a call for prospective studies of newer imaging techniques. *Eur Respir J*. 2007;29:418-22.

Barna BP, Culver DA, Abraham S, Malur A, Bonfield TL, John N, Farver CF, Drazba JA, Raychaudhuri B, Kavuru MS, Thomassen MJ. Depressed peroxisome proliferator-activated receptor gamma (PPARγ) is indicative of severe pulmonary sarcoidosis: possible involvement of interferon gamma (IFN-γ). *Sarcoidosis Vasc Diffuse Lung Dis*. 2006; 23:93-100.

Culver DA, Barna BP, Raychaudhuri B, Bonfield TL, Abraham S, Malur A, Farver CF, Kavuru MS, Thomassen MJ. Peroxisome proliferator-activated receptor gamma activity is deficient in alveolar macrophages in pulmonary sarcoidosis. *Am J Respir Cell Mol Biol* 2004;30:1-5.

## Sarcoidosis Care and Available Studies at Cleveland Clinic

Established in 2000, the Cleveland Clinic Sarcoidosis Center of Excellence is dedicated to providing comprehensive clinical care and advancing research for this disease. Our mission is to provide a coordinated approach to this multi-system disease for patients and providers. Since 2005, we have treated nearly 600 unique sarcoidosis patients a year.

To facilitate this goal, we have assembled a collaborative core of physicians with interest in sarcoidosis, including dedicated specialists in ophthalmology, dermatology, neurology, hepatology, heart failure, electrophysiology and otorhinolaryngology. For patients with difficult-to diagnose disease, we collaborate with the Granuloma Clinic in the Department of Infectious Diseases. Typically, we arrange for patients to be seen by all the relevant providers during their visit here.

We recently started a dedicated joint neurosarcoidosis clinic with one of our core neurologists, Jinny Tavee, MD. As an additional service,

we will soon begin offering same-day biopsy testing for small fiber neuropathy (SFN), a common but under-recognized complication of sarcoidosis. Cleveland Clinic is one of only five centers in the U.S. to provide this diagnostic test.

We are currently participating in two multicenter clinical trials: a 1:1:1 randomized, double-blind study comparing a novel TNF antagonist (golimumab), an IL-12/IL-23 antagonist (ustekinumab) and placebo for chronic treatment-requiring pulmonary or cutaneous sarcoidosis; and, a randomized, double-blind placebo controlled trial of bosentan for sarcoidosis-associated pulmonary hypertension.

For further information, please contact Karla Pearson, PA-C at 216.444.6508 or pearsok@ccf.org, Daniel Culver, DO, at 216.444.6508 or culverd@ccf.org, or Joseph Parambil, MD, at 216.444.7567 or parambj@ccf.org.



## In the Spotlight: Critical Care Transport

Cleveland Clinic's Critical Care Transport team is ready to respond 24/7 to just about any emergency, anywhere in the world. Our transport team can start tertiary care during transfer to one of our many facilities, thus improving the outcomes for many serious and complex conditions.

### STAFF

Our team is made up of Cleveland Clinic physicians and pediatric intensivists, nurse practitioners, critical care nurses and allied health professionals. Each medical team is customized to meet the needs of the patient and is ready at a moment's notice for regular patient transfers, as well as transfers of highly acute patients.

### SERVICES OFFERED

24/7 Adult critical care transport by ground or air by team experienced in critical care and/or emergency services and trained in transport environment care, 24/7 pediatric critical care transport by ground or air by team specially trained in neonatal and pediatric intensive care, emergency and transport medicine and flight physiology.

### NEW BEDS

To make sure your patients get the specialized care he or she needs, we now have 24 dedicated Cardiovascular ICU beds with adjacent imaging and cath labs, and a cardiology fellow in attendance, 24/7. Our medical intensive care unit (MICU) has recently been expanded by eight beds and will expand to a total of 43 beds by 2010. The unit is staffed by a board certified intensivist in-house 24 hours and receives patient transfers from the region and neighboring states, constituting 31.2 percent of all admissions to the unit.

### OUR FLEET

Local patients can be transferred to Cleveland Clinic by fully staffed Mobile Intensive Care Units. Our air transport capabilities include a Sikorsky S-76 A++ for our immediate 250-mile radius, and a Beechjet 400A and Hawker 800 for longer distances – both staffed and equipped as “flying ICUs.”

**For more information, visit [clevelandclinic.org/cct](http://clevelandclinic.org/cct)**

## Instructions for Transport

NEW! Acute transfers, call 877.379.CODE (2633). One call to this number immediately launches a flight – with no delay-causing dispatch protocols.

Routine transfers, call 216.444.8302 or 800.533.5056

### Have the following information ready

- Patient name
- Date of birth
- Cleveland Clinic medical record number
- Insurance information
- Diagnosis and location of patient
- Need for telemetry
- If the patient has invasive lines, assistive devices or drip; if the patient is hemodynamically stable

# What's New in Interstitial Lung Disease

## IPF Research Update

By Mitchell Olman, MD

### Examining Fibroblast Migration and Proliferation

Pulmonary fibrosis (PF) is a devastating disease, and those afflicted have an average survival similar to that seen with cancer. Current treatment is focused on the amelioration of symptoms, without addressing the underlying problem or staying the inexorable progressive of the disease. This disease affects more than 100,000 patients a year in the United States alone.



The driving force behind my move to the Department of Pathobiology and the Respiratory Institute at Cleveland Clinic was to help patients through pushing forward the boundaries of translational and basic research into this devastating disorder. To this end, our basic laboratory studies the pathways by which fibroblasts, the cells that form the scar in PF, are activated to do so. We study the factors and processes that induce fibroblast migration and proliferation in the context of PF. Specifically, we are interested in the ability of the naturally occurring proteins of the coagulation/fibrinolytic (blood clotting/dissolving) system's capacity to modulate fibroblast pro-fibrotic processes.

In the clinic, we are currently enrolling, and will start several new clinical trials for PF as one of 22 sites selected by the National Institutes of Health to participate in the Idiopathic Pulmonary Fibrosis clinical research network (IPF-Net). In fact, work in our labs has allowed me the honor and privilege of developing the first national clinical trial to use treatments directed toward the coagulation system in patients with PF.

*Dr. Mitchell Olman recently joined Cleveland Clinic in the Department of Pathobiology and the Respiratory Institute.*

## IPF Network Update

By Jeffrey T. Chapman, MD

As a new member of the NHLBI-sponsored Idiopathic Pulmonary Fibrosis Research Network (IPF-Net), we recently completed enrolling patients in two clinical trials for patients with newly diagnosed IPF, the BUILD 3 and STEP trials.

This group of 22 sites throughout the U.S. formed to evaluate multi-drug therapeutic trials for stabilizing IPF is now enrolling patients for two additional trials for early IPF, ARTEMIS and MUSIC (see box for study criteria).

At Cleveland Clinic's Respiratory Institute, we also have been busy with our multidisciplinary, weekly IPF conference, which is designed to bring together experts from pulmonology, thoracic surgery, lung transplantation, radiology, to review IPF cases for both multidisciplinary clinical management decisions and education. This also provides a forum to discuss new treatment protocols or experimental therapies.

## Actively Enrolling IPF-Net Trials:

### **AMBRISENTAN (ARTEMIS)**

This randomized clinical trial, sponsored by Gilead Sciences, Inc., is studying ambrisentan (endothelin receptor blocker) vs. placebo in patients with early idiopathic pulmonary fibrosis for 12-24 months. The primary outcome is delay in disease progression or death.

#### **ELIGIBILITY:**

Patients age 40 to 80 years with IPF diagnosis  $\geq 3$  months via a surgical lung biopsy or HRCT. Exclusion criteria include  $>5\%$  honeycomb on HRCT scan and  $FVC < 50\%$  predicted.

#### **PRINCIPAL INVESTIGATOR:**

Jeffrey Chapman, MD

#### **STUDY COORDINATOR:**

Diane Faile, BS, RRT, 216.444.9975

### **MACITENTAN (MUSIC)**

This randomized clinical trial, sponsored by Actelion, is studying macitentan (endothelin receptor blocker) vs. placebo in patients with idiopathic pulmonary fibrosis for one year. The primary outcome is change in forced vital capacity. Randomization will be 2:1 in favor of the treatment arm.

#### **ELIGIBILITY:**

Patients age 18 years or older with IPF diagnosis  $< 3$  years via a surgical lung biopsy. Exclusion criteria include extensive honeycomb on HRCT scan,  $FVC < 50\%$  predicted or  $DLCO < 30\%$  predicted.

#### **PRINCIPAL INVESTIGATOR:**

Jeffrey Chapman, MD

#### **STUDY COORDINATOR:**

Ron Wehrmann, RRT, 216.445.0574

## Examining the Pathobiology and Therapeutics of Ischemia Reperfusion Injury

by Kenneth McCurry, MD

Ischemia reperfusion injury not only causes acute problems within a day or two of heart and lung transplantation, it also can make organs more susceptible to rejection and decrease long-term survival rates. What has not been fully explained is what causes that process. What are the triggers? What exacerbates it?

In my lab, I am looking for answers to these questions in hopes of developing techniques, strategies, pharmacological agents or other approaches to try and protect the heart or lungs during the transplant process. Specifically, I am examining several therapeutic agents that might have a protective effect in heart and lung transplant models.

One of the agents I have been studying in recent years is carbon monoxide. While it is toxic in higher doses, it is quite protective for ischemia reperfusion injury in lower doses.

In previous studies, my colleagues and I found that carbon monoxide provides protection against oxidative stress via anti-inflammatory and cytoprotective actions as well as that a carbon monoxide-saturated preservation solution protects lung grafts from ischemia-reperfusion injury. I expect to report additional findings later this year.

A second agent I have more recently begun examining is nitrite, a common anion in the body. Nitrite is a metabolite of nitric oxide that appears to have a very significant protective effect against ischemia reperfusion injury. We are working to develop a delivery system for nitrite to a point where it can be evaluated in a clinical trial in lung transplantation.

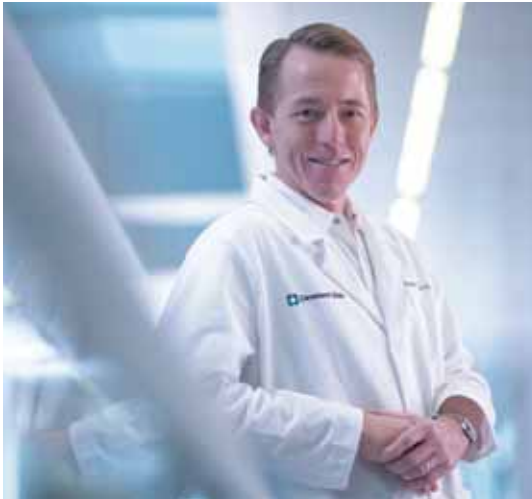
I have been collaborating on this work with Mark T. Gladwin, MD, Director of the Hemostasis and Vascular Biology Research Institute at the University of Pittsburgh Medical Center, and hope to secure funding for a multicenter study of nitrites in pulmonary and cardiac transplantation.

On the clinical research side, I have recently focused on alternative immunosuppressive strategies for both heart and lung recipients, but lung recipients, in particular, because they suffer from amongst the worst outcomes of all organ transplants.

Together with John Fung, MD, PhD, Chairman of General Surgery and Hepato-Pancreato-Biliary and Transplant Surgery at Cleveland Clinic, I hope to begin studying a novel immunosuppressive strategy to better understand the immunologic responses of the lungs and liver. We're interested in trying to understand the relationship of various parts of the immune system and how they each respond to different immunosuppressant strategies. To achieve this, I am the Principal Investigator of a multi-institutional grant that is pending review at the National Institutes of Health.

Also in the works, I will be the chair of the data safety and monitoring board for a pivotal trial involving TransMedics, Inc. Organ Care System, a heart preservation device designed to keep the heart beating while being transported from the donor to the recipient. I also am supplying input to the company for developing a similar device for lungs, which is currently being evaluated in Europe.

**Contact Dr. McCurry at 216.445.9303 or [mccurrk@ccf.org](mailto:mccurrk@ccf.org).**



**Kenneth McCurry, MD**, joined the Department of Thoracic and Cardiovascular Surgery at Cleveland Clinic in 2008. Dr. McCurry's specialty interests include lung and heart transplantation, ventricular assist devices, heart failure surgery, and lung and heart ischemia-reperfusion injury. Dr. McCurry received his medical degree from the University of Florida College of Medicine, Gainesville, Fla. He completed his residencies in general surgery and cardiothoracic surgery at the University of Michigan Medical Center, Ann Arbor, Mich., where he was honored with Frederick A. Collier Award for Research Excellence. He completed a CT transplant fellowship at the University of Pittsburgh Medical Center, Pittsburgh, Pa. and a research fellowship at Duke University Medical Center, Durham, N.C. He joined Cleveland Clinic from UPMC, where he served as director of its Lung and Heart-Lung Transplantation program.



## Lung Transplant Center of Excellence

The year 2009 is on track to be a record year of growth for the Cleveland Clinic Lung and Heart/Lung Transplant Program, one of the most active in the country.

The program has completed 752 transplants since its inception in 1990, performing 82 thus far in 2009\* – with a projected 170 cases for the entire year, reinforcing Cleveland Clinic's position among the leading lung transplantation programs, both in Ohio and nationally.

This unprecedented growth is due to an increasing availability of donor lungs, more aggressive criteria for evaluating donor lungs, addition of new transplant staff, as well as increased referrals from across the country.

In 2008, the program performed 57 lung transplants, including 29 double lung transplants and 28 single lung transplants. Patients came from 11 states and abroad.

### PROGRAM HIGHLIGHTS:

Offers combination transplants, as well as combined heart/lung with simultaneous CABG surgery

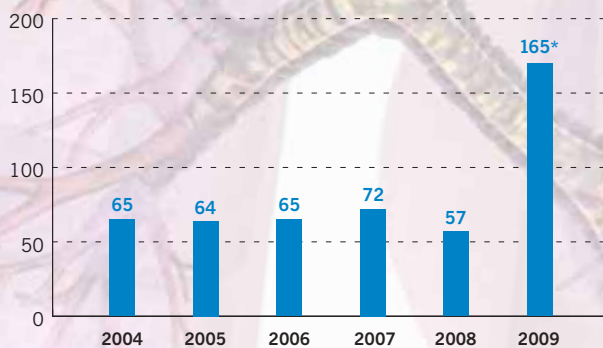
Quick evaluation and waiting list approvals

Accepts challenging, complex cases

High volume center with excellent clinical outcomes

The Transplant Center continues a reputation for accepting and transplanting challenging, complex cases. Cleveland Clinic's Lung Transplant team is involved in a series of multicenter trials aimed at therapy of primary graft dysfunction, acute rejection and induction therapy. In addition, our surgeons have pioneered certain transplant surgical techniques, which include bronchial artery revasculariza-

Number of transplants in 2004–2009



\* = Projected Number

tion, which may improve outcomes further by reducing ischemic injury.

The average wait time for a graft in our program remains stable. Currently, our average waiting time is 82 days. The Transplant Center has achieved very strong survival rates that are at or above the national average. Median and long-term outcomes continue to remain steady or improve, with a one-year survival rate of 86 percent and a two-year survival rate of 76 percent. Post-transplant length of stay is an average of 24 days.

The U.S. Department of Health and Human Services has identified Cleveland Clinic as one of six Best Practices “high performing” centers for lung transplantation, based on volume, growth and clinical outcomes.

**To refer a patient for consideration for lung transplant or heart/lung transplant, please call our transplant coordinator at 216.444.8282, option 3.**

### Recommended Reading:

Pettersson GB, Yun JJ, Nocero J, Mason DP, Murthy SC, Kapadia S, Mangi AA, Mehta AC, Budev MM – “Lung transplantation with direct bronchial arterial revascularization (BAR): feasible and effective – time to revisit?” Presented at the International Society of Heart Lung Transplantation 29th Annual Meeting and Scientific Sessions, April 22-25, 2009, Palais des Congres, Paris, France.

## The BAR Continues to Rise in Lung Transplantation at the Cleveland Clinic

By James J. Yun, MD, PhD, Marie M. Budev, DO, MPH and Gösta B. Pettersson, MD, PhD

Impaired airway healing after lung transplantation leads to bronchial necrosis and stenosis, which may contribute to infections and rejection. In standard lung transplant surgery, only pulmonary artery blood flow to the lungs is restored; bronchial artery blood supply is sacrificed. In December 2007, Cleveland Clinic lung transplant surgeons, led by Gösta Pettersson, MD, PhD, initiated a study offering bronchial artery revascularization (BAR). BAR refers to primary restoration of bronchial arterial circulation to transplanted donor lungs. During a lung transplant with BAR, surgery includes an additional connection between a recipient artery and the diminutive donor lung bronchial arteries. Thus, a normal bronchial blood supply is restored.

Currently, 16 patients have been transplanted with BAR. All patients are alive, and 15 of 16 had excellent early airway healing. Selective angiography in 13 of these patients has demonstrated revascularization success, with two not yet examined. No patients have evidence of chronic rejection to date. One patient had evidence of airway ischemia, but still had healing within 10 weeks.

In April 2009, these early results were presented at the International Society for Heart and Lung Transplant meeting in Paris. Currently, more than 50 patients are enrolled in this BAR pilot study. Because the early experience with BAR at Cleveland Clinic is promising, our long term hope is that BAR will improve airway healing, reduce the incidence of infections and rejection, and therefore improve survival. To our knowledge, this remains the only study of its kind being conducted in the world.

