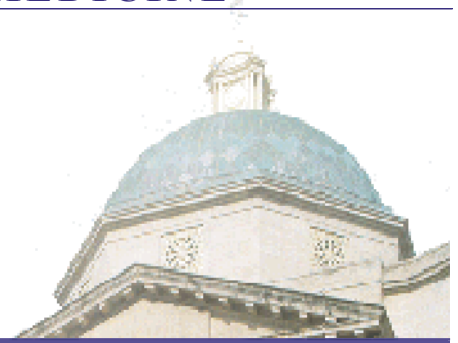


THE DEPARTMENT OF
**INTERNAL
MEDICINE**



Newsletter of the Department of Internal Medicine

Volume 1 • Number 14

Yale Occupational and Environmental Medicine Program

In May, the Yale Occupational and Environmental Medicine Program will celebrate its 25th anniversary as an organized unit in the Department of Internal Medicine at Yale. Promoted by then chairman Sam Thier as part of his broad vision for the nascent academic section in General Internal Medicine, the Program has flourished. Originally a niche unit comprised of a single junior faculty member, two eager trainees and small support staff, it is now a dynamic division, with 10 full-time faculty, a dedicated specialty clinic and referral service, a federally funded fellowship training program and a diverse and well funded research portfolio spanning the gamut from epidemiologic to clinical, translational and bench research. Housed except for laboratories at 135 College, YOEMP has emerged as one of the best established and largest among the 30 or so comparable units at academic medical centers in the US.

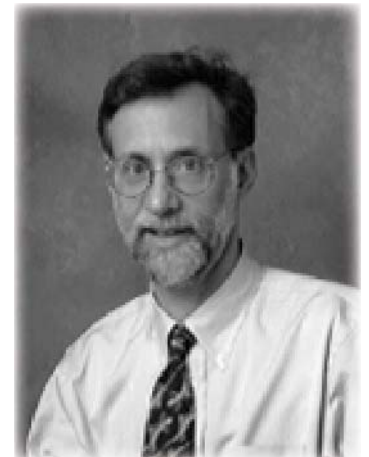
Clinic Services

Yale Occupational and Environmental Medicine is a regional referral center for the early diagnosis, treatment, and prevention of diseases due to chemical, biological, and physical hazards in the workplace and environment. Common diagnoses seen in our diagnostic clinic include asbestos-related lung disease, occupational asthma, noise-induced hearing loss, contact dermatitis, and toxicity due to exposures to metals, solvents, pesticides, and carbon monoxide. Clinical staff performs specialized testing for conditions such as Chronic Beryllium Disease, hypersensitivity pneumonitis, and occupational ototoxicity. Other specialized services include site investigations by our Certified Industrial Hygienist, investigation of outbreaks of occupational illness, and hospital consultations for acute exposure-related conditions. We

also provide contract services to worker populations including firefighters, police departments, and factory workers. The clinical site serves as a training resource for Yale medical students, Internal Medicine Residents (approximately 20 per year) and the Fellows in the Occupational and Environmental Medicine Program.

Training Program

The Yale Occupational and Environmental Medicine Fellowship Training program is an ACGME accredited program now entering its 21st year. The primary goal of the program is to train physicians interested in pursuing academic careers by fostering comprehensive development of clinical education and scientific investigation skills. The training program offers an integrated 2-year academic and practicum program (including a Master of Public Health degree) with an optional third year for additional research experience. Because of the unique nature of the institution and the philosophy of integration of clinical and public health aspects of the field, trainees are usually recruited after completing a residency in a primary care specialty. The program admits two new fellows annually, with full support provided through a combination of the NIOSH training grant and other departmental funds. Approximately half of our graduates have gone on to full-time academic jobs; the remainder are in clinical practice or



Mark Cullen, M.D.
Program Director

working in the corporate setting, often teaching on a part-time basis. To date Yale's program has been quite successful in producing faculty able to expand training opportunities and research experience nationwide.

