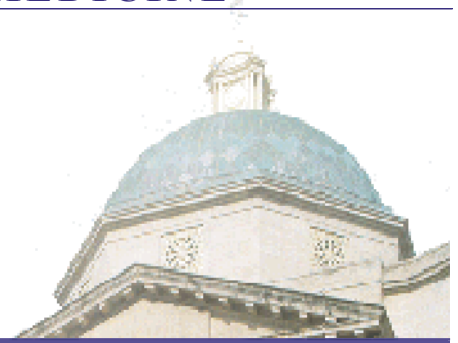


THE DEPARTMENT OF
**INTERNAL
MEDICINE**



Newsletter of the Department of Internal Medicine

Volume 1 • Number 12

The Section of Pulmonary and Critical Care Medicine

INTRODUCTION

The Section of Pulmonary Medicine has been in existence at Yale for approximately 40 years. In the early 1970s the Section was directed by Dr. Arend Bouhuys. In 1976 Dr. Herbert Reynolds was recruited from the NIH to direct the Section. He stayed in this position until 1989. In keeping with national trends, responsibility for medical critical care was added to the sections portfolio in the 1980's. Since 1990 the Section has expanded its clinical, research and educational programs. As a result, it is now internationally recognized (US News and World Report top 16) for its patient care, investigative and training activities. Each is reviewed below.

CLINICAL PROGRAMS

To address the diversity of the diseases and disorders of the respiratory tract, the Section provides consultative care to all adult inpatient services and primary care in the Medical Intensive Care Units at Yale New Haven Hospital (Y-NHH) and the VA-CT Medical Center and runs the Yale Sleep Center which has offices throughout CT. It also runs a large outpatient program out of the Winchester Chest Clinic that includes subspecialty programs in a variety of chest disorders.

Consultations. The Y-NHH and VA Consult Services are mainstays of pulmonary care at both institutions. Each is staffed by a Section attending and year 01 Pulmonary and Critical Care Medicine (PCCM) fellow on a rotating basis. These services provide consults in all of the adult non-MICU wards at Y-NHH and VA-CHS. The Consult Service also covers all pulmonary issues on surgical and other non-medical wards at both institutions. An average 3-6 new consults are seen daily.

MICU. The Medical Intensive Care Unit (MICU) at Y-NHH is regarded as one of the region's elite ICUs. The MICU proper, housed on 5-4, has 14 beds and admits approximately 1,000 patients per year. As a "non-capped" service, the MICU team cares for an average census of 18-24 critically ill patients throughout the hospital. This census can rise into the thirties during busy months. Because

of the high census, the MICU is now covered at all times by two teams, each consisting of a PCCM attending, a PCCM fellow, two residents, and two interns, in addition to Emergency Medicine residents and Yale medical students. Yale faculty spend an average of 10-14 hours per day in the MICU, leading work rounds seven days per week and conducting attending rounds 3-5 days per week. Recent achievements include the development and implementation of several successful management protocols, inauguration of a new Step Down Unit on 5-7, creation of a new MICU syllabus for house staff on CD-ROM, and dramatic decreases in the incidence of nosocomial catheter and pulmonary infections. In addition, the MICU is a haven for clinical research, with multiple faculty conducting studies in cognitive impairment, diabetes management, weaning from mechanical ventilation, and end-of-life care. The activities in the MICU were recently recognized with a Press Ganey Compass Award.

The Bronchoscopy Service. Pulmonary procedures are becoming an increasingly important aspect of the Section. The Section's bronchoscopy service performs approximately 225 procedures annually. An integral part of the training program for post-doctoral fellows, the bronchoscopy service offers diagnostic and therapeutic capabilities for neoplastic, infectious and inflammatory disorders of the lungs and bronchial tree. Recently, airway stenting and balloon dilation for malignant and non-malignant airways obstruction have been added. A focus in the next twelve months is to expand our capabilities to include electrocautery and cryotherapy for the management of more challenging airway tumors.



Jack Elias, M.D.
Section Chief

The Y-NHH Pulmonary Function Laboratory. Pulmonary function testing and training in pulmonary function test (PFT) evaluation are undertaken in the Y-NHH PFT laboratory. Under the direction of Dr. Geoffrey Chupp and with the technical leadership of Mr. Jim Virgolto, the lab has tripled in patient volume over the last few years. In addition to state of the art spirometry, lung volume and diffusion assessments the laboratory is being increasingly called on for methacholine challenges, airplane/altitude simulations, shunt studies and exercise evaluations.

The Winchester Chest Outpatient Practice. The Winchester Chest Clinic at Y-NHH is the primary outpatient practice site for the Section of Pulmonary and Critical Care Medicine. The history of the Clinic dates back decades to a bequest by Sarah Winchester, which established an endowment in the memory of her husband William Wirt Winchester and their young daughter, both of whom succumbed to tuberculosis. This bequest resulted in the establishment in the early 1900s of the original Winchester Hospital in West Haven, which was dedicated to the care of persons with tuberculosis. Over the years, the Winchester Hospital evolved from a freestanding facility to become part of Y-NHH, always with the ongoing mission of pursuing tuberculosis treatment and research. The Winchester Chest Clinic continues this tradition of commitment to tuberculosis. Presently, the Clinic serves a much broader role in research and patient care in all facets of chest diseases. General consultation is available for all pulmonary diseases. Specialty clinics for specific disease areas have also been developed over the past 10 years, which serve as referral sites for consultation, as well as centers for clinical research in those areas. The specialty centers and their directors within the Winchester Chest Clinic include tuberculosis (Lynn Tanoue, MD), asthma (Geoffrey Chupp, MD), interstitial lung disease (Paul Noble, MD), sleep medicine (Vahid Mohsenin, MD), adult cystic fibrosis (Saadia Akhtar, MD), pulmonary hypertension (John McArdle, MD), COPD (Carolyn Rochester, MD), and lung cancer (Lynn Tanoue, MD).

Patient visits to the Clinic have increased substantially over the last ten years. The Clinic has seen an increase in annual volume from 2670 visits in 1992 to 5049 visits in 2003. This growth has been ably facilitated by the Clinic staff, led by nurse manager Joyce D'Amato. Mrs. D'Amato has managed the Clinic since 1972, and has been a vital resource to patients and physicians. The rest of the clinic staff, all of whom deserve great praise for the effort they give, include the Clinic nurses Linda Martin, RN and Mengqing Lai, RN, Patient Care Associate Dorothy Whitfield and clinic secretaries Victoria Pabon and Susan Porto. The quality of care in Winchester Chest Clinic has been nationally recognized by Press Ganey Compass Awards in 2002 and 2003.

(a) **The Yale Asthma Clinic.** To meet the medical needs

of asthmatics in our medical community, the Section established the Yale Asthma Clinic 4 years ago. Under the direction of Geoffrey Chupp, MD and staffed by Tao Zheng, MD and Lauren Cohn, MD, this Center has become one of the busiest programs in the Section and is an established referral source for the most difficult asthmatic patients in southern New England. To facilitate translational research patient data, DNA and serum have been banked. As a result of this effort the clinic is now at the center of ongoing clinical research studies on a variety of issues including the roles of chitinases in asthma, the pathogenesis of refractory asthma, the vascular basis of asthma and the natural history of asthma (sponsored by Wyeth, Inc.).

(b) **The Yale Interstitial Lung Disease Center.** The interstitial lung diseases are difficult to diagnose and treat even for experienced pulmonologists. To address the needs of these patients, Dr. Paul Noble established the multidisciplinary Interstitial Lung Disease Center 3 years ago. This program is now staffed by Dr. David Morris, with Pathology input provided by Robert Homer, MD, PhD (Pathology). In the short time since it began, the Center has become a recognized center of excellence with patients being referred from all over the USA and the world. The Center recently served as one of the major sites for the investigation of the efficacy of gamma interferon in Idiopathic Pulmonary Fibrosis (IPF).

(c) **The Yale Center for Sleep Medicine.** The Yale Center for Sleep Medicine is a multidisciplinary and interdepartmental program that deals with the complexities of sleep disordered breathing including diseases like obstructive sleep apnea and obesity hypoventilation syndrome. Originally established as a result of the efforts of Dr. Vahid Mohsenin, it now includes the efforts of Dr. Francoise Roux and Dr. H. Klar Yaggi and coordinates the efforts of Yale faculty from the Departments of Neurology, Otolaryngology, Psychiatry and Cardiology. The Center is known nationally and internationally for its research and educational endeavors and is recognized by The American Academy of Sleep Medicine as a Center of Excellence. The Center has laboratories in Norwich, Guilford and New Haven CT and at VA-CHS in West Haven. At these locations it studies over 2,000 patients a year and sees over 600 outpatient visits. The Center also offers electives in Sleep Medicine for medical house staff and postgraduate fellows. The patients that are seen at the Center have also been data based to allow the clinicians and scientists at the Center to study the features of the disorder. Prospective studies of the cardiovascular and cerebrovascular pathologic consequences of sleep apnea and gender differences in the phenotypic expression of sleep-disordered breathing are presently ongoing. (<http://www.info.med.yale.edu/intmed/sleep>)

(d) **The Yale COPD Center.** Chronic obstructive pul-

monary disease (COPD) is a major focus of both scientific and clinical interest in the Section of Pulmonary and Critical Care. Drs. Jack Elias, Tao Zheng, Min Jong Kang, Chun Geun Lee and David Morris have recently identified novel mechanisms that likely contribute to the pathogenesis of pulmonary emphysema using transgenic and other mouse models of emphysema and airways inflammation. Numerous members of PACC are currently collaborating in translational studies that are testing the applicability of these findings to human disease, investigating the molecular mechanisms underlying clinical heterogeneity in this disorder and the factors that affect the rate of decline in lung function among COPD patients. Clinical faculty members with particular expertise and interest in COPD include Dr. Carolyn Rochester (Winchester Clinic and VA) and Dr. Hilary Cain (VA). A broad base of patients with COPD, ranging from those with mild disease to those in need of rehabilitation, assisted ventilation or under consideration for Lung Volume Reduction Surgery or Lung Transplantation are seen at the Winchester Chest Clinic COPD Center and the two campuses (West Haven and Newington) of the VA-CT Medical Center. An outpatient Pulmonary Rehabilitation Program was developed at the West Haven VA to improve the functional capacity, exercise tolerance and symptoms of patients with COPD and other forms of chronic respiratory disease. Dr. Rochester is the Medical Director of this program. Drs. Rochester and Cain are also participating in a multi-center, randomized, placebo-controlled trial investigating the effects of the long acting anticholinergic, Tiotropium, on lung function in COPD (based at the West Haven VAMC).

(e) **Adult Cystic Fibrosis Care.** Another exciting new development is the expansion of the Section to include an adult cystic fibrosis (CF) program. CF was previously considered to be a disease of childhood. With improving nutritional and other medical support, however, the median survival of CF patients is now 32 years and continuing to rise. Despite this, pulmonary disease remains the primary cause of morbidity and mortality for these patients. Over the past year members of the Section (Drs Saadia Akhtar and John McArdle) have worked with Dr. Caroline Kim (MedPeds) to transition adult CF patients to adult inpatient and outpatient care. To accomplish this, a multidisciplinary team has been established that includes CF-trained nurses, respiratory therapists, dieticians, social workers and physicians. It is expected that this program will provide optimal medical care to this cohort of patients, create new educational opportunities for trainees and, ultimately, open new avenues of research.

(f) **The Yale Lung Cancer Center.** The Yale Lung Cancer Center is a new initiative supported by the New Clinical Program Development Fund, a joint effort of Yale School of Medicine and Y-NHH. It is expected to open in early 2004 as a multidisciplinary program that coordinates and interdigitates the efforts of faculty from Internal Medicine

(Section of Pulmonary and Critical Care), the Yale Cancer Center (Section of Medical Oncology), Surgery (Section of Cardiothoracic surgery), and Radiation Oncology. The Medical Director of the Lung Cancer Center is Lynn Tanoue, MD. Patient referrals to the Lung Cancer Center are handled centrally through the nurse coordinator for the Center. The physicians of the Lung Cancer Center meet weekly for Tumor Board, which is also supported by the Departments of Pathology and Diagnostic Imaging. This approach maximizes the patient's access to the many physicians involved in the Lung Cancer Center. The result is a streamlined evaluation process, ensuring that optimal therapy is delivered in an efficient manner.

Occupational and Environmental Lung Diseases. Under the direction of Carrie A. Redlich, M.D. a nationally recognized referral practice evaluates patients with potential occupational or environmental lung diseases through a collaborative effort involving faculty from the Yale Pulmonary Section and the Yale Occupational and Environmental Medicine Program. Patients with asthma, interstitial lung disease and other pulmonary disorders are evaluated to determine whether environmental and / or occupational exposures may be causing or exacerbating the patients' lung diseases. Workplace and home environmental assessments are performed with the assistance of Judy Sparer, CIH. Pathology input is provided by Robert Homer, MD, PhD (Pathology). Specific inhalation challenge testing is performed for diagnostic and research purposes, the only such facility in the United States.

PCCM at VA-CT. The Section of Pulmonary and Critical Care Medicine at the VA, directed by Dr. Richard (Rick) Enelow, has active clinical, educational, and research activities, and provides the bulk of the outpatient training for the pulmonary fellowship. Clinics at the West Haven and Newington campuses received over 1,200 new consultations last year under the direction of Drs Carolyn Rochester and Hilary Cain, respectively. As noted above, an active sleep laboratory has been established and will be expanding to 4 beds in the spring, under the direction of Drs Francois Roux and H. Klar Yaggi. Under Dr. Cain the medical intensive care unit recently expanded to 6 beds. A Pulmonary Rehabilitation Program under Dr. Rochester has now been established and has been accepting patients for over a year. Dr. Cain also runs the VA PFT Laboratory which is an active site of fellow physiology training.

RESEARCH

The Section has a wide and varied research portfolio that extends from basic bench-focused studies of disease pathogenesis and target gene validation to human-based studies of clinical issues such as cognitive impairment in the MICU. A unifying theme amongst the bench focused investigators is the desire to elucidate the cellular and molecular events involved in lung injury and repair. The result has been an intense focus on immunology and

molecular biology and the development of scientific approaches at Yale that are now used throughout the world. The investigators and their programs are highlighted below.

