



ATSPAR NEWS

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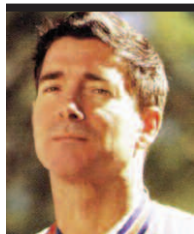
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We help the world breathe
PULMONARY • CRITICAL CARE • SLEEP

ATS 2008: WHERE SCIENCE MEETS PATIENT CARE



One of the defining qualities of the annual ATS International Conference is the wide range of topics and perspectives presented during the six-day meeting. With more than 400 sessions, 800 speakers and 5,600 original research abstracts, ATS 2008 will draw thousands of physicians, scientists and researchers, as well as many patients and patient advocates, to Toronto, Canada, May 16 to 21.

“The International Conference is the ideal forum for patients and public interest organizations to interact and network with clinicians, researchers and other healthcare professionals who specialize in pulmonary, critical care and sleep medicine,” said Donna J. Appell, R.N., chair of the Society’s Public Advisory Roundtable (PAR), which is sponsoring a number of events at the meeting. “Not only does it allow us to inform these professionals that ATS PAR can be a resource to their patients, but it also keeps us abreast of the latest advances in disease diagnosis, management and treatment.”

ATS PAR will host its 8th annual symposium, “Rebuilding the Pulmonary Patient from Laboratory to Lifestyle,” on Tuesday, May 20 from 8:15 to 11 a.m. The symposium will include discussions ranging from new technologies to regenerate organs to new approaches to clinical rehabilitation in a range of pulmonary diseases.

“Ideas about rebuilding the lungs are changing very rapidly, and new data is emerging about the causes of disability

in diseases such as COPD and post-critical illness,” said ATS Immediate-Past President John E. Heffner, M.D., who will co-chair the symposium with Ms. Appell. “The goal is to bring together different kinds of investigators to address this important clinical problem.”

Presenters will include:

- Len Geiger—“Patient Perspective: Reevaluation, Rehabilitation and Resiliency: An Alpha-1 Patient’s Journey from Diagnosis and Lung Transplant to Today” (see “Spotlight on Patients” on page 3 for more on Mr. Geiger)
- Dan Weiss, M.D.—“Cellular and Molecular Strategies for Rebuilding the Lungs of the Pulmonary Patient”
- Annemie Schols, M.D.—“The Role of Inflammation as a Limiting Factor in Pulmonary Rehabilitation”
- Francois Maltais, M.D.—“Targeting Skeletal Muscles in Pulmonary Rehabilitation”

(continued on page 2)

ATS 2008: WHERE SCIENCE MEETS PATIENT CARE *(continued from page 1)*

- Margaret Herridge, M.D.—“Strategies for Post-Hospital Rehabilitation After Critical Illness”
- Dee Story—“Patient Perspective” *(title to be determined)*
- Andrew Ries, M.D.—“The New Evidence Base for Rehabilitation in Chronic Respiratory Disease”
- Jean Bourbeau, M.D.—“Putting the Patient in Charge: The Benefits of Self-Management and Education”
- Bartolome Celli, M.D.—“Disease Modification Strategies in Chronic Lung Disease”

In total, PAR will bring patients to share their experiences at 15 scientific sessions during ATS 2008, including at its annual symposium *(a complete list of patient speakers will be published in the March ATS PAR News)*.

Attendees can also learn more about ATS PAR at its 8th annual poster session, which will feature highlights and information on a variety of lung public interest organizations. It will be on display in the Metro Toronto

Convention Centre from Sunday, May 18 to Tuesday, May 20.

Finally, ATS PAR will hold its second “Breathing Better with the ATS” forum, at which patients will have the unique opportunity to network, meet other patients and learn more about their diseases. The event will take place on Saturday, May 17 from 1 to 4 p.m. at the Sheraton Centre Toronto Hotel.

“This event is a wonderful example of how patients can be involved in their care and have their voices heard by the physicians who treat them and are working to find treatments and cures,” said Judy Simpson, former chair of PAR, who oversaw last year’s inaugural event.

For more about programming sponsored by ATS PAR at the 2008 International Conference, please send an e-mail to par@thoracic.org or call Karen Belgiovine at (212) 315-8640. ■

2008 ATS/PARTner Research Grants

Now in its sixth year, the ATS Research Program continues to advance pulmonary, critical care and sleep medicine by providing individuals at the beginning of their careers with opportunities to conduct independent research and gather data to secure other grants. Eight of the 17 grants awarded this year are co-funded by organizations that belong to ATS PAR.

ATS/ALPHA-1 FOUNDATION RESEARCH GRANT



Shivraj S. Tyagi, Ph.D., Brigham and Women’s Hospital, Harvard Medical School: “The Role of Bronchio-Alveolar Stem Cells in Cigarette Smoke-Related Emphysema”

ATS/ASTHMA AND ALLERGY FOUNDATION OF AMERICA RESEARCH GRANT



Njira L. Lugogo, M.D., Duke University Medical Center: “Obesity and Asthma: Modulation of Airway Inflammation by Adipokines”

ATS/CYSTIC FIBROSIS FOUNDATION RESEARCH GRANT



Lucas R. Hoffman, M.D., Ph.D., University of Washington, Seattle: “S.aureus and Polymicrobial Interactions in CF Lung Disease: Observational Study”

ATS/COALITION FOR PULMONARY FIBROSIS RESEARCH GRANT



Andrew M. Tager, M.D., Massachusetts General Hospital: “Mechanisms of Fibrosis Driven by Lysophosphatidic Acid and its Receptor LPA1”

ATS/LAM FOUNDATION RESEARCH GRANT



Elena A. Goncharova, Ph.D., University of Pennsylvania: “Defining the Role of RhoA GTPase in Modulating LAM Cell Growth”

ATS/PULMONARY HYPERTENSION ASSOCIATION RESEARCH GRANT



Kewal Asosingh, Ph.D., Cleveland Clinic Foundation: “Role of Pulmonary Vascular Wall Resident Endothelial Progenitors and Circulating Bone Marrow-Derived Angiogenic Precursors in Idiopathic Pulmonary Arterial Hypertension”

ATS/RESPIRATORY HEALTH ASSOCIATION OF METROPOLITAN CHICAGO RESEARCH GRANT



Qing Lu, Ph.D., Brown University: “TGF-Beta1 and Pulmonary Artery Hypertension”

ATS/RESPIRATORY HEALTH ASSOCIATION OF METROPOLITAN CHICAGO RESEARCH GRANT



Jerry A. Krishnan, M.D., Ph.D., The University of Chicago: “Repeated High-Dose Inhaled Corticosteroids for Acute Asthma (ReHICS) Study”

NEWS BRIEFS

NHLBI ANNOUNCES NEW STRATEGIC PLAN



The National Heart, Lung, and Blood Institute (NHLBI) has announced that a new strategic plan will guide its next decade of research, training and education to reduce the national burden of cardiovascular, lung, blood and sleep disorders.

“This plan sets the institute on a trajectory toward preempting disease by using emerging and sophisticated research approaches, adapting to a rapidly changing healthcare environment and remaining flexible to invest in new research opportunities that offer the best potential for improving the nation’s health,” said NHLBI director Elizabeth G. Nabel, M.D.

The plan sets forth three major goals: 1) to increase understanding of the molecular and physiological basis of health and disease; 2) to enhance knowledge of the clinical mechanisms of disease and thereby identify better approaches to prevention, diagnosis and treatment; and 3) to improve the translation of research into practice for the benefit of personal and public health by seeking a better understanding of the processes for health behavior change.

To read the document in full, visit www.nhlbi.nih.gov.

TRAVEL REQUIREMENTS FOR ATS 2008 TORONTO, MAY 16-21



New travel regulations will require all individuals planning on attending the 2008 ATS International Conference in Toronto, Canada, to present a valid passport to enter the country (and to re-enter the United States).

As of January 23, 2007, all passengers, including U.S. citizens, traveling by air or sea to and from Canada, Mexico, Central or South America, the Caribbean and Bermuda must have a passport. This is a change from prior requirements, which allowed travelers to cross these borders with only a U.S. driver’s license.

For more information on the new travel requirements and instructions on how to apply for or renew a U.S. passport, visit <http://travel.state.gov>.

CORRECTION TO JANUARY ATSPAR NEWS

The January 2008 *ATSPAR News* incorrectly stated that one in 18,000 Puerto Ricans have been diagnosed with Hermansky-Pudlak Syndrome. According to current statistics, one in 1,800 Puerto Ricans have been diagnosed with HPS. For more information, please visit www.hpsnetwork.org.



Spotlight On Patients

Fourteen years ago, I was given the worst news I thought I'd ever receive. After several years of being told that asthma was causing my increasing breathing troubles, my internist had ordered a simple blood test.

As my physician explained it over the phone, "Len, you have Alpha-1 antitrypsin deficiency, a genetic protein deficiency that has caused you to develop a form of severe, progressive and irreversible COPD. You've already lost over 60 percent of your lung function and you'll now need IV infusions every week for the rest of your life to slow the rapid progress of your lung disease."

She continued, "Here's the phone number for your new pulmonologist. At some point he'll probably refer you to a center to be evaluated for a lung transplant. Any questions?"

It is heartbreaking to hear you aren't going to live a normal life or have a normal lifespan. You see, I had just turned 35 and still thought I was going to live forever. Because of my successes in medical sales, I had recently been promoted to our corporate office. The job paid well. I had a nice house and a nice family in a nice neighborhood. By my own definition, it was a great life. With one phone call, I was suddenly forced to recognize my own swiftly approaching mortality for the very first time. It was an uncomfortable moment, to say the least.

Even though the weekly IV infusions certainly helped slow the disease's progression, within two years I had become so ill that I could no longer work. There went the great job, the money and the house. Eventually, my wife and I divorced. I had lost everything by which I had defined myself. I was evaluated and placed on the list for a double lung transplant.

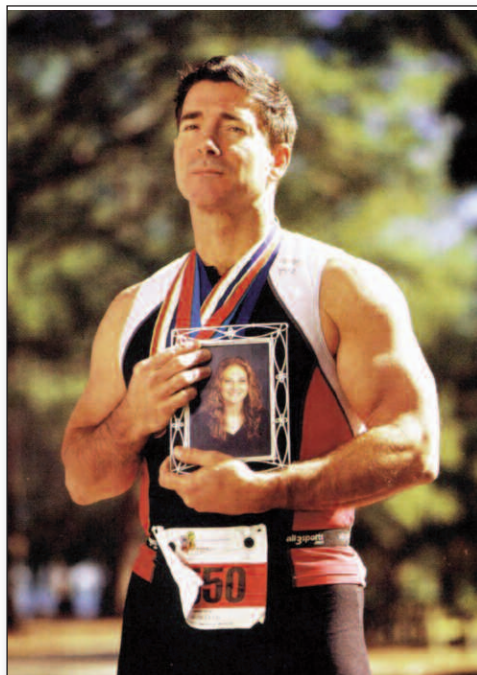
During this difficult time, I recognized two unalterable facts. First, I could not survive without a positive attitude—negativity would kill me, so it was time for a change. Second, I knew my breathing would only get worse, not better. So I'd better push to get in the best shape possible to prepare for whatever the future would bring.

It was during an exercise session that I first noticed a new pain in my lower back, which turned out to be "bilateral avascular necrosis of the femoral heads"—caused by the steroids I'd taken to help my breathing. In plain English, this meant that blood was not reaching my hips and the bone was dying. The pain was agonizing, and the only solution was for an orthopedic surgeon to remove my hip bones and replace them with pieces of titanium over a three-month period in early 2000.

The surgeries made exercise even tougher and my lungs continued to deteriorate for another two difficult years, but I managed to keep a positive attitude despite the pain and a remaining lung function in the mid-teens. To anyone who asked, I always said I'd be "fine." Exactly what "fine" meant, I wasn't sure, but I did know everything would work out the way it was supposed to.

Then during Memorial Day weekend in 2002, I finally got the call for which I had waited years. It was the University of Virginia's transplant center calling to say they had lungs for me. In a flurry of activity, I was taken to UVA and underwent the eight-and-a-half-hour double lung transplant procedure. I didn't know it at the time, but not only was a 14-year-old young woman named

Len Geiger



Korinne Shroyer about to save my life, but I would also live to meet her family and compete in a 5K, 8K, two half-marathons, one full marathon and a triathlon with her father, Kevin. I am forever grateful to Korinne and her family for my second chance at life.

Just a few days after surgery, I was walking again on a treadmill, faster than I had in years. My recuperation was remarkably uneventful and within two weeks, I was released from the hospital. Now that I could breathe again, I felt the urge to elevate my exercise regimen to a higher level, but because of my previous hip replacements I was unable to run. On a friend's recommendation, I took up mountain biking. I spent that summer of 2002 building up my legs and my wind, racing on trails through the woods, pushing myself to my limits. And then, on one unfortunate and unforgettable occasion, I pushed to a point beyond my limits.