† = As of July 1, 2009



Serpil Erzurum, MD

## A Bridge to Better Patient Care

As Director of the Clinical Research Unit of the Cleveland Clinical Science and Translational Consortium, Serpil Erzurum, MD, is particularly well positioned to encourage interaction between clinicians and researchers.

“I really see the benefit of an environment that lets clinicians and researchers talk and share their experiences. You can learn so much from one another in informal settings,” she says. “There are so many times when I hear what a researcher is doing that could apply to my patients, or what I’m seeing with patients that could have an impact on laboratory projects.”

Formalizing this interaction was possible through a Clinical and Translational Science Award (CTSA), a \$64 million National Institutes of Health grant that provides resources for the coordinated development of clinical and translational sciences. One of 38 academic health center awards nationally, CTSA is a partnership of Cleveland Clinic, Case Western Reserve University, University Hospitals Case Medical Center, MetroHealth Medical Center, and the Louis Stokes Cleveland VA Medical Center.

### FROM BENCH TO BEDSIDE

The Clinical Research Unit (CRU) provides the equipment, nursing support and support staff for more than 200 investigators carrying out more than 125 clinical research projects. Most such projects are NIH-supported and are under way at Cleveland Clinic, from diabetes research and exercise studies to storing and shipping samples and investigating acute heart attacks. All projects in the CTSA undergo review by its Protocol Review Committee.

The services range from the ordinary, such as echocardiograms, to the extraordinary, such as apheresis and elutriation. With the support of the CTSA, Cleveland Clinic researchers launched this new service, in which healthy human volunteers undergo collection of their blood to obtain human circulating cells, which are then separated into the various components for use by basic science researchers.

“Bridging the gap between laboratory and clinical research is integral to patient care, and it would be much more challenging to do without the CTSA,” says Dr. Erzurum. “Our Clinical Research Unit allows rapid translation of our findings in the lab to the patient.”

Just as important, the CRU serves as an advocate for the members of the public who volunteer for the various research projects. “Our participants are equal partners in the clinical research enterprise. Without them, we couldn’t advance medical care, and in the CTSA structure, they are partners in the research in the CTSA,” she says.

## INSTRUMENTAL SUPPORT

Raed Dweik, MD, Director of the Pulmonary Vascular Program in the Respiratory Institute values the help the Clinical Research Unit has provided for several of his clinical and translational projects. "Some of these projects would not have been possible without it," he says.

One such example is the Whole Lung Allergen Challenge, a study in which individuals with asthma were exposed to ragweed or grass antigen in order to induce a mild asthma attack. This study helped researchers unravel many of the mysteries of asthma that could not be answered using laboratory or animal studies and that would be difficult to study in naturally occurring asthma because of its variable nature.

"Having the CRU resources allowed me to secure the necessary FDA approval for the study and perform it in a safe and closely monitored environment," says Dr. Dweik.

Another example is the performance of pharmacodynamic studies. Prior to the CRU, Dr. Dweik's Pulmonary Vascular group declined requests for such studies from industry because volunteers require hospitalization and frequent and rigorously timed blood drawing requirements. Dr. Dweik notes that the group recently signed up for a pharmacodynamic study for the first time in years and anticipates excellent enrollment with CRU support.

## ROOM FOR EXPANSION

As much as the Clinical Research Unit provides to investigators, Dr. Erzurum sees potential for growth.

"We have a need to expand the Clinical Research Unit, in particular into nutritional and metabolic areas," she says. "We are starting to organize for the development of a nutritional research center to focus on that facet of the disease process, which is so important for diabetes and obesity research. We have also begun to create a research participant membership that will allow greater and more meaningful involvement of our volunteers in our ongoing studies, including the sharing of research findings."

**Dr. Serpil Erzurum is Chair of the Department of Pathobiology and Co-Director of Cleveland Clinic's Asthma Center. She sees patients in the Department of Pulmonary, Allergy and Critical Care Medicine and can be reached at 216.445.5764 or [erzurus@ccf.org](mailto:erzurus@ccf.org).**

## Clinical Research Unit Resources

The Clinical Research Unit provides molecular biology, specimen processing and analytical work. Its primary functions are to provide technical support for sophisticated chemical analyses called assays and to develop or validate new laboratory methods. The unit provides staffing for specific laboratory procedures.

### SPECIMEN PROCESSING

The unit performs minimal to complex specimen processing. Among its services are blood, serum, plasma or urine collection; highly consistent, project-specific processing; specimen shipping; and large-volume blood cell separation.

### RESEARCH ASSAYS

The unit can provide chemical analysis assays that offer a complete chemical analysis of blood and the detection of antibodies or antigens, among other services.

### SPECIMEN STORAGE

Researchers have access to a 4°C refrigerator, one upright -20°C and one -70°C freezer for short-term specimen storage. All refrigerators and freezers are equipped with centrally monitored alarm systems for efficient and accurate temperature control.

### SPECIMEN SHIPMENT

The unit has the capability to ship ambient or frozen specimens to other laboratories.

## CTSA by the Numbers

- 2,359 outpatient visits
- 310 overnight research admissions
- 15,000 samples processed in laboratory
- 139 research projects
- 35 departments involved
- 225 principal investigators who use the Clinical Research Unit
- 41 refereed journal publications from studies done on the CRU

12-month period 2007-08

# Eosinophilic Esophagitis: Utility of Allergy/Immunology Evaluation

By David M. Lang, MD

In recent years, eosinophilic esophagitis (EoE) has emerged as a condition encountered more frequently by allergy/immunology and gastroenterology specialists. In patients with EoE, esophageal symptoms occur in association with an eosinophil-rich infiltrate in the esophagus, defined as >15 eosinophils per high-power field in the appropriate clinical context.

The etiology, appropriate management and natural history of EoE are poorly understood. At Cleveland Clinic, we recently carried out a study to assess the utility of routine allergy/immunology evaluation in adults with EoE<sup>1</sup>.