Jack A. Elias, MD. The Elias Laboratory is intensely interested in chronic inflammatory and remodeling responses in the lung. To optimally address these issues, the lab has established the techniques that allow one to express transgenes in a lung-specific fashion. In addition, the lab established systems that allow transgenes to be eternally regulated giving the investigator the ability to selectively express a gene at a specific point in time during development and the ability to turn a gene on and off at will. Studies in the lab are presently focusing on the inflammation and remodeling in asthma and COPD, the pathogenesis of pulmonary fibrosis and mechanisms of cytoprotection in acute lung injury. These studies are funded by multiple NIH RO1 grants, an NIH Program Project Grant (Dr. Elias is the Principal Investigator) and multiple industrial research awards. Recent scientific highlights include:

- (a) The demonstration that chitinases are an essential part of the effector response induced by IL-13 and antigen in the lung that can be detected in the serum of humans with asthma where they correlate with disease severity.
- (b) The elucidation of a novel cathepsin-dependent apoptotic pathway that plays a key role in the pathogenesis of emphysema in murine models and in human COPD.
- (c) The demonstration that an early growth response gene-1 (Egr-1)-mediated apoptotic response plays a critical role in TGF- β_1 -induced tissue fibrosis.
- (d) The demonstration that VEGF is a critical mediator in asthma where it induces tissue inflammation, airway remodeling, airway hyperresponsiveness and links in innate and adaptive immunity.
- (e) The demonstration that IL-11 is a critical mediator of IL-13 effects in the lung.
- (f) The demonstration that A1 is a critical mediator of tissue cytoprotective responses in the setting of oxidant-induced lung injury.

Many of these findings have led to patentable intellectual property and collaborations between Yale and Pharmaceutical companies developing new pulmonary therapeutics.

Paul Noble, MD. Dr. Noble's lab is focused on studies of the pathogenesis of idiopathic pulmonary fibrosis and mechanisms that regulate lung fibrosis. He is particularly interested in the roles of the extracellular matrix glycosaminoglycan, hyaluronan in the generation of tissue fibrosis and the ability of hyaluronan degradation products to stimulate tissue inflammation via tissue Toll-like receptors. He continues his research into the interactions of matrix and

inflammation in the setting of pulmonary fibrosis. Recent highlights included his publication in the Journal Science demonstrating that CD44 plays a critical role in the resolution of non-infectious inflammation and the demonstration that low molecular weight hyaluronan signals via Toll 2 and 4. His laboratory has also recently identified a novel role for the chemokine receptor CXCR3 in regulating lung fibrosis. This work demonstrated that CXCR3 is required for in the production of interferon-gamma following non-infectious lung injury. Interferon-gamma was found to inhibit the development of lung fibrosis. Most recently he developed an interest in mechanisms that promote fibroblast survival. His laboratory has discovered that the anti-apoptotic protein survivin that has been implicated in cancer pathogenesis is also expressed by fibroblasts from patients with IPF. These studies are supported by multiple NIH RO1 awards and industrial funding

David Morris, MD. David Morris' research focuses in two broad areas. The first is in the development of translational genomic and proteomic approaches to both interstitial lung diseases and pulmonary emphysema. He is also deeply involved in studying in the mechanisms of post-natal lung remodeling in response to injury with a particular emphasis on Transforming Growth Factor β regulation and signaling. These studies are supported by NIH and American Thoracic Society funding.

Lauren Cohn, MD. Dr. Cohn studies the mechanisms of airway inflammation. The two primary areas of her focus are: (1) the effects of inflammation on mucus metaplasia and (2) mechanisms regulating T cell persistence in asthma. One goal is to determine if inhaled antigen can be used to down-regulate T cell responses in the lung. These studies show that tolerance can be induced in mice during active allergic airways disease. This supports using low-dose, inhaled allergens as immunomodulatory treatments in asthma. As director of the Animal Physiology Core for the Sections Asthma Program Project Grant, she has also set up new methods to measure lung function in mice. These studies have been supported by NIH (RO1, PPG) and American Thoracic Society funding

Patty Lee, MD. Dr. Patty Lee conducts research into the role of apoptosis in acute lung injury and the cytoprotective mechanisms of the enzyme system heme oxygenase-1 (HO-1) using hyperoxia (95% oxygen inhalation) and lung ischemia-reperfusion injury are models of oxidant-induced acute lung injury. Using these models, Dr. Lee has demonstrated that apoptosis, via the induction of a family of signal transduction proteins the mitogen-activated protein kinases (MAPK), is a central mechanism of oxidant-induced lung injury. HO-1 is an inducible isoform of the gene HO, which catalyzes the initial and rate-limiting step in the degradation of heme to biliverdin with the generation of carbon monoxide (CO) and iron. Her studies reveal that HO-1 is not only

strongly induced by oxidant stress but also protects against oxidant-induced lung injury. Importantly, HO-1 can modulate oxidant-induced apoptosis through the MAPK signaling pathway. A reaction product of HO-1 catalysis, carbon monoxide (CO), appears to have significant anti-apoptotic properties as well. Her lab maintains active collaborations within the Pulmonary section; with Dr. Elias she is investigating the role of apoptosis and MAPK in IL-13 transgenic mice and the role of HO-1 in VEGF transgenic mice and with Dr. Paul Noble she is investigating the role of toll-like receptors in hyperoxic lung injury. In addition, Dr. Lee collaborates with investigators from the Vascular Biology and Transplant group at the Boyer Center, the Vascular Biology Center at London University, Ontario, Canada, and Pulmonary investigators at Cambridge University. These studies have been and are supported by NIH (RO1) and American Lung Association funding.

Rick Enelow, MD. Dr. Enelow, the Section Chief at VA-CT, maintains an NIH funded research program investigating the immunopathologic mechanisms of lung injury associated with respiratory virus infection (influenza and respiratory syncytial virus), and CD8+ T cell responses to infectious and non-infectious antigens in the lung. He was recently named a permanent member of the NIH Lung Cellular, Molecular, and Immunobiology study section, and has been an ad hoc member of the Experimental Virology study section, as well as numerous Special Emphasis Panels.

Tao Zhang, MD. Dr. Zheng has focused her energies on the mechanisms of Th2 cytokine-induced tissue alterations and Th1 cytokine-induced tissue remodeling. She has made impressive insights as regards the role of IL-13 receptor alpha 2 in the regulation of IL-13 tissue responses and the important role that IL-11 plays in the pathogenesis of IL-13-induced tissue alterations. She has also generated inducible IL-13 overexpressing transgenic mice that reproduce many of the features of the Dutch Hypothesis of emphysema pathogenesis and defined a novel gamma interferon-induced apoptosis pathway that plays a critical role in the pathogenesis of pulmonary emphysema. These studies are supported by NIH funding.

Zhou Zhu, MD, PhD. Dr. Zhu is an accomplished scientist who has contributed impressively to our understanding of the effector pathways that IL-13, the major effector cytokine at sites of Th2 inflammation, uses to induce tissue and physiologic alterations. He has done this, in part by generating IL-13 overexpressing transgenic mice and by defining the roles that chemokines play in the pathogenesis of the IL-13 phenotype in these animals. He has also used these animals for genetic mining and appreciated the essential role of chitinases in the pathogenesis of IL-13 tissue responses. Most recently, Dr. Zhu's studies have focused on the role of phosphatases in the regulation of Th2 inflammation. These studies are supported by NIH and

American Lung Association funding.

Chun Geun Lee, MD, PhD. Dr. Lee is an accomplished molecular biologist who has focused his energies on the inflammatory and remodeling responses in the lung. His early studies demonstrated that IL-13-induced Th2 inflammation generates tissue fibrosis via inducing and activating TGF- β_1 (a known mediator of fibrosis). He subsequently developed the constructs that are needed to allow bioactive TGF- β to be expressed in the lung and demonstrated that that TGF- β_1 induces tissue fibrosis via an Egr-1-mediated apoptosis pathway. Most recently, he generated mice in which vascular endothelial growth factor was overexpressed in the lung and defined the impressive asthma-like phenotype that develops in the lungs of these animals. These studies are supported by NIH and industry funding.