Research on Isocyanate Asthma / Exposures

A major research focus of the YOEMP is the pathogenesis and prevention of isocyanate asthma, the most common cause of occupational asthma. Dr. Carrie A. Redlich leads a large multidisciplinary team of laboratory, epidemiological and clinical investigators investigating isocyanate exposures and asthma, including Meredith Stowe PhD, Adam Wisnewski PhD, Yucheng Liu PhD, Mark Cullen MD, Kim Bottomly PhD (Immunobiology), Christine Herrick MD (Dermatology), Susan Woskie PhD (Industrial Hygiene UMass), Ellen Eisen ScD (Biostatistics UMass), and Dimitri Bello PhD (Industrial Hygiene UMass). These multidisciplinary studies include a longitudinal epidemiologic study of isocyanate-exposed workers, laboratory-based studies, an intervention study to reduce workplace skin and respiratory exposures, and a murine model of isocyanate asthma. We have also developed an isocyanate exposure chamber to perform specific inhalation challenge testing for diagnostic and research purposes.

Recent findings from these studies have provided new insights into assessing respiratory and skin isocyanate exposures in the workplace, characterizing biologically relevant isocyanate antigens, and defining human immune responses to exposure, including isocyanate-induced γ/δ T cells and mixed Th1/Th2 responses. These studies have advanced our understanding of the pathogenesis of isocyanate asthma and may lead to improved diagnostic laboratory assays and preventive strategies. 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.

The Yale-Alcoa Partnership

In 1996 the CEO of the world's largest aluminum company approached the Program Director to forge an historic research/service partnership with Yale in order to further advance a ten year campaign to eradicate injuries and develop a comparable plan to control health. In addition to assuming the responsibilities

of running the corporate medical department for an organization of 140,000 employees world-wide, and extraordinary panoply of research opportunities were opened, centered around the availability of personnel, exposure, injury and health claims data on the entire population and its dependents. Currently Drs. Cullen, Taiwo and Rabinowitz, a research staff of 7, fellows and graduate students are studying many fundamental questions in occupational health studies, ranging from esoteric questions about dose-response relations for certain occupational diseases, to establishing a more fundamental understanding of the causes of chronic disease and injury in a large industrial workforce.

In addition to Alcoa's core contribution, funding for the research has come from the MacArthur Foundation and NIOSH. Among the highlights ongoing are the following research projects:

- Work culture as an underlying cause of ASCVD, COPD, asthma and depression in the population
- Physical and psychologic demands of specific jobs as risks for chronic disease, injury and absenteeism
- Extended work hours (overtime) as a risk factor for workplace injury
- Time on the job as the underlying causal factor in workplace injury
- Dose-response of fluoride induced asthma
- Solvents as co-factors in the cause of noise-induced hearing loss
- Weight gain as the mediator of health effects associated with non-traditional work shifts

Other Research Activities

Dr. Peter Rabinowitz has been focusing research on the effects of noise as an occupational and environmental hazard. Dr. Rabinowitz's team recently published a study of the natural history of hearing loss in a large industrial working population, using the Alcoa database. He is the principal investigator of a NIOSH funded study of industrial workers exposed to noise and organic solvents, determining whether solvents increase the risk of occupational hearing loss. He is also investigating host risk factors for hearing loss susceptibility, and has published data linking a polymorphism of the glutathione S-transferase M1 gene to increased hearing loss in a group of noise-exposed workers. He is

currently working with the US Navy on a randomized, controlled trial of N Acetyl cysteine for the prevention of noise-induced hearing loss in military recruits.

In his role as director of Clinical Services at Yale Occupational and Environmental Medicine, Dr. Rabinowitz directs the investigations of unusual clusters of occupational illness, and has recently been involved with a contact investigation for tuberculosis exposure in a workplace and an outbreak of diarrheal illness among workers in an enteric pathogen research laboratory.

In addition, Dr. Rabinowitz is directing a National

Library of Medicine project to create a database of scientific studies of animals as “sentinels” of human environmental health hazards. The project will create a web-based, curated database of such studies, which will be available for the general scientific community later this fall. Collaborators in this effort include Dr. Prakash Nadkarni and Daniel Chudnov of the Yale Center for Medical Informatics.

