CREIGHTON
MEDICINE

CREIGHTON UNIVERSITY ✦ DEPARTMENT OF MEDICINE ✦ APRIL 2002 ✦ VOL. III, NO. 1

Infectious Diseases Laboratory Investigates Detrimental Effects of Smoking and Drinking

by **Martha Gentry-Nielsen, Ph.D.**
ASSOCIATE PROFESSOR OF MEDICAL MICROBIOLOGY AND IMMUNOLOGY, AND OF MEDICINE


Martha Gentry-Nielsen, Ph.D.

In 1991, the Creighton University Infectious Diseases Laboratory, under the direction of **Laurel Preheim, M.D.**, Professor of Medical Microbiology and Immunology, and of Medicine, published the first paper describing a rat model to examine the detrimental effects of chronic alcohol ingestion on host resistance to pneumococcal pneumonia. The bacterium *Streptococcus pneumoniae,* or the pneumococcus, was chosen for this model because it is the most common cause of community-acquired pneumonia in humans. Alcoholics have a higher incidence of pneumococcal pneumonia than the general population, and they have a greater likelihood of developing complications that increase their mortality rate. Although this propensity of alcoholics to develop fatal pneumococcal pneumonia has been recognized for years, the exact host immune defects responsible for their greater susceptibility is not completely understood.

Studies of the effects of ethanol on host defense mechanisms against pneumonia are difficult to perform in humans because it is almost impossible to control for the amount of ethanol consumed and the length of time of abuse. Many of the early studies with animals had focused on the effects of a single acute dose of ethanol administered orally or intravenously just before the animals were infected. The model described by Dr. Preheim's group was unique, in that it allowed the study of events leading to fatal pneumococcal pneumonia in a chronically intoxicated host. Rats, unlike humans, do not drink ethanol willingly. Removing their normal sources of food and water and offering them only a nutritionally complete liquid diet containing 36% of its calories as ethanol overcame this difficulty. To control for the rats' natural aversion to the ethanol diet, a weight- and age-matched group of control rats was fed an identical volume of a liquid control diet with the ethanol calories replaced by dextrin-maltose. It was discovered in these initial studies that ingestion of the ethanol-containing diet for only 7 days reduced the lethal dose of *S. pneumoniae* 10-fold in comparison to the rats fed the liquid control diet.

Dr. Martha Gentry-Nielsen joined Dr. Preheim in the Infectious Diseases Laboratory in 1990. She received a FIRST award (R29) from the National Institute of Alcohol Abuse and Alcoholism in 1992 to continue work in the ethanol-fed rat model. In a series of papers published from 1993-2001, their laboratory has demonstrated that one of the primary immune defects in the ethanol-fed rat was a dysfunction of their neutrophils. Although adequate numbers of neutrophils were recruited to the lungs of the ethanol-fed rats after infection, the cells did not effectively kill the organisms, at least when isolated from the bloodstream and tested *in vitro.* Continuing studies in this model include comparing the ability of neutrophils from ethanol-fed vs. control rats to kill *S. pneumoniae* within the rats' lung tissues and examining the importance of certain pneumococcal virulence factors in this particular example of an immunocompromised host.

In September of 2001, the research of the Infectious Diseases Laboratory took another exciting turn as a unique twist was added to the ethanol-fed rat model. Because 80-90% of patients in alcohol

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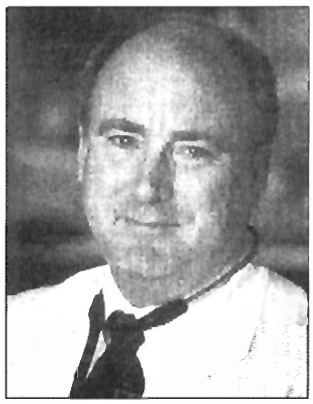
From the Chair


Eugene Rich, M.D.

As I write this column for CREIGHTON Medicine, our office is preparing for the annual process of faculty evaluations. We first share with the chiefs of our eleven specialty divisions various information we've received over the year relevant to faculty accomplishments. This information includes teaching evaluations by medical students and residents, clinical service evaluations from patients and referring physicians, quality of care chart reviews supervised by **Dennis Esterbrooks MD**, Associate Professor of Medicine and of Radiology, and his Office of Quality Management, and faculty research accomplishments. Through the Creighton School of Medicine Mission Based Management Initiative, we also obtain detailed, sophisticated analyses of individual faculty, as well as divisional, productivity in the clinical, educational and research missions.

The individual faculty review this and other information with their division chief, and discuss the objectives they wish to accomplish in the coming year. I then review this extensive information with each division chief, reflecting on individual and group accomplishments over the past 12 months, and discussing together how best to achieve faculty and Departmental aspirations over the next academic year.