Carrie Redlich, M.D., M.P.H. Dr. Redlich is an accomplished clinical investigator whose research is focused on the pathogenesis and prevention of isocyanate asthma, the most common cause of occupational asthma. She leads a large multidisciplinary team of laboratory, epidemiological and clinical investigators, including Adam Wisniewski PhD (Pulmonary), Kim Bottomly PhD (Immunobiology), Mark Cullen MD (Occupational Medicine), Christine Herrick MD (Dermatology), and Robert Homer MD, PhD (pathology), Youcheng Liu (Occupational Medicine), and Meredith Stowe PhD (Occupational Medicine). These multidisciplinary studies, which include a longitudinal epidemiologic study of isocyanate-exposed workers, laboratory-based studies (see Adam Wisniewski Ph.D), an intervention study to reduce workplace exposures, and a murine model of isocyanate asthma, have made substantial progress in understanding the pathogenesis of this important occupational lung disease and developing greatly needed diagnostic laboratory assays and preventive strategies. Recent findings have provided new insights into the exposures that cause isocyanate asthma, the biologically relevant antigens, and the specific human immune responses to exposure. Dr. Redlich's other research interests focus the adverse effects related to indoor air problems. These research efforts are funded by grants from the NIH-NHLBI, NIH-NIEHS, and CDC-NIOSH:

Adam Wisniewski, Ph.D. Dr. Wisniewski's research focuses on two areas, (a) the pathogenesis of occupational asthma and the immunobiology of (b) γ/δ T-cells. Studies on occupational asthma focus on isocyanates, the leading chemical cause of occupational asthma world-wide. His laboratory investigations involve in vitro and clinical studies aimed at understanding the key immunologic and molecular differences between the normal and asthmatic response to exposure. Ultimately his studies may lead to the development of immunotherapeutics, the identification of risk factors for disease, and much needed diagnostic assays for sensitivity. From these studies has grown an interest in

γ/δ T cells, an unusual T-cell subset enriched in mucosal tissue, which appear to specifically respond to isocyanates as well as unknown signals from the normal host epithelium. Molecular characterization and recombinant expression of the antigen receptors from these cells is being pursued to better understand the stimuli that activate these cells as well as their role in health and disease.

Mark Siegel, MD. Dr. Mark Siegel, the director of the Y-NHH MICU, is involved in multiple clinical research studies. For several years he has participated in multicenter clinical research trials investigating new treatments for sepsis and acute respiratory distress syndrome (ARDS), in addition to other facets of critical illness. He participated in all phases of the development of Drotrecogin alpha (activated), now marketed as Xigris, which has been shown to significantly decrease mortality among patients with severe sepsis. Dr. Siegel has several ongoing research projects conducted with Yale House staff, in areas such as end-of-life care and decision making, weaning from mechanical ventilation, detection of pain in the ICU, and the use of CT scanning to predict complications from pulmonary emboli. A major project in development is the development of a Translational Research Program, to be conducted in collaboration with bench scientists in the Section, to better understand the mechanisms that underlie sepsis and ARDS. These studies are supported by industrial funding.

H. Klar Yaggi, MD, MPH. As a Sleep Medicine specialist, Dr. H. Klar Yaggi's research focuses on the clinical epidemiology of sleep-disordered breathing and its relationship to cardiovascular disease, stroke, and cardiovascular disease risk factors. His multidisciplinary research team includes general internists, neurologists, and health services researchers. The team has recently completed an observational cohort study of patients recruited through the Yale Center of Sleep Medicine which demonstrated that obstructive sleep apnea significantly increases the risk for the composite outcome of transient ischemic attack, stroke, and death independent of traditional cardiovascular risk factors. In addition, using the Massachusetts Male Aging Cohort, they are investigating the impact of "sleep debt" on the development of overt clinical diabetes. This ongoing work entails constructing a prognostic system to identify patients suspected of sleep-disordered breathing with incrementally increased risk for cardiovascular complications. As a result of these studies, Dr. Yaggi plans to explore the impact treatment of sleep disordered breathing on the primary and secondary prevention of cardiovascular disease and stroke.

Margaret Pisani, MD. Dr. Pisani's research focuses on outcomes in older intensive care unit patients. Specifically, she has looked at the prevalence of pre-existing cognitive impairment of patients admitted to the MICU and physician recognition of the impairment. Currently she is looking at risk factors for poor outcomes from ICU care in older

patients. Her work is focusing on baseline risk factors as well as modifiable ones such as medication use. Her studies are funded by the Yale Pepper Center on Aging, American Lung Association, The Chest Foundation and Merck/American Federation on Aging Research. She is the recipient of a T. Franklin Williams Aging Scholars Award.

Lynn Tanoue, MD. Recently the PCCM Section received a grant from Y-NHH and Yale University School of Medicine for a new program in lung cancer. Dr. Lynn Tanoue, is the PCCM Section Director of this Program, which will feature innovative clinical research in conjunction with the Clinical Oncology Section, the Department of Surgery and the Yale Cancer Center. Dr. Tanoue is also the PI of an industry-sponsored grant looking at the effects of TNF-based interventions (Infliximab) on the natural history of sarcoidosis.

John McArdle, MD. Dr. McArdle is the Co-Investigator of the industry sponsored study evaluating the effects of Infliximab in Sarcoidosis.

The Yale University Asthma and COPD Working Group
The leadership of the PCCM Section are committed to the belief that the most impressive rates of research progress will be seen when we integrate the efforts of clinicians, translationally-focused investigators and basic scientists. In keeping with this belief, the Section of PCCM served, in 1992, as the center for the formation of the interdisciplinary Yale University Asthma and COPD Working Group. This group contains 75 members from many different departments at Yale including Pathology, Immunobiology, Comparative Medicine, Pediatrics, the Howard Hughes, other sections from Internal Medicine, Genetics and Cell Biology. It meets on a monthly basis where it holds scientific, research in progress and clinical presentations designed to foster asthma and COPD research on the Yale Campus. During its existence it has been a hotbed for collaborations and interactions that have led to NIH funding. Early interactions led to the receipt of a NIH Specialized Center in Research Award from the NHLBI. It also led to the present Program Project Grant entitled "Initiation and Effector Mechanisms in Th2 Inflammation" which is funded by the National Heart, Lung, and Blood Institute, Principal Investigators of Projects and Cores on the Program Project Grant include Jack A. Elias, MD (PCCM), Kim Bottomly, PhD (Immunobiology), Richard A. Flavell, PhD (Immunobiology and Howard Hughes), Anuradha Ray, PhD (Medicine) Lauren Cohn MD (PCCM) and Robert Homer MD, PhD (Pathology). Numerous other awards have also been derived from these interactions including multiple RO1s and Sandler Family Foundation Asthma Awards.

FELLOW TRAINING

The PCCM Fellowship Program continues to enjoy an outstanding national and international reputation for quality

and continues as one of the top PCCM training programs in the nation. Under the Directorship of Geoffrey Chupp, our program has expanded to 5 fellows, bringing the total to 18. Graduates of our Program are highly sought after having recently assumed faculty positions at the McGill University, the University of Rochester, the University of Vermont, the University of Maryland and Georgetown University. Under the sponsorship of the Section's T32 NIH sponsored training grant, present day fellows are receiving advanced training in molecular biology, cell biology, statistics, study design and clinical research. Two fellows are in the Department's PhD in Investigative Medicine Program, and 2 are getting MPH degrees at the School of Public Health.

STUDENT EDUCATION

Yale Medical students in years 03 and 04, as well as medical students from various medical schools in the United States and other countries, routinely rotate on the PCCM section consult service at Y-NHH and the West Haven VA Hospital. A structured education program is provided, including instruction in the interpretation of chest radiographs and chest CT scans, interpretation of pulmonary function tests, differential diagnosis for respiratory problems and airway anatomy at bronchoscopy.