Dr. Ben Hur Mobo, full time at the West Haven Veterans Administration Medical Center, has developed several lines of investigation using the Agent Orange Registry and newly computerized health system database.

Occupational and Environmental Medicine Program Faculty and Staff

Faculty

Brenda Cartmel, PhD
Associate Research Scientist
Primary Appointment: EPH

Peter Rabinowitz, MD, MPH
Assistant Professor of Medicine
Director, Clinic Services

Judy Sparer, CIH, MSCE
Industrial Hygienist,
Lecturer in Medicine

Mark R Cullen, MD
Professor of Medicine
Director, Occupational
And Environmental Medicine
Program

Carrie A. Redlich, MD, MPH
Associate Professor of Medicine
Associate Director, Occupational
and Environmental Medicine Program

Oyebode Taiwo, MD, MPH
Assistant Professor of Medicine
Director, Fellowship Training

Youcheng Liu, ScD
Assistant Professor of Medicine

Mark Russi, MD, MPH
Associate Professor of Medicine

Adam Wisnewski, PhD
Assistant Professor of Medicine

Ben Hur Mobo, Jr., MD, MPH
Clinical Assistant Professor
Veterans Administration Medical Center

Meredith Stowe, PhD
Associate Research Scientist

Research Staff

Linda Cantley
Liang Chen
Martha Fiellin
Qing Liu

Jian Liu
Martin Slade
Sally Vegso

Support Staff

Chris Daly
Claire Lutgendorf
Elizabeth Malarney
Frank Nusdeu

Linda Oliva
Brynn Taylor
Sylvia Ullman

Federal Grant Activity

Principal Investigator	Title	Grant Period	Annual Funding Total
Mark Cullen	“Longitudinal Study of Isocyanate Asthma in Body Shops”	9/01/02-8/31/07	\$366,267
	“Carotene and Retinol Efficacy Trial”	6/1/99-5/31/04	\$161,385
Youcheng Liu	“Isocyanate Exposure Intervention Study in Body Shops”	9/30/01-9/29/05	\$420,427
	“Efficacy Study of Skin Protection”	10/1/03-9/30/04	\$76,827
Peter Rabinowitz	“Noise, Solvents and Hearing Loss”	8/30/02-9/29/05	\$225,000
	“Genetic Susceptibility to Noise-induced Hearing Loss”	12/1/03-11/30/06	\$250,000
	“Animals as Sentinals of Human Environmental Hazards”	5/15/03-5/14/06	\$150,000
Carrie A. Redlich	“Health and Socioeconomic Consequences of NSBRI”	4/01/01-3/31/04	\$125,000
	“Program for Patient-Oriented Environment Health Research Training”	7/1/00-6/30/05	\$105,958
Adam Wisnewski	“Isocyanate Antigens and T-cells that Cause Asthma”	1/1/99-4/30/06	\$150,000
	“Human Lung Gamma/Delta T Cells, Antigens and Functions”	9/30/01-7/31/05	\$200,000

The Department of Internal Medicine and AIDS in South Africa

*Gerald Friedland, MD, Director, Yale AIDS Program
Professor of Medicine and Epidemiology & Public Health*

The most severe impact of HIV infection and AIDS in the world is in Sub-Saharan Africa. In South Africa alone, over 5.4 million persons, or one in four adults, are currently thought to be living with HIV/AIDS. This number is higher than in any other country in the world and is expected to double over the next decade. The province of KwaZulu Natal has the highest HIV seroprevalence and seroincidence rates in South Africa, with 36% of antenatal clinic attendees found to be HIV positive in the year 2000 and an annual incidence rate of 20%.

Although Highly Active Antiretroviral Therapy (HAART) has dramatically altered and improved the natural history of HIV disease in the individuals for whom it has been available in the developed world, these therapies remain largely unavailable in Africa and most of the world. This unacceptable disparity in access is the result of the high cost of drugs, lack of infrastructure and political will in both the developing and developed world

Since 2001, a Yale team led by Gerald Friedland, MD, Director of the Yale AIDS Program, has been working to develop strategies and projects to provide access to antiretroviral therapy in KwaZuluNatal, South Africa. These projects were developed and initiated during a sabbatical in Durban, South Africa at the Nelson R Mandela School of Medicine. They have been moved forward with colleagues in South Africa, and at Yale, including Robert Wood Johnson Clinical Scholars Neel Gandhi, MD and Kim Zeller, MD and Ann Williams, RN, Professor of Nursing and others from the Yale School of Nursing. The projects have received support from Yale President Levin, The Irene Diamond Fund, Doris Duke Charitable Foundation and the National Institutes of Health.

Most efforts have been based upon the close biologic, epidemiologic and clinical relationship between HIV/AIDS and tuberculosis (TB). In areas of high prevalence of both infections, such as Africa, secondary and dramatic epidemics of TB follow in the path of HIV disease. Tuberculosis is the leading cause of morbidity and mortality in people with HIV disease and in KwaZuluNatal up to 2/3 of newly diagnosed cases of TB are coinfecting with HIV. Despite this, as is the case throughout the world, the care and treatment of TB and HIV are carried out in separate medical infrastructures.

The integration of TB and HIV care and treatment is a logical but untested approach to address these issues and provide treatment for both diseases. In South Africa and over 150 other countries, TB treatment is carried out using WHO recommended directly observed treatment programs (TB/DOT) in established TB clinics and in community-based outreach programs. TB medicines are provided in once a day regimens and taken under direct observation. The recent availability of once a day antiretroviral therapy has enabled construction of once daily HIV regimens, which could be administered at the same time as TB drugs and within the same already existing TB treatment infrastructure. To test this strategy as a way of providing access to HIV treatment, the Yale and Nelson R. Mandela teams have developed and implemented projects in both the large City of Durban, and in rural Tugela Ferry in KwaZuluNatal.

A pilot project in the Prince Cyril Zulu Communicable Diseases Clinic (Durban Municipal TB clinic) has been completed. Although preliminary and designed as a feasibility study, the results clearly demonstrate that; *a*) it is indeed feasible to introduce HAART into an existing TB/DOT program in an urban clinic without disrupting or compromising clinic routines and practice, *b*) a once daily HAART regimen of efavirenz, 3TC and ddI administered concomitantly with a standard rifampicin based TB treatment regimen during TB/DOT 5 days per week and self administered on weekends is effective and well tolerated, *c*) adherence with self-medication of HAART over weekends is excellent, and *d*) a high TB cure rate can be achieved and *e*) the additional cost of the strategy is largely related to the cost of antiretroviral therapy.

Two additional projects are now underway to extend these observations and more precisely determine the relative risks and benefits of this strategy. A large randomized controlled trial of TB and HIV integrated and concomitant vs traditional sequential TB and HIV therapy is now commencing, supported by the National Institutes of Health. The same procedures and regimens used in the pilot study will be employed. Perhaps more challenging and innovative is expansion of the strategy to rural Tugela Ferry, a traditional Zulu community, where most families remain without electricity and piped water. With superb and inspiring South African colleagues, lead by Dr.

Tony Moll, we have begun this project in co-infected patients, in collaboration with a provincial government hospital (serving 300,000 patients) and a non-government community based HIV support program (Philanjalo) and are using trained community based treatment supporters. Community members and staff have named the project Sizonq'oba ("We shall overcome") Because of the limited infrastructure, expertise and availability of antiretroviral therapy, the project has included training of physicians, nurses and community health care workers, strengthening the TB/DOT program, developing supportive laboratory and back up services and purchasing and providing antiretrovirals.

Patients with active and newly diagnosed TB are offered HIV testing and if positive, the opportunity to receive treatment for both diseases. Under supervision, patients construct and package a month's supply of their own regimens in individual daily packets, together with others in supportive groups, as is typical of African culture. This seemingly simple, yet powerful individual and community process is a particular strength of the project. Patients are seen daily at home by community treatment supporters and monthly at the hospital to monitor efficacy and side effects and toxicity. The early results of this project have been encouraging with excellent adherence and clinical response and minimal toxicity. Observing patients who would otherwise have died, successfully taking pills for both diseases in remote rural huts, will convince even the most skeptical, that HIV treatment is possible in resource poor settings. Additional studies evaluating patients' HIV transmission risk behavior using a confidential interactive computer based interviewing in Zulu, designed for a non-literate population, and studies of the cost effectiveness of the integrated HIV/TB treatment strategy are in progress. The early results from the Durban pilot will be published in the Journal of Acquired Immunodeficiency Syndrome and those from Sizonq'oba in Tugela Ferry, and will be presented at the XV International Conference on AIDS in July, 2004.

This is but one of among many strategies to make HIV treatment available in resource-limited settings. Demonstrating its success, we hope, will convince and motivate international agencies and others to incorporate this strategy into worldwide HIV treatment roll out plans. In the meantime, we are grateful for the opportunity to pursue this work with colleagues in South Africa and attempt to address the enormous tragedy and challenges of the world's worst AIDS epidemic. Developing the projects and participating in their early success has been more gratifying than can be adequately expressed.

We welcome colleagues to join in this project and help carry the work forward.



Patient family compound in Tugela Ferry, KwaZuluNatal, South Africa



The first seven Sizonq'oba patients displaying their monthly medication calendars and packets



Volunteer community based treatment supporters



Dr. Friedland with Yale and South Africa study team and patients

Training on Treating Opioid Addiction

Faculty from the Department of Internal Medicine at Yale University School of Medicine, in conjunction with the American Society of Addiction Medicine, the Connecticut Society of Addiction Medicine and the Connecticut AIDS Education and Training Center will provide a training on the treatment of prescription opioid (e.g. oxycodone, hydrocodone) and heroin dependence on June 12, 2004 at the Omni Hotel in New Haven. This training will allow physicians to take advantage of new federal legislation and recently approved medication and qualify for a special DEA registration to prescribe buprenorphine/naloxone in an office-based, clinic and hospital setting. Faculty from Yale Department of Internal Medicine will include Drs. David Fiellin, Patrick O'Connor, Lynn Sullivan, and Mark Kraus. To register for this course please contact Tammy Baldwin at 888-362-6784 or tbaldwin@xperience-ny.com. For further information please contact David Fiellin, M.D. at david.fiellin@yale.edu.

Kudos



DR. JOSEPH CRAFT, Chief of the Section of Rheumatology and Professor of Medicine and Immunobiology and **DR. AUGUSTE FORTIN IV**, Assistant Clinical Professor of Medicine were selected as the 2004 recipients of the Charles W. Bohmfalk Teaching Prize. The prize committee consisting of faculty and medical students selected Drs. Craft and Fortin from the list of nominees submitted by the department chairmen, directors of medical studies, faculty members and students.



Dr. Craft will receive the prize for his outstanding teaching in the basic sciences. He is credited with revitalizing and revamping the immunology course taught to the medical students. Dr. Fortin will be awarded the prize for his excellent teaching of clinical sciences, emphasizing the importance of skill and compassion in caring for patients. They will both presented their awards at the medical school commencement on May 24.

In April, **DAVID A. FIELLIN, M.D.**, Associate Professor of Medicine, Section of General Internal Medicine, began his service on the White House's Office of National Drug Control Policy's (ONDCP), Drug Control Research, Data, and Evaluation Advisory Committee. The purpose of the committee is to determine the adequacy of existing federal research and data systems to inform the national drug control strategy. The ONDCP is divided into efforts at demand reduction (treatment) and supply reduction (interdiction). Specific topics addressed include implementation of the President's \$100 million voucher system to increase access to treatment services, student drug testing, prescription drug abuse, screening, brief intervention and referral to treatment, the marijuana initiative, international drug trafficking and harm reduction efforts, and ONDCP's media campaign.



DR. ASHWIN BALAGOPAL, Chief Resident in Internal Medicine, was chosen by the Yale School of Medicine Class of 2004 to receive the Betsy Winters House Staff Award for outstanding teaching. The award is named in honor of the former director of the Office of Student Affairs, Betsy Winters. It is awarded annually to the member of the house staff who the graduating class feels has made the most significant contribution to teaching the medical students. As this year's recipient, Dr. Balagopal will be honored at the medical school commencement on May 24.

DR. DEVAN KANSAGARA, PGY 3 resident and future chief resident in the Primary Care Program, is among the four chief residents in Internal Medicine selected by the American Board of Internal Medicine to attend the European Society of Internal Medicine (ESIM) Fall 2004 Conference in Alicante, Spain. This weeklong interactive, multinational retreat on education and training brings together approximately 70 senior residents from Europe, Australia, New Zealand, Israel, Turkey, the United Kingdom and United States. The European Federation of Internal Medicine (EFIM), a partner with the ABIM Foundation and the ACP Foundation in the Medical Professionalism Project sponsors the conference. Dr. Harry Kimball, President Emeritus, ABIM, and Dr. Esther Torres, Professor and Chair, Department of Medicine, University of Puerto Rico School of Medicine will join 20 distinguished international faculty from ESIM's member societies as participants. From nominations submitted by residency programs nationwide, the candidates were judged on their excellence in improving graduate medical education, advancing medical professionalism and quality improvement in residency, and future aspirations and professional goals. Congratulations to Dr. Kansagara on his selection!



DR. JANET HENRICH, Associate Professor of Medicine, is this year's recipient of the Society of General Internal Medicine (SGIM) National Award for Scholarship in Medical Education in the area of "Scholarship of Integration." This prestigious national award recognizes the impact of a body of scholarly work on medical education and clinical practice. The award selection committee felt that Dr. Henrich's work with the federal government to help medical institutions with the development of both educational and training initiatives in women's health education to be of great significance in shaping medical education nationally in the area of women's health. Dr. Henrich's involvement at the national level has included the NIH Office of Research on Women's Health, the Health Resources and

Services Administration, the Office for Women in the U.S. Department of Health and Human Services, and the Council on Graduate Medical. The committee also recognized Dr. Henrich's leadership on a survey on curriculum on women's health education in collaboration with the American Association of Medical Colleges as well as her report to Congress which defined the educational philosophy, scope, and content of a model curriculum on women's health. This award was presented at the SGIM 27th Annual Meeting in Chicago, on Friday May 14th. Congratulations and Bravo!

Medical Grand Rounds

- June 3, 2004 “BNP in the Clinical Assessment of Decompensated CHF”
Stuart D. Katz, MD, Associate Professor of Medicine, Section
of Cardiovascular Medicine
- June 10, 2004 “From Research to Application: Reducing Time to Reperfusion”
Harlan Krumholz, MD, Professor of Medicine, Section of Cardiovascular
Medicine
Elizabeth Bradley, M.D., Associate Professor, Epidemiology &
Public Health
Robert McNamara, MD, Assistant Professor of Medicine, Section of
Cardiovascular Medicine
Harry Moscovitz, MD, Assistant Professor, Surgery, Emergency Medicine
- June 17, 2004 Title To Be Announced
Stefan Somlo, MD, Professor of Medicine and Chief, Section
of Nephrology
- June 24, 2004 No Grand Rounds This Week

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

Research in Residency Reminder

2nd Annual Research in Residency Day

The Department of Internal Medicine will be hosting its 2nd Annual Research in Residency Day on May 27, 2004 at 11 am in the Fitkin Amphitheatre. The structure of the program will consist of a poster session (in which 5 residents will present the results of their research) followed by a slide session for two additional residents to present. The Department has placed a strong emphasis on housestaff pursuing scholarly and independent research and they have worked hard on their projects. We are hoping for another large turnout of faculty and housestaff for this important Departmental initiative. Please join us and give the housestaff encouragement, advice, and critiques of their work. Thank you.

THE DEPARTMENT OF INTERNAL MEDICINE

Yale University School of Medicine

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

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