While this effort can be time consuming (just the meetings with the chiefs of the larger divisions, like Cardiology, Endocrinology, and General Internal Medicine, often take 2 hours each), I have found this process extraordinarily informative and rewarding. Although, inevitably, the Division chiefs and I find opportunities for individual and programmatic improvement, I view these as simply the natural result of Medicine's longstanding philosophy of continuous striving for excellence. A wise mentor once said to me, "if someone does everything perfectly, they probably aren't trying to accomplish enough." Our faculty is working hard to accomplish many things, so of course there will always be opportunities for improvement. What I always find most impressive is all that our faculty have done, and done extraordinarily well.

Just in the last few months, Creighton Medicine faculty have reported discoveries of genetic mechanisms related to bone mass, important new therapies for allergic rhinitis, and enhanced understanding of the drivers of pharmaceutical costs. They have earned national grants for important new initiatives, been elevated to leadership roles in national professional organizations, and been appointed to consultant roles on important federal panels. They have developed new medical school programs, helped residents and fellows accomplish excellent performance on in-training and certification exams, earned teaching awards, and published educational evaluations. They have served thousands of patients, developed new clinical programs, and worked hard to improve existing services.

I look forward to learning more about all our Creighton Medicine faculty have done this past year, and all they hope to accomplish in the next. Their skill, energy and dedication are a credit to themselves, and bring great credit to Creighton University.

Eugene Rich, M.D.
Tenet Professor and Chair
Department of Medicine
Director, Center for Practice Improvement
and Outcomes Research

Clinical Trials Office

by **Thomas Casale, M.D.**
PROFESSOR OF MEDICINE

If you have patients who would benefit from participation, please contact either the Principal Investigator or the Study Coordinator for the respective trial.

Clinical trials outside the Department of Medicine

Treatment of community-acquired pneumonia of suspected pneumococcal origin in countries with a high prevalence of drug-resistant respiratory pathogens. For more information, please contact **Mark Goodman, M.D.**, Assistant Professor of Family Practice, Principal Investigator, or Study Coordinators: **Penny Fredrick, R.N.** at 402-280-5562 and **Sharon Kochanowicz, R.N.** at 402-280-5972.

Adolescent outpatients with social anxiety disorder. For more information, please contact **Shashi Bhatia, M.D.**, Associate Professor of Psychiatry and of Pediatrics, Principal Investigator, or Study Coordinators: **Davin Dickerson, R.N.**, at 402-345-7100 and **Sharon Kochanowicz, R.N.** at 402-280-5972.

Management of post-operative pain control in patients undergoing ACL repair. For more information, please contact **Charles Giangarra, M.D.**, Assistant Professor of Orthopedics Sports Medicine, Principal Investigator, or Study Coordinators: **Sami Zeineddine, M.D.** at 402-280-4356 and **Tony Romero, M.S.** at 402-280-5960.

Management of post-operative pain in patients undergoing lower abdominal surgery. For more information, please contact **Robert McQuillan, M.D.** Associate Professor of Anesthesiolgy and Clinical Ethics, Principal Investigator, or Study Coordinators: **Tony Romero, M.S.** at 402-280-5960 and **Sharon Kochanowicz, R.N.** at 402-280-5972.

Management of post-operative pain in patients undergoing hip arthroplasty. For more information, please contact **Robert McQuillan, M.D.**, Principal Investigator, or Study Coordinators: **Tony Romero, M.S.** at 402-280-5960 and **Sharon Kochanowicz, R.N.** at 402-280-5972.

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Echocardiography: More Than A Few Reflections

by **M. Jeffrey Holmberg, M.D., Ph.D.**
ASSISTANT PROFESSOR OF MEDICINE

M. Jeffrey Holmberg, M.D., Ph.D.

Echocardiography is one of the most frequently used modalities for diagnosing cardiovascular diseases. Its role has expanded greatly since its introduction into the clinical practice of cardiology in the late 1960s. It is a noninvasive, portable, and extremely versatile technology, which is currently used clinically across the entire spectrum of cardiovascular diseases. Echocardiography allows evaluation of structural, functional, and hemodynamic abnormalities of the heart and peripheral vasculature.

Evaluation of the heart using ultrasound was first performed in 1954. M-mode echocardiography was first used clinically in the 1960s and allowed a single plane evaluation of chamber sizes, ventricular function, and valve structure and motion. A significant enhancement in diagnostic capabilities and imaging of cardiac structures was made possible by real-time 2-D imaging. At nearly the same time, Doppler echocardiography was developed and was applied to evaluation of valvular stenosis and regurgitation. In the early 1980s, color flow Doppler became available. This allowed real-time imaging of blood flow and semi-quantitative analysis of valvular regurgitation. The next advancement, tranesophageal echocardiography (TEE), opened a new window for evaluation of structural heart disease, valvular heart disease, as well as disease states involving the thoracic aorta, especially when transthoracic images were sub-optimal. Several newer technologies have developed over the past decade and will soon become clinically useful. These include automated border detection, contrast echocardiography, tissue Doppler imaging, three-dimensional echocardiography, and advancements in digital acquisition and storage.

Before Doppler echocardiography, determination of cardiac hemodynamics required cardiac catheterization. Doppler echocardiography can be used to assess hemodynamic variables such as stroke volume, cardiac output, regurgitant volume and fraction, pulmonary-systemic flow ratios (Qp/Qs), and pressure gradients. Valve areas and estimations of intra-cardiac pressures such as pulmonary artery pressure, left atrial pressure (LAP), and left ventricular end-diastolic pressure (LVEDP) are also possible.

Quantitative assessment of mitral regurgitation is now possible through determination of regurgitant volumes and fractions using the volumetric method or the proximal isovelocity area (PISA) method. PISA can be used to calculate effective regurgitant orifice area (ERO) and regurgitant volume.

Intra-cardiac pressures can be estimated using different Doppler and color M-mode measurements combined with systemic systolic and diastolic blood pressures and estimated right atrial pressure (RAP). For example, tricuspid regurgitation velocity and RAP are used to calculate right ventricular systolic pressure (RVSP), which correlates with pulmonary artery systolic pressure. LA and LVEDP can be estimated in similar fashions, using arterial systolic and diastolic BP with mitral and aortic regurgitation, respectively. The mitral regurgitation jet can also be used to determine dp/dt. LVEDP can also be estimated using many variables determined from Doppler-derived mitral inflow, pulmonary vein flow, and mitral annular velocities. Measurements from color M-mode derived flow propagation velocities and tissue Doppler imaging (TDI) of the mitral annulus are also used to predict increased LVEDP.

Echocardiography is the most widely used technique for evaluation of left ventricular systolic function (LVSF). However, evaluation is highly subjective and dependent on the experience of the interpreter and sonographer. Manual tracings of endocardial borders in one or two orthogonal views is an accurate method to quantify LVSF, but this procedure is time consuming. Acoustic quantification (AQ), or automated border detection, is a new method where the endocardial border is automatically detected. Real-time volume changes in two orthogonal views can be averaged to obtain quantitative assessment of left ventricular volumes and ejection fraction. AQ has also been developed to assess regional ventricular function and in the future, may allow real-time evaluation of regional systolic and diastolic performance in order to detect regional dysfunction secondary to coronary disease or cardiomyopathies. Real-time AQ reconstruction of the endocardial surface in three dimensions may be possible and it may offer improved analysis of regional wall motion abnormalities.

We are currently evaluating a new program using acoustic quantification in conjunction with contrast echocardiography in our laboratory. Hopefully, this will allow real-time beat-to-beat accurate determination of global left ventricular systolic function, even in those patients with poor images.

Tissue Doppler Imaging (TDI) was recently developed to evaluate the low velocity characteristics of wall motion, both during systole and diastole. TDI provides superior signal to noise ratio and a basis for quantitative assessment of regional left ventricular function. The primary use of this technique would be to look at regional left ventricular contractility objectively. TDI has also been used to assess diastolic function through measurement of mitral annular motion. Combining this information with mitral diastolic filling velocities provides objective load independent evidence of either normal or elevated left ventricular end diastolic pressures. Mitral annular TDI can also help differentiate constrictive pericarditis from restrictive cardiomyopathy, which can be difficult at times. (See Figure 1 on page 4.)

Contrast echocardiography has been used for many years to diagnose right to left shunts but did not allow visualization of left heart structures. Echocardiographic contrast agents have been developed, which can be given IV, pass through the pulmonary system, and help visualize the left heart. Two agents are currently approved by the FDA and used for left ventricular opacification and improved endocardial border definition. Contrast agents have been proven to improve accuracy in interpretation of stress echocardiograms, especially in those patients with poor images.

Myocardial perfusion imaging will likely become the major clinical use of IV echo contrast agents. Several new imaging modalities have been developed to allow visualization of myocardial perfusion using contrast micro-bubbles. Preliminary studies demonstrate the possibility of quantifying myocardial blood flow and improved detection of coronary artery disease. Dobutamine-induced perfusion defects occur much earlier in the infusion stages and happen prior to dobutamine-induced wall motion abnormalities or electrocardiographic changes. These studies have correlated well with findings using thallium or sestamibi radio-nucleotide imaging.

Myocardial viability can also be assessed by contrast echocardiography. Intact micro-vascular circulation and contractile reserve with

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Echocardiography: More Than A Few Reflections

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low dose dobutamine can be identified using contrast echocardiography. This combination of modalities may become the best test for determining viability in akinetic myocardium.

Three dimensional (3-D) echocardiography has progressed from long acquisition times and offline reconstruction to real-time imaging. This will allow evaluation of chamber volumes and assessment of regional wall motion abnormalities and left ventricular function. Three-D echocardiography will provide realistic evaluation of valve structures and direct the surgical approach to valve repair. More accurate determination of severity of regurgitation may be allowed by reconstructing color flow regurgitant jets. The ultimate goal of 3-D echocardiography will be to objectively display the anatomy and complex relations between different structures of the heart, especially in congenital heart disease.

new technologies, we are currently doing research in the area of automatic border detection (AQ) with contrast echocardiography and quantitative analysis of left ventricular function. Application of this modality to stress echocardiography is also being considered. Research using contrast myocardial perfusion imaging has also been initiated in the past year. We plan to enhance our ability to evaluate the hemodynamic status of the heart, especially in regard to evaluation of left ventricular diastolic function and noninvasive estimation of intra-cardiac pressures.

In the more distant future, I foresee integration of contrast echocardiography into a daily evaluation of myocardial perfusion, as well as increased use during stress echocardiography. Real-time 3-D imaging, which enhances evaluation of valvular abnormalities, congenital heart disease, and ventricular function, will also become routine.

Creighton Cardiac Center Noninvasive Laboratory

Our noninvasive laboratory consists of the inpatient laboratory at Saint Joseph Hospital and the outpatient laboratories at the Creighton Cardiac Center and Creighton Cardiology West, in Columbus. They are staffed by 11 sonographers. Currently, we perform over 2,800 inpatient, 1,500 outpatient, and 2,300 outreach echocardiograms each year. Peripheral vascular studies are offered in our outpatient noninvasive laboratory and outreach centers. These include carotid duplex studies, peripheral arterial studies, venous Doppler studies, as well as abdominal and renal duplex studies to evaluate for abdominal aortic aneurysm and renal artery stenosis. Over 500 vascular procedures were completed last year. Transesophageal echocardiography is performed in our outpatient and inpatient labs, and in Columbus. Over 400 TEEs were completed last year.

In the near future, we will be converting to a digital echocardiography laboratory. We hope this will improve the ease of reviewing the studies performed as well as decreasing the time for generation of reports. In regard to

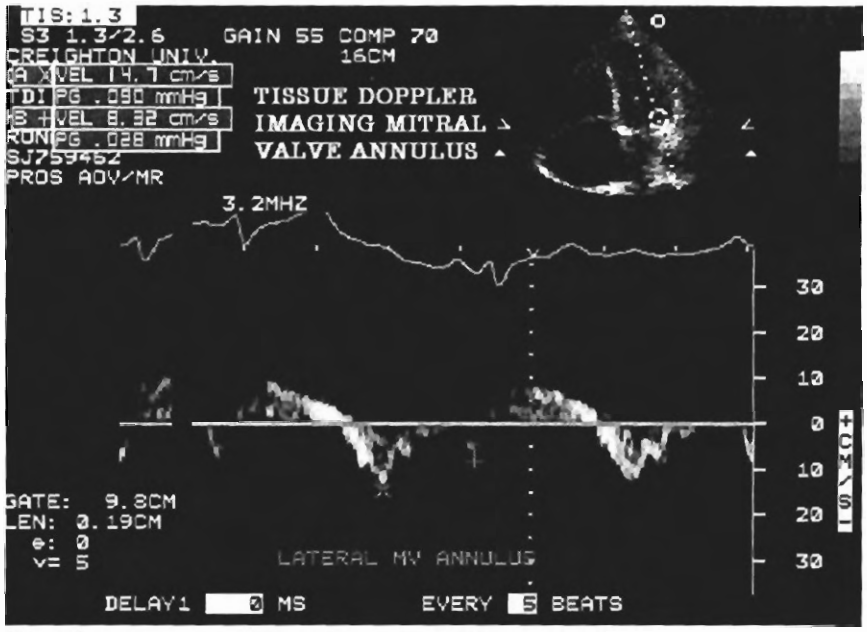

Figure 1

Division News

Allergy

submitted by **Thomas Casale, M.D.**

Fellowship program

Henry Lin, M.D. began his fellowship in December. Dr. Lin comes to us from Loma Linda University Medical Center, where he completed his Residency in Internal Medicine.

Christopher Clark, M.D. began his fellowship in March. Dr. Clark comes to us from East Carolina University, where he began his fellowship in 2001.

Clinical trials

If you have questions and/or patients who would benefit from participation, please contact either the Principal Investigator or the Study Coordinator for the respective trial.

Trial assessing the safety and efficacy of tablet containing ibuprofen, pseudoephedrine hydrochloride, and dextromethorphan Hydrobromide in patients with cold or flu symptoms. For more information, please contact **Thomas Casale, M.D.**, Principal Investigator, or Study Coordinator, **Sharon Kochanowicz, R.N.** at 402-280-5972.

Trial assessing the safety and efficacy of an allergy/decongestant medication in people with seasonal allergic rhinitis and concomitant mild to moderate asthma. For more information, please contact **Thomas Casale, M.D.**, Principal Investigator, or Study Coordinator, **Kristi Farrington, B.C.S., R.R.T.** 402-280-3427.

