CREIGHTON
MEDICINE

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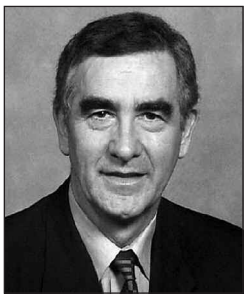
Skeletal Role of Low Endogenous Estrogen Levels In Elderly Women

by **Prema Rapuri, Ph.D.**
ASSISTANT PROFESSOR OF MEDICINE
AND
J.C. Gallagher, M.D.
PROFESSOR OF MEDICINE, DIVISION OF ENDOCRINOLOGY


Prema Rapuri, Ph.D.


J.C. Gallagher, M.D.

Osteoporosis and its related fractures are a major public health threat to post-menopausal women. In the United States, an estimated 250,000 hip fractures and 500,000 vertebral fractures occur annually with direct medical expenditure approximating $10 to $15 billion per year. It is well known that the rapid bone loss immediately following menopause is due to estrogen deficiency and this phase lasts for five to seven years. Estrogen replacement therapy at or after menopause prevents bone loss. Following the initial rapid phase, bone loss occurs more slowly. This second stage of age related bone loss has been attributed to secondary hyperparathyroidism, nutritional deficiency of vitamin D in the elderly and impaired bone formation at the cellular level; however, estrogen may also play a role in age related bone loss. Although it has been known for a long time that estrogen treatment prevents bone loss in elderly women, earlier studies, which looked at the role of endogenous estrogens in maintaining bone mass did not always show positive results. This was probably due to a lack of reliable methods for detecting very low levels of serum estradiol. Recent evidence supports the hypothesis that low levels of endogenous estrogen in postmenopausal women have an important physiological effect on the skeleton.

In a recent study of 489 elderly women aged 65-78 years who participated in a three year randomized, double blinded osteoporosis trial; we found that women in the lowest tertile compared to the highest tertile of serum bioavailable estradiol had significantly higher indices of bone resorption (20% higher). There was a significant positive association between serum estradiol (both bioavailable and unbound forms) and bone density. Women with serum total estradiol greater than 13 pg/ml (tertile 3) had bone density mineral (BMD) that was 6-14% higher at the spine, femoral sites and total body compared to women with serum estradiol less than 9 pg/ml (tertile 1). The correlations were stronger for serum bioavailable estradiol with women with levels of greater than 4 pg/ml (tertile 3) having BMD that was 8-19% higher at various skeletal sites, compared with that of women with less than 2.4 pg/ml (tertile 1) (Figure 1).

After three years treatment with estrogen, we demonstrated that there was a significantly larger increase (4-6%) in BMD in women with the lowest baseline serum estradiol (tertile 1) (Figure 2) compared to women with higher levels (tertile 3).

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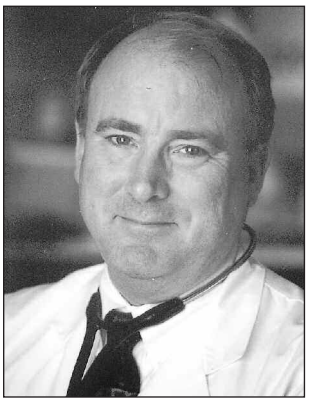
From the Chair



Eugene Rich, M.D.

As we finalize this April 2005 Issue of Creighton Medicine, the faculty and staff in the Chair's Office are already busy planning for the 2005-06 academic year. This begins with developing our objectives for the upcoming year, and then formulating our budget priorities to meet these objectives. We have identified many exciting initiatives to undertake next year.

Of course, Medical Education is one of our core missions, and we have ambitious plans for new programs in this area. With anticipated increases in the number of Creighton medical students, we are expanding our rotation options for third year students on inpatient medicine. Our approach to case-based learning for second year students is evolving to improve the students' introduction to clinical medicine. We are also beginning new fellowship programs in interventional cardiology and endocrinology. For our Alumni, we intend to incorporate a "Come Home to Creighton Medicine" component into our annual CME update.

In research, we continue to recruit investigators to enhance our existing areas of scholarly expertise, as well as fostering new multidisciplinary research programs investigating pathogenic mechanisms and innovative treatments. Airway Disease, Endocrinology, and Cardiovascular Disease are all areas of research excellence we intend to expand. We are also committed to expand research training opportunities for medical students, residents, and fellows.

In the area of clinical service, we hope to develop enhancements in both service and performance in 2005. The new LARA (Lab and Radiology Access) system at CUMC instantaneously connects physicians to clinical data on hospital inpatients using advanced PDAs with "Wi-Fi" capability. In 2005, we are committed to securing this technology for all of our residents and clinical services in internal medicine. We are also working with Creighton leadership to develop improved outpatient clinical facilities on the CUMC Campus as well as offering more of Creighton Medicine's specialized services to the physicians and patients of West Omaha.

We are beginning the fifth year of publishing Creighton Medicine (our inaugural issue was January 2000), so another one of our objectives is to learn from you, the readership, how else these publications can be of service; in the coming months we plan to query recipients of our newsletter and Annual Report to identify potential improvements. Thanks in advance for your help with this effort, and thanks for your interest in Creighton Medicine.

Sincerely,

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

We Need Your Help!

In January 2000, the Department of Medicine at Creighton University printed the first issue of the Creighton Medicine newsletter. We are interested in your ideas and comments about the overall appearance and topics within the newsletter.

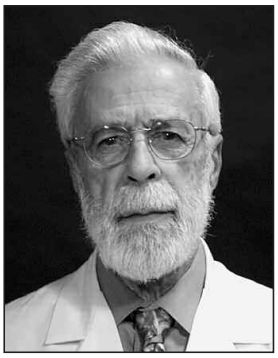
Please visit **http://medicine.creighton.edu/medschool/medicine** and click on Department Newsletter to complete a short survey.

Thank you for your interest in Creighton Medicine!

CREIGHTON MEDICINE is published three times a year by the Creighton University Department of Medicine. Address all mail to Joann Reynolds, 601 North 30th Street, Omaha, NE 68131 or email: *jreynolds@creighton.edu.*

Creighton UNIVERSITY Medical Center

Pillars, Past and Present



Ramon M. Fusaro, MD, MS, Ph.D.