My lung transplant was less than three months old when I wrecked my mountain bike. My left femur had shattered into numerous pieces, and it took many hours of surgery and a lot of stainless steel plates, wires and screws to put my leg back together. Even then the doctors weren't sure I'd ever walk again, much less walk normally. Worse yet, shortly after the surgery, my new lungs decided to stop breathing for me. I was put on life support and placed into a drug-induced coma with the hope of giving my body a chance to heal.

Almost three weeks passed before I could breathe on my own. UVA had saved my life once again. Four days later, I went home in a wheelchair, weak and almost forty pounds lighter than when I'd entered. Even with extensive physical rehabilitation, it was weeks before my knee would bend and several months before I could put any weight on the repaired leg. Still, I focused on my attitude and my

(continued on page 8)

NEWS BRIEFS

'VIRTUAL ASTHMA CENTER' FOR PROVIDERS, PATIENTS



Since its launch in December 2007, the ATS "Virtual Asthma Center" has received more than 3,000 hits, making it one of the most popular features on the ATS Web site.

The Web-based portal, which was developed by the Assembly on Asthma, Immunology and Inflammation, houses peer-reviewed links to online asthma-related resources for clinicians, researchers and patients.

"With the overwhelming amount of information now available on the Web, being able to easily access relevant and reliable material related to asthma in one central location is very important," said John G. Mastronarde, M.D., chair of the assembly's Asthma Advisory Committee and Virtual Asthma Center Committee, which spearheaded the project and will continue to maintain and add to the site over the next several years.

The center includes nine sections with information on disease epidemiology, guidelines for diagnosis and management, patient education materials and clinical cases submitted by ATS members, which provide "practical demonstrations of real-world asthma care."

The site is already getting rave reviews from ATS members. "I typically spend a lot of time online trying to track down up-to-date statistics and reliable resources for patients, so having all of this information readily available is going to be invaluable to me," said Anne Dixon, M.D., who serves as assistant professor at the University of Vermont College of Medicine.

Although the site's primary audience is currently asthma care providers like Dr. Dixon, the committee plans to expand existing content of interest to researchers and trainees, including clinical case submissions, links to quality of life instruments, asthma-related clinical trials and funding opportunities.

One of the site's other benefits is that it houses all material the ATS has published on asthma—including statements, workshop proceedings, patient education resources and teaching slides. The center also provides links to the ATS Reading List and asthma-related programming at past International Conferences.

"Like the ATS itself, the Virtual Asthma Center is global in scope," said Peter G. Gibson, M.B.B.S., of the Department of Respiratory and Sleep Medicine at John Hunter Hospital in Australia, who brought an international perspective to the project as one of seven members of the assembly's asthma advisory committee. "It really serves as a forum where national and international members can access case discussions and the latest trends in care, as well as educational materials relevant to both healthcare professionals and their patients."

To access the Virtual Asthma Center, visit www.thoracic.org. On the drop-down menu under "Clinical Information," click "Asthma Center."

RESEARCH IN BRIEF

SUMMARIES OF RESEARCH FINDINGS IN PULMONARY, CRITICAL CARE, AND SLEEP MEDICINE FROM AROUND THE WORLD

EXHALED NITRIC OXIDE USEFUL IN EVALUATION OF CHRONIC COUGH

NEW YORK (Reuters Health) - In patients with chronic cough, measurement of exhaled nitric oxide accurately predicts response to inhaled corticosteroid (ICS) therapy, clinicians from the Mayo Clinic, Rochester, Minnesota report based on a retrospective observational study.

"Patients with a positive exhaled nitric oxide test result had a strong likelihood of response to ICS, whereas a negative exhaled nitric oxide test result indicated an unlikely response to ICS," Dr. Peter Y. Hahn and colleagues report in the *Mayo Clinic Proceedings* for November.

Of 114 patients evaluated for chronic cough with measured exhaled nitric oxide and methacholine challenge, 64 met study inclusion criteria in that they were either started on ICS therapy or their current ICS dosage was increased. These patients had documented follow up ranging from 4 weeks to 16 months.

According to Dr. Hahn and colleagues, 36 of 41 patients (88%) found to have elevated nitric oxide levels, defined as 35 ppb or greater, had significant improvement in their chronic cough documented in their charts. The likelihood ratio of a positive response to ICS was 4.9.

Twenty-three patients with exhaled nitric oxide levels in the normal range (less than 35 ppb) were also prescribed ICS therapy, but only two had significant improvement in chronic cough. The likelihood ratio of a negative response was 0.07.

"A cutoff of 38 ppb was found to best differentiate ICS responders and non-responders," the team reports.

Exhaled nitric oxide proved more accurate in predicting response to ICS for chronic cough than methacholine challenge. At the 38 ppb cutoff, exhaled nitric oxide had a sensitivity, specificity, positive predictive value, and negative predictive value of 90%, 85%, 90% and 85%, respectively. For methacholine challenge, these percentages were 66%, 46%, 64%, and 48%, respectively.

"The results of our study suggest that exhaled nitric oxide may have a role in the evaluation and treatment of patients with chronic cough and may preclude the need for more invasive testing," Dr. Hahn and colleagues conclude.

They also note that compared with methacholine challenge or induced sputum, measurement of exhaled nitric oxide is less time consuming and costly. ■

Last Updated: 2007-12-26 11:30:05 -0400

Mayo Clin Proc 2007; 82:1350-1355.

MEPOLIZUMAB OF LITTLE HELP TO MOST ASTHMATICS

By David Douglas

NEW YORK (Reuters Health) - Mepolizumab, a humanized anti-interleukin-5 monoclonal antibody, does not appear to give additional benefit to the majority of patients whose asthma is incompletely controlled by corticosteroid therapy, UK and U.S. researchers report.

In the December 1st issue of the *American Journal of Respiratory and Critical Care Medicine*, Dr. Neil C. Barnes of the London Chest Hospital and colleagues observe that they studied 362 such patients.

The patients were randomized to monthly infusions of mepolizumab 250 or 750 mg or to placebo. At 3 months, the team found a reduction in the rate of exacerbation in the 750 mg group, but this did not reach statistical significance. In 37 patients in whom levels were measured, there was a significant reduction in both sputum and blood eosinophils in the active treatment groups.

However, in the whole cohort, no differences overall were found in a variety of factors including lung function, symptom scores and quality-of-life measures.