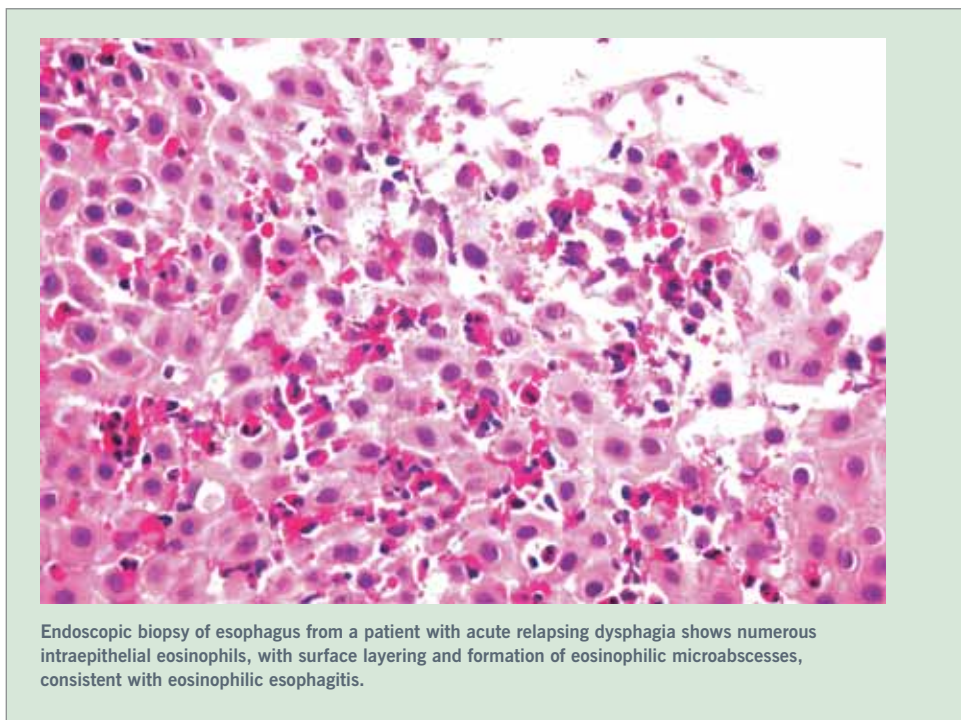
## CONSENSUS-BASED RECOMMENDATIONS FOR MANAGEMENT

The high rate of allergic rhinitis, atopic dermatitis and asthma reported in case series of pediatric and adult EoE patients, combined with the established role of eosinophils in atopic disease, implies that, at least in some patients, an IgE-mediated or IgE-associated response to one or more antigens may provoke and perpetuate this inflammatory disorder.

Recent consensus-based recommendations for EoE management state that patients should undergo allergy/immunology evaluation<sup>2</sup>; however, these recommendations are based primarily on pediatric studies. Although immediate hypersensitivity skin testing has been associated with excellent negative predictive value and can reliably detect clinically relevant inhalant and/or food allergens in individuals with IgE-mediated disorders<sup>3</sup>, the value of skin (or in vitro) testing has not been established in adult patients with EoE.

## CLEVELAND CLINIC EXPERIENCE

In a study carried out at Cleveland Clinic of 26 subjects with EoE (confirmed by history and upper gastrointestinal endoscopy with biopsy and referred for allergy/immunology evaluation), 13 (50 percent) exhibited wheal/flare reaction to >1 food. Of the 15 subjects with EoE who had concomitant respiratory symptoms, 14 (93 percent) had wheal/flare reaction to one or more inhalants. Twenty-



one of these 26 subjects (81 percent) had >1 allergen identified, 16/26 (62 percent) had >5 allergens identified and 4/26 (15 percent) had >10 allergens identified (range: 0-20 allergens identified). Peanut, egg, soy, cow's milk and tree nuts (including walnut, almond and Brazil nut) were the most common food allergens identified in our series.

Allergy/immunology evaluation frequently leads to detection of allergens via skin (or in vitro) testing that can direct avoidance measures<sup>3</sup>. In patients with EoE, avoidance measures carry the potential for improving outcomes by encouraging reduced symptoms and medication reliance. These findings provide further support for the utility of routine allergy/immunology evaluation for adults with EoE.

**Dr. David Lang is Head of Cleveland Clinic's Section of Allergy/Immunology, Co-Director of the Asthma Center, and Director of the Allergy/Immunology Fellowship Program. He can be reached at 216.445.5810 or at [langd@ccf.org](mailto:langd@ccf.org).**

## Note

This study was carried out in collaboration with Cleveland Clinic colleagues Joshua Penfield, MD, (Chief Medical Resident), John Goldblum, MD, (Anatomic Pathology), and Gary Falk, MD (Digestive Disease Institute).

## References

1. Penfield JD, Lang D, Goldblum JR, Falk GW. The role of allergy evaluation in adults with eosinophilic esophagitis. *J Clin Gastroenterology*. 2009. In Press.
2. Furuta GT, Liacouras CA, Collins MH, et al. Eosinophilic esophagitis in children and adults: A systematic review and consensus recommendations for diagnosis and treatment. *Gastroenterology*. 2007;133:1342-63.
3. Bernstein IL, Li JT, Bernstein DI, et al. Allergy diagnostic testing: An updated practice parameter. *Ann Allergy Asthma Immunol*. 2008;100:S1-148.



## James Stoller, MD, Appointed Chairman of Education Institute

James K. Stoller, MD, MS, Head, Section of Respiratory Therapy, was recently named Chairman of the Education Institute.

Dr. Stoller joined Cleveland Clinic in 1986 as a staff member in the Department of Pulmonary, Allergy and Critical Care Medicine (currently the Respiratory Institute). His interest in organizational development and education led to his involvement in developing the Cleveland Clinic Academy, where he serves as Executive Director of Physician Leadership.

Dr. Stoller holds the Jean Wall Bennett Professorship of Medicine at the Cleveland Clinic Lerner College of Medicine of Case Western Reserve University. He has a secondary appointment as Professor of Organizational Behavior in the Weatherhead School of Management of Case Western Reserve University, where he completed a Master of Science in Organizational Development and Analysis in 2001.

Dr. Stoller graduated from Yale University School of Medicine in 1979 and obtained advanced fellowship training in pulmonary medicine at Yale-New Haven Hospital and the Brigham and Women's Hospital and in critical care medicine at Massachusetts General Hospital. He is the author of more than 11 books, 70 chapters, 210 original peer-reviewed reports, and over 85 abstracts; actively involved in professional societies and editorial boards and currently serves as an associate editor for the journal *Respiratory Care*. He has been continuously included in the "Best Doctors in America" list and in "America's Top Doctors."



## CME Calendar

Physicians are welcome to attend the following upcoming symposia:

### Obesity Summit 2009

Sept. 9-11

InterContinental Hotel and Bank of America Conference Center, Cleveland Clinic  
Cleveland, Ohio

### Pulmonary Hypertension Symposium

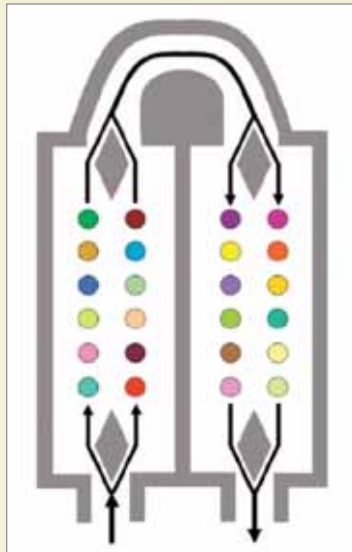
Nov. 20-21

InterContinental Hotel and Bank of America Conference Center, Cleveland Clinic  
Cleveland, Ohio

### 17th World Congress for Bronchology, and the 17th World Congress for Bronchoesophagology

June 16-19, 2012

For more information about the above events, call the Cleveland Clinic Department of Continuing Education at 216.444.5696 or 800.762.8173 or visit [ccfcme.org](http://ccfcme.org).



The redesigned colorimetric sensor array provides many advantages over the prior device. It is easier to handle via the thumb tab, avoiding prints on the array that could affect its imaging. It has improved seals to eliminate environmental contamination. The airflow is directed over the sensing elements to produce consistent exposure to all elements and reproducible results. Response times are shortened by the new design.

## Identifying and Validating Exhaled Breath Biomarkers for Detecting Early-stage Lung Cancer

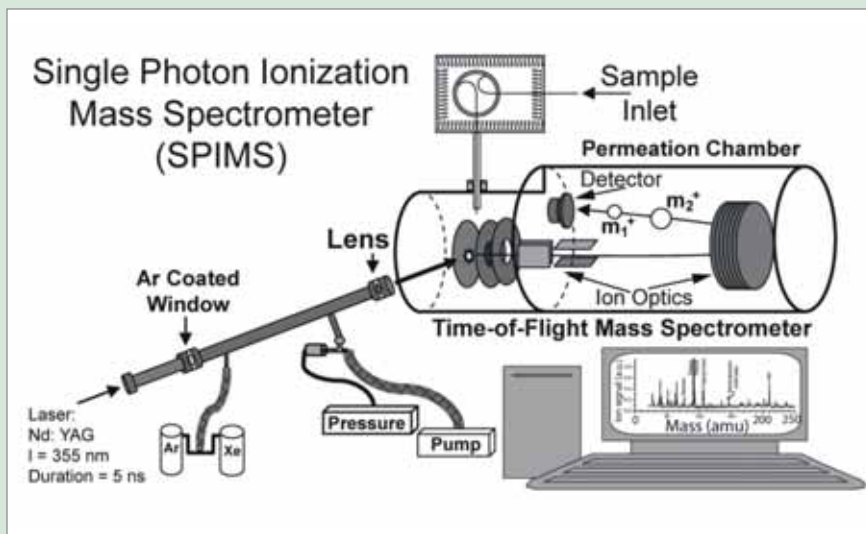
By Peter Mazzone, MD, MPH

Too often, lung cancer presents late in its course. Symptoms, often non-specific, may not occur until the cancer has progressed. Studies assessing imaging technologies as a screening tool have yet to prove a reduction in lung cancer-specific mortality from their use. Many benign nodules have been identified in CT screening studies, leading to patient concern and expensive, potentially morbid follow-up testing. Many patients' lives could be saved if an accurate, inexpensive, and non-invasive test for early-stage lung cancer were available.

Current research aimed at identifying biomarkers associated with lung cancer has shown a great deal of promise. Biomarkers are being developed that may help with the diagnosis of lung cancer, determine the prognosis of an individual patient, or predict a patient's response to therapy. Our group's research is aimed at identifying and validating exhaled breath biomarkers for lung cancer. In addition to nitrogen, oxygen and carbon dioxide, the exhaled breath contains trace components called volatile organic compounds (VOCs). These exhaled breath VOCs are felt to be produced or metabolized through cellular biochemical processes that are likely to differ in lung cancer cells. To date, studies that have evaluated exhaled breath VOC profiles in lung cancer patients have used various mass spectrometry technologies and chemical sensor matrices to find a unique lung cancer signal in the exhaled breath. Our group has led studies using two of these types of systems<sup>1,2</sup>. The accuracies of technologies that have been available to date have ranged from 70 to 85 percent<sup>3,4</sup>. This is quite promising, but not yet accurate enough to be clinically useful. Additional promise for this line of investigation has come from an unusual source. A study assessed the ability of dogs to detect

lung cancer from the exhaled breath. The dogs were 99 percent accurate in their determinations<sup>5</sup>.

We have been fortunate to bring two advanced sensing technologies to our breath biomarker research group. The first is called a single photon ionization mass spectrometer (SPIMS). The benefits of this system are that it is able to detect VOCs at an order of magnitude lower concentration than previously available devices (down to the parts per trillion – parts per quadrillion level), and can do so in near-real time (other devices requiring processing of the breath with one hour analysis times). We have one of only two SPIMS systems in the world (the other is with the EPA). The second technology we are studying is a colorimetric sensor array (COSAT). This disposable cartridge is impregnated with compounds that change their color upon exposure to VOCs. The output from the sensor is the pattern of color changes seen on the array. We have studied an early version of this system previously<sup>2</sup>. The current version has been significantly improved, warranting further investigation. The information we gather from the SPIMS analysis will allow us to refine sensor systems, such as the COSAT system, which are ultimately better suited to become point of care tests.



The ultra-sensitive SPIMS instrument can detect VOCs in the parts per trillion to parts per quadrillion range. Results of analysis take only a few seconds. It does not require breath collection onto concentration devices and media. Breath can be delivered directly into the system. This system will be used to analyze the breath of study subjects in the current proposal.

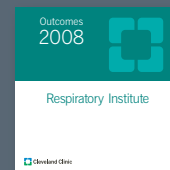
Our team's next step is to analyze the breath of patients with early-stage lung cancer, and compare the breath VOCs to those from patients at risk for developing lung cancer. We are currently using both the SPIMS and COSAT systems to identify and validate the presence of breath biomarkers of early-stage lung cancer. Subjects with early-stage lung cancer are being recruited from our busy multidisciplinary lung cancer clinic. The at-risk control group will be recruited from a lung cancer screening trial that is currently underway at our institution. We hope this work will help move us closer to our goal of developing a breath test that can accurately screen for, and diagnose, lung cancer in a noninvasive manner.

**Dr. Peter Mazzone, MD, MPH, is the Director of the Lung Cancer Program and Director of the Pulmonary and Critical Care Fellowship Program. He can be reached at 216.445.4812 or mazzonp@ccf.org.**

#### Recommended Reading

- 1 Machado RF, Laskowski D, Deffenderfer O, et al. Detection of lung cancer by sensor array analyses of exhaled breath. *Am J Respir Crit Care Med* 2005;171:1286-1291.
- 2 Mazzone PJ, Hammel J, Dweik RA, Na J, Czich C, Laskowski D, Mekhail T. Lung cancer diagnosis by the analysis of exhaled breath with a colorimetric sensor array. *Thorax*, 2007;62:565-568. doi: 10.1136/thx.2006.072892.
- 3 Mazzone PJ. Analysis of volatile organic compounds in the exhaled breath for lung cancer diagnosis. *J Thorac Oncol* 2008;3:774-780.
- 4 Mazzone PJ. Progress in the development of a diagnostic test for lung cancer through the analysis of breath volatiles. *J Breath Res* 2008;3:10.1088/1752-7155/2/3/037014.
- 5 McCulloch M, Jezierski T, Broffman M, Hubbard A, Turner K, Janecki T. Diagnostic accuracy of canine scent detection in early- and late-stage lung and breast cancers. *Int Can Therap* 2006;5:30-39.

## Outcomes Data Available



The latest outcomes data from Cleveland Clinic departments involved in the treatment of respiratory diseases

are available. Our outcomes booklet offers summary reviews of medical and surgical trends and approaches. Charts, graphs and data illustrate the scope and volume of procedures performed in our departments each year. To view outcomes booklets for respiratory diseases as well as many other Cleveland Clinic medical and surgical disciplines, visit [cleveland-clinic.org/quality](http://cleveland-clinic.org/quality).

## CME Opportunities: Live and Online

Cleveland Clinic's Center for Continuing Education's website, [ccfme.org](http://ccfme.org), offers convenient, complimentary learning opportunities, from webcasts and podcasts to a host of medical publications and a schedule of live CME courses. Many live CME courses are hosted in Cleveland, an economical option for business travel. Physicians can manage their CME credits by using the myCME Web Portal, available 24/7.

## Cleveland Clinic Ranked One of America's Top Hospitals

Cleveland Clinic is ranked among the top hospitals in the country, according to the latest *U.S. News & World Report's* annual survey of "America's Best Hospitals." In the Respiratory Disorders category, Cleveland Clinic is ranked #4. For details, visit [clevelandclinic.org](http://clevelandclinic.org).

# Compassionate-use of Mepolizumab for Treating Life-threatening HES

By Fred H. Hsieh, MD

At Cleveland Clinic, we have recently been able to offer access to mepolizumab (recombinant anti-interleukin-5 monoclonal antibody) through a compassionate-use, open-label study to subjects with life-threatening hyper-eosinophilic syndrome (HES). The study subjects' disease could not be adequately controlled with steroid or other steroid-sparing therapies.

## MULTISYSTEM DISORDER

HES is a heterogeneous multisystem disorder characterized by persistent peripheral blood eosinophilia and end-organ involvement by eosinophils. Classically it has been defined as having prolonged peripheral eosinophilia of  $>1.5 \times 10^9$  cells/L for at least six months, with no evidence of other recognized causes of eosinophilia and evidence of target-organ damage.

Affected organs and systems can include the heart, gastrointestinal tract, nervous system, bone marrow, skin, lung, eye and coagulation system. Although several variants have been described, including the myeloproliferative variant (characterized by a clonal expansion of eosinophils harboring the FIP1L1-PDGFR $\alpha$  fusion kinase), and the lymphocytic or lymphoproliferative variant (characterized by a clonal expansion of abnormal T cells overexpressing cytokines such as interleukin-5), in many cases the specific molecular defects associated with HES have not been identified.

Untreated, the disorder is associated with severe disability, and mortality is primarily due to cardiac disease.

## TRADITIONAL THERAPY

The goal of HES therapy is to control peripheral blood and tissue eosinophilia, and prevent irreversible organ damage and thromboembolic events associated with uncontrolled eosinophilia. First-line therapy usually includes systemic steroids for HES in general or imatinib mesylate in patients with documented myeloproliferative variant HES. Steroid therapy, however, typically does not induce a complete remission, and prolonged steroid therapy with its attendant toxicity usually is required for long-term management of HES patients.

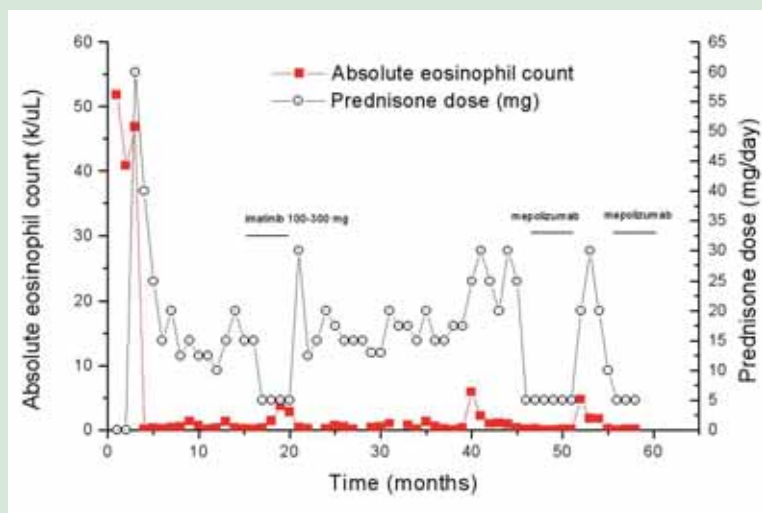
## COMPASSIONATE-USE STUDY

Mepolizumab is given via monthly IV infusions and binds to serum interleukin-5 (IL-5) with high affinity and specificity, preventing it from binding to the IL-5 receptor on the surface of eosinophils. Recent publications have suggested its efficacy in investigational use in subjects with asthma, eosinophilic gastrointestinal disorders and HES, and it may be efficacious as a steroid-sparing agent and as a primary therapy to prevent organ damage.

Our own experience suggests that this product is well-tolerated with minimal drug-related toxicity, and is effective in controlling peripheral blood eosinophilia and modulating target-organ damage in subjects with steroid-sensitive disease.

The study currently is open at 32 sites worldwide and is targeted to enroll 75 subjects. Inclusion criteria include: age  $>12$  years old, presence of life-threatening HES and failure of at least three standard therapies for disease control. Subjects with eosinophil-related disorders not diagnosed as life-threatening HES are not eligible. The study is scheduled to close in 2011.

**Dr. Fred Hsieh is a Cleveland Clinic allergist and local site PI for investigational mepolizumab therapy. He can be reached at 216.445.3504 or at [hsieh@ccf.org](mailto:hsieh@ccf.org).**



Mepolizumab efficacy in one subject with HES. Representative clinical course of one subject diagnosed at age 15 with idiopathic HES and biopsy-proven lung, gastrointestinal and skin involvement. Subject had steroid-responsive disease, but experienced recurrence of eosinophilia and symptoms when steroids were tapered to less than 15 mg of prednisone per day. Introduction of imatinib mesylate at increasing doses failed to control eosinophilia. A trial of mepolizumab at 45 months controlled eosinophilia and symptoms, and allowed prednisone to be tapered to 5 mg per day. Withdrawal of mepolizumab was associated with a flare in peripheral eosinophilia, so mepolizumab therapy was resumed.



# Respiratory Institute Staff Directory

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**Herbert P. Wiedemann, MD, MBA**  
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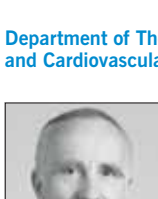
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**Sudish Murthy, MD, PhD****Surgical Director, Center for Major Airway Diseases**

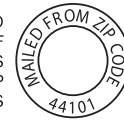
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**RESPIRATORY EXCHANGE** ●●● **RESEARCH AND NEWS FOR PHYSICIANS FROM  
THE CLEVELAND CLINIC RESPIRATORY INSTITUTE**

**CONTACT US**

**General Patient Referral**

24/7 hospital transfers or physician consults  
800.553.5056

**Pulmonary Appointments/Referrals**

216.444.6503 or 800.223.2273, ext. 46503

**Allergy Appointments/Referrals**

216.444.3386 or 800.223.2273, ext. 43386

**On the Web** at [clevelandclinic.org/pulmonary](http://clevelandclinic.org/pulmonary)

**SERVICES FOR PHYSICIANS**

**Physician Directory**

View all Cleveland Clinic staff online at [clevelandclinic.org/staff](http://clevelandclinic.org/staff).

**Physician Liaison**

Referring physicians have a direct and personal link to Cleveland Clinic with our Physician Liaison. For help with any interaction involving Cleveland Clinic, contact Physician Liaison Kate Kenny at [clevelandclinic.org/ContactKate](http://clevelandclinic.org/ContactKate).

**Track Your Patient's Care Online**

Whether you are referring from near or far, DrConnect offers secure access to your patient's treatment progress at Cleveland Clinic. To establish a DrConnect account, visit [clevelandclinic.org/drconnect](http://clevelandclinic.org/drconnect) or email [drconnect@ccf.org](mailto:drconnect@ccf.org).

**Remote Consults**

Request a remote medical second opinion from Cleveland Clinic. MyConsult is particularly valuable for patients who wish to avoid the time and expense of travel. Visit [clevelandclinic.org/myconsult](http://clevelandclinic.org/myconsult),

**SERVICES FOR PATIENTS**

**Critical Care Transport Worldwide**

Cleveland Clinic's critical care transport team serves critically ill and highly complex patients across the globe. The transport fleet comprises mobile ICU vehicles, helicopters and fixed-wing aircraft. The transport teams are staffed by physicians, critical care nurse practitioners, critical care nurses, paramedics and ancillary staff, and are customized to meet the needs of the patient. Critical care transport is available for children and adults.

To arrange a transfer for STEMI (ST elevated myocardial infarction), acute stroke, ICH (intracerebral hemorrhage), SAH (subarachnoid hemorrhage) or aortic syndromes, call 877.279. CODE (2633).

For all other critical care transfers, call 216.444.8302 or 800.553.5056.

**Medical Concierge**

Complimentary assistance for out-of-state patients and families 800.223.2273, ext. 55580, or email [medicalconcierge@ccf.org](mailto:medicalconcierge@ccf.org)

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