

Academic Physician Quarterly

A DEPARTMENT OF MEDICINE BULLETIN



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FLORIDA
College of Medicine
Jacksonville

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CHAIRMAN'S MESSAGE

Dear colleagues:

I am proud to share with you an exciting program at our institution. Shands Jacksonville Cardiovascular Center, recognizing the needs of women in our community, created the Women's Cardiovascular Health Program. In this issue, Dr. Gladys Velarde, University of Florida Associate Professor of Medicine in the Division of Cardiology, describes the rationale for establishing this program and the current services offered. Working in close collaboration with the Shands Jacksonville Cardiac Rehabilitation Program, the Sleep Disorders Center, the YMCA Fitness Center, the UF&Shands Jacksonville Employee Wellness Program, the Valvular Heart Disease Program and Cardiothoracic Surgery, the Women's Cardiovascular Health Program offers individualized, advanced, and gender-specific care to our female patients with a variety of risk profiles.



The scholarly activities of our trainees are described by Dr. Nilmarie Guzman in this issue's GME Corner. Our residents continue to present their research in regional and national meetings. The exceptional performance of our residents would not have been possible without the dedication and commitment of our faculty members. We are proud to report that this year, 14 members of the Department of Medicine were recipients of the 2013 University of Florida College of Medicine's Exemplary Teachers Award for their exceptional contributions to the teaching mission of the university.

Also in this issue is an update on drug therapy of dyslipidemia in people with diabetes. This is a timely review of the topic especially considering the recent release of data from drug trials targeting the lipid disorders.

I believe we have put together an interesting and informative issue of the Academic Physician Quarterly and I hope you will find it an informative and enjoyable read.

Arshag D. Mooradian, MD
Professor of Medicine
Chairman, Department of Medicine



Gladys Velarde, MD
Associate Professor of Medicine

Division of Cardiology

Department of Medicine

University of Florida College of
Medicine-Jacksonville

Heart Disease in Women - An Old Mysterious Foe

Cardiovascular disease is the number one killer of women and men in the United States, far outdistancing all other causes of death, including every kind of cancer combined. Since 1984, more women die of cardiovascular disease (CVD) than men. The statistics are particularly sobering when seen as one female death from CVD in the U.S. every minute. That represents over 420,000 deaths per year. Of these deaths more than one quarter of a million are due to coronary heart disease (CHD). Additionally, roughly 64% of women who die suddenly of CHD will have no prior symptoms.

Due to improved therapies, preventive strategies and public awareness over the last decade, CVD mortality overall has been on the decline. Unfortunately, that decline has been less prominent for women. This is, in large part, due to poorly understood gender differences in clinical presentation, as well as management and application of therapeutic and preventive strategies. Another important contributing factor has been the under representation of women in CVD research to date.

WHAT'S DIFFERENT IN CHD IN WOMEN?

The development of CHD in women may lag 10 to 15 years behind that of men, but after menopause the atherosclerotic process appears to significantly accelerate.

Among black women death rates are about 15% greater than those of white women, and stroke rates are 30% greater than for white women. When Hispanic women are included, i.e. Caribbean, South American and Mexican-Americans, statistics are not seen to be more favorable for them, with rates lying somewhere between black women and white women.

Special consideration needs to be given to racial differences and to metabolic profiles. Diabetic women deserve special consideration given the alarming CV morbidity and mortality that affects this population. The metabolic syndrome, especially in postmenopausal women, should receive special attention with emphasis

on early recognition (high triglycerides, low HDL, insulin resistance, abdominal obesity, and hypertension) and intervention due to its strong association with diabetes and increased risk for CVD events. For reasons still not completely understood, these recognizable and treatable risk factors appear to hit women harder.

Several biological variables and pathophysiological mechanisms differ in women and continue to remain poorly understood. Obvious differences, such as vessel size and increased number of co-morbidities in the older female, do not entirely explain the gender differences we see in terms of frequency and type of angina and heart failure signs and symptoms. Both differences are often discordant with the smaller number of obstructive coronary artery lesions found in women by coronary angiography and also with the better left ventricular systolic function in women as seen on echocardiography.

Disorders such as gestational diabetes, hypertension, preeclampsia or eclampsia commonly occur during pregnancy and significantly increase the risk of cardiovascular events later in life. Similarly, psychosocial factors, such as anxiety, depression, inadequate social and economic resources, caregiver stress, marital stress, and adversities early in life are highly prevalent in women.

A significant number of health care professionals still fail to recognize symptoms of CVD in women of all ages, leading to under-diagnosis of acute coronary syndromes and subsequently delayed treatment. Finally, according to the most recent AHA survey, despite increased awareness of CVD in women, almost 50% of U.S. women currently fail to recognize CVD as their major health problem. The level of awareness is even lower in minority women, putting them at a distinct disadvantage.

CALL FOR ACTION

To address the needs of women in our community, the Shands Jacksonville Cardiovascular Center created the Women's Cardiovascular Health Program in January of 2012.