Trial assessing the safety and efficacy of a long-acting beta agonist in the treatment of patients with persistent stable asthma. For more information, please call **Robert Townley, M.D.**, Professor of Medicine and of Microbiology, Principal Investigator, or Study Coordinator: **Rene Sueiro** at 402-280-5964.

Treatment of patient with allergy to bee stings via intranodal vaccination. For more information, please contact **Againdra Bewtra, M.B.B.S., M.D.**, Principal Investigator, Professor of Medicine, or Study Coordinator: **Rene Sueiro** at 402-280-5964.

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Pillars, Past and Present

Harry J. Jenkins, Jr., M.D. Creighton School of Medicine 1954, Saint Joseph Hospital Intern 1955, St. Francis Hospital in Wichita OB-GYN Residency 1955-56, USAF 1956-58, University of Colorado Internal Medicine Residency 1958-61, Creighton School of Medicine faculty Department of Internal Medicine 1961-2002, Gastroenterology Division 1972-2002.

Who was your most influential teacher? My most influential teacher lived at "our" house. He was a hard working, dedicated physician. Patients who entrusted their care to him could always count on his genuine concern, ready availability, and honesty (with a touch of unique humor thrown in). He took great pride in the sensible quality of care he provided, and made a concerted effort to ensure that the quality of that care was in no way dependent on his patient's ability to pay. He felt that passing his medical skills on to young physicians was not only a privilege, but also his clearly defined responsibility. I am proud to say that he was a "man for others" long before that phrase slipped into our current day lexicon. I am equally proud to say that my most influential teacher was my Father.

What would be your advice to a newly qualified physician? Always be grateful for the opportunity you have to serve others. I am told that compassion is the highest attribute to which we humans can aspire. As physicians, we are challenged and privileged to attempt to achieve that disposition each and every day.

What is your worst habit? I don't understand the question.

What book are you reading now? *Man of the House.* It is a story of Tip O'Neal's political life recommended by my favorite historian, Doris Kearns Goodwin.

What is your greatest regret? Not putting aside some of my selfish goals to spend more time with my exceptional wife and family.

What patient interaction gave you the greatest satisfaction? I cared for a patient with a chronic difficult disease for many years. This lady didn't seem to care for doctors in general, and me in particular. She rarely smiled, and never showed appreciation for the extra time she regularly consumed. I just thought that came with the doctor's "territory." This struggle went on for 25-30 years. Then one day for no apparent reason, she came in with a beautiful smile on her face and expressed her sincere appreciation for my long-term kindness and concern for her.

What has been your most compelling research interest? Although I made some honest efforts in the area of research, I frankly saw my role as that of a clinician and a clinical teacher. I have no apologies for that, since I believe schools like Creighton need a blend of individuals with clinical expertise, combined with talented serious researchers.

Did you enjoy your career at Creighton? Most assuredly! I was fortunate enough to have had the opportunity to work with credible clerical associates, wonderful nurses and truly exceptional colleagues. I believe that working in Creighton's Ignatian environment has had a favorable effect on my outlook toward myself and others. It has also given me a better opportunity to strive to be a more integrated, and joyful person.

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Cardiology

submitted by **Syed Mohiuddin, M.D.**

Professional activity

Tom Hee, M.D., Associate Professor of Medicine, and **Timothy Ryan, R.N.**, will attend the 23rd Annual Scientific sessions of the North American Society of Pacing and Electrophysiology May 8-11, 2002 in San Diego. They will make a poster presentation entitled, *Arrhythmias in Nonagenarians,* Tom Hee, Karen Rovang, Huagui Li, Timothy Ryan, Richard Clark, Syed Mohiuddin.

Xuedong Shen, M.D., Research Fellow, has authored or co-authored three papers accepted for presentation at the American College of Cardiology 51st Annual Scientific Session in 2002. The first paper is *Transesophageal Echocardiography Before Cardioversion of Atrial Fibrillation: Is it Needed for Patients Receiving Conventional Anticoagulation But Having Sub-Therapeutic INR?,* Xuedong Shen, Huagui Li, Karen Rovang, Tom Hee, Mark J. Holmberg, Syed M. Mohiuddin.

The second paper is entitled *Hyperglycemia Worsens Myocardial Microcirculation Reperfusion: Validation By Power Pulse Inversion Imaging and Neutron Activated Microspheres,* Xuedong Shen, Thomas R. Porter, John Lof, Leng Jiang.

The third paper is entitled *Insulin Improves Myocardial Microcirculation Reperfusion After Acute Ischemia With Hyperglycemia,* Leng Jiang, Xuedong Shen, John Lof, Thomas R. Porter.

CARSI Program

Cardiovascular disease (CVD) in African-American patients involves a complex interplay of risk, geographic, socio-economic, and cultural factors. Modifiable cardiac risk factors, such as high blood pressure, diabetes, cigarette smoking, obesity, and physical inactivity, contribute to the excessive CVD mortality and morbidity in the African-American population.