Thus, Dr. Barnes told Reuters Health, "mepolizumab is not going to be a viable treatment for the majority of patients with asthma."

"However, it is possible that if one took a group with continuing eosinophilic inflammation and exacerbations, there may still be a role for treatment in this group, as it appears to be very safe and well-tolerated," he said. ■

Last Updated: 2007-12-27 14:00:14 -0400

Am J Respir Crit Care Med 2007; 176:1062-1071.

ROFLUMILAST REDUCES SPUTUM INFLAMMATORY CELL COUNTS IN COPD PATIENTS

By Will Boggs, MD

NEW YORK (Reuters Health) - The PDE4 inhibitor roflumilast reduces sputum neutrophil and eosinophil counts in patients with chronic obstructive pulmonary disease (COPD), according to a report in the December *Thorax*.

"Roflumilast treatment has anti-inflammatory effects in patients with COPD that are accompanied by an improvement in lung function," Dr. Diana C. Grootendorst from Leiden University Medical Center, The Netherlands, told Reuters Health. "Whether such treatment also reduces airway remodeling, the progressive decline in

FEV₁, and the associated mortality risk in patients with COPD remains to be examined in long-term follow-up studies."

Dr. Grootendorst and associates examined the efficacy of oral roflumilast treatment compared with placebo on the reduction in sputum inflammatory cell counts and improvements in FEV₁ in a crossover study of 38 patients with COPD.

Overall sputum cell counts decreased by 34% during roflumilast treatment compared with placebo, the authors report, including significant reductions in neutrophil, eosinophil, and lymphocyte numbers. Differential cell counts did not change.

Pre- and post-bronchodilator FEV₁ improved significantly during roflumilast treatment, the report indicates. Roflumilast also significantly reduced markers of inflammation and microvascular leakage in sputum supernatant and reduced TNF-alpha secretion by whole blood cultures following ex vivo stimulation by lipopolysaccharide.

Diarrhea and headache were the most frequent adverse events with roflumilast, the researchers note, and there were no serious adverse events.

"Based on the mode of action of PDE4 inhibition and bronchodilators (both increase intracellular cAMP, albeit in a different manner), one would expect that combination of these treatments would yield more pronounced bronchodilation," Dr. Grootendorst said. "However, we have shown in a small study that this is not the case, thereby suggesting that the effect on lung function that is seen after treatment for at least 4 weeks is due to anti-inflammatory effects." ■

Last Updated: 2007-12-19 14:30:08 -0400

Thorax 2007; 62:1081-1087.

OSA BLUNTS HEART RATE RECOVERY AFTER EXERCISE

NEW YORK (Reuters Health) - In young, overweight men, untreated obstructive sleep apnea (OSA) alters the cardiovascular response during recovery from maximal exercise, suggesting impaired autonomic regulation, new study findings suggest.

"Research into the exercise response of OSA subjects is limited and equivocal," Dr. William G. Herbert and colleagues write in the January 1 issue of the journal *Sleep*. Such information could be of value, they surmised, given the increased risk of hypertension and cardiovascular disease associated with OSA.

In their study, they employed maximal ramping exercise testing on a cycle ergometer to evaluate cardiovascular responses in young sedentary men (ages 18 to 26). The study was conducted at

Virginia Polytechnic Institute and State University in Blacksburg.

Included were 14 overweight men with OSA (mean BMI 32, mean apnea/hypopnea index score 23 events/hour). Responses were compared with those of men without OSA, including 16 men matched for BMI and central adiposity, and 14 men of normal weight. During exercise, the groups did not differ in heart rate, blood pressure, or oxygen consumption.

However, heart rate recovery was significantly attenuated in the OSA group throughout the 5-minute recovery period compared with the other groups (p=0.009). Dr. Herbert's team also observed that for patients with OSA, up to 49% of the degree of blunting in blood pressure response was explained by severity of OSA.

Attenuated heart rate recovery has been identified as an independent predictor of cardiovascular and all-cause mortality, the authors point out.

"These results suggest that ramping exercise testing may be a useful tool in identifying significant clinical signs in the early stages of OSA progression, which may aid clinicians in improving risk stratification and patient selection for overnight polysomnography." ■

Last Updated: 2008-01-09 16:40:30 -0400

Sleep 2008.

VALUE OF HYDROCORTISONE QUESTIONED IN SEPTIC SHOCK

NEW YORK (Reuters Health) - In a randomized, placebo-controlled study of patients with septic shock, hydrocortisone did not improve survival, regardless of the patients' adrenal responsiveness to corticotropin administration.

Dr. Charles L. Sprung from Hadassah Hebrew University Medical Center, Jerusalem and an international team report their findings in the January 10 issue of *The New England Journal of Medicine*. From this study, writes the author of an editorial, "it should be clear that substantial uncertainty over the role of corticosteroids (in septic shock) persists."

Treatment with physiologic doses of hydrocortisone is currently recommended in patients with septic shock, even though a survival benefit has been reported only in patients who remained hypotensive after fluid and vasopressor resuscitation and who had a reduced response to corticotropin, Dr. Sprung and colleagues note in their report.

In their study, 499 well-matched patients were randomly assigned within 72 hours of the onset of septic shock to 50 mg intravenous hydrocortisone (n=251) or placebo (n=248) every 6 hours for 5 days. The dose was then tapered over the next 6

days. Before treatment, all 499 patients underwent a corticotropin stimulation test and 233 (46.7%) failed to respond to the test—125 in the hydrocortisone arm and 108 in the placebo arm.

Dr. Sprung and colleagues found that use of low-dose hydrocortisone had no significant effect on the rate of death at 28 days—the primary outcome. This finding was consistent in the overall population and in patients who had a response to corticotropin and in those who did not. Specifically, at 28 days, 34.3% of patients in the hydrocortisone group and 31.5% in the placebo group had died. In those who responded to corticotropin, death rates were 28.8% and 28.7% in the hydrocortisone and placebo groups, respectively. In those who did not respond to corticotropin, death rates at 28 days were 39.2% and 36.1%, respectively.

Shock was reversed more quickly in patients treated with hydrocortisone but this did not result in improved survival. Editorialist Dr. Simon Finfer of the University of Sydney, Australia, makes the point that this study, despite being the largest to date of corticosteroids in patients with septic shock, was “inadequately powered to detect a clinically important treatment effect.”

Although this study was unable to define the role of corticosteroids in septic shock, the investigators performed a “valuable service,” Dr. Finfer writes, by “reminding us that few critical care practices or treatment recommendations are based on unequivocal evidence and that, in some instances, critical appraisal and an open mind may be more appropriate than unquestioning adherence to guidelines.” ■

Last Updated: 2008-01-09 17:00:45 -0400

N Engl J Med 2008; 176:685-690.

VITAMIN D INSUFFICIENCY COMMON IN CYSTIC FIBROSIS PATIENTS

By Will Boggs, MD

NEW YORK (Reuters Health) - Vitamin D insufficiency is common in patients with cystic fibrosis (CF), according to a report in the December *American Journal of Clinical Nutrition*.

“Children with CF have vitamin D insufficiency despite routine supplementation with vitamin D,” Dr. Babette S. Zemel from The Children’s Hospital of Philadelphia told Reuters Health. “Further research is needed to determine the optimal dose of vitamin D for CF patients.” Dr. Zemel and associates compared the vitamin D status in children, adolescents, and young adults with CF who were being treated with routine vitamin D and pancreatic enzyme supplements with the status in healthy controls.

The mean serum concentrations of 25-hydroxyvitamin D were significantly lower in the CF group (20.7 ng/mL) than in healthy controls (26.2 ng/mL), the authors report. Mean 1,25-dihydroxyvitamin D levels were also significantly lower in the CF group.

Seven percent of CF patients had vitamin D deficiency, and 90% had vitamin D insufficiency, while 2% of healthy sub-

jects had vitamin D deficiency and 74% had vitamin D insufficiency.

More CF patients (25%) than healthy controls (9%) had elevated parathyroid hormone (PTH) concentrations, the researchers note.

There was no significant correlation between PTH and 1,25-dihydroxyvitamin D levels in CF patients, the investigators say, and there was no correlation between dietary intake of vitamin D and 25-hydroxyvitamin D concentrations in either group.

These data suggest that the 800 IU vitamin D daily dose is too low to maintain the desired 25-hydroxyvitamin D concentrations between 30 and 60 ng/mL in CF patients.

“Serum vitamin D levels should be monitored and increased supplemental doses considered for those patients with vitamin D insufficiency,” Dr. Zemel said. ■

Last Updated: 2007-12-27 15:15:15 -0400

Am J Clin Nutr 2007; 86:1694-1699.

THREE-GENE PANEL PREDICTS SURVIVAL IN NON-SMALL CELL LUNG CANCER

NEW YORK (Reuters Health) - The expression of three specific genes in microarray studies provides information on overall survival in non-small cell lung cancer (NSCLC), Canadian investigators report.

Dr. Ming-Sound Tsao of Princess Margaret Hospital in Toronto and colleagues analyzed 158 possible prognostic genes, identified in previous studies as being potentially linked to NSCLC, by reverse transcription quantitative polymerase chain reaction (RT-qPCR) in the tumors of 14 patients with NSCLC.

As reported in the December 10 issue of the *Journal of Clinical Oncology*, they identified a three-gene classifier, involving genes STX1A, HIF1A and CCR7, that was predictive of overall survival, with a hazard ratio of 3.8.

“The classifier was also able to stratify stage I and II patients and further improved the predictive ability of clinical factors such as histology and tumor stage,” Dr. Tsao and colleagues report. “The predictive value of this three-gene classifier was validated in two large independent microarray data sets from Harvard and Duke Universities.”

Dr. Tsao’s team says that STX1A is associated with more aggressive forms of colon and rectal carcinomas and the chemokine receptor CCR7 is highly expressed in a number of tumors, including NSCLC, and is linked to increased invasion, lymph node infiltration, metastasis, and poor prognosis. Similarly, HIF1A is correlated with a poor prognosis.

“Once further validated in other independent patient cohorts and with standardized protocols in hand, a significant advantage of our robust three-gene classifier for NSCLC is that it may be easily implemented in the clinic using cost-effective multiplex RT-qPCR assays,” Dr. Tsao and colleagues point out. ■

Last Updated: 2008-01-02 14:33:33 -0400

J Clin Oncol 2007; 25:5562-5569.

SEVERE PNEUMONIA IN CHILDREN CAN BE TREATED AT HOME

NEW YORK (Reuters Health) - Ambulatory management with high-dose oral amoxicillin is effective treatment for severe pneumonia without underlying complications in children below 5 years of age, according to a study in Pakistan.

In fact, this regimen is so successful that WHO guidelines for hospitalizing these patients and treating them with parenteral ampicillin should be changed, the authors recommend in the January 5 issue of *The Lancet*.

Calling these findings “a milestone,” Dr. Shams El Arifeen and Dr. Abdullah H. Baqui note in an editorial that “the potential impact here is enormous, particularly for the many children with severe pneumonia who are referred to hospitals but never reach them.”

Dr. Donald M. Thea, at Boston University, and colleagues enrolled 2,037 children aged 3 to 59 months with severe pneumonia (cough and/or difficult breathing plus lower chest indrawing) at seven sites in Pakistan. They excluded patients with signs of very severe pneumonia, such as inability to drink, convulsions, or central cyanosis.

Patients were randomly assigned to ambulatory treatment for 5 days with oral amoxicillin 80-90 mg/kg per day in two doses (n=1025), or to hospitalization and parenteral ampicillin 100 mg/kg per day in 4 doses for 48 hours, followed by at-home treatment for 3 days with oral amoxicillin 80-90 mg/kg per day (n=1012).

The treatment failure rate at day 6 was 8.6% in the hospitalized group and 7.5% in the home-based group. After 2 weeks, 88% and 90%, respectively, were cured.

Young infancy (age 3 to 5 months), very fast breathing (>70 breaths per min for children younger than 12 months old, >60 breaths per min for older children), and being underweight for age were associated with increased treatment failure rates. Thus, Dr. Thea’s group suggests that for patients with these risk factors, close monitoring and possibly hospitalization may be warranted.

They maintain that their results are generalizable to most other developing countries.

Dr. El Arifeen, at the International Centre for Diarrhoeal Disease Research in Bangladesh, and Dr. Baqui, at Johns Hopkins University in Baltimore, point out that hospitalization rates in these cases is low, “which makes current guidelines ineffective in practice.”

They conclude: “We would benefit from considering severe pneumonia without any danger signs, complications, or other severe conditions as a distinct category that could be safely and effectively treated with oral antibiotics outside hospitals.” ■

Last Updated: 2008-01-03 18:30:20 -0400

Lancet 2008; 62:861-867.

LUNG-ORIENTED IMMUNOASSAY ACCURATELY DIAGNOSES ACTIVE TB

NEW YORK (Reuters Health) - A rapid lung-oriented immunoassay accurately diagnoses sputum smear-negative active tuberculosis (TB), according to a report in the January *Thorax*.

Small clinical studies using bronchoalveolar lavage (BAL) have suggested that antigen-specific responses can be used to make a rapid diagnosis in cases of extrapulmonary and HIV-related tuberculosis with greater sensitivity than if blood was used, the authors explain.

Dr. R. A. M. Breen from Royal Free and University College Medical School in London and colleagues evaluated a flow cytometric assay measuring the percentage of interferon-gamma synthetic CD4+ lymphocytes following stimulation with purified protein derivative of *M. tuberculosis* (PPD). They tested BAL fluid from 250 sputum smear-negative individuals with possible TB.

In the 111 patients found to have TB (including 23 co-infected with HIV), the median percentage of PPD-specific CD4+IFN-gamma synthetic lymphocytes was significantly higher for those with culture-proven TB (14.6%) and for those with clinical diagnoses (10.4%) than in the 139 patients without a diagnosis of TB (0.21%), the authors report.

A value of 1.5% for PPD-specific CD4+IFN-gamma synthetic lymphocytes gave a sensitivity of 95% and a specificity of 76% in diagnosing TB.

Both the PPD-specific immunoassay and the nucleic acid amplification test (NAAT) were highly sensitive in smear-positive BAL fluid, the investigators say, but only the performance of the immune test was maintained in smear-negative BAL fluid.

“Our data strongly suggest that immunological assays, which can be combined with conventional culture and NAAT in BAL samples, have the potential to improve the diagnosis of patients with suspected TB,” the authors conclude. “Simplification of sample collection and processing would enable this technique to be applied beyond its current research setting.”

“Should we use the new tests for latent tuberculosis in the examination of BAL fluid?” asks Dr. Graham H. Bothamley from Homerton University Hospital, London, in a related editorial. “The answer remains unclear, but the excitement is palpable.”

“At last, the investment made during the last decade may begin to pay dividends in the clinical management of patients with suspected tuberculosis,” the editorial concludes. ■

Last Updated: 2008-01-07 14:47:13 -0400

Thorax 2008; 63:4-5,67-71.

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Additional summaries are published each month on the ATS Web site at www.thoracic.org

WHO'S WHO *at* ATS PAR

EILEEN ZACHARIAS

In June 1995, Eileen Zacharias was a thirty-three-year-old, hard-driven trial attorney who was not slowed by a little back pain, even when it became excruciating. A few days later, however, when breathing became difficult, her life changed forever.

Although she went to see a doctor who sent her home with muscle relaxants, she continued to deteriorate and was soon admitted to the medical intensive care unit. "Two days later, I was on a respirator fighting for my life," she said.

Her doctors diagnosed her with acute respiratory distress syndrome (ARDS), a life-threatening condition in which intense inflammation of the lung tissue causes moderate to severe loss of lung function. As Ms. Zacharias learned firsthand, the disease can be caused by more than 60 precipitating factors, including pneumonia, sepsis, trauma and aspiration. It presents itself quickly and patients usually require mechanical ventilation within 72 hours.

After spending nine weeks in the hospital—eight on the ventilator and four in a drug-induced coma—she was surprised to discover that there was little information available about ARDS, except for descriptions in medical literature that showed autopsy photos.

"From my perspective and experience, it was easy to see that there was a tremendous need for information on ARDS for patients and their families written in plain English," said Ms. Zacharias, who co-founded the ARDS Foundation in December 2000 with Paula Blonski, who had lost her sister to the disease in 1998. "Many people discouraged us, stressing that without financial backing, the task would be monumental. But we felt strongly that something needed to be done."

What they lacked in funding, she added, they compensated for with a shared passion and desire to make a difference for those in the ARDS community.

And make a difference they did. In 1995, Ms. Zacharias didn't know of any other patients with ARDS. Her family only had each other for support. And the only available literature was intended for healthcare professionals.

Since then, the landscape has vastly changed. There are about 150,000 cases of ARDS reported each year in the U.S. and 2.3 million reported worldwide. And through the ARDS Foundation, survivors and their families can easily find information and support.

Public awareness of the disease, though still lacking, has grown tremendously. When the Foundation first launched its Web site in March 2001, it consisted of five pages. Today, it has more than 100 pages filled with educational materials, links to online resources, articles from medical and scientific journals, and stories of survivors and families who have lost a loved one to ARDS.

But the fact remains that ARDS is still not well-known or well-understood. "It is a vicious circle: without awareness, fundraising is difficult. Without funds, we can only do so much to raise awareness. And without sufficient financial support, it is extremely difficult to advance research," said Ms. Zacharias.

As a result, patients with ARDS continue to face an uphill battle. Even with life support, at least 40 percent of those diagnosed in the United States will die. Only one-third



of survivors are discharged directly home, and many suffer from post-traumatic stress disorder and depression. Some face cognitive impairment, while others are diagnosed with asthma, COPD and even pulmonary fibrosis.

Despite these sobering statistics, Ms. Zacharias is inspired by the patients and physicians she meets as president of the ARDS Foundation.

"We receive e-mails and phone calls from patients all over the world who have survived ARDS and feel so alone," she said. "They want information and advice from someone who has gone through this before. And we can give that to them."

The physicians and scientists who work tirelessly to better understand and treat ARDS, she adds, are "sincere, caring and generous with their time, knowledge and expertise. Without their commitment, it would be difficult for us to offer patients what they need most: reliable information."

Belonging to ATS PAR has bolstered the ARDS Foundation's profile and provided a number of opportunities for partnering with other lung organizations. "Our goals and the patients we serve have tremendous commonalities and, as such, our collaborations are mutually beneficial," Ms. Zacharias said.

Since joining PAR in 2005, the Foundation has co-funded one partnership research grant with the ATS, participated in advocacy efforts on Capitol Hill, and attended the annual ATS International Conference.

"Having the opportunity to present our poster at the conference and offer patient speakers at sessions has allowed us to network with medical professionals and introduce them to the ARDS Foundation as a resource for their patients," said Ms. Zacharias, who has spoken about her experience as an ARDS survivor at six sessions.

As for the future, she hopes the ARDS Foundation will continue to partner with other organizations to fund research, publish patient resources and participate in joint fundraising efforts. "As a young organization, our future is boundless," she said.

Ms. Zacharias lives in Chicago with her husband, Paul, and their two daughters, Lily, 11, and Dana, 9. In addition to serving as president of the ARDS Foundation, she works part time as a criminal defense attorney and administrative law officer. ■

NEWS BRIEFS

INTRODUCING THE ATS PAR EXECUTIVE COMMITTEE

Donna J. Appell, R.N., Chair

The Hermansky-Pudlak Syndrome (HPS) Network, Inc. was founded in 1992 for individuals and families dealing with HPS, a rare genetic metabolic disorder that affects the way cell membranes are made and which can cause albinism, legal blindness, a platelet bleeding disorder, colitis, and pulmonary fibrosis.

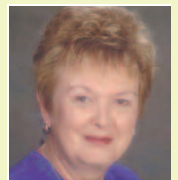


The Network's mission is to gather and disseminate information, produce educational materials, promote awareness, support research and give hope to individuals and families affected by the disease. Toward those ends, the organization maintains a patient registry to assist with networking and medical research. It also holds annual conferences in New York and Puerto Rico, which bring together members, their families and friends, researchers and healthcare professionals. For more information, please visit www.hpsnetwork.org.

Eileen Zacharias, Chair-Elect (please see profile to left)

Judy Simpson, R.N., Immediate-Past Chair

Founded in 1990, the Pulmonary Hypertension Association's (PHA) mission has grown to "seek a cure for pulmonary hypertension and provide hope for the pulmonary hypertension community through support, education, advocacy and awareness." PH, a rare blood vessel disorder of the lung in which the pressure in the pulmonary artery rises above normal levels and may become life threatening, affects tens of thousands of patients in the U.S. and abroad.



Although the cause of pulmonary hypertension is not known, the PHA works with physicians to improve diagnosis and treatment. The organization hosts a Web site that averages 170,000 visitors per month, publishes the world's only medical journal dedicated to PH and sponsors more than 150 support groups, a patient-to-patient telephone helpline and an advocacy program. For more information, please visit www.phassociation.org.

Teresa Geiger, Membership Action Team Chair

The Coalition for Pulmonary Fibrosis (CPF) was founded in 2001 to accelerate research efforts leading to a cure for idiopathic pulmonary fibrosis (IPF), while educating, supporting and advocating for the community of patients, families and medical professionals fighting the disease. It is the largest non-profit organization in the U.S. dedicated to advocating for improved diagnosis and treatment of IPF.



IPF is a debilitating disease marked by pulmonary fibrosis or progressive scarring of the lungs that gradually interferes with a person's ability to breathe and thus obtain enough oxygen for vital organs to function normally. The CPF funds promising research into new approaches to treat and cure the disease. For more information, please visit www.coalitionforpf.org.

the ADVOCATE

CONGRESS AND WHITE HOUSE AGREE ON FEDERAL SPENDING



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NIH INSTITUTE & VA FUNDING (in millions)				
PROGRAM	FY06 ACTUAL	FY07 ACTUAL	FY08 ACTUAL	% CHANGE
NIH Total	\$28,311	\$28,900	\$29,229	+1.1
NHLBI	\$2,922	\$2,922	\$2,922	0
NIAID	\$4,383	\$4,264	\$4,265	+0.02
NIEHS	\$636	\$647	\$642	-7%
NINR	\$137	\$137	\$137	0
VA Research	\$412	\$413.7*	\$480	+16.2

CDC & USAID PROGRAMS (in millions)				
PROGRAM	FY06 ACTUAL	FY07 ACTUAL	FY08 ACTUAL	% CHANGE
CDC Total	\$6,366B	\$6,227	\$6,400	+3.0
NIOSH (including WTC)	\$262M	\$253M	\$381M	+17.50
Tobacco Control	\$104M	\$104M	\$104M	0
Domestic TB	\$136.6 M	\$137M	\$140.3M	+2.5%
USAID Global TB	\$80M	\$100M	\$152M	+52%

* The VA research program received a 32.5 million increase in FY07 funding as part of the Iraq War emergency supplemental, bringing FY07 funding to \$446.2 million.

In late December, Congress passed an omnibus appropriations bill for fiscal year 2008 that includes funding for all Labor, Health and Human Services and Education (Labor-HHS-ED) programs, including the National Institutes of Health (NIH) and the Centers for Disease Control and Prevention (CDC).

The NIH is slated to receive a modest funding increase of 1.1 percent, most of which will be earmarked for administrative activities and for a \$300 million contribution to the Global Fund for AIDS, TB and Malaria (up from \$100 million in 2007). As a result, nearly all institutes received slightly more funding than in FY07, except for the National Institute for Environmental Health Sciences (*see table*).

The CDC fared better than the NIH with a 3 percent budget increase for FY08, including \$56.5 million in newly authorized funding to improving health conditions related to the World Trade Center collapse. The National Institute of Occupational Safety and Health, which saw a significant budget increase, will administer these funds.

The U.S. Agency for International Development's (USAID) global TB control program and the VA research program received the largest increases of 52 percent and 16.2 percent, respectively.

Congress Mandates Public Posting of NIH-Funded Articles

A provision in the omnibus appropriations bill requires all manuscripts produced with funding from the NIH be submitted to PubMedCentral within 12 months of publication, making what was a voluntary policy now mandatory. The ATS already participates in a program where all NIH-funded manuscripts published in the Society's journals are automatically submitted in compliance with the policy.

ATS Comments on Research Involving Impaired Patients

The ATS and several sister societies submitted joint comments to the Office for Human Research Protection (OHRP) in response to its request for public input on rules protecting patients with temporary "decision-making" impairments who participate in clinical research protocols. Existing regulations focus primarily on individuals with permanent mental impairments.

After describing the need for and challenges associated with conducting clinical research in the critical care unit, where patients are often temporarily impaired, the comments concluded that:

1. Ethical clinical research in the ICU must be preserved and enhanced with national standards.
2. The unique needs of critically ill patients participating in clinical research must be recognized.
3. Surrogate consent must be preserved.
4. Cross institution procedural consistency and simplification should be enhanced.
5. A waiver of informed consent should be required in certain emergency research.

ATS Tells EPA to Tighten Ozone Standard

Last month, ATS leaders, along with representatives of the American Lung Association and other medical organizations, met with Environmental Protection Agency Administrator Stephen Johnson to discuss the EPA's pending final rule on the National Ambient Air Quality (NAAQS) for ozone pollution.



Stephen Johnson

In June, the EPA issued a proposal to tighten the NAAQS for ozone pollution from the existing standard of .084 ppm/8 hours to a new standard in the range of 0.075 to 0.070 ppm/8 hours. While this standard is stricter than what is currently in place, the EPA is also considering a range of policy options, including retaining the existing standard.

At the meeting, ATS Executive Director Stephen Crane, Ph.D., M.P.H., and William Rom, M.D., chair of the ATS Environmental Health Policy Committee, voiced the Society's support for a stricter standard of 0.060 ppm/8 hours. Dr. Rom highlighted numerous studies that show the need for a tighter standard, countering industry arguments that scientific data on the adverse effects of exposure to ozone pollution at or even below the current standard is "uncertain." By court order, a new standard must be issued by March 12. ■

Organizational Highlights

The ARDS Foundation



- Founded and incorporated in 2000.
- Mission: to increase awareness, foster medical research and offer a forum where ARDS patients and families around the world can find caring and effective guidance and support.
- Maintains survivor registry to collect data for ARDS researchers who want to locate ARDS survivors for future research projects.
- Hosts an online petition to gather signatures for submission to the U.S. government to urge additional research for ARDS.
- Hosts events to raise funds for educational materials, research and public awareness of ARDS, both locally and nationally.
- Maintains personal accounts of patients who have survived or succumbed to ARDS

To learn more about ARDS, please visit www.ardsusa.org. The ATS and the ARDS Foundation co-produced a patient information pamphlet on the disease, which was published in the *American Journal of Respiratory and Critical Care Medicine* in 2007, and can be downloaded from the "Patient Education" section of the ATS Web site.

Spotlight  Patients

Len Geiger

(continued from page 3)

goals, ultimately emerging ten months later in better shape than I'd been in my entire life.

What followed over the next several years was a series of revelations, road races, introductions, interviews and introspection far too extensive to describe here. I can say this: I cherish my life now more than ever before. Both the best and worst things that have happened in my life were directly related to Alpha-1 and I wouldn't trade it in for a "normal" life for all the money in the world.

I'm working hard in healthcare again, but this time as an Alpha-1 patient advocate, actively promoting aware-

ness, early detection and treatment and supporting individuals diagnosed with the disease. One of the first things I tell a newly diagnosed patient is that they have a long road in front of them. The decision they must make is what attitude they will carry on their journey.

Fourteen years after my diagnosis of Alpha-1 and six years after my transplant, I am enjoying my new opportunity for life and love with my wife, Christina, and our two-year-old daughter, Ava Corinne. It may have had a lot of twists, turns, detours, and even a washed out bridge or two, but it's still a glorious road that I continue to travel.

Len Geiger has been featured in *Sports Illustrated*, HBO's "Real Sports," the Discovery Channel's "Mystery Diagnosis" and, most recently, on "World News Tonight." To learn more about his personal journey or Alpha-1, please visit www.alphaonefoundation.org. ■

CALENDAR OF ATS PAR EVENTS

DATE	MEETING	CONTACT
March 8, 2008	LUNGeivity Foundation: <i>Playing for a Cure</i> Memphis, Tennessee	Phone: (773) 281-LUNG www.lungevity.org
March 11-12, 2008	PAR/RAC Lobbying Day on Capitol Hill Washington, D.C.	Phone: (212) 315-8640 E-mail: kbelgiovine@thoracic.org
March 28-30, 2008	The 15 th Annual HPS Conference Uniondale, New York	www.hpsnetwork.org
March 29, 2008	ALA California: <i>Climb California Former Bank of American Building - San Francisco, California</i>	E-mail: kstone@alac.org www.climbcalifornia.org
April 3-4, 2008	Alpha-1 Foundation: 10 th Gordon L. Snider Critical Issues Workshop "Quantitative Chest Tomography in COPD Research" Bethesda, Maryland	Phone: (305) 567-9888 www.alphaone.org
April 6, 2008	LUNGeivity Foundation: <i>Ann Arbor Walk for Lung Cancer - Ann Arbor, Michigan</i>	Phone: (773) 281-LUNG www.lungevity.org
April 18, 2008	LUNGeivity Foundation: <i>A Step 4 Life</i> Brighton, Colorado	Phone: (773) 281-LUNG www.lungevity.org
May 13, 2008	ALA California: <i>Breath of Fresh Air, A Women's Lung Health Initiative - San Francisco, California</i>	E-mail: asullivan@alac.org www.alac.org
May 16-21, 2008	American Thoracic Society International Conference - Toronto, Canada	E-mail: ats2008@thoracic.org
May 17, 2008	PAR: <i>Breathing Better with the ATS</i> Toronto, Canada	Phone: (212) 315-8640 E-mail: kbelgiovine@thoracic.org
May 20, 2008	PAR Symposium: "Rebuilding the Pulmonary Patient, From Laboratory to Lifestyle" Toronto, Canada	Phone: (212) 315-8640 kbelgiovine@thoracic.org
June 1, 2008	LUNGeivity Foundation: <i>NYC Walk for Lung Cancer - New York, New York</i>	Phone: (773) 281-LUNG www.lungevity.org

ABOUT
ATS PAR

The ATS Public Advisory Roundtable (PAR) represents a core component of the Society and a mutually beneficial partnership wherein organizations that represent persons affected by respiratory diseases, sleep-related conditions or critical illnesses collaborate to advance their shared educational, research, patient care and advocacy missions.



Members of ATS PAR

Donna Appell, Chair
Hermansky-Pudlak Syndrome Network, Inc.

Eileen Rubin Zacharias, JD, Chair-Elect
ARDS Foundation

Willard A. Fry, MD
The Respiratory Health Association
of Metro Chicago

Karen Fulton Holine
American Lung Association
of California

Teresa Geiger
Coalition for Pulmonary Fibrosis

Edward Grandi
American Sleep Apnea Association

Bill McLin
Asthma and Allergy Foundation of America

Suzanne Pattee, JD
Cystic Fibrosis Foundation

Paula Y. Polite
Sarcoidosis Research Institute

Gregory R. Porta
Children's Interstitial Lung Disease Foundation, Inc.

Judith A. Simpson, MS, RN
Pulmonary Hypertension Association

Beth I. Stern
LUNGeivity Foundation

John W. Walsh
Alpha-1 Foundation

Vicky Holets Whittemore, PhD
Tuberous Sclerosis Alliance

For more information about ATS PAR, please visit the Society's Web site at www.thoracic.org. Under the "About ATS" drop-down menu, click "ATS PAR."