We offer an innovative approach to women with established CVD as well as those who need aggressive preventive care. Working in close collaboration with the Shands Jacksonville Cardiac Rehabilitation Program, Sleep Disorders Center, YMCA Fitness Center, UF&Shands EmployeeWellness Center, Valvular Heart Disease Program and Cardiothoracic Surgery, we are ideally suited to offer individualized, advanced, gender-specific care to those female patients with a variety of risk profiles.

Our Program offers:

- a) Comprehensive risk assessment, diagnostic

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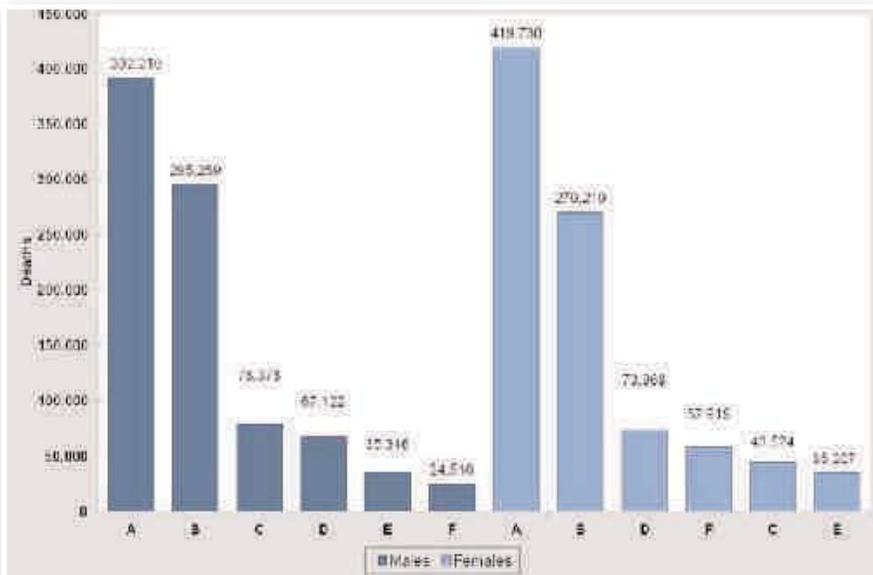
screening, primary and secondary prevention and risk reduction. Evidence-based treatment strategies

- b) Comprehensive care, evaluation, treatment and follow-up of patients with peripartum cardiomyopathy, as well as women with high cardiovascular risk pregnancies from other reasons (congenital valvular disease and/or cardiomyopathies)
- c) Referral services to advanced testing and intervention such as complex coronary or vascular procedures, valvular surgical consultation, and electrophysiology interventions when deemed appropriate
- d) Education of patients and providers
- e) Community outreach
- f) Clinical research enrollment and participation

Our active and successful clinical research in platelet biology, thrombosis, metabolic issues unique to women, and advanced interventional coronary and vascular treatment as well as arrhythmia management by our EP service, gives our patients a unique access to the most advanced and up-to-date therapeutic and research interventions.

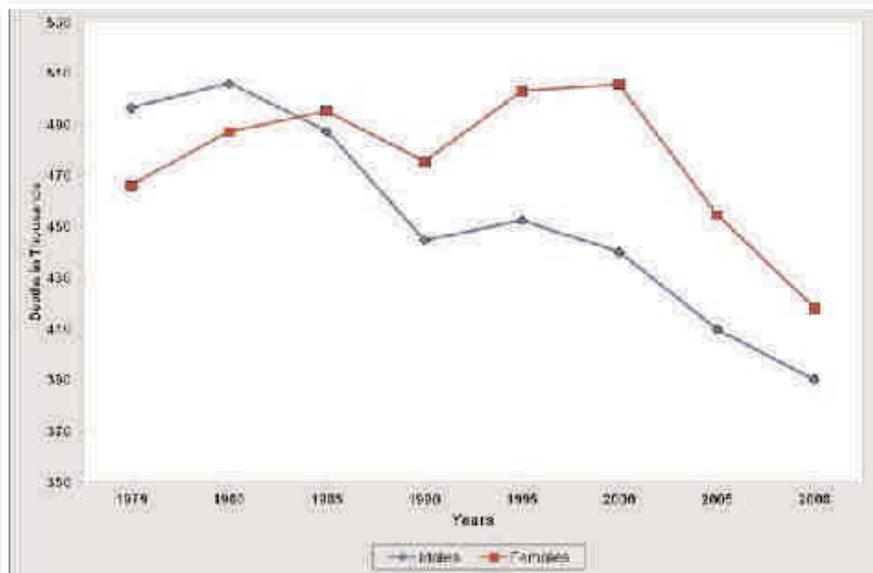
We believe that local and national educational and research efforts in cardiovascular health in women and minority populations will not only serve us well as we head into a very challenging future, but are paramount to keeping pace with an evolving field. As we face an older, more obese, more diverse, and more cardiometabolically-impaired population, we believe we need to be prepared to prevent disease in massive groups of patients will be disproportionately accruing risk if we do not intervene in time.

MAJOR CAUSES OF DEATