Pulmonary Diseases, Critical Care & Environmental Medicine News

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Message from the Section Chief

This issue of the Tulane Pulmonary/Critical Care News Letter largely focuses on regional and school educational efforts of the section. We offered two robustly attended community programs, specifically in pulmonary fibrosis and sarcoidosis this past year, and look forward to facilitating more programs in the future. So please drop me an email with any suggestions on topics that would be helpful for your practice (jlasky@tulane.edu).

Joseph A. Lasky, MD
Professor of Medicine
Deming Educational Fund Chair of Internal Medicine
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Dr. Ross Klingsberg Selected to Serve on the USMLE® Acute Care Test Material Development Committee

Tulane Pulmonary Medicine physician-educator, Ross Klingsberg MD, has been selected to serve on the United States Medical Licensing Examination® (USMLE®) Acute Care Test Material Development Committee. The USMLE® is sponsored by the National Board of Medical Examiners® (NBME®) and the Federation of State Medical Boards (FSMB).

The USMLE program conducts a periodic review of standards for each USMLE Step examination. Congratulations to Dr. Klingsberg for his selection to work on this important committee that helps set the national standards for medical licensure. His participation will give our region representation on this important committee. He will also bring standardized test-writing skills back to Tulane to help improve our educational mission.
Tulane Multi-Specialty Sarcoidosis CME Conference and Tulane/Foundation for Sarcoidosis Research (FSR) Patient Conference

Saturday, February 27, 2016 held the first New Orleans Sarcoidosis Multi-Specialty and Patient conferences. It was a tremendous success on all counts. Of fifteen years of FSR patient conferences, FSR proudly reports that the New Orleans patient conference was 'out of the ball park!' with over 120 patient attendees - the largest Sarcoidosis Patient conference ever held in the United States or elsewhere!

The CME Multi-Specialty Conference in Sarcoidosis was the first CME conference dedicated to non-WASOG members providing high-level specialty specific and generalist knowledge for clinicians with 122 registrants (generalists, pulmonologists, cardiologists, neurologists and ophthalmologists as well as nurses and therapists). In addition to the medical specialty tract, a special session for pulmonary, physical and occupational rehabilitationists was also conducted.

We would like to thank our combined specialty moderating panels, that included regional and national experts and trainees, for the presentation of highly educational and thought-provoking cases.

The feedback from patients and clinicians was very positive and comments were congratulatory, for which we thank you, and are looking forward to the next one. The invited international conference faculty also report having a wonderful stay and engagement with audiences in New Orleans. With such strength of response, Tulane and the FSR are considering an annual New Orleans Patient conference and a bi-annual CME conference. Thanks to all for making this inaugural event a magnificent success!

Any comments or questions for the faculty activity director are welcomed by emailing Dr. Lesley Ann Saketkoo, lsaketk@tulane.edu.

Tulane University, Center for Continuing Education has been accredited as an Accredited Provider by the International Association for Continuing Education and Training (IACET). Tulane University, Center for Continuing Education is authorized by IACET to offer .8 CEUs for this program or 7.75 AMA PRA Category 1 Credits™.
Available Pulmonary Clinical Trials

The following clinical trials are currently available and enrolling patients. If your patient would like to be considered for any of these trials, please contact the Pulmonary section: 504-988-4040, 504-988-0743, or 504-988-2325.

**Pulmonary Fibrosis**
- Pulmonary Fibrosis Foundation Patient Registry Protocol
- A Phase 2, randomized, double-blind, placebo-controlled study of GBT440 to evaluate the safety, tolerability, pharmacokinetics, and effect on hypoxemia in subjects with idiopathic pulmonary fibrosis.
- A twelve week, open-label, randomized, parallel-group study evaluating safety, tolerability and pharmacokinetics (PK) of oral nintedanib in combination with oral pirfenidone, compared to treatment with nintedanib alone, in patients with idiopathic pulmonary fibrosis.
- Idiopathic Pulmonary Fibrosis Prospective Outcomes (IPF-PRO) Registry
- Comparison of Transbronchial, Cryoprobe and Vats Biopsy for the Diagnosis of Interstitial Lung Disease

**Pulmonary Hypertension**
- A Multicenter, Randomized, Double-Blinded, Placebo-Controlled Trial to Evaluate the Safety and Efficacy of Inhaled Treprostinil in Subjects with Pulmonary Hypertension due to Parenchymal Lung Disease

**Cystic Fibrosis**
- VX15-371-101: A Phase 2a, Randomized, Double-blind, Placebo-controlled, Incomplete Block, Crossover Study to Evaluate the Safety and Efficacy of VX-371 in Subjects Aged 12 Years or Older With Cystic Fibrosis, Homozygous for the F508del-CFTR Mutation, and Being Treated With Orkambi.
- Novartis CTBM100C2407: A prospective Observational Study in cystic fibrosis patients with chronic respiratory Pseudomonas aeruginosa infection treated with TOBI® Podhaler™ (tobramycin inhalation powder) or other FDA approved inhaled antipseudomonal antibacterial drugs

**Scleroderma and Sarcoidosis**
- Acthar Gel for Chronic Pulmonary Sarcoidosis
- (GRASP)-Genome Research in African American Scleroderma Patients
- A double blind, randomized, placebo-controlled trial evaluating efficacy and safety of oral nintedanib treatment for at least 52 weeks in patients with Systemic Sclerosis associated Interstitial Lung Disease (SSc-ILD)

**Eosinophilic Disorders**
- Human Eosinophilic Disorders in Health and Disease
Dr. Jay Shames was honored by the Louisiana Thoracic Society at the 60th Annual Tri-State Case Conference in New Orleans on January 16th, 2016 with the Outstanding Clinician Award recognizing a brilliant professional career that has greatly impacted our local and regional community. Dr. Jay Shames was also elected as the national Outstanding Clinician Awardee by the American Thoracic Society; he will be receiving this recognition during the international American Thoracic Society Meeting in May 2016 at San Francisco.

Dr. Shames, originally from Iowa, received his Medical Degree from Tulane University; he underwent an Internship at Jackson Memorial Hospital in Miami, followed by Internal Medicine residency at Touro Infirmary and subsequently a fellowship in Pulmonary Diseases at Tulane University. During his medical career, Dr. Shames has served as a Clinical Professor at Tulane University and Louisiana State University. He has served in different very prominent roles in the Orleans Parish Medical Society, Louisiana State Medical Society and American Medical Association, societies that have also recognized his great work and have honored him with several awards in the past. Dr. Shames is also one of the original founders of one of the most prestigious medical groups in the city of New Orleans, Internal Medicine Specialists, Inc.

In addition to the great impact in the health of his patients during his career, Dr. Shames has been a highly valued teacher and mentor to many medical students, residents and fellows. He continues mentoring Tulane pulmonary fellows during academic activities and outpatient clinics, serving as one of their best role models for their future practice.
NIH Awards Dr. Derek Pociask R21 Research Grant

Dr. Derek Pociask’s laboratory is focused on ways to improve the immune response during influenza infection and reduce the subsequent injury that occurs. A hallmark of severe influenza infection is thymic atrophy and associated peripheral lymphopenia. Given that lymphopenia is strongly associated with secondary bacterial pneumonia, Adult Respiratory Distress Syndrome (ARDS) and mortality, understanding and targeting ways to promote thymic regeneration and reduce lymphopenia can have great impact on patient care. Dr. Pociask’s laboratory is focused on the balance between the cytokine interleukin-22 (IL-22) and its soluble receptor IL-22Ra2 (IL-22 binding protein or IL-22BP). He has found that IL-22 is integral in reducing thymic atrophy during severe influenza infection. The studies in this R21 are focused on ways to boost IL-22 activity in the thymus. We believe the development of such therapies can reduce the impact of influenza on the thymus and subsequently allow for an improved immune response, allowing for quicker patient recovery.

Dr. Fayez Kheir Receives AABIP Research Award

Dr. Fayez Kheir was the recipient of the American Association of Bronchology and Interventional Pulmonology (AABIP) research award (2016-2017) for his project entitled “Silicone Airway Stents for Excessive Dynamic Airway Collapse: A Randomized Placebo Controlled Double-Blinded Trial”. He will carry on the project during his Interventional Pulmonology fellowship at Beth Israel Deaconess Medical Center and Massachusetts General Hospital, two major teaching hospitals of Harvard Medical School under the mentorship of Dr. Adnan Majid.

The mission of the American Association for Bronchology and Interventional Pulmonology is to advance the care of patients with thoracic diseases through the synergy of innovative technologies, minimally invasive procedures, and transformative education and research.
Welcome Dr. Karin Halvorson!

Dr. Karin Halvorson earned her medical degree from the University of Hawaii. She completed a combined residency in Internal Medicine and Emergency Medicine at the University of Illinois at Chicago. Subsequently she attended Brown University for her Pulmonary and Critical Care Fellowship. While at Brown she was inducted into the Alpha Omega Alpha Honor Society and earned the 2014 Fellow Teaching Award. She served as the liaison between the emergency department and the intensive care unit during her time at Brown.