Community-based programs can broaden health education and facilitate behavior change to reduce such risk factors by providing interventions consistent with existing socio-cultural norms and beliefs.

The CARSI (Cardiovascular Risk Factor Screening and Intervention) in African-American Adults) study will implement and evaluate the effectiveness of a community-based cardiovascular risk assessment and intervention program for African-American adults. The ultimate goal of the program is to provide cost-efficient, uncomplicated risk factor reduction to a large segment of the African-American community over a 3-5 year period.

Outcome evaluation will include program success factors including patient satisfaction rates, program compliance, and reduction in modifiable CVD risk factors.

The CARSI study is seeking 200 African-American participants (at the rate of 50 per year) between the ages of 40-80 with two or more of the following risk factors for CVD (hypertension, hypercholesterolemia, smoking habituation, obesity). Participants will receive intensive 1:1 cardiac risk factor reduction counseling and attend group classes on nutrition, physical activity, and smoking cessation.

A group of 60 African-American community members (at the rate of 12 per year), preferably with backgrounds in healthcare or education, will be recruited and trained as Community Health Advocates to provide the community-based intervention programs.

Syed Mohiuddin, M.D., Leah Jorgensen, R.N., M.S.N., and **Charlotte Flick, M.P.A.** of the Clinical Research Section of The Cardiac Center, are conducting this grant-funded intervention study.

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Dermatology

submitted by **Sharon Kochanowicz, R.N.**

Clinical trial

The enrollment period remains open for the study of treatment of patients with Actinic Keratoses on the head. If you have questions and/or patients who would benefit from participation, please contact **Christopher Huerter, M.D.**, Principal Investigator, or Study Coordinators: **Tony Romero, M.S.** at 402-280-5960, or **Sharon Kochanowicz, R.N.** at 402-280-5972.

Endocrinology

submitted by **Mark Johnson, Ph.D.**
ASSOCIATE PROFESSOR OF MEDICINE AND OF BIOMEDICAL SCIENCES

Professional activities

Joan Lappe, R.N., Ph.D., Associate Professor of Nursing and of Medicine, was appointed to the Scientific Advisory Board of the National Osteoporosis Foundation. Dr. Lappe, along with **Joan Stubby, R.N.** and **Gina Lypaczewski, R.N.**, were members of the National Association of Orthopedic OPTIONS task force (Osteoporosis Prevention: Teaching in our Nation's Schools). They developed the content and visual aids for the OPTIONS program which will be presented to teens across the United States.

Dr. Lappe has been appointed to the Editorial Board for Women's Health Issues.

Robert Recker, M.D., Professor of Medicine and Director of the Osteoporosis Research Center, and Dr. Mark Johnson were featured in the cover story of the Spring Issue of the CREIGHTON MAGAZINE. The story describes their research relating to the discovery of a mutation in the Lrp5 gene that causes high bone mass and may have important implications for treatment of osteoporosis in the future.

The Third Annual Meeting of the Great Plains States Society for Molecular Biology and Genetics will be held in Omaha, June 3-4. Several exciting talks, including the keynote speaker, Dr. Mary Claire King, will be presented at this year's meeting. More information, including registration, can be found at the Creighton University CME Division Website: http://medicine.creighton.edu/medschool/cme/

Grant funded

Robert Anderson, M.D., Professor of Medicine and of Biomedical Sciences, grant entitled, Thyroid Hormone Metabolism by Sulfate Conjugation" was funded as a VA Merit Award for three years.

Clinical trial

Dr. Anderson is a participating Principal Investigator in the 7-year VA Diabetes Trial (Cooperative Study #465). After the first year, their nurse coordinators, **Diana Dunning, R.N., M.A., C.D.E.**, **Claire Korolchuk, R.N., C.R.C.**, and **Beth Lemek, L.P.N., C.R.C.**, led the nation (20 different VA sites) in enrollment and level of control of the intensive treatment group. **Tammy Chadwell**, a Creighton employee, is the Research Assistant for the study.

Gastroenterology Division

submitted by **MaryAnn Scramstad**
ADMINISTRATIVE COORDINATOR FOR ACADEMIC AFFAIRS,
DEPARTMENT OF MEDICINE

Staff

On January 1, 2002, **John Ferry, M.D.**, Associate Professor of Medicine, retired from practice at Creighton University. On February 12, 2002, **Father John Schlegel**, Creighton University President, bestowed Professor Emeritus status on **Joseph Holthaus, M.D.**, who retired from practice on July 30, 2001 and to Harry Jenkins, M.D., who retired from practice on August 31, 2001.

Dr. Holthaus was given the Distinguished Administrator Award at the President's Convocation in February 12, 2002.

General Internal Medicine

submitted by **Wendy Taylor**
ADMINISTRATIVE ASSISTANT

Meetings

Dr. Rich co-directed the Genetics in Primary Care Workgroup Meeting, February 21-22, 2002 in Baltimore.

Presentations

Bruce Houghton, M.D., Assistant Professor of Medicine, was one of three finalists for the President's Award for Innovative Use of Instructional Technology. He presented "Use of Technology" on January 18, 2002.

Consultations

Dr. Rich attended the Step 3 Computer-Based Case Simulation Committee, National Board of Medical Examiners meeting, February 7-8, 2002 in Philadelphia.

Review panel

Dr. Rich was on the Health Care Training Study Section, Agency for Healthcare Research and Quality, January 2002.

Clinical trial

The enrollment period for the study of treatment of Type II Diabetes Mellitus in treatment-naïve patients is still open. If you have questions and/or patients who would benefit from this study, please contact **Anna Maio, M.D.**, Principal Investigator. or Study Coordinators: **Tony Romero, M.S.** at 402-280-5960, or **Sharon Kochanowicz, R.N.** at 402-280-5972.

Hematology/Oncology

submitted by **MaryAnn Scramstad**

Staff

We are pleased to announce the arrival of **Peter Silberstein, M.D.**, on May 1, 2002 as Interim Hematology/Oncology Division Chief. Prior to that time, Dr. Silberstein will be at Creighton approximately one week a month, working on program development.

Peter Silberstein, M.D.

Dr. Silberstein graduated from Amherst College in 1975, where he was Summa Cum Laude, and Phi Beta Kappa. He completed medical school at the State University of New York at Buffalo in 1979, where he was a member of Alpha Omega Alpha Honor Society. He completed three years of Internal Medicine Residency at the University of Iowa Hospitals and Clinics in Iowa City. He then went to the University of Minnesota Medical School for Hematology/Oncology Fellowship training, which he completed in 1985. He was certified by the American Board of Internal Medicine in 1982, in Hematology in 1984 and in Oncology in 1985.

Since completion of his fellowship, Dr. Silberstein has been in private practice at the Mercy Cancer Center in Mason City, Ia, where he has been the Medical Director of Research. He is quite interested in offering state-of-the-art, compassionate, multi-modality cancer care. He is

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married and has two daughters. He is an avid exerciser and marathoner.

We are pleased to have Dr. Silberstein join the faculty of the Department of Medicine and we look forward to the new ideas he is bringing with him. In July 2002, Adrian Caracioni will be joining the Hamatology/Oncology Division and we will have more about him in the next issue.

Clinical trials

If you have questions and/or patients who would benefit from participation, please contact the principal Investigator or the Study Coordinator for the respective trial.

James Mailliard, M.D., Professor of Medicine, is the Principal Investigator of five new trials which compliment the already existing studies we have open:

A Phase III trial of the investigational drugs Oxaliplatin and Bevacizumab (VEGF) alone or in combination as a third line treatment for advanced colorectal cancer. For more information, please contact Study Coordinator, **Bethany Mills**, at 402-280-4398.

A Phase III trial of IV chemotherapy with or without the investigational drug iressa for patients with inoperable stage III non-small cell lung cancer. For more information, please contact Study Coordinator **Bethany Mills**, at 402-280-4398.

A Phase II trial testing a combination or oral and IV chemotherapy for extensive stage small cell lung cancer. For more information, please contact Study Coordinator, **Bethany Mills**, at 402-280-4398.

Trial testing the efficacy of IV chemotherapy with Herceptin in advanced Her2 positive breast cancer. For more information, please contact Study Coordinator, **Bethany Mills**, at 402-280-4398.

A Phase II trial of neoadjuvant IV chemotherapy followed by surgery then adjuvant radiation and IV chemotherapy for localized gastric cancer. For more information, please contact Study Coordinator, **Bethany Mills**, at 402-280-4398.

Infectious Diseases/VA Hospital

submitted by **Marvin Bittner, M.D.**
ASSOCIATE PROFESSOR OF MEDICAL MICROBIOLOGY AND IMMUNOLOGY, AND OF MEDICINE

Educational and professional activities

The Division is preparing for its 22nd Annual Infectious Diseases Symposium, scheduled on May 3, from 8:00 a.m. – 3:30 p.m., at the Embassy Suites Hotel Downtown/Old Market. Speakers will address topics ranging from the public health response to bioterrorism to the relation between perinatal infection and cerebral palsy. For more information, please contact the Creighton CME Office at 402-280-1830.

David Dworzack, M.D., Professor of Medical Microbiology and Immunology, and of Medicine, who is Chairman of Creighton's Institutional Review Board, and five other members of the IRB attended a December 2001 national IRB meeting in Boston, entitled "Public Responsibility in Medicine and Research." Seminars dealt with special populations, including prisoners, children, the mentally incompetent, pregnant women, and minorities.

The Omaha VA Medical Center was recently involved in an administrative reorganization. The facilities in Nebraska and Iowa are now joined to form a region that includes Minnesota and the Dakotas.

Pulmonary

submitted by **Naresh Dewan, M.D.**
PROFESSOR OF MEDICINE

Professional activities

Walter O'Donohue, M.D., Professor of Medicine, participated in a nontreatment study of transfusion rates among patients in the ICU (CRIT Study), sponsored by Ortho Biotech.

Naresh Dewan, M.D. was elected to serve as the Co-Chair of the Continuing Medical Education Committee of the American Association of Physicians of Indian Origin (AAPI). He will be involved in coordinating the "Update in Internal Medicine" meeting to be held in Las Vegas on March 29-31, 2002. Dr. Dewan also attended the Governing Body meeting of the American College of Chest Physicians, held in Puerto Rico on March 7-10, 2002.

Clinical trials

If you have patients who would benefit from participation, please contact either the principal Investigator or the Study Coordinator for the respective study.

Effect of 12-week treatment on exercise endurance in patients with chronic obstructive pulmonary disease. For more information, please contact **Naresh Dewan, M.D.**, Principal Investigator, or Study Coordinators: **Tony Romero, M.S.** at 402-280-5960, or **Sharon Kochanowicz, R.N.** at 402-280-5972.

Trial evaluating comparative inhalation treatments in patients with chronic obstructive pulmonary disease. For more information, please contact **Naresh Dewan, M.D.**, Principal Investigator, or Study Coordinator: **Mike Caldwell** at 402-346-8800 Ext 3312.

Rheumatology

submitted by **Sharon Kochanowicz, R.N.**

Clinical trials

The enrollment period for the following two studies remains open. If you have patients who would benefit from participation, please contact either the Principal Investigator or the Study Coordinator of the respective study.

Trial assessing the safety and efficacy of COX-2 selective inhibitor as compared to naproxen in patients with primary osteoarthritis. For more information, please contact **John Hurley, M.D.**, Principal Investigator,Associate Professor of Medicine, or Study Coordinator, **Sharon Kochanowicz, R.N.** at 402-280-5972.

The second study enrolling patients is a trial assessing the gastrointestinal safety of COX-2 selective inhibitor as compared to naproxen in patients with osteoarthritis of the knee or hip who are taking low-dose enteric-coated aspirin. For more information, please contact **John Hurley, M.D.**, Principal Investigator, or Study Coordinator, **Sharon Kochanowicz, R.N.** at 402-280-5972.

Infectious Diseases Laboratory Investigates Detrimental Effects of Smoking and Drinking

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treatment programs smoke and >50% of multi-pack/day smokers are considered "alcohol dependent," Drs. Preheim and Gentry-Nielsen felt it was imperative to consider the additional effects of smoking when studying alcohol-induced defects in host defense against a respiratory disease such as pneumonia. Therefore, Dr. Gentry-Nielsen submitted an Exploratory/Developmental (R21) grant proposal to the NIAAA, with a goal of developing another novel rat model to study the compounding effects of cigarette smoking and alcohol abuse on susceptibility to severe pneumococcal disease. In this model, the rats are exposed in whole body chambers twice daily to room air (sham-exposure) or to the smoke generated from 30 cigarettes lit 5 at a time by an automated smoking machine. After 6 weeks of sham or smoke exposure, the rats within each exposure group are divided into 4 feeding groups and switched to liquid diets containing 0%, 16%, 26%, or 36% ethanol calories to simulate different drinking habits. After an additional 5 weeks of concurrent smoke-exposure and ethanol-ingestion, the rats are infected with *S. pneumoniae*. The effects of smoking and drinking then are assessed in terms of the rats' relative resistance to infection.

Dr. Gentry-Nielsen's proposal received a score in the very meritorious range, and the NIAAA stated it expected to begin funding the grant at the maximum level for an exploratory grant ($100,000/year for 3 years) beginning in March of 2002. While awaiting funding, the laboratory performed the first major experiment for the grant, which ran from the beginning of September to November 29, 2001. In this particular experiment, the rats were infected intranasally with *S. pneumoniae* and then euthanized 4 hours later so that movement of the bacteria down their respiratory tracts and into their lungs could be correlated with alterations in the beat frequency of the cilia lining their tracheas. It was determined that smoke-exposure alone was not particularly detrimental for the rats, as long as they were not drinking ethanol as well. Ethanol ingestion, on the other hand, did have a detrimental effect on the ability of the rats' to keep bacteria out of their lungs, and cigarette smoke exposure further exacerbated the damage within each drinking group.

One of the other most exciting results of this recent experiment was the realization of the potential for collaboration with other research groups at Creighton and the Omaha VA Medical Center. Because the Creighton group is one of the first laboratories in the country to devise an animal model of concurrent smoking and drinking, a number of other local researchers expressed an interest in obtaining samples from the rats used in these studies. Already eight laboratories are collaborating. So, stay tuned, as it appears you may be hearing a lot more in the future about the Creighton smoking/drinking rat model.

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