Ramon M. Fusaro, MD, MS, PhD, Adjunct Professor Emeritus Department of Internal Medicine, and active Adjunct Professor of Preventive Medicine & Public Health of Creighton University, graduated from the University of Minnesota.

Why did you come to Creighton?

To participate in undergraduate and graduate education and continue basic and clinical medical research.

Who were the most influential in your career?

At the University of Minnesota, Drs. S. Schwartz, C. Watson, H. Michaelson, and at Creighton, Drs. Henry Lynch and Robert Heaney. Dr. H. Michaelson got me interested in Dermatology as a specialty, which allowed me to invade many areas of medicine. Drs. S. Schwartz and C. Watson were two men who influenced me to do research and were always supportive of me in my academic pursuits. At Creighton, Dr. Henry Lynch gave me the opportunity to do genetic research in cancer with my background in dermatology as an asset. Dr. Robert Heaney influenced me because he was always a good individual to talk to about a new concept. In addition, he was someone who gave thoughtful reflection and advice.

Would you identify rewarding periods in your career?

Participating in undergraduate or graduate education, but most gratifying was research in such areas as:

- Exploring cutaneous glucose physiology and establishing anaerobic glycolysis as primary in the skin
- Developing methodologies for measuring carbohydrates in the skin, liver, and muscle
- Investigating with immunologic studies bullous dermatoses
- Determining the erythropoietic origin of excess blood protoporphyrin in protoporphyria
- Treating and curing leprosy patients with intravenous infusions of histocompatible normal white cells
- Defining hereditary polymorphic light eruption in American Indians and non-Indians
- Clarifying the occurrences of systemic cancers in the FAMMM syndrome
- Classifying Muir-Torre's syndrome within the HNPCC syndrome
- Developing computer programs and data mining for use in the assessment and therapy of hereditary cancer syndromes
- Discovering keratin bound melanoidins for broad UVB/A/Soret band photoprotection
- Becoming the primary advocate of the first multimedia information retrieval and learning center in the library at University Minnesota's Health Sciences

Were there any disappointments in your career?

Yes, the termination of the joint (CU & UNMC) dermatology training program in which 40% of our residents ranked in top 10th percentile of all dermatology residents in the nation when tested by the American Board of Dermatology, 55% in the top 20th percentile, and 80% in the top 50th percentile.

Would you identify a singular rewarding moment in your career?

My most rewarding moment was when Dr. Steve Lemon nominated me for the Outstanding Research Career Award at Creighton University because of all the various research that I had completed. I was awarded the honor in 1996-97.

What is my philosophy of practice?

To do the best that I can with the tools and knowledge I have; but, I also enjoy thinking of new ideas and ways to practice medicine and improve healthcare.

What should Creighton University stand for?

Creighton University is a religious school that projects the christian moral philosophy of the Jesuits in education.

Why do you see patients?

I enjoy helping patients with their medical problems but observing diseases in men and women also allows the developing of new ideas that can result in improved health care.

Calcium Phosphate and Parathyroid Metabolism in Chronic Kidney Disease: New Treatment Options

by **Muhammad N. Firoz, M.D.**
Assistant Professor of Medicine
Division of Nephrology


Muhammad N. Firoz, M.D.

End stage renal disease (ESRD) now known as stage 5 kidney disease affects more than 300,000 patients in the United States. The overall mortality rate from ESRD remains high at around 25% per year and has not changed much since 1994. The leading cause of death remains the atherosclerotic cardiovascular disease (CVD).

The risk of CVD begins even before the onset of ESRD and increases by 10 to 100 folds after dialysis is initiated. The traditional risk factors for the atherosclerotic cardiovascular disease (CVD) do not adequately explain the high cardiovascular mortality seen in these patients.

Though the exact etiology of the increased incidence of CVD in this group remains unclear, a number of studies point towards a deranged mineral metabolism as a risk factor for CVD; especially the abnormalities in calcium, phosphorus, parathyroid hormone (PTH) and vitamin D seen frequently in patients with chronic kidney disease (CKD). Furthermore, there is increasing evidence that the current management of these abnormalities which involves the suppression of parathyroid hormone level by vitamin D analogues and the use of calcium containing phosphate binders may have an adverse effect on the vessels and may be responsible for this increased risk of CVD.

Serum phosphorus, which is a potent stimulator of vascular calcification is now considered perhaps the most important mineral abnormality that links ESRD and a high risk of CVD. Its level gradually increases with the decline in renal function due to inadequate renal excretion and high PTH levels. The relative risk of death resulting from coronary artery disease has been reported to increase by 41% in patients with serum phosphate levels greater than 6.5mg/dl, as has a 20% increase in mortality from sudden death. The relative risk of death increases by 5-8% for each 1mg/dl increase in serum phosphorus level above normal.

In dialysis patients, serum phosphorus is maintained in normal range by dietary phosphorus restriction of <1000mg/day, use of phosphate binders and by reducing the phosphorus flux from the bone by controlling hyperparathyroidism. Despite these measures, serum phosphorus control remains a challenge due to multiple factors including poor patient compliance with diet, lack of a good phosphate binder and the inability of dialysis to remove the daily phosphorus load.

It is not surprising that 60% of the dialysis patients have a phosphorus level of more than 6mg/dl.

Phosphate Binders

In 1970s and 80s, aluminum salts were widely used as phosphate binders; however, their use was discontinued because of osteomalacia and dementia.

In 1980s and 90s, calcium carbonate and calcium acetate (Phoslo) replaced aluminum as phosphate binders. Calcium salts are potent phosphorus binders but their use is associated with hypercalcemia in 17-40% of the patients, especially when a vitamin D analogue is concomitantly used to suppress PTH.

In response to the accumulating evidence linking mineral metabolism and CVD, the National Kidney Foundation **K/DOQI** (Kidney Disease Outcomes Quality Initiative) issued guidelines to restrict the daily calcium intake to less than 2000mg of elemental calcium and to maintain serum calcium, phosphorus and calcium-phosphorus product close to normal range.