Dr. Halvorson is currently board certified in Emergency Medicine, and Internal Medicine, Pulmonary Medicine, and is board-eligible in Critical Care Medicine. She comes to Tulane University as the Medical Director of the Intensive Care Unit for the new Southeast Louisiana Veterans Health Care System (SLVHCS). She is working on her Masters in Public Health with an emphasis in Healthcare Policy here at Tulane University. With this degree she hopes to help shape the structure of SLVHCS to improve the health care of our nation’s Veteran population. A focus of this new medical center is developing practice guidelines with the most recent evidence-based literature. While her main research interests are on ED to ICU transitions and optimizing early critical care, she plans to assess various aspects of pulmonary and critical care diseases associated with the large population of Veterans exiting the Iraq and Afghan Wars. She is also invested in medical education. She has published research on procalcitonin as a biomarker of infection in both pulmonary and neurological diseases. She is a contributing author in Ultrasound in the Intensive Care Unit by Springer (2015) and has also published 12 children’s books on the human body. Super Simple Body Series with Abdo Publishing (2013 and 2016).
Dr. Astha Chichra was born in New Delhi, India and graduated from Kasturba Medical College, Manipal University, India in 2008. She completed her Internal Medicine residency and her fellowship in Pulmonary and Critical Care Medicine at the Hofstra North Shore-Long Island Jewish School of Medicine. She joined as Assistant Professor of Clinical Medicine in Tulane School of Medicine this academic year.

During her fellowship she focused on the field of critical care ultrasonography and was trained under nationally and internationally recognized leaders including Dr. Paul Mayo, MCCP and Dr. Seth Koenig. Her clinical and research interests include critical care ultrasonography, critical care transthoracic and transesophageal echocardiography, simulation training and medical education. In addition to basic goal directed critical care ultrasonography, she also performs advanced echocardiography and was the principal investigator of a novel study involving simulator-based training of pulmonary and critical care fellows in critical care transesophageal echocardiography. She also serves as faculty for national critical care ultrasonography courses organized by the American College of Chest Physicians in addition to similar courses at the regional level. Her knowledge and experience in the field of critical care ultrasonography, echocardiography and medical simulation combined make her ideal to expand the growth of this field at Tulane University.

Dr. Chichra is board certified in Internal Medicine, Critical Care Medicine and Pulmonary Diseases. She is a member of American College of Chest Physicians, American Thoracic Society and Society of Critical Care Medicine. She currently sees patients at Tulane Medical Center and University Medical Center of New Orleans. She also serves as the director of respiratory services and medical director of laboratory services at Kindred hospital. She has a clinic at Tulane Medical Center where she will be focusing on patients with COPD, Cystic Fibrosis and other general pulmonary disorders. She will be collaborating with the heart failure team at Tulane towards early screening of pulmonary comorbidities in heart failure patients.
A 56 year-old man with a history of common variable immunodeficiency (CVID), along with recurrent bronchitis and pneumonia, presented with progressively worsening shortness of breath over a period of a few months. His baseline NYHA functional class I declined to class II. He also developed a frequent dry cough and wheezing. He denied fever, chest pain, and hemoptysis. His CVID was diagnosed in 1968 after episodes of recurrent bronchitis and pneumonia, and was treated with intravenous immunoglobulin (IVIG) monthly for decades. He was a non-smoker and had no significant environmental or occupational exposures.

Physical Examination: Temperature 98.2°F, heart rate regular at 95/minute, respirations 20/minute, blood pressure 106/70 mmHg, oxygen saturation 95% on room air, BMI of 31; no acute distress; bilaterally mild rhonchi without crackles, and there was a prolonged expiratory phase; no jugulovenous distention or peripheral edema; no clubbing; no hepatomegaly or splenomegaly; musculoskeletal examination was unremarkable.

Laboratory and Radiographic Results: CBC and differential: WBC 10.3/μL (73.8% PMNs, 13.9% lymphocytes, 7.3% monocytes, 1.2% eosinophils); Hct 39.9%. The BMP was entirely within the normal range. HIV serology was negative. PFTs demonstrated severe obstruction and the FVC and FEV1 were significantly reduced from his baseline (FEV1 43% (1.56 L) and FVC 64% (3.04 L) declined to 26% (0.97 L) and FVC 40% (1.89 L). A CT scan of the chest was obtained:

The chest CT was summarized as showing evidence of old granulomatous disease, peribronchial thickening with bilateral reticulonodular infiltration, and ground glass opacity. Scarring was present in the lingula and lower lung fields.

Pathology Results:
A diagnostic VATS was performed and demonstrated a fibrotic interstitial lung disease that was temporally and spatially uniform. There were no spared areas of lung parenchyma. There were rare microgranulomas, areas of patchy lymphohistiocytic interstitial inflammation, sparse organizing regions, and a rare fibroblast focus. The lung tissue did not appear to be honeycombed, but did show centrilobular bronchiolarization and the beginning of restructured lung. A very prominent desquamative component with pneumocyte hyperplasia suggested the possibility of a late fibrotic phase of DIP, but the "desquamative" component lacked the light brown cytoplasmic pigment of classic DIP macrophages. Moreover in many areas the alveolar desquamative component was mixed with a sprinkling of neutrophils, eosinophils, and rare microgranulomas. AFB, GMS, and
Common Variable Immunodeficiency (CVID) with Worsening Dyspnea (cont’d from page 8)

PMS strains did not reveal organisms.

**Diagnosis:** Common variable immunodeficiency with granulomatous and lymphocytic interstitial lung disease (GLILD).

**Discussion:** Common variable immunodeficiency (CVID), the most common clinically significant primary immunodeficiency, is a disorder with impaired B cell differentiation and immunoglobulin production and is estimated to affect about 1:25,000 people in the US. CVID is defined by a markedly reduced serum concentration of IgG in combination with low levels of IgA and/or IgM, a poor response to immunizations, and the absence of other primary immunodeficiency disorders. (1)

Clinical manifestations of CVID include recurrent infections, most commonly involving the sinuses, lung and skin. Long-term treatment for this condition involves administration of immunoglobulin to decrease the incidence of infection. Chronic pulmonary disease is a common problem among patients with CVID, and may manifest as obstructive or restrictive lung disease. It is also associated with the occurrence of granulomatous lymphocytic interstitial lung disease (GLILD), as demonstrated in this patient.

Approximately 10-18% of patients with CVID develop interstitial lung disease, such as GLILD. GLILD is characterized by histologic changes that include lymphocytic interstitial pneumonitis, follicular bronchiolitis, and non-necrotizing granulomas. The pathobiology of GLILD is unclear, however, one study suggests an association with HHV8, which is also associated with HIV-related pulmonary hypertension and Castleman’s Disease. (2) Patients with GLILD usually present with worsening shortness of breath, a declining FEV1, and on occasion splenomegaly and diffuse adenopathy. Laboratory tests may demonstrate cytopenia, and the HRCT most commonly displays patchy ground glass and nodular opacities. The definitive diagnosis most often requires a VATS lung biopsy to rule out cryptogenic organizing pneumonia and neoplastic process (e.g. lymphoma).

GLILD is associated with increased mortality and is not responsive to treatment with cortico-
Common Variable Immunodeficiency (CVID) with Worsening Dyspnea
(cont’d from page 9)

steroids. (3) There are no standard treatment guidelines for this condition, so suggestions for treatment are based on small series and case reports. A recent retrospective study reported on the treatment of GLILD with a combination of rituximab for 4 weeks and azathioprine therapy for 18 months in 6 patients, and described a significant improvement in FEV1, FVC, and HRCT scoring. (4) The 4-week regimen of rituximab was employed at 6 months intervals for 3 cycles in total. However, there are no published long-term data regarding efficacy of this regimen beyond the 18 months of treatment. Another study published last year reported clinical improvement following treatment with infliximab. (5) Our patient had typical CT scan and histologic findings of GLILD. He was treated with rituximab weekly (375 mg/m2/infusion) for 4 weeks, followed by treatment with azathioprine 200 mg per day. Three months after starting treatment there was a significant decrease in his DOE, his chest CT showed decreased interstitial densities, and his PFTs demonstrated improvements in the FEV1 (0.97 L) and FVC (1.89 L) to (1.42 L) and (2.98 L) respectively. A second cycle of rituximab, 6 months after the first cycle, did not result in further improvements in symptoms or PFTs, but neither was there a decline, so a third cycle of rituximab was not administered.

Clinical pearls:
1. GLILD occurs in 10-18% of patients with CVID.
2. Clinicians should consider GLILD in the setting of CVID when patients complain of worsening dyspnea.
3. CT scans in patients with GLILD demonstrate diffuse ground glass or nodular opacities, and VATS biopsy is generally required to make a definitive diagnosis.

4. There is no current standard treatment regimen for GLILD. However, the combinations of rituximab and azathioprine, or solo treatment with infliximab, are reported to be effective.

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