Training in sleep medicine is also provided. These trainees rotate through the Yale Sleep Disorders Center where they learn fundamentals of neurobiology and sleep structure, the classification and recognition of sleep disorders and the physiologic control of ventilation in wakefulness and sleep. During their rotations they become familiar with and observe the performance of full nocturnal polysomnography with emphasis on sleep stages and cardiorespiratory monitoring. They also rotate through the Sleep Clinic where they learn a sleep disorder-focused physical examination, a full wake-sleep history, and initiate treatments for sleep-related breathing disorders.

CONFERENCES AND COURSES

The Yale PCCM Section schedule contains several conferences that educate students, residents, fellows and faculty. The CT State Chest Conference, which was started in 1975, is held on Wednesdays from 2:30 to 5 pm in the Fitkin Amphitheater. It includes Yale faculty and fellows, and faculty and fellows from throughout the State. This conference features a one-hour didactic lecture followed by case presentations. Didactic lectures are given by Yale faculty and visiting professors from throughout the United States, Canada, and Europe. Starting on July 1 each year, a structured curriculum is followed during the Summer Lecture Series at the CT State Conference. This curriculum is designed to expose the new fellows and rotating residents to key basic topics in PCCM. The case presentation portion of the State Chest Conference provides a special opportunity for Yale PCCM fellows to present interesting and

challenging cases in a public forum. Moreover, community physicians throughout the State bring interesting cases to the State Chest Conference for discussion. The Tumor Board Conference is held on Thursday afternoons from 4-5 pm in the Greenspan Conference Room in Diagnostic Radiology. The Friday at noon, Lung Biology Conference is held on the fourth floor of The Anlyan Center (TAC) where it focuses on clinical and bench research advances, and provides a forum for research in progress presentations and a fellows' journal club.

The Respiratory Pathophysiology Module is an important component of the Second Year Medical Student "Mechanisms of Disease" Course. Under the directorship of Dr. Carolyn Rochester, this module has been very popular and has received excellent student reviews. Dr. Rochester also directs the Respiratory Physiology and Pathophysiology Module for the Physician Associate Program.

EDUCATIONAL AWARDS

The Section is very excited by its educational mission. This is reflected in the teaching awards that PCCM faculty have been given. Dr. Mark Siegel received the Faculty Teaching Award from the Medical House Staff in 1999. Dr Lynn Tanoue is a member of the Dean's Society of Distinguished Teachers and a recipient of the Leah Lowenstein Teaching Award. Lastly, the pulmonary fellows gave their inaugural Faculty Teaching Award to Patty Lee in 2003.

COMMUNITY OUTREACH

The Winchester Chest Clinic TB Community Outreach Program was established in 1997 as a joint effort between Y-NHH and the Hill Health Center. The program is based at the Adult Education Center for the City of New Haven, and offers targeted tuberculosis screening to foreign-born students enrolled in classes in English as a Second Language. Since 1997, over 4,000 students have been tested. Approximately 20% of these students have been found to have latent TB through the screening program, and have been referred to the Winchester Chest Clinic for further evaluation. Through this Program we have been able to offer evaluation and treatment for latent TB to this group of individuals who are at risk for TB, but in general do not have access to medical care. We have also identified several cases of active TB, and in doing so have minimized the inherent public health hazard. In addition, several serious medical issues not related to TB have been identified, with subsequent appropriate medical intervention.

The TB community outreach program has also been extended to outlying areas, including Adult Education centers in Hamden and the East Shore, and has also recently initiated TB screening at the Migrant Children's Program in New Haven. The Outreach Program is directed by Lynn Tanoue, MD, working with the program nurse Mengqing Lai, RN and the Program outreach worker Marta Hilares.

Match Results 2004

The annual NRMP Match results were released on March 18th. Overall, Internal Medicine saw an increase in the number of U.S. medical students matching in categorical residency programs for the first time since 1998. In percentage terms, 54.8% of positions in traditional Internal Medicine programs were filled by U.S. seniors, 63.7% in Primary Care Internal Medicine programs, and 74.0% in Medicine-Pediatrics programs. Family practice continued to show a decline in the number of matched U.S. seniors with a 41.4% US student fill rate.

Each of our Department's programs did very well in the Match. A summary of the demographic information about our new interns is listed below followed by their names and medical schools.

Traditional Internal Medicine Program

- 45 new interns (32 in the categorical program and 12 in the preliminary year program)
- 14 of the 45 are women, 1 is a member of an under-represented minority group. Of the 32 categorical interns one is a M.D./PhD and three others have Masters degrees.

Primary Care Internal Medicine Program

- 28 new interns (14 in the categorical program and 14 in the preliminary year program)
- 12 of the 28 are women, 6 are members of an under-represented minority group. Of the 14 categorical interns, 4 have a Masters degree in Public Health.

Combined Medicine/Pediatrics Program

- 4 new interns
- 3 of the 4 are women, 1 is a member of an under-represented minority group

Yale Traditional Internal Medicine Residency 2004-2005 Match Results

James Alberti	State University of New York at Syracuse College of Medicine
James Bartscher*	Cornell University Medical College
Robert Bercovitch	Brown Medical School
Devina Bhasin	Emory University School of Medicine
Leonard Calo	University of Rochester School of Medicine & Dentistry
Annie Chandrankunnel*	Finch University of Health Sciences/Chicago Medical School
Tommy Chau	New York Medical College
Severine Chavel*	Yale University School of Medicine
Keith Choate*	Yale University School of Medicine
Oscar Colegio*	Yale University School of Medicine
Michael Greenspan	Yale University School of Medicine
Isaac Hall	University of New Mexico School of Medicine
James Hansen	University of Illinois College of Medicine
Joseph Harburger	Yale University School of Medicine
Scott Heysell	Oregon Health Sciences University School of Medicine

Kenar Jhaveri	State University of New York at Syracuse College of Medicine
Sammy Kang*	University of Maryland School of Medicine
George Kihiczak*	University of Medicine & Dentistry of New Jersey/RW Johnson Medical School
Johnny Kim	University of Medicine & Dentistry of New Jersey/RW Johnson Medical School
Stuart Klein	State University of New York at Brooklyn College of Medicine
Seth Lessner	New York University School of Medicine
Hung-Kei Li	State University of New York at Brooklyn College of Medicine
Elin Lisska	Yale University School of Medicine
Sam Madoff*	University of Rochester School of Medicine & Dentistry
Rupa Mukherjee	Johns Hopkins University School of Medicine
Albert Nayeri	State University of New York at Syracuse College of Medicine
Jesse Nussbaum	Duke University School of Medicine
Himati Patel	University of Medicine & Dentistry of New Jersey/RW Johnson Medical School
Natalie Pauli	Columbia University College of Physicians & Surgeons
Mai Pho	University of Massachusetts Medical School
Kyriaki Poumpouridis	Albert Einstein College of Medicine/Yeshiva University
Maria Rodriguez	Creighton University School of Medicine
Alex Ryzhikov	Cornell University Medical College
Amit Shah*	Duke University School of Medicine
Danny Sodano	University of Medicine & Dentistry of New Jersey/RW Johnson Medical School
Mukta Srivastava	University of Virginia Medical School
Jonathan Stoehr	University of Wisconsin Medical School
Mohamedtaki Tejani	Dartmouth Medical School
Po Tsai*	Tufts University School of Medicine
Loida Viera	Tulane University School of Medicine
Vivian Vlamakis	Finch University of Health Sciences/Chicago Medical School
Lillian Wang*	Cornell University Medical College
Oliver Wang	Columbia University College of Physicians & Surgeons
Sean Wilson*	Albert Einstein College of Medicine/Yeshiva University

44 New Interns

* Preliminary

Yale Internal Medicine Primary Care Program Match List

Gelareh Abedi*	University of Vermont College of Medicine
Kevin Baran	University of Connecticut School of Medicine
Vernee Belcher	Yale University School of Medicine
Jerry Brewer*	Wayne State University School of Medicine
Gordon Buchanan*	University of Illinois College of Medicine

Carla Casulo	State University of New York at Brooklyn College of Medicine
Karl Dauphinais	University of Miami School of Medicine
Maryann Deak*	Georgetown University School of Medicine
Rina Garcia	Yale University School of Medicine
Karl Haglund*	Yale University School of Medicine
Michael Harma	University of Connecticut School of Medicine
Stephen Holt	Columbia University College of Physicians and Surgeons
Elaine Kung*	Yale University School of Medicine
Reed Levine*	New York University School of Medicine
Lisbeth Lopez*	Stanford University School of Medicine
Yamini Naidu*	State University of New York at Syracuse College of Medicine
Haakon Nygaard*	Creighton University School of Medicine
Michael Phipps*	Medical College of Virginia Commonwealth University
Ali Rahimi	Medical College of Georgia
Robert Rusher	Boston University School of Medicine
Susan Samuel*	Temple University School of Medicine
Salil Shukla*	New York Medical College
Mark Simone	Jefferson Medical College of Thomas Jefferson University
Adam Smith*	West Virginia School of Medicine
Steve Taylor	Duke University School of Medicine
Laura Triano	University of Connecticut School of Medicine
Alexander Truong	Tulane University School of Medicine
Parita Vasa	University of Maryland School of Medicine

28 New Interns

*Preliminary

Yale Medicine/Pediatrics Internal Medicine Residency 2004-2005 Match Results

Lana Lee	University of Illinois at Chicago College of Medicine
Sarah Rowan	University of Oklahoma College of Medicine-Oklahoma City
Kapil Saharia	Duke University School of Medicine
Tania Thomas	Oregon Health Sciences University School of Medicine

4 New Interns

West Haven Clinical Epidemiology Research Center (CERC)

The Clinical Epidemiology Research Center (CERC), created recently with a five-year grant from the Department of Veterans Affairs (VA), is the newest research center on the West Haven campus of the VA Connecticut Healthcare System. The mission of West Haven CERC is to conduct cutting-edge multidisciplinary research, provide comprehensive training in patient-oriented research, and support investigators based at the Center. As a component of the VA Cooperative Studies Program, the CERC—combined with the (existing) Cooperative Studies Program clinical trials unit—provide the West Haven VA campus with a broad capacity to conduct a range of patient-oriented clinical research. Faculty in the Department of Internal Medicine at Yale University School of Medicine, including the Center's Director (John Concato, M.D., M.S., M.P.H.), Associate Director (Catherine Viscoli, Ph.D.), and investigators (Joseph Agostini, M.D., Dawn Bravata, M.D., Liana Fraenkel, M.D., M.P.H., Terri Fried, M.D., Barbara Gulanski, M.D., M.P.H., Richard Marottoli, M.D., M.P.H., and Lisa Walke, M.D.), account for the majority of CERC activities.

The Medical Service at the West Haven VA campus, led currently by Dr. Gary Desir, Acting Chief, has a tradition of excellence in clinical care, medical education, and laboratory-based research. Although the history of patient-oriented research can be traced back to the 1960s (when the late Dr. Alvan Feinstein directed the VA Eastern Research Support Center), much has evolved over the past ten to fifteen years. The current era of patient-based research at West Haven can be attributed to the creation of the VA Health Services Research and Development (HSR&D) Service, including an opportunity to compete for faculty career development awards, beginning in the early 1990s. (The National Institutes of Health (NIH) would

follow, several years later, in establishing K23 and K24 career development awards for patient-oriented researchers.) During the last decade, the West Haven VA campus has utilized this opportunity on a frequent and consistent basis. Several faculty in Internal Medicine receive (or have received) support via the HSR&D Career Development Award mechanism, including Drs. Dawn Bravata, John Concato, Liana Fraenkel, Terri Fried, Richard Marottoli, and M. Carrington Reid (who was subsequently recruited to direct geriatric research at Cornell). The faculty concurrently obtained VA Merit Review awards, the VA's "R01 equivalent" funding mechanism for investigator-initiated research. Organized from 1998 to 2003 as the West Haven VA Clinical Epidemiology Unit (also directed by Dr. Concato), these and other West Haven based investigators conducting patient-oriented research have also competed successfully for NIH and private (e.g., Donaghue Medical Research Foundation) awards.

The West Haven CERC was created in response to a request-for-applications to broaden the capacity of VA research. The Center has three specific aims:

- To serve as a center-of-excellence for epidemiological research within the Veterans Health Administration—by conducting high quality studies that are relevant to the health and health care of veterans, and by maintaining a rapid response capability to investigate issues and problems as they arise.
- To conduct methodological projects that improves the standards of research design and data analysis in patient-oriented research.
- To create an educational environment in support of collaborative epidemiological research, including training in methods of research design, biostatistics, and data processing.



A distinctive aspect of the Center is the extensive integration of clinical and statistical personnel and resources. The CERC was formed with seven M.D. or Ph.D. investigators (and has since added two new faculty recruits), five Center staff, and an array of project team members. The CERC's core support was leveraged to an overall budget of more than \$2 million in fiscal year 2003.

The objective of producing pertinent epidemiological research is addressed by coordinating a talented cadre of physician investigators, epidemiologists, statisticians, and other personnel to develop and conduct corresponding projects. The CERC is intended to be far reaching in terms of its benefits to investigators at West Haven and beyond, including VA and non-VA institutions, and ranging across categories of specialty and subspecialty training. In this context, Carolyn Wells, M.P.H., provides core methodological support, and Nancy Cummings, R.N., oversees CERC activities as the Center Administrator. Dr. Mihaela Aslan from Internal Medicine, along with Drs. Haiqun Lin and Robert Makuch from the Yale Department of Epidemiology and Public Health, provide part-time biostatistical support. From the Department of Psychiatry, Drs. Mayur Desai and Douglas Leslie are CERC-affiliated investigators; and Drs. Robert Rosenheck and Michael Sernyak are part of the senior leadership of the Center. Among numerous examples of CERC-related research initiatives, Drs. Lawrence Brass and Albert Lo from the Yale Department of Neurology have ongoing or pending projects with the Center.

The main theme of the Center involves a broad effort to improve diagnosis, prognosis, and therapy for common, chronic conditions affecting veterans, including both physical and mental health. The CERC's portfolio of projects currently includes studies of cancer, stroke, lupus, osteoporosis, geriatric syndromes, and pharmaco-epidemiology. The focus of these investigations involves determining the effectiveness of screening tests, evaluating prognosis, assessing outcomes of therapy, measuring quality of care, assessing patient preferences for the site of care, and exploring patient decision-making regarding treatment options. The clinical topics themselves are diverse (representing the training and interests of each principal investigator), but the projects are linked by clinical relevance and methodological rigor in the pursuit of research to improve the health of, and health care for, veterans. Each CERC-affiliated investigator maintains his or her identity within an academic section and clinical service (at Yale and the West Haven VA campus); the Center serves to provide opportunities for shared ideas and resources. A representative sample of publications by CERC investigators in Internal Medicine is cited at the end of this article.

The CERC also provides a rapid response capability that can respond to medical and mental health issues arising

in the Veterans Health Administration. For example, the Center was asked recently to design and conduct a new study evaluating a possible association of anxiety (and other symptoms) with acetylcholinesterase (and other enzyme) levels among veterans of the Persian Gulf War. The study combines questionnaire data on physical signs and symptoms collected previously from Persian Gulf veterans living in Iowa, with results from laboratory assays done on stored serum samples for these veterans. This initiative evolved more than ten years after the Persian Gulf War ended in 1991, with veterans continuing to report various health problems, and new theories proposed regarding acetylcholinesterase having a possible pathophysiological role in this context. The project, directed by Dr. Catherine Viscoli, also illustrates the CERC's ability to conduct investigations that include aspects of both patient-oriented and laboratory-oriented research.

The objective of conducting methodological (patient-oriented) research includes a continuation of local efforts to examine the strengths and limitations of observational research design and statistical analyses. The pertinence of this work includes both internal and external components. From an internal perspective, methodological advances serve to refine the basic science of patient-oriented research, in disciplines such as epidemiology and statistics. From an external perspective, understanding patient-oriented research is an increasingly relevant and important skill. For example, Dr. Concato recently presented a talk on "Overview of Research Design" to more than 50 federal and state court judges at a Science for Judges symposium (held at Brooklyn Law School), sponsored by the National Academy of Sciences, the Federal Judicial Center, and the National Center for State Courts. The judges preside over "toxic tort" cases, and are often put in a position of having to evaluate the quality of epidemiological evidence, presented in an adversarial setting.

The objective of promoting a strong educational environment involves further development of ongoing activities that already provide a comprehensive range of training opportunities at West Haven. These options include: for junior faculty—mentoring for Career Development Awards, from all branches of VA research and across all clinical specialties (the CERC currently has three such awards, with one application pending); for fellows—a research-intensive fellowship, via the Office of Academic Affiliations (Sarwat Chaudhry, from General Internal Medicine at Yale, is the current fellow; and John Chang, from Nephrology at Yale, is the incoming fellow for 2004); and for trainees at any level—less formal training options (e.g., a summer course in epidemiology and statistics offered by the Cooperative Studies Program). Other educational options provide "hands on" experience with research using administrative or clinical trial databases, and electronic medical records; and several pilot projects were also approved with the ini-

tial funding of the CERC. Finally, technical assistance and consultation capacity for VA-based investigators is available, within a feasible scope in terms of availability, and on a first-come, first-served basis.

The CERC is affiliated with the Cooperative Studies Program (CSP), a unit directed at West Haven by Dr. Peter Peduzzi, which itself provides a framework for conducting multicenter clinical trials. The CSP allows for the development of proposals by VA-based investigators, supported by an extensive network of biostatisticians, health economists, pharmacists, programmers, administrators, and support staff. In addition to West Haven, Cooperative Studies Program Coordinating Centers are located at Hines (IL), Palo Alto (CA), Perry Point (MD), Boston (MA), and Albuquerque (NM; pharmacy center only). As a network, these coordinating centers oversee approximately 60 multicenter randomized trials at any one time; each conducted usually over a 5-year period. Studies are assigned to one of the coordinating centers, which in turn provides statistical and methodological guidance to VA investigators conducting the clinical trials. The CERC also has links with the Veterans Aging Cohort Study (VACS), directed by Dr. Amy Justice, the new Chief of General Internal Medicine at West Haven. Oversight of all research activities at the West Haven VA campus is coordinated by Dr. Fred Wright, Associate Chief of Staff for Research. Many senior faculty in internal medicine have contributed to the evolution of the CERC, including, but not limited to, Dr. David Coleman (as former Chief of the Medical Service at the VA, and current Interim Chair of Medicine at Yale), Dr. Leo Cooney (as former Chief of General Internal Medicine, and current Chief of Geriatrics at Yale), Dr. Patrick O'Connor (as current Chief of General Internal Medicine at Yale), and Dr. Mary Tinetti (as former Chief of Geriatrics at Yale).

The Clinical Epidemiology Research Center adds a new capability to VA research in general, and to the West Haven VA campus in particular. Along with other centers-of-excellence, the CERC will help to maintain the tradition of West Haven consistently ranking within the top three VA facilities nationwide, in terms of total dollars of research funding. The CERC was also a critical component of a successful initiative to build 20,000 square feet of new space for patient-oriented research, currently under construction (see photo). Thus, in addition to the intellectual resources of the CERC, the West Haven VA campus is also gaining new physical resources. The Department of Medicine at Yale has contributed to, and will benefit from, the establishment of the CERC, both now and in the foreseeable future.

SELECTED CITATIONS BY CERC-AFFILIATED INVESTIGATORS

Agostini JV, Leo-Summers LS, Inouye SK. Cognitive

and other adverse effects of diphenhydramine use in hospitalized older patients. *Archives of Internal Medicine* 2001; 161:2091-2097.

Bravata DM, Kim N, Concato J, Krumholz HM, Brass LM. Thrombolysis for acute stroke in routine clinical practice. *Archives of Internal Medicine* 2002; 162:1994-2001.

Chaudhry SI, Olofinboba KA, Krumholz HM. Detection of errors by attending physicians on a general medicine service. *Journal of General Internal Medicine* 2003; 18:595-600.

Concato J. Challenges in prognostic analysis. *Cancer* 2001; 91:1607-1614.

Concato J, Shah N, Horwitz RI. Randomized, controlled trials, observational studies, and the hierarchy of research designs. *New England Journal of Medicine* 2000; 342:1887-1892.

Fraenkel L, Bodardus S, Wittnik DR. Understanding patient preferences for the treatment of lupus nephritis with adaptive conjoint analysis. *Medical Care* 2001; 39:1203-1216.

Fried TR, Bradley EH, Towle VR, Allore H. Understanding the treatment preferences of seriously ill patients. *New England Journal of Medicine* 2002; 346:1061-1066.

Kalish GM, Barrett-Connor E, Laughlin GA, Gulanski BI. Association of endogenous sex hormones and insulin resistance among postmenopausal women: results from the Postmenopausal Estrogen/Progestin Intervention Trial. *Journal of Clinical Endocrinology & Metabolism* 2003; 88:1646-1652.

Reid MC, Boutros NN, O'Connor PG, Cadariu A, Concato J. The health-related effects of alcohol use in older persons: a systematic review. *Substance Abuse* 2002; 23:149-164.

Richardson ED, Marottoli RA. Visual attention and driving behaviors among community-living older persons. *Journal of Gerontology Series A-Biological Sciences & Medical Sciences* 2003; 58:M832-836.

Viscoli CM, Brass LM, Kernan WN, Sarrel PM, Suissa S, Horwitz RI. A clinical trial of estrogen-replacement therapy after ischemic stroke. *New England Journal of Medicine* 2001; 345:1243-1249.

Walke LM, Gallo WT, Tinetti ME, Fried TR. The burden of symptoms among community-dwelling older persons with advanced chronic disease. *Archives of Internal Medicine* (in press).

Faculty Achievement Awards

The Department has established Faculty Achievement Awards in the areas of Clinical Care, Education, and Research. The Award recipients will be acknowledged at a Departmental Faculty Meeting and in the Department's Electronic Newsletter. Our goal in creating these Awards is to provide a mechanism whereby our Departmental Faculty recognize outstanding achievement by their peers in the three core areas of our Departmental mission.

All full-time faculty within 15 years of their initial appointment as an Assistant Professor will be eligible for the Awards in Clinical Care or Education. All full-time faculty in the first 5 years of their appointment will be eligible for the Award for Research.

Faculty to be considered for one of these three Awards should be nominated by their respective Section Chief. The Nomination should include:

1. A nominating letter from the Section Chief that must include a description of qualitative and quantitative measures of achievement in Clinical Care, Education or Research. For the Award in Clinical Care, a compilation of patient satisfaction and outcome data, and a description of Programmatic achievement would be very useful. For the Award in Education, data on educational innovation, teaching evaluations, or publications in the field of Education would be helpful. A description of the impact of publications, significance of the work, and promise of the investigator would be used to assess candidates for the Research Award. The nominating letter should be limited to two pages.
2. CV in Yale Format.
3. Description of Activities in Yale Format.

The Nominating Letter, CV, and Description of Activities should be submitted to the Department of Medicine, Attention: Rosemary Slattery by May 1, 2004.

David L. Coleman, M.D.
Interim Chair

Medical Grand Rounds

- | | |
|----------------|---|
| April 1, 2004 | “Young Woman, 4 Month Postpartum with Dyspnea”. John Setaro, M.D., Associate Professor of Medicine, Section of Cardiovascular Medicine. |
| | “Patient with AMI and Low Platelets”. Thomas Duffy, M.D, Professor of Medicine and Director, Program for Humanities in Medicine; |
| April 8, 2004 | “The Brain – Heart Interaction; The Impact of Stress in Coronary Disease”. Robert Souffer, M.D., Associate Professor of Medicine, Section Chief, Cardiovascular Medicine at VA Connecticut Healthcare System. |
| April 15, 2004 | “T-Cell Immunity to Myeloid Leukemias”. Jeffrey Molldrem, M.D., Associate Professor, University of Texas Medical Center, MD Anderson Cancer Center, Section of Transplant Immunology. |
| April 22, 2004 | “Patient with SLE and New Onset CHF”. John Hughes, M.D. Associate Professor of Medicine, Section of General Medicine, VA Connecticut Healthcare System. |
| April 29, 2004 | “Caring for Patients and Community: Lessons from the Cuban Experience”. Maya Salameh, M.D., Chief Resident, Department of Medicine. |

Grand Rounds begins at 8:30 a.m. in the Fitkin Amphitheatre.

New Faculty

Jason Carlyon recently joined the Section of Rheumatology as an Associate Research Scientist



Dr. Jason Carlyon's research focuses on invasion and intracellular survival strategies of *Anaplasma phagocytophilum*, the etiologic agent of human anaplasmosis, an emerging, potentially deadly tick-transmitted disease in the United States and Europe. *A. phagocytophilum* is the only known pathogen with a specific tropism

for neutrophils, which indicates that it utilizes specific strategies for targeting and surviving within the hostile intracellular environment of its host cell. Dr. Carlyon is specifically interested in defining the bacterial molecules involved in cellular adhesion. Such molecules would be likely candidates for vaccine targets. A second focus of Dr. Carlyon's work is dissecting the mechanisms by which *A. phagocytophilum* subverts neutrophil superoxide production, which may potentially lead to the development of novel anti-inflammatory therapies. Furthermore, studying *A. phagocytophilum*'s interactions with its host will not only lead to a greater understanding of intracellular pathogenesis, but also offers a unique approach to comprehending neutrophil function in the context of human disease.

Rachel Gallagher recently joined the Section of Nephrology as an Associate Research Scientist



Rachel Gallagher, PhD, joined the faculty on July 1, 2003 as an Associate Research Scientist. After obtaining both her Bachelors and Doctorate from the Department of Biochemistry, at University of Wales, Cardiff, in the UK, she subsequently moved to Germany for her postdoctoral training under

the guidance of Professor Ralph Witzgall. It was at the University of Heidelberg where her research interests took her into the field of polycystic kidney disease, which enabled her to establish a successful collaboration with Dr Stefan Somlo, the current chief of Nephrology, here at Yale. Rachel is the recipient of a 2004 Polycystic Kidney Disease Foundation 'grant in aid' award that will enable her to continue to investigate the molecular mechanisms underlying autosomal recessive polycystic kidney disease.

Werner Gurr recently joined the Section of Endocrinology as Research Associate



Dr. Werner Gurr graduated from the Swiss Federal Institute of Technology and was awarded a PhD from the University of Zürich in 1993 for studies on the role of components of the myelin sheath in the development of peripheral neuritis. His interest in autoimmunity then led him to work at the University of Cambridge,

UK, where he demonstrated cross-immunoreactivity between a composite protein of the parasite which causes river blindness and a protein present in the eye. He completed a second Post Doc in the group of Dr Robert Sherwin at Yale in 2001. After undertaking research in Geneva for one year, Werner obtained funding from the Juvenile Diabetes Foundation to continue his research at Yale where he is developing a protein-based therapy to prevent the progression of type 1 diabetes.

Kenric Maynor joins the Section of General Medicine as a Clinical Instructor



After graduating from the University of North Carolina School of Medicine, Dr. Maynor joined the housestaff in the Yale Primary Care Internal Medicine Residency Program. He completed his Chief Residency in June 2003 and continued on as faculty as a clinician educator.

Currently, Dr. Maynor's research interests include the detection of medical errors and the implementation of patient safety practices. Beginning July 2004, Dr. Maynor will begin a two year fellowship as a Robert Wood Johnson Clinical Scholar at Johns Hopkins Medical Center.

Kudos

DAWN BRAVATA, M.D., Assistant Professor of Medicine, Section of General Medicine, has been selected for the RWJ Generalist Faculty Scholars Program. This prestigious award is exceedingly well deserved. “Her application was one of the most well written career development award documents that I have ever seen”, said Dr. Patrick O’Connor. “Obviously the high quality of her proposal came through in her interviews”. Bravo to Dr. Bravata!

Special Lectures

April 1, 2004

Program for Humanities in Medicine

Liza Cariaga-Lo, Ed.D., Assistant Dean and Director of the Office for Diversity and Equal Opportunity at the Graduate School and Assistant Clinical Professor at the Child Study Center at Yale School of Medicine will present the 2004 Multicultural Lecture entitled: **ESTABLISHING A COLLECTIVE IDENTITY: ASIAN-AMERICANS AND THEIR LEGACY TO AMERICAN MEDICINE**

5:00 p.m., Beaumont Room, SHM

April 19, 2004

Biomedical Research Seminar

REGULATING INFLAMMATION IN ASTHMA: TRUE TAILS OF MICE WITH AIRWAY INFLAMMATION

Lauren Cohn, M.D.

12 Noon, Fitkin Amphitheatre

April 23, 2004

A Symposium in Honor of Stephen E. Malawista, M.D., Professor of Medicine, Section of Rheumatology
NEUTROPHILS AND INFLAMMATION

Registration deadline: April 16, 2004

For further details contact MaryAnn Livieri at 785-7063

April 26, 2004

Faculty Development Seminar

ETHICS OF CLINICAL INVESTIGATION

Robert Levine, M.D.

12 Noon, Fitkin Amphitheatre

THE DEPARTMENT OF INTERNAL MEDICINE

Yale University School of Medicine

<http://info.med.yale.edu/intmed/newsletter/>

Editor: Lynn Gambardella

Assistant Editor: Steven Wormsley, Ph.D.

Designed by: Sarah Walls

For questions, comments, and submissions,
Please contact:

Lynn Gambardella

Chairman's Office

LMP-1072

(203) 737-4249 Tel. (203) 785-6954 Fax