New Phosphate Binders

In the last few years, **Sevelamer HCL (Renagel)** has emerged as an effective non-calcium containing binder. In a study comparing calcium acetate with sevelamer HCl, both were comparable in reducing phosphorus levels, but the group receiving calcium acetate had an incidence of hypercalcemia over 20% whereas those taking the sevelamer had an incidence of less than 5%. Sevelamer is relatively well tolerated and has the added benefit of lowering LDL levels. Its main disadvantages are GI side effects, metabolic acidosis and a high pill burden.

Lanthanum is a "rare earth element," which is found widely in nature. **Lanthanum Carbonate (Fosrenol)** was approved by FDA earlier this year for use as a phosphate binder in dialysis patients. Fosrenol is formulated as chewable pills and when taken with food, it binds the phosphorus throughout GI tract and has a very low systemic absorption. Its ability to lower phosphorus is comparable to calcium carbonate but the main advantage is significantly lower incidences of hypercalcemia (20.2% vs. 0.4%).

Lanthanum Carbonate was well tolerated in clinical studies for up to two years and has no major side effects reported so far.

Hyperparathyroidism and CKD

CKD is associated with an increase in PTH by multiple mechanisms, including hypocalcemia, hyperphosphatemia and low levels of active form of vitamin D (see Figure 1).

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Calcium Phosphate and Parathyroid Metabolism in Chronic Kidney Disease: New Treatment Options

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Hyperparathyroidism (HPTH) has also been shown to increase the risk of death in chronic kidney disease. Until recently, the only treatment options to control HPTH were calcium supplements, adjusting dialysate calcium concentration and the use of vitamin D sterols. This often caused mineral imbalance and may actually exacerbate calcification. Physicians were forced to make a trade-off between lowering PTH and controlling calcium-phosphorus product.

Calcium Sensing Receptors

Many different organs in the body contain receptors on their cell surface called calcium-sensing receptor (CaSr). Activation of this receptor on the parathyroid chief cells decreases synthesis and secretion of PTH. CaSr is sensitive to changes in serum calcium.

In 2004, **Sensipar (Cinacalcet)** became available for use in the United States. Cinacalcet belongs to a new class of medicines called calcimimetics. Calcimimetics are small organic compounds that can be administered orally and act as allosteric effectors to the calcium sensing receptors. They increase the sensitivity of the receptor to the extracellular ionized calcium and thus suppress PTH secretion without causing an elevation in the serum calcium or phosphorus.

In a recent randomized controlled trial, Cinacalcet lowered the PTH by 30% compared to placebo over an 18-week period. At the same time, the calcium-phosphorus product decreased by 12% instead of an increase seen when vitamin D analogues were used. This reduction reflects a change in calcium as well as phosphorus levels.

Though these new medicines have shown promising results in managing a very important problem of mineral metabolism in CKD, it remains to be seen if they will improve the high mortality rate in this population.

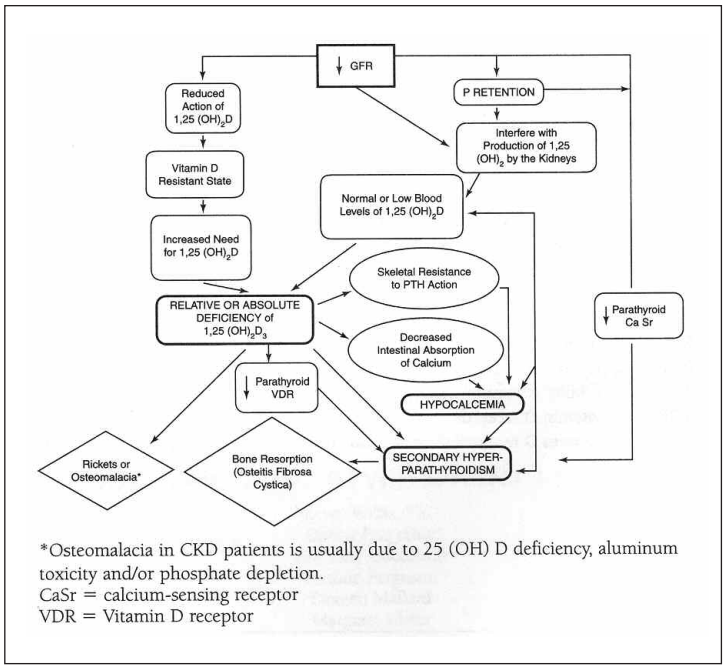

Figure1: Pathogenesis of Abnormalities in Mineral Metabolism and Bone Disease in CKD

For more information about these treatment options, please contact Dr. Muhammad Firoz at (402) 341-3141 or via email at muhammadfiroz@creighton.edu.

Current Research Opportunities Osteoporosis Research Center (ORC)

Web site: http://osteoporosis.creighton.edu

Clinical Trials

Bon-Mark

A six-month study to evaluate the change in bone turnover markers after once monthly oral ibandronate therapy in treatment naïve post-menopausal osteoporosis patients. For more information, please contact **Robert R. Recker, M.D.**, Principal Investigator, or **Jeanette LeMaster, RN, CCRC**, Study Coordinator, at (402) 280-4839.

Carb-Phos

A twelve-month study to determine whether the phosphorus-containing calcium supplements provide better skeletal protection than calcium alone with the use of Forteo(tm). For more information, please contact **Robert P. Heaney, M.D.**, Principal Investigator, or **Joy Egan, RN**, Study Coordinator, at (402) 280-4827.

Fosbon

A twelve-month study comparing the efficacy and safety of once monthly oral ibandronate with once weekly alendronate in postmenopausal osteoporosis. For more information, please contact **Robert R. Recker, M.D.**, Principal Investigator, or **Jeanette LeMaster, RN, CCRC**, Study Coordinator, at (402) 280-4839.

Nuclear Family

A genetic study looking for four to five members of a family that includes at least one parent. Children must be between the ages of 25

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Current Research Opportunities at the Creighton Osteoporosis Research Center (ORC)

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to 50. DXA scan and health promotion provided at a one-time visit. For more information, please contact **Robert R. Recker, M.D.**, Principal Investigator, or **Theresa Conway, BSN, RN, CCRC**, Study Coordinator, at (402) 280-4676.

Idiopathic Osteoporosis in Premenopausal Women

This study involves an intensive work up for the diagnosis of osteoporosis in **premenopausal** women. We are looking for women with low bone mass as well as those that are experiencing fragility fractures. For more information, please contact **Robert R. Recker, M.D.**, Principal Investigator, or **Jeanette LeMaster, RN, CCRC**, Study Coordinator, at (402) 280-4839.

IVZA

A two-year study to determine the efficacy and safety of zolendronic acid (Zometa™) that they receive intravenously once a year in postmenopausal women with **osteopenia.** For more information, please contact **Robert R. Recker, M.D.**, Principal Investigator, or **JoAnn Wilde, BSN, RN, CCRC**, Study Coordinator, at (402) 280-4959.

Long-term Bisphosphonate Study

This study is to compare the long-term effect of Fosamax(tm) and Actonel(tm) on bone quality. For more information, please contact **Robert R. Recker, M.D.**, Principal Investigator, or **Theresa Conway, BSN, RN, CCRC**, Study Coordinator, at (402) 280-4676.

PTH Bisphosphonate Study

A study to determine how prior therapy with Fosamax or Actonel in postemenopausal women with osteoporosis influences the clinical effectiveness of Forteo™. For more information, please contact **Robert R. Recker, M.D.**, Principal Investigator, or **JoAnn Wilde, BSN, RN, CCRC**, Study Coordinator, at (402) 280-4959.

Ultraviolet B rays (UVB)

Raising serum vitamin D levels using an ultraviolet light box. For more information, please contact, **Dr. Laura Armas**, Principal Investigator, at (402) 280-4241.

Skeletal Role of Low Endogenous Estrogen Levels In Elderly Women

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In summary, very small variations in endogenous serum estradiol determine the differences in BMD and age related bone loss and affect the response to treatment with estrogen. Thus, women with greatest degree of relative estrogen deficiency benefit the most with estrogen treatment compared to those who are better able to maintain their endogenous estradiol levels. For practical management, using ultra sensitive assays of serum estradiol allow better selection of women for treatment with estrogen. A serum estradiol level of less than 10 pg/ml is a reasonable cutoff point. By keeping in perspective with the findings of the Women's Health Initiative (WHI) and other studies of estrogen, it is likely that much smaller doses of estrogen could be used in elderly women for prevention of bone loss and this is likely to lead to fewer side effects. The use of serum estradiol measurement should allow for individual titration of the estrogen dose similar to that done for patients with hypothyroidism on thyroxine, using serum T_4 and TSH. Women on estrogen do not need to exceed a serum estradiol level greater than 20 pg/ml.

For more information, please contact Dr. Prema Rapuri via email at thiyyari@creighton.edu.

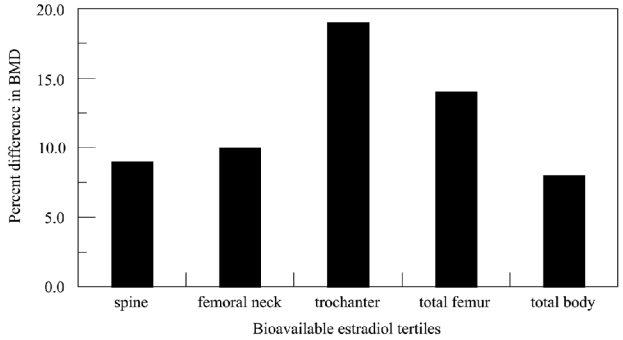

Figure 1: Relation between baseline serum bioavailable estradiol and BMD at various skeletal sites. The data represents the percent difference in BMD between the lowest (<2.4 pg/ml) and highest tertiles (>4 pg/ml) of serum bioavailable estradiol.

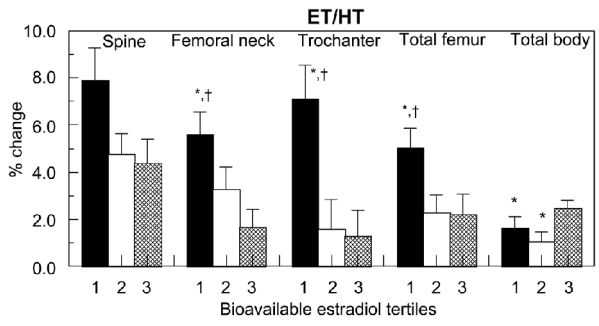

Figure 2: Mean percent change in BMD in women receiving the hormone therapy according to tertiles of serum bioavailable estradiol. * P<0.05 compared to tertile 3, † p<0.05 compared to tertile 3

Division News

Allergy and Immunology

Submitted by **Barb Dineen**

Faculty Activities

Publications

Townley RG, Barlan IB, Patino C, Vichyanond P, Basaran MM, Minervini MC, Simasathien T, Nettagul R, Bachceciler NN, Fyrat A, Basdemir D, Sezgin G, Pongprueksa S, **Hopp RJ**. The Effect of BCG at Birth on the Development of Atopy of Allergy Disease in Young Children, Annals of Allergy and Immunology, Ann Allergy Asthma, Immunology 92: 35-355, 2004.

Hopp RJ. Genetics and Epidemiology of Allergic Disease. Allergy and Immunology Secrets 2nd Edition. Eds: Naguwa SM, and Gershwin ME. Elsevier Mosby, pp1-7, 2004.

Presentations

Jeffrey R. Stokes, M.D.

Asthma and Allergy in Children: PTA – Parents, Omaha, Nebraska, September 21, 2004.

Awards

Thomas Casale, M.D.

Selected to Joint ERS/ATS Task Force on Asthma Control and Exacerbation Outcomes, 2004 - Present.

Jaros Memorial Lecturer Award, American College of Allergy, Asthma and Immunology (awarded 11-3-04), 2004.

Russell J. Hopp, D.O.

American Lung Association of Nebraska, Outstanding Volunteer Recognition, 2004.

Clinical Trials

A randomized, phase I, double-blind, placebo-controlled dose escalating study to examine the effects of a Toll-4 receptor agonist for ragweed-induced allergic rhinitis. For more information, contact **Thomas Casale, M.D.**, Principal Investigator, or **Jean Kessler, R.N.**, Study Coordinator, at (402) 280-5965.

A randomized, double-blind, placebo-controlled trial of omalizumab, an anti-IgE monoclonal antibody, for people allergic to peanuts. For more information please contact **Thomas Casale, M.D.**, Principal Investigator, or **Deb Law, L.P.N.**, Study Coordinator, at (402) 280-5964.

A randomized, double-blind, placebo-controlled trial examining the effects of omalizumab, an anti-IgE monoclonal antibody on airway hyperresponsiveness. For more information, please contact **Thomas Casale, M.D.**, Principal Investigator, or **Kristi Farrington, R.R.T.**, Study Coordinator, at (402) 280-3427.

A randomized, double-blind, placebo-controlled trial evaluating the effects of a novel bioavailable compound for patients with mild to moderate asthma. For more information, please contact **Thomas Casale, M.D.**, Principal Investigator, or **Kristi Farrington, R.R.T.**, Study Coordinator, at (402) 280-3427.

Cardiology

Web site: http://thecardiaccenter.creighton.edu

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

New Faculty

Monique G. Kusler, M.D.

The Division of Cardiology welcomes **Monique G. Kusler, M.D.**, Assistant Professor of Medicine. Dr. Kusler graduated with her medical degree from the University of North Dakota School of Medicine and completed both her Internal Medicine Residency and Cardiovascular Fellowship at the University of Nebraska Medical Center. She was appointed Chief Cardiology Fellow during her final year of fellowship, received the Outstanding Fellow Teaching Award in 1998 and was honored as the 2002 Teacher of the Year in Cardiology from the University of Nebraska Medical Center. Dr. Kusler is board certified in Internal Medicine and Cardiovascular Medicine. Her specialty is echocardiography with an interest in women and heart disease.

Staff News

Athena Ramos has joined The Cardiac Center as a health educator to support two grants from the Nebraska Health and Human Services System funded through June 2006. The grants are part of the Tobacco Free Nebraska program and are designed to implement strategies to reduce tobacco use and exposure to tobacco smoke in Douglas and Sarpy county schools and communities, while working to eliminate health disparities.

Excellence in Nursing Awards

The Nebraska Chapter of the March of Dimes held its first annual Excellence in Nursing Awards dinner on November 20, 2004. The awards reflect the level of respect and appreciation these nurses have attained for their accomplishments. Fifty-two Omaha-area nurses were nominated in 17 categories, including four nurses from The Cardiac Center: Lisa Christiansen (Cardiac), Karen Hardy (Rehabilitation), Lori Umberger (Management) and Tami Ward (Advanced Practice).

Milagro Award

The Cardiac Center of Creighton University Medical Center was honored by OneWorld Community Health Center as the recipient of the 2004 Milagro Award. The award was presented at OneWorld's annual Milagro Dinner on Wednesday, November 17, 2004. OneWorld Community Health Center (formerly known as the Indian-Chicano Health Center) provides culturally-respectful, quality health care to underserved populations in the Omaha area. The Milagro Award is presented to individuals or organizations that give unselfishly of themselves to provide services to OneWorld's patients that the center is not equipped to give.

Heart Month Activities

The yellow rubber bracelets made popular with cyclist Lance Armstrong's LiveStrong campaign have become a fashion statement. To celebrate American Heart Month, The Cardiac Center at Creighton University Medical Center is making its own statement with red

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Division News

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bracelets for heart health. The inscription on the bracelets reads, "HEART HEALTH – YOU HAVE THE POWER," and is meant to raise awareness of heart health while empowering the wearer to take charge of his or her own well-being by committing to a heart-healthy lifestyle. The bracelets cost $1 each and can be purchased at The Cardiac Center reception desk and the CUMC gift shop. Proceeds will go to the American Heart Association.

Other Heart Month-related events included the second annual Girls' Night Out, a fundraiser sponsored by The Cardiac Center and the local chapter of the American Heart Association, and the ICAN Conference, a day-long event sponsored by The Institute for Career Advancement Needs, Inc. (ICAN).

Emergency Alarm System

In January 2005, an updated Emergency Alarm System was put into operation in the CUMC cardiac nursing pods. This system designed by the CCC Information Technology team is compatible with the hospital monitoring system installed in July 2003. The stand-alone alarm system allows cardiac technicians to notify the nursing unit of life-threatening arrhythmias using a touch screen monitor. Once the alarm is enabled, the bed number is displayed and a distinct audible tone is activated until it is manually disabled by a nurse.

Expansion of ICD Coverage

On January 27, 2005, the Centers for Medicare and Medicaid Services (CMS) released the final coverage policy regarding the implantation of implantable cardioverter defibrillators (ICD) for primary prevention. The inclusion of patients who have low ejection fractions, class II and class III heart failure and cardiomyopathy allows those who were previously not eligible for ICD therapy to receive this life-saving device. This policy change was made in the wake of the publication of the SCD-HeFT trial. This trial revealed that patients with this profile who had received an ICD had a 23% decrease in mortality.

Cardiovascular Fellowship Training Program

The Cardiovascular Fellowship Program has been approved by the RRC to increase the program by one fellow each academic year beginning in 2004-2005. At the conclusion of the 2006-2007 academic year, the program will consist of 12 fellows.

Interventional Cardiovascular Fellowship Training Program

In July 2005, The Cardiac Center will begin an Interventional Cardiovascular Fellowship Training Program. One fellow will be accepted into the one-year program and will be assigned primarily to the Catheterization Lab.

Faculty Activities

Publications

Lanspa TJ, **Reyes AP**, Oldemeyer JB, **Williams MA**. Ulnar artery catheterization with occlusion of corresponding radial artery. *Catheter Cardiovasc Interv* 2004;61:211-213.

Leon AS, Franklin BA, Costa F, Balady GJ, Berra KA, Stewart KJ, Thompson PD, **Williams MA**, Lauer MS. Cardiac rehabilitation and secondary prevention of coronary heart disease. *Circulation* 2005;111:369-376.

Lanspa TJ, **Esterbrooks DE**, **Williams MA**. Stenting of the left carotid artery to relieve anginal symptoms. *Catheter Cardiovasc Interv* 2005;64:223-226.

Lanspa TJ, **Williams MA**, Heirigs RL. Effectiveness of ulnar catheterization after failed attempt to cannualte a radial artery. (accepted) *Am J Cardiol* June, 2005.

Chapter Publications

Williams MA. Cardiovascular and respiratory structure and function. In: R Earle, T Baechle (eds.) *Essentials of Personal Training*. Human Kinetics Publishers. Champaign, IL. 2004;19-34.

Presentations

Buckley MS, Nolan PE, Slack MK, Tisdale JE, **Hilleman DE**, Copeland JG – Amiodarone dose response for preventing atrial fibrillation following cardiac surgery: a meta-analysis. ACCP annual meeting, Dallas TX, October 26, 2004.

Buckley MS, Nolan PE, Slack MK, Tisdale JE, **Hilleman DE**, Copeland JG – Prophylactic amiodarone decreases atrial fibrillation and hospital length of stay following cardiac surgery: a meta-analysis. ACCP annual meeting, Dallas TX, October 26, 2004.

Faulkner MA, **Hilleman DE.** – Fixed-dose combination antihypertensive therapy with trandolapril/verapamil: a meta-analytic comparison against monotherapy. ASHP mid-year clinical meeting, Orlando FL, December 7, 2004.

Faulkner MA, **Hilleman DE**, **Reyes AP.** – Cost-effectiveness of a fixed-dose combination agent in high-risk hypertensive patients. ASHP mid-year clinical meeting, Orlando FL, December 7, 2004.

Lakkireddy D, **Shen XD**, **Huagui Li**, Thambidorai S, Cloutier D, **Holmberg MJ**, **Mooss AN**, **Mohiuddin SM**. Carotid artery stenosis, left atrial thrombus and aortic plaques: the impact of co-existing risk factors on the incidence of embolic stroke. Presented in American Heart Association 77th Annual American Scientific Session in 2004. Circulation 2004; 110 (17): III-376.

Lakkireddy D, Valasareddi S, **Shen XD**, Korlakunta H, **Li HG**, **Mohiuddin SM**. Cleaning Subcutaneous Pockets with Povidone-Iodine Prior to an Implantable Device Doesn't Improve Pocket Infection Rates. Presented in 53rd Annual Scientific Sessions of American College of Cardiology in 2004. J Am Coll Cardiol 2004; 43(5): 140A.

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Shen XD, Xie F, Lof J, Porter TR, Jiang L. – Cyclic variation and measurement of myocardial blood flow by real-time contrast echocardiography: comparison with neutron activated microspheres. Presented in 53rd Annual Scientific Sessions of American College of Cardiology in 2004. J Am Coll Cardiol 2004; 43(5): 310A.

Clinical Studies

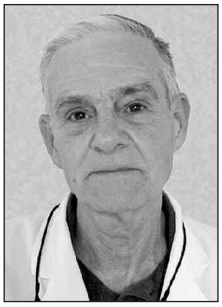
The Home Automatic External Defibrillator Trial (HAT) studies the survival from risks of previous myocardial infarction, either through emergency training and CPR, versus training and use of an AED. For more information, please contact **Syed Mohiuddin, M.D.**, Principal Investigator, or the Study Coordinator, **Sandy Byers, R.N., B.S.N.**, at (402) 280-4961.

The Division of Cardiology is conducting a study to assess the relationship between lipoproteins and the function of blood vessels in both smokers and non-smokers of Asian Indian or African American descent. Non-smokers are provided a stipend for time and travel, while smokers are provided smoking cessation courses at no cost. For more information, please contact the Study Coordinator, **Stephanie Maciejewski, Pharm.D.**, at (402) 280-4292.

The ARISE trial studies the reduction of vascular inflammation and coronary atherosclerosis with AGI-1067, a vascular protectant, in patients with coronary artery disease. For more information, please contact **Syed Mohiuddin, M.D.**, Principal Investigator, or the Study Coordinator, **Eddy Butkus, R.N., B.S.N.**, at (402) 280-4665.

The MADEITT is a study to evaluate the effect of valsartan and hydrochlorothiazide, combined and alone, on insulin sensitivity in patients with metabolic syndrome (waistline greater than 35 inches for women or 40 inches for men, and one of the following: elevated triglycerides, elevated blood glucose, or low levels of HDL). For more information, please contact the Study Coordinator, **Eddy Butkus, R.N., B.S.N.**, at (402) 280-4665.

The Trial to Reduce Cardiovascular Events with Aranesp Therapy (TREAT) protocol aims to assess the effect of anemia therapy with Aranesp(r) on long-term cardiovascular events in patients with type II diabetes and chronic kidney disease. For more information, please contact the Study Coordinator, **Sandy Byers, R.N., B.S.N.**, at (402) 280-4961.



James J. Woodbury, M.D.

Gastroenterology Division

Submitted by **Mary Ann Scramstad**

Dr. James J. Woodbury Returns

We are pleased to welcome back **James J. Woodbury, M.D.** who retired in May 2004. He is returning under a new division chief, Dr. John O'Brien who joined Creighton in August 2004. Dr. Woodbury will be returning to patient care and will be actively involved in resident and student teaching. In addition, Dr. Woodbury plans to participate in the Gastroenterology fellowship program after it is implemented. If you would like to schedule an appointment with Dr. Woodbury, please call the Gastroenterology clinic at (402) 449-4692.

General Internal Medicine

Submitted by **Mary Ann Scramstad**

Faculty Activities

Joann Porter, M.D.

We are pleased to announce that **Joann Porter, M.D.** has been promoted to section chief of Creighton University General Internal Medicine at the Omaha Veterans Administration Medical Center (VAMC). As a full-time Creighton faculty member, she will continue her educational duties, including those of associate program director of the internal medicine residency program. Dr. Porter's new clinical duties will include outpatient clinic and the inpatient service at the Omaha VAMC. After March 15, 2005, she will no longer see patients at Creighton Family Healthcare – South. This is a great opportunity for Dr. Porter.

We are also fortunate to announce **Temple Brannan, M.D.**, who joined Internal Medicine in July 2004, will move her practice to the Creighton Family Healthcare – South Clinic to join Drs. Theresa Townley and Martina Tribulato. If you would like to schedule an appointment, please call the Creighton Family Healthcare – South Clinic at (402) 449-5750.

Hematology/Oncology

Submitted by **Mary Ann Scramstad**

New Faculty

The Division of Hematology/Oncology is pleased to announce the addition of two new physicians, **Peter M. Townley, M.D.** and **Luke T. Nordquist, M.D.** Drs. Townley and Nordquist joined the Creighton family along side their father (father-in-law), Dr. Robert Townley, Division of Allergy and Immunology, and sister (sister-in-law), Dr. Theresa Townley – Creighton Family Healthcare – South and Program Director for the Medicine/Pediatrics Residency Program.

Peter M. Townley, M.D.

In July 2004, **Peter M. Townley, M.D.** joined Division of Hematology/Oncology as a part-time physician. Dr. Townley was born in Boston, Massachusetts and he and his wife, Annette, have three sons and three daughters. Dr. Townley graduated from Creighton Prep High School and received his Bachelor of Science degree from Creighton University. After receiving his Medical Degree from Creighton University School of Medicine, he completed his residency in Internal Medicine and fellowship in Hematology/Oncology at the Mayo Clinic in Rochester, Minnesota. Dr. Townley is board certified by the American

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Board of Internal Medicine and Medical Oncology. In addition, he is a member of the American College of Physicians, American Medical Association, and the American Society of Clinical Oncology and serves as a member of the Executive Committee for Creighton University School of Medicine. Dr. Townley's practice will focus on the treatment and management of oncology patients with solid tumors as well as patients with hematological diseases.

Luke T. Nordquist, M.D.

In August 2004, **Luke T. Nordquist, M.D.** joined the Hematology/Oncology Division as a part-time physician. Dr. Nordquist was born in Beresford, South Dakota and he and his wife, Rachel, have one son and one daughter. Dr. Nordquist received a Bachelor of Science degree in pharmacy from Creighton University School of Pharmacy. After receiving his Medical Degree from Creighton University School of Medicine, he completed his internship, as well as residency in Internal Medicine at the University of South Florida/H. Lee Moffitt Cancer Center in Tampa, Florida. Then, Dr. Nordquist completed his Medical Oncology/Hematology Fellowship at Memorial Sloan Kettering Cancer Center in New York City and returned to Omaha to practice medicine. Dr. Nordquist is board certified in Internal Medicine and Medical Oncology and board eligible in Hematology. He is a member of the American Society of Clinical Oncology and the American Society of Hematology. As a member of the Hematology/Oncology Division, Dr. Nordquist will provide treatment and care to various oncology patients and he has a particular interest and expertise in bladder and prostate cancer.

Please welcome Drs. Townley and Nordquist to the Division of Hematology/Oncology. Both are available to see patients in the Hematology/Oncology clinic located at the Creighton University Medical Center, 601 North 30th Street, Suite 2565. If you would like to schedule an appointment with Dr. Townley or Dr. Nordquist, please call the Creighton Hematology/Oncology clinic at 280-4364.

Infectious Diseases

Submitted by **Gary Gorby, M.D.**
and **Marvin Bittner, M.D.**

Symposium

The Division of Infectious Diseases of the Department of Medicine and the Department of Medical Microbiology and Immunology hosted the 25th Annual Infectious Diseases Symposium on April 22, 2005 at the Embassy Suites Downtown Old Market. The program included the following topics and speakers:

- **Adolescent Immunizations** by Archana Chatterjee, M.D., Ph.D., Creighton University Medical Center, Omaha, Nebraska
- **Prevention of Ventilator Associated Pneumonia (VAP)** by Victoria J. Fraser, M.D., Washington University School of Medicine, St. Louis, Missouri
- **Update on Sexually Transmitted Diseases** by Matthew R. Golden, M.D., University of Washington, Seattle, Washington
- **Community Acquired MRSA in Pediatrics** by Sheldon L. Kaplan, M.D., Baylor College of Medicine, Houston, Texas
- **Predicting Outcomes of Hepatitis C (HCV)** by Mark E. Mailliard, M.D., University of Nebraska Medical Center, Omaha, Nebraska
- **Infectious Disease Issues of Refugees on Arrival to the United States**, William M. Stauffer, M.D., M.S.P.H., D.T.M.&H., University of Minnesota, Minneapolis, Minnesota

For more information, please contact the CME Office at 280-1830 or Dona Goodrich at 449-0650.

Computer Updates

In January 2005, the Omaha Veterans Administration Medical Center (VAMC) took another step toward a truly paperless medical record by replacing paper progress notes with electronic notes. To facilitate this move, the Medicine Department at the Omaha VAMC developed templates for rapid entry of data, often using so-called "objects." For example, with the click and drag of a mouse, a resident can incorporate a patient's current medication list into a progress note.

In addition, the Omaha VAMC has moved to computerized physician order entry, so-called CPOE, which replaces paper order sheets with computer systems. CPOE has the potential to eliminate certain types of errors. Misinterpreted handwriting can never occur in a system that doesn't use handwritten orders. The computer system can generate an immediate warning if a physician writes an order for penicillin in a penicillin-allergic patient.

Faculty Activities

Marvin J. Bittner, M.D.

Marvin J. Bittner, M.D. was appointed chief of infectious disease at the Omaha VAMC. Dr. Bittner earned his M.D. at Harvard Medical School, completed his internal medicine residency at the University of Michigan, and completed his infectious diseases fellowship at the University of Minnesota. He is a Fellow of the American College of Physicians, a Fellow of the Infectious Diseases Society of America, and a Fellow of the Society for Healthcare Epidemiology of America. Twenty-two years after graduating from medical school, he moved into his old dorm for a couple summers to complete the coursework for his master's degree in epidemiology from the Harvard School of Public Health's Program in Clinical Effectiveness. His master's research project was published as the lead article in the March 2002 *Infection Control and Hospital Epidemiology* and was accompanied by a favorable editorial-even though it reported negative results.

Dr. Bittner has garnered a half-dozen teaching awards and nominations, was the key developer of the Travel Clinic at the Douglas County Health Department, and was honored as one of "The Best Doctors in America." He is editor of the Metro Omaha Medical Society's bimonthly magazine, Editorial Review Group chair for infectious diseases for Doody Enterprises, a member of the editorial board of

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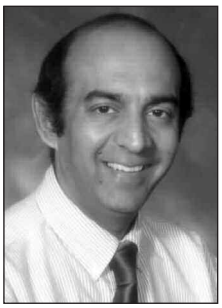
this newsletter, a member of the membership committee of the Society for Healthcare Epidemiology of America, and chair of the communications committee of the International Health Medical Education Consortium. He has traveled over a half-dozen times to the Dominican Republic and Nicaragua with medical students providing services for impoverished communities. In his role as hospital epidemiologist at the Omaha VAMC, he spearheaded a smallpox immunization program that was more than 25 times as successful as the national program and which immunized more than three times as large a segment of healthcare workers as the next most successful hospital in Omaha. This winter, he wrote a one-page guide to anti-influenza drugs that was distributed nationally to VA's by the Acting Under Secretary for Health.

Nephrology

Submitted by Mary Ann Scramstad

New Faculty



Khalid Bashir, M.D.

The Department of Medicine is pleased to welcome **Khalid Bashir, M.D.**, who joined the Nephrology Division on April 1, 2005 after several years in private practice in Delnorte, Colorado.

Dr. Bashir received his medical education at King Edward Medical College at Lahore, Pakistan and completed his residency in Pakistan. He then moved to the United States to finish his internal medicine internship at the Hospital of Saint Raphaels in New Haven, Connecticut and an internal medicine residency at Danbury Hospital in Danbury, Connecticut. After completing a nephrology and hypertension fellowship at the University of Colorado Health Sciences Center in Denver, Colorado, Dr. Bashir completed a critical care fellowship at the University of Massachusetts Medical Center in Worcester, Massachusetts in 1998. He then went into private practice and has been affiliated with the University of Colorado School of Medicine since 1999.

Pulmonary and Critical Care Medicine

Submitted by **Dan Schuller, M.D.**

Clinical Trials

A Multidisciplinary Intervention to Optimize the Recovery of Elderly Patients Hospitalized with Community Acquired Pneumonia. For more information, please contact **Lee E. Morrow, M.D.**, Principal Investigator, at (402) 449-4486.

Multi-Center Clinical Trial of the Bard Silver-Coated Endotracheal Tube to Reduce Ventilator Associated Pneumonia (VAP). For more information, please contact **Lee E. Morrow, M.D.**, Principal Investigator, at (402) 449-4486.

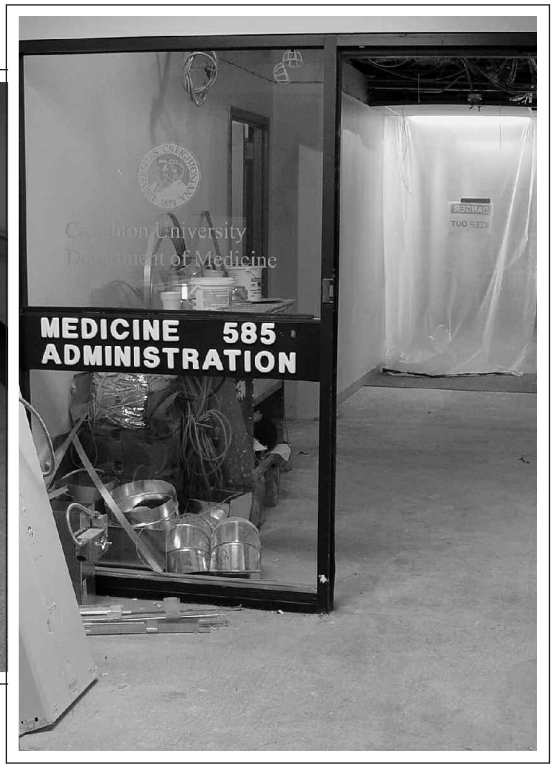
Lactobacillus GG in the Prophylaxis of Ventilator Associated Pneumonia: A Prospective, Randomized, Placebo Controlled, Double-Blind Study. For more information, please contact **Lee E. Morrow, M.D.**, Principal Investigator, at (402) 449-4486.

A Multicenter, Randomized, Controlled Trial Comparing the Safety and Effectiveness of Surfaxin (Lucinactant) Delivered Via Bronchopulmonary Segmental Lavage to Standard of Care in Patients with Acute Respiratory Distress Syndrome (ARDS). For more information, please contact **Dan Schuller, M.D.**, Principal Investigator, at (402) 449-4487.

A Randomized Double-Blind, Placebo-Controlled Study to Determine the Efficacy and Safety of Epoetin Alfa in Critically Ill Subjects. For more information, please contact **Dan Schuller, M.D., Principal Investigator**, at (402) 449-4487.

A Randomized, Double-Blind, Parallel Group, 52-week Study to Compare the Effect of the Fluticasone Propionate/Salmeterol DISKUS Combination Product 250/50mcg BID with Salmeterol DISKUS 50mcg BID on the Annual Rate of Moderate/Severe Exacerbations in Subjects with Chronic Obstructive Pulmonary Disease (COPD). For more information, please contact **Dan Schuller, M.D.**, Principal Investigator, at (402) 449-4487.

Renovation of the Department of Medicine Administration Suite



The Department of Medicine is near completion of the renovation of its administration suite area. The project began in late February and will finish in early May. Renovated areas include the classroom, computer lab, small conference room and room 5849. The Medicine Department appreciates the patience of staff and physicians for this temporary inconvenience.

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