

CREIGHTON MEDICINE

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“Sulfator Status” in Drug and Hormone Metabolism

by **Robert J. Anderson, M.D.**

PROFESSOR OF MEDICINE AND OF BIOMEDICAL SCIENCES



Robert J. Anderson, M.D.

drug therapy by developing personalized medicines that will be genotype-specific.

Sulfation is an important process for regulating the biological activity of many drugs, hormones and neurotransmitters in humans. For example, the antihypertensive and hair growth-stimulating drug, minoxidil, is converted to its active form by sulfation, whereas the hormones estradiol and triiodothyronine are inactivated by sulfation.

A detailed understanding of the enzymes responsible for these reactions eventually will allow us to develop drugs that will take advantage of a person's unique capacity for sulfation, the so-called “sulfator status,” to enhance a desired response and to avoid adverse reactions.

The sulfation reaction of current interest is catalyzed by a super family of cytosolic sulfotransferase enzymes, now called SULTS, that are different from the membrane-bound sulfotransferases such as chondroitin, glycoprotein and tyrosylprotein sulfotransferases. In humans there are at least 11 known cytosolic sulfotransferases divided into three major groups based on their primary amino acid sequences. The Phenol Sulfotransferase Family includes seven enzymes in the Phenol SULT and Estrogen SULT subfamilies. The Hydroxysteroid SULT Family includes 3 enzymes, and an orphan

family named SULT 4 includes only one enzyme that is present in the brain.

The Phenol SULTs can metabolize an impressive array of substrates including endogenous hormones and neurotransmitters, such as dopamine, epinephrine, norepinephrine, serotonin, 6-hydroxymelatonin, thyroid hormones, and estrogens, as well as exogenous compounds that include phenol, alpha-methyldopa, L-DOPA, acetaminophen, plus several phytoestrogens such as genistein, and xenoestrogens such as bisphenol A.

The Hydroxysteroid SULTs primarily metabolize dehydroepiandrosterone (DHEA) to DHEA sulfate, an adrenal steroid of current nutraceutical and dietary supplement fame. No clear endogenous substrate has been identified for the SULT4 group, although thyroid hormone is a likely candidate in brain metabolism. Of course, many of the hormones will be metabolized in a similar fashion whether they are internally synthesized and secreted, or administered as replacement medicines (e.g., thyroid hormones).

All SULTs use PAPS (3'-phosphoadenosine-5'phosphosulfate) as the co-substrate in the reaction to transfer a sulfuryl group to the acceptor substrate to form the sulfated product. In general, sulfation renders a compound more water soluble for excretion or changes a hormone to a receptor-inactive ligand.

Our research efforts have focused on identifying specific substrates for the various SULTs, characterizing their biochemical properties, and identifying individual variations (genetic and environmental) in the specific SULT activities that would allow prediction of a patient's enzyme level and subsequent response to an administered hormone or drug.

A brief review of minoxidil sulfation will help to demonstrate one approach to identifying individual variations in SULT activities.

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From the Chair



Eugene Rich, M.D.

As I write this column for **Creighton MEDICINE**, I am finalizing our annual report to Dean Wilson and Father Schlegel regarding our Department contributions to service and community outreach. I am once again impressed and gratified by the extent, range and diversity of our faculty and staff contributions in this area. Below are just a few highlights of the numerous activities I identified!

- For the past 18 months, the department sponsored the weekly Thursday evening clinic for the homeless, held in the Sienna

Francis House. Each year one of the Medicine Chief Residents (this year it is actually the Medicine-Pediatrics Chief Resident) accepts responsibility for managing this service. They oversee the schedule, as well as provide supplies, free medications, etc., for this clinic; CU Internal Medicine Residents and faculty staff this weekly free clinic and CU medical students have begun to participate as well. A number of Medicine faculty regularly volunteer in this and other Hope Medical Outreach Clinics around Omaha.

- The Medicine-Pediatrics program has developed and is implementing a rotation and formal curriculum on community service.
- Department Administrative staff took the leadership in securing grant funding, and then implementing a clinic "Language Line," i.e., dedicated language interpretation phone lines in clinic exam rooms to facilitate care of limited English proficiency (LEP) patients.
- The General Internal Medicine faculty devotes some of their earnings to paying the cost of a part-time Sudanese interpreter to assist in the care of these challenging LEP patients.
- The Osteoporosis Research Center, The Cardiac Center, and the new Community Center of Excellence (CCOE) for Women's Health (being established by **Chris Gallagher, M.D.**, Professor of Medicine) conduct numerous Educational community outreach efforts, and participate in local health fairs.
- The Cardiac Center is also in the midst of implementing the CARSI Program, a public health initiative to evaluate the effectiveness of a community-based cardiovascular risk assessment and intervention program for African-American adults.
- A number of Creighton Medicine Clinical programs work hard to enroll their patients in pharmaceutical industry programs to help indigent patients receive expensive medications to manage chronic illnesses. The most extensive of these efforts is the Medication Assistance Program of The Cardiac Center. This program endeavors to provide cardiac medications to their patients who cannot afford them. A team of five clinic nurses each devote approximately five hours a week to manage the program, assuring that patients meet the eligibility criteria of the drug companies and receive their medications in a timely fashion.

The very abbreviated list above is powerful testimony to the deep commitment of the Medicine faculty and staff to the Creighton Mission. It is this mission, and our employees' dedication to it, that make Creighton such a wonderful place to practice internal medicine.

Eugene Rich, M.D.
Tenet Professor and Chair
Department of Medicine

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

Management of post-operative pain in patients undergoing lower abdominal surgery. For more information, please contact **Robert McQuillan, M.D.**, Associate Professor of Anesthesiology and of 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 knee 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.

Creighton University Clinical Research Coordinators are invited to attend Creighton University Research and Education (CURE) meetings held from 12:00 - 1:00 p.m. on the 4th Wednesday of each month. The purpose of the meetings is to discuss issues related to clinical research conducted at Creighton University, network with other coordinators and attend guest lectures. For more information, contact **Sharon Kochanowicz, R.N.** at 280-5972, or **Patsy Nowatzke, R.N.** at 280-3586.

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General Internal Medicine Update

by **Larry L. Brown, M.D.**

ASSISTANT PROFESSOR OF MEDICINE, AND OF PEDIATRICS



Larry L. Brown, M.D.

Transportation Service

Creighton University, Creighton Family Healthcare and Creighton University Medical Center are working together to provide transportation services to Omaha's growing Hispanic community. In July, Creighton University was awarded its third year of funds from the Excellence in Health Care Trust Fund grant for the project entitled, "Healthcare Transportation for the Hispanic Community." Funds from the grant, as well as from CUMC and Creighton University,

are used to provide free transportation services for Limited English speaking residents living in South Omaha. The transportation service is offered to individuals who need to see a doctor, go to the hospital, or for the purpose of attending a free health screening or a health education class anywhere within 10 miles of our Creighton Family Healthcare location on 25th and L Streets.

Since February 2001, employees at Creighton Family Healthcare have been coordinating transportation services for the community under the direction of **Lori Pinkerton**, Project Director, and **Rita Garcia**, Grant Coordinator. A van was purchased in January 2001 and **Sal Savala**, a bi-lingual van driver, was hired in February 2001. We transport patients to any area healthcare provider. Some examples include, CUMC, Excel Physical Therapy, Boys Town National Research Hospital, and Children's Hospital.

Rita Garcia reports, "We are happy to have given over 1,500 rides to those in need. So many people tell me how much they appreciate the service and that they love Sal, our driver." She adds, "Before we had the van service, a couple of winters ago, we had an elderly patient in her 80's, who walked four blocks with a walker in the snow and ice to get to her appointment. She could have slipped and fallen down, and we were all very worried about her. She inspired us to apply for the grant funds. Now, with the van, we can make sure she and others like her get to and from their appointments safely."

If you are interested in learning more about this service, or have patients who could benefit from it, please call Rita Garcia at 449-5740.



Over 1,500 rides to those in need.

ACP-ASIM Award

The Internal Medicine interest group at Creighton University has won the top award in the ACP-ASIM Medical School Awards Program. Medical student membership in the ACP-ASIM by students from Creighton increased by 45.9% in the period from July 1, 2001 to March 15, 2002. The award was presented during the Annual Session in Philadelphia on April 13, 2002.

New Faculty

We are pleased to welcome **Devin Fox, M.D.**, Assistant Professor of Medicine, to the faculty of the General Internal Medicine Division and the Primary Care Section of the Department of Medicine. Dr. Fox graduated from the University of Nebraska College of Medicine in 1998. He then pursued his training in Internal Medicine at Creighton. Dr. Fox was one of the Chief Medicine Residents last year. As an Omaha native, he feels a particular tie to the community. He will have his office at the Dundee Clinic at 115 North 51st Street, with **Kirk Muffly, M.D.**, Assistant Professor of Medicine, and Primary Care Section Chief.



Devin Fox, M.D.

We are pleased to welcome **Theresa Townley, M.D.**, Assistant Professor of Medicine, to the General Internal Medicine Division and the Primary Care Section of the Department of Medicine. Dr. Townley has joined the Creighton Family Healthcare South Clinic at 4628 South 25th Street. Dr. Townley is a 1992 graduate of the University of Minnesota School of Medicine. She completed a four-year Internal Medicine/Pediatrics Combined Residency there. After working one year at Regions Hospital in St. Paul, Minnesota, she then joined Doctors Without Borders in 1997 and spent three years in various countries, such as Liberia, South Sudan, Macedonia and Kosovo. In 2000, Dr. Townley began working on her Masters in Public Health, which she received in May 2001 from The Johns Hopkins University. She has been working with Health Partners Medical Group as a "locum tenens" in various areas of the country. Dr. Townley is Board Certified in Internal Medicine.



Theresa Townley, M.D.

Meetings and Presentations

Dr. Rich attended the Precourse: "Health Policy in the 21st Century" at the 2002 Annual SGIM Meeting, May 3-5, 2002 in Atlanta. He also attended meetings on "Medicare Financing of Graduate Medical Education: Current Problems, Future Solutions," on "Genetics in Primary Care Curriculum: Hands-On Instruction," and a workshop on "Enhancing the Professional Work Life of General Internists: Does the Future of General Medicine Depend Upon It?" while at the 2002 SGIM Annual Meeting.

Dr. Rich gave a presentation on "Family History" at the SACGT Program, May 13, 2002 in Baltimore.

Henry Sakowski, M.D., Assistant Professor of Medicine, **Ronald Markert, Ph.D.**, and Dr. Rich gave a poster presentation entitled, "Declining Student Interest in Primary Care" at the 2002 SGIM Annual Meeting.

Grants Awarded

EC Rich, KA Galt, JD Bramble, M Bittner, G. Nugent, grant entitled "Evaluation of Pharmaceutical Costs in VA Health Care" was funded through a subcontract from the VA HSRD, April 1, 2002 - May 31, 2003.

Division News

Allergy

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



Jeffrey R. Stokes, M.D.

New faculty

The Division of Allergy/Immunology welcomes **Jeffrey R. Stokes, M.D.**, as a new faculty member, effective July 1, 2002. Dr. Stokes was appointed as an Assistant Professor in the clinician-educator track. Dr. Stokes is board certified in pediatrics, pediatric pulmonary diseases, and allergy and immunology. He will be a valuable asset to the division in expanding our clinical opportunities outside of the Creighton University Medical Center campus and in

helping to maintain and improve the quality of the Allergy & Immunology training program.

Professional activities

Dr. Casale received the 2001-2002 Pfizer Visiting Professorship in Allergic Diseases and Asthma. He presented five lectures at UMDNJ-New Jersey Medical School in May as part of this award.

Robert Townley, M.D., Professor of Medicine and of Microbiology, presented a poster at the World Congress of Tuberculosis in Washington, DC in March 2002 on "Effects of BCG Vaccine in Patients With Allergic Asthma." He also presented in March 2002 at Grand Rounds at Albany Medical College in New York on "New Immunomodulatory Treatments of Allergy and Asthma Including Anti-IgG and Use of BCG Vaccine."

Clinical trials

Evaluation of the onset of action (day-in-the-park) of a single dose of 400 μ loteprednol etabonate nasal spray in adults and adolescents with ragweed-induced seasonal allergic rhinitis. For more information, please contact **Thomas Casale, M.D.**, Principal Investigator, or Allergy Asthma and Immunology Study Coordinators at 402-280-5975.

Evaluation of tecastemizole administered to subjects with seasonal allergic rhinitis. For more information please contact **Thomas Casale, M.D.**, Principal Investigator, or Allergy Asthma and Immunology Study Coordinators at 402-280-5975.

Study assessing the efficacy and safety of fexofenadine 120 mg bid in subjects with mild to moderate persistent asthma. For more information, please contact **Thomas Casale, M.D.**, Principal Investigator, or Allergy Asthma and Immunology Study Coordinators at 402-280-5975.

Evaluation of the safety and clinical activity of idec-152 (anti-cd23) monoclonal antibody in patients with mild persistent to severe persistent allergic asthma. For more information, please contact **Thomas Casale, M.D.**, Principal Investigator, or Allergy Asthma and Immunology Study Coordinators at 402-280-5975.

Study comparing the efficacy and safety of fexofenadine 120 mg BID, fexofenadine 240 mg QD, and placebo in subjects with perennial allergic rhinitis. For more information, please contact **Robert Townley, M.D.**, Principal Investigator, or Allergy Asthma and Immunology Study Coordinators at 402-280-5975.

Cardiology

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



Ademola K. Abiose, M.D.

New faculty

Ademola K. Abiose, M.D., Assistant Professor of Medicine, joined the Division on July 1, 2002. Dr. Abiose graduated from the College of Medicine, University of Lagos, Nigeria in 1985 and subsequently completed his Internal Medicine Residency training at the Lagos University Teaching Hospital. He received his M.Sc. degree in Pharmacology from the Lagos University Medical College in 1992, and joined the faculty as a lecturer. Dr. Abiose was a Merck Fellow in the Division of Clinical Pharmacology at Stanford University Medical Center between 1995-97. He then completed his Internal Medicine Residency and Cardiology Fellowship training at the University of Connecticut Health Center in June 2002. He is Board Certified in Internal Medicine. Dr. Abiose is the first Creighton cardiologist to work full-time in Onawa, Iowa. The Cardiac Center has opened an office in Onawa to provide consultation to area primary care providers on an ongoing basis. Dr. Abiose's sub-specialty is non-invasive cardiology.

Intravascular brachytherapy at CUMC

Intravascular brachytherapy is now being performed at the Creighton University Medical Center. It is being used in the treatment of coronary in-stent restenosis. Brachytherapy involves the very short exposure of an artery to a radiation source.

In-stent restenosis occurs in approximately 15% of patients who receive a stent. This process occurs as a result of inflammation of the stented segment of the artery. During intravascular brachytherapy, radioactive seeds are placed directly in the artery for approximately three minutes to prevent this inflammatory process from recurring.

The first patient underwent treatment in June and has done well with no evidence of recurrence. The procedure is done in the same way an angioplasty is performed. The interventional cardiologists and radiation oncologists participate in this procedure.

Publications

Ijaz Khan, M.D., Assistant Professor of Medicine, had an article entitled, "Transient Atrial Mechanical Dysfunction (Stunning) After Cardioversion of Atrial Fibrillation and Flutter," in the July 2002 American Heart Journal.

Dr. Khan also co-authored with **Chandra Nair, M.D.**, Professor of Medicine, an article entitled, "Clinical, Diagnostic, and Management Perspectives of Aortic Dissection" in the July 2002 CHEST Journal.

Clinical trials

Amlodipine vs. valsartan in the treatment of hypertension compares the efficacy of angiotensin II receptor antagonist valsartan (Diovan™) to calcium channel blocker amlodipine (Norvasc®) in the management of mild to moderate hypertension in African-Americans. For more information, please contact **Kathleen Packard, Pharm.D.** at 402-280-4292.

The I-PRESERVE Study assesses the use of angiotensin II receptor blocker irbesartan (Avapro®) in the treatment of heart failure in patients with preserved systolic function. For more information, please contact **Tony Reyes, M.D.**, Assistant Professor of Medicine, Principal Investigator, or Study Coordinator, **Lois Rasmussen, R.N.**, at 402-280-4618.

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Pillars, Past and Present



Alfred W. Brody, M.D., D.Sc., Professor of Medicine.

Who was your most influential teacher?

I was greatly influenced by Dr. J. Comrow; his ideas greatly advanced the development of the science of physiology in this country. He was also an outstanding teacher who could not only immediately charm, but also educate the most sophisticated of audiences.

What was your first medical paper? My first paper, published in the Armed Forces Medical Journal in 1948, was a case report of a 58 year-old male who had bicuspid aortic valve and died of a rupture of the aortic aneurysm. This paper was written under the tutelage and guidance of Dr. Herwig Hamperl, Head of the Department of Pathology at Allgemeine Krankenhaus (General Hospital) in Salzburg, Austria. Dr. Hamperl not only was an eminent pathologist and a scholar, but he also opposed the idea of Austrian union with Nazi Germany.

Who brought you to Omaha and Creighton Medical School? Dr. J. Raymond Johnson brought me to Omaha and introduced me to Dr. Harold Neu and led to the establishment of the first Pulmonary Function Lab at Creighton. He also introduced me to Dr. Fredrick Gillick, Dean of the School of Medicine, who helped me acquire my first multi-channel recorder for my experimental lab, then located in the Medical School basement.

What was different or newly discovered when you were a student? Ninety-five percent of my class was male and no one was interested in the "business aspects" of medicine. Antibiotics were unheard of and accidental discovery of sulfanamide was an anecdotal finding. During my internship, penicillin had been discovered but was nearly impossible to obtain for the civilian population. An anti-serum for the treatment of pneumococcal pneumonia was available, but there was a high risk of serum sickness. We had to desensitize and treat a very sick patient with great difficulty and at a high risk to the patient. Today's medical graduates have the good fortune of having appropriate and effective therapies available to them.

News From Other Departments

The Creighton University Department of Psychiatry is conducting clinical research trials using licensed medications to treat Post-Traumatic Stress Disorder (PTSD), at our Psychiatry Clinic at 3528 Dodge Street, Omaha, NE 68131.

We are looking for trauma survivors who have experienced a serious trauma such as rape, domestic violence or serious injury, and who currently experience symptoms related to the trauma such as nightmares, depression, anxiety, and/or intrusive memories.

To be eligible for these trials, subjects must be medically stable, not currently abusing drugs or alcohol, age 19-65, male or female, and

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Division News

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The Gemini Study evaluates the efficacy of a fixed combination tablet of amlodipine/atorvastatin (Norvasc®/Lipitor®) in subjects with concomitant hypertension and hyperlipidemia. For more information, please contact **Aryan Mooss, M.D.**, Professor of Medicine, or Study Coordinator, **Lois Rasmussen, R.N.** at 402-280-4618.

The Sitostanol Margarine (Benecol) Study evaluates the combined efficacy of statin drugs and Benecol spread in patients with LDL cholesterol not at NCEP goal on current statin therapy. For more information, please contact **Roger Riedel, M.D.**, Cardiology Fellow and Principal Investigator, or Study Coordinator, **Lois Rasmussen, R.N.**, at 402-280-4618.

Dermatology

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

Clinical trial

Trial comparing the efficacy, safety, and tolerability of new oral formulation terbinafine in patients with onychomycosis of the toenails. For more information, please contact **Christopher Huerter, M.D.**, Associate Professor of Medicine and 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

The Creighton Osteoporosis Research Center welcomes the referral of persons of all ages interested in research participation. Please call 280-BONE (280-2663) for details about current clinical research studies.

Hematology/Oncology

submitted by **MaryAnn Scramstad**

ADMINISTRATIVE COORDINATOR OF ACADEMIC AFFAIRS,
DEPARTMENT OF MEDICINE

New faculty

We are pleased to welcome **Adrian Caracioni, M.D.**, Assistant Professor of Medicine, to the faculty of the Hematology/Oncology Division of the Department of Medicine. Dr. Caracioni comes to Creighton University from the Moses Cone Health System of Greensboro, North Carolina.

Dr. Caracioni is a graduate of the Timisoara Medical School in Romania. He completed an Internal Medicine Residency in Romania before coming to the United States. After his arrival, Dr. Caracioni completed Internal Medicine Residency training at Meridia Huron Hospital in Cleveland, Ohio. He became a full-time faculty member at the same hospital until he went into an Oncology and Hematology Fellowship at St. Louis University. Dr. Caracioni has been in private practice the last two years in Greensboro. He is Board Certified in Internal Medicine, Hematology and Medical Oncology. His interests include benign hematology, myelodysplasia and general oncology.



Adrian Caracioni, M.D.

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Clinical trials

A randomized selenium, vitamin E vs. placebo prostate prevention trial for men 55 and older (African-American men may be 50 and older) with no prior history of prostate cancer. For more information, please contact **Peter Silberstein, M.D.**, Assistant Professor of Medicine and Principal Investigator, or Study Coordinator, **Penny Anzures** at 402-280-5274.

A randomized tamoxifen vs. raloxifene breast cancer prevention trial for postmenopausal women who are at increased risk for breast cancer. For more information, please contact **Peter Silberstein, M.D.**, Principal Investigator, or Study Coordinator, **Penny Anzures** at 402-280-5274.

A colorectal cancer screening study for patients 50-80 years old, who have had no prior GI testing in the last 10 years. For more information, please contact **Peter Silberstein, M.D.**, Principal Investigator, or Study Coordinator, **Penny Anzures**, at 402-280-5274.

A randomized treatment trial of Gemcitabine, 5-Fluorouracil and Radiation therapy for patients with resected pancreatic cancer. For more information, please contact **Peter Silberstein, M.D.**, Principal Investigator, or Study Coordinator, **Bethany Mills**, at 402-280-4398.

A randomized trial of DepoProvera vs. Venlafaxine for women receiving Tamoxifen, Raloxifene, or Aromatase inhibitors, who experience bothersome hot flashes. For more information, please contact **Peter Silberstein, M.D.**, Principal Investigator, or 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

Professional activities

Dr. Bittner published the lead article in the March 2002 issue of *Infection Control and Hospital Epidemiology*. His article described a hand hygiene improvement study.

He also presented six lectures at the American College of Physicians-American Society of Internal Medicine's Midwest Internal Medicine Board Review in May. Dr. Bittner is the Chief Consultant for Infectious Diseases and International Travel for the Travel Clinic of the Douglas County Health Department.

Martha Gentry-Nielsen, Ph.D., Associate Professor of Medical Microbiology and Immunology, and of Medicine, was Visiting Professor at the medical schools at Louisiana State University on April 8-9, and at the University of Texas Medical Branch at Galveston on April 30, 2002. She spoke on the rat models she uses to study the effects of alcohol ingestion, alcohol-induced liver cirrhosis, and smoking on susceptibility to pneumococcal infections.

Gary Gorby, M.D., Associate Professor of Medical Microbiology, and of Medicine, gave an invited presentation on "Modulation of Gonococcal Invasion by the Immune Response" at the June 9 meeting of the American Society for Reproductive Immunology in Chicago.

Meetings

Dr. Bittner attended the annual meeting of the International Health Medical Education Consortium (IHMEC) March 19-22 in Havana, Cuba and was elected to the IHMEC Governing Council. IHMEC encourages international electives for medical students.

Dr. Gentry-Nielsen attended the Ninth Microbiology and Immunology Educational Strategies Workshop in Myrtle Beach, SC May 4-8, 2002. One day of the workshop was devoted to the develop-

ment of uniform bioterrorism learning objectives for medical students throughout the country.

Clinical trials

Trial assessing the safety and efficacy of gemifloxacin in community-acquired pneumonia. This is limited to VA patients and focuses on the efficacy in penicillin-resistant pneumococcal infection.

Trial comparing the safety and efficacy of piperacillin/tazobactam with that of ampicillin/sulbactam in the treatment of diabetic foot infections. This is limited to VA patients.

Trial studying the relationship between *Legionella* colonization of health facility water systems and *Legionella* nosocomial pneumonia. This trial is underway at the VA Medical Center.

If you have questions or patients who would benefit from participation, please contact the Principal Investigator, **Marvin Bittner, M.D.**, or the Study Coordinator, **Willy Arnold, M.S.** at 402-221-8052.

Pulmonary Division

submitted by **Cindy Hanneman**

ADMINISTRATIVE ASSISTANT, PULMONARY/CRITICAL CARE MEDICINE

Professional activities

Naresh Dewan, M.D., Professor of Medicine, was invited to give a presentation on "Pharmacology of Chronic Obstructive Pulmonary Disease" at the annual meeting of the American Association of Physicians from India in Chicago. He also served as the moderator for the symposium on COPD and a session on sepsis and lower respiratory tract infections.

Rheumatology Division

submitted by **John Hurley, M.D.**

ASSOCIATE PROFESSOR OF MEDICINE

Grant awarded

The Rheumatology Division has received an educational grant from Pharmacia for an arthritis learning center.

Outreach clinic to move

The Rheumatology Division's Alegent Health Bergan Mercy Outreach Clinic will move from the hospital to the South Tower office building to see patients starting in January 2003.

Clinical trials

Jay Kenik, M.D., Associate Professor of Medicine, and **Dr. Hurley** are currently involved in a Novartis drug study, evaluating a selective COX-2 inhibitor vs. a comparative nonsteroidal in the treatment of patients with osteoarthritis. For more information, please contact **Dr. Hurley**, Principal Investigator, or Study Coordinator, **Sharon Kochanowicz, R.N.**, at 402-280-5972.

News from other departments

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able to attend regular clinic visits for a 10-12 week period. Stipends are available to compensate subjects for travel and other study-related expenses. Subjects will receive a thorough psychiatric evaluation, study medication, and weekly or bi-weekly clinic visits.

If you have patients who might benefit from our research trials, please refer them to: **Maggie Kenney, L.C.S.W.**, at 402-981-8250.

Walter J. O'Donohue, M.D.

from the Editor

Few people get the chance to do what they like and even fewer do it with great success. Walter did both. He loved to practice medicine, to teach medicine, and to contribute new knowledge to the field of clinical medicine—and he was a master at all three. He was that rare man who lived, thought and felt with style; a style with a unique combination of a scholar, teacher, and a physician, greatly loved by his patients.

Allow me to quote from his colleagues, friends and students:

"Dr. O'Donohue epitomized the ideals of Creighton University; he provided outstanding patient care, promoted a family-friendly work environment, and always strove towards excellence."

—Nancy Koster, M.D., Chief Resident, Medicine

"Walter was the ideal friend and colleague; always supportive and encouraging. He was a teacher who inspired confidence and care. He was the best mentor we have had for scores of students and residents, as well as faculty colleagues."

—Robert Recker, M.D., Osteoporosis Research Center

"Walter O'Donohue fostered, and exemplified the ethos of the Creighton Department of Medicine that clinical faculty are great teachers or great scholars BECAUSE of (not instead of) being great physicians. He was a great clinician who was also a superb teacher, and thoughtful and productive scholar. Even more important, he was a great friend, to me personally, and to all at Creighton. We will miss him deeply."

—Eugene Rich, M.D., Chairman, Department of Medicine

"I have known Walter since he came to Creighton, first as Director of Pulmonary Medicine, then as Chairman of Medicine, then as Director of Graduate Medical Education. When a problem arose, in every instance, he was always very helpful. He was truly a "man for others" in the fullest sense of the Creighton tradition."

—Robert Townley, M.D., Professor of Medicine

"When I came to Creighton to assume the role of Dean of the School of Medicine in 1982, Walter O'Donohue was one of the first faculty members who offered a warm welcome. In a short time it became apparent that he was one of the most productive and respected members of the faculty. He was committed to students, to colleagues, and to the Creighton mission. His years as Chair of the Department of Medicine were years of growth of size and quality. He is sorely missed."

—Richard L. O'Brien, M.D., Professor of Medicine
Center for Health Policy and Ethics

"For the past 40+ years, the Department of Medicine has been the premier department in the Medical School; inpatient care, research, and

teaching. Walter O'Donohue inherited and nurtured that legacy admirably during his 11 years in the chair. Then, on leaving the chair, he effectively defined the Associate Dean's job for Clinical Affairs at a time when great external pressures were being placed on the school to formalize graduate medical education. In both assignments, he was fully professional, committed, effective, and perhaps equally important, self-effacing."

—Robert Heaney, M.D.,
John A. Creighton
University Professor



Walter J. O'Donohue, M.D.
September 23, 1934 - July 22, 2002

"Dr. O'Donohue's passion for academic medicine was very apparent in his role as Associate Dean for Graduate Medical Education. He had an impact on many young physicians, providing them with guidance, support, and encouragement along the way. He was highly respected and admired by the House Staff and the postgraduate programs for his leadership, knowledge, compassion, and fairness."

—Angie Alberico, Administrative Assistant,
Graduate Medical Education

"The teacher who walks in the shadow of the temple, among his followers, gives not of his wisdom, but rather of his faith and his loving self. If he is indeed wise, he does not bid you enter in the house of his wisdom, but rather, leads you to the threshold of your own mind."

—Khalil Gibran, *The Prophet*

Gifts are currently being sought in Dr. O'Donohue's honor in order to fund in perpetuity an endowment in Internal Medicine at Creighton University Medical Center. If you would like to donate to the Walter O'Donohue, M.D. Endowment, please send your gifts to Tom Schuyler, Office of Development, Creighton University School of Medicine, 2500 California Plaza, Omaha, NE 68178, or call (800) 561-1649.

Residency Program News

submitted by Robert Dunlay, M.D. • Assistant Professor of Medicine, and of Pharmacology

CHIEF RESIDENTS FOR 2002-2003

VA Medical Center Outpatient Clinic: Sean Denney, M.D., is a 1999 graduate of the Creighton University School of Medicine. Dr. Denney is married. He will do a Cardiology Fellowship at Creighton, beginning in 2003.

Creighton University Medical Center: Nancy Koster, M.D., is a 1999 graduate of the Creighton University School of Medicine. Dr. Koster is married with one child. She will do a Cardiology Fellowship at Creighton, beginning in 2003.

VA Medical Center Inpatient: Randy Reister, M.D., is a 1999

graduate of the University of South Dakota School of Medicine. Dr. Reister is married with one child.

Creighton University Medical Center: John Sype, M.D., is a 1999 graduate of the University of Nevada School of Medicine. Dr. Sype is married with one child. He will do a Cardiology Fellowship at Creighton, beginning in 2003.

Medicine/Pediatrics: Matt Zollinger, M.D., is a 1999 graduate of the Creighton University School of Medicine. He speaks and writes fluently in Spanish. Dr. Zollinger is married with three children.

“Sulfator Status” in Drug and Hormone Metabolism

continued from page 1

Minoxidil is unusual because sulfation activates rather than inactivates this compound to express its vasodilatory and hair growth properties. Initially, only one of the Phenol SULTs, SULT1A1, was thought to be responsible for the reaction. This enzyme is readily measured in the human platelet, and can be used as an indicator of enzyme activity in other tissues.

To test the utility of this approach, we measured blood platelet SULT1A1 activity and a scalp biopsy sample SULT1A1 activity from each of 28 volunteers. Inter-individual variations in the activity were 13 to 60-fold. The level of activity in the scalp was significantly correlated with the activity in the platelet. The results supported the conclusion that we could predict an individual's scalp hair growth response to minoxidil based on the level of SULT1A1 in the platelet. The final test of this hypothesis, an early foray into pharmacogenetics, with potential applications for pharmacogenomics, has not been completed. Thus, for now, an individual must take the usual and customary route in modern medicine: trial and error. Try it for three months. If it doesn't work, we'll try something else. In the meantime, we hope the patient doesn't experience a severe adverse reaction. In the future, the precise identification of the patient's “sulfator status” by genotyping with regards to the SULT enzymes and levels of activities will lead to customizing the type and dose of medicine to provide the safest and most effective response.

Sulfation of endogenous estrogen during menstrual cycle provides a fascinating overview of the tissue-specific action of SULTs in the regulation of the availability of a steroid hormone to its receptor, a paradigm for pre-receptor ligand regulation. Estrogen sulfotransferase (SULT1E1) is present in the endometrium and is involved in the local regulation of estrogen available to the nuclear estrogen receptors. During the follicular phase of the menstrual cycle when estradiol is increasing, the endometrial SULT1E1 activity level is low. This makes physiologic sense because the full effect of the estrogen present is maintained with diminished estrogen sulfotransferase activity. During the luteal phase, elevated progesterone induces

SULT1E1 to 5-fold higher levels of activity. Again, this makes sense because the sulfation of estradiol in the cytosol prevents it from binding nuclear steroid receptors and decreases the overall estrogen effect in the tissue.

Thus, the local SULT levels within the endometrium contribute to the tissue regulation estradiol during the menstrual cycle - somewhat different from the predominant model that labels the circulating hormone level as the determining factor in the final hormone effect. The paradigm of tissue-specific pre-receptor regulation can be applied to our ongoing studies of thyroid hormone sulfation because thyroid hormone also acts through a nuclear receptor.

What does the future hold for “sulfator status?” For now, our studies are still in the descriptive phase as we learn the normal physiology, biochemistry, substrate interactions and pathophysiology of the human SULT enzymes. We have detected and characterized Phenol SULTs in human osteoblast cells. Because estrogen and thyroid hormone are important mediators of bone metabolism in men and women, the thorough description of the role of SULTs in normal bone and in osteoporosis may lead to tissue-specific therapies.

Hormone replacement therapy for women is receiving extensive negative reviews today as results of long-term studies raise concerns about adverse events. There is little information about the tissue-specific metabolism of estrogen preparations by SULTs. Sulfation may be protective in certain tissues by decreasing the potency of the estrogens. It is possible that the “one dose, or a few doses, fit all” approach to replacement therapy has exposed women with low levels of certain tissue SULTs to excessively high tissue doses of estrogens.

With personalized medicine, it will be possible to identify a SULT genotype, the “sulfator status,” and then choose the appropriate estrogen dose or perhaps a customized estrogen analog that will avoid the adverse effects of the parent compound. The possibilities of tailor-made medicines for numerous diseases are being evaluated and developed today.



Attn: Larry Maxwell

3006 Webster Street • Omaha, NE 68131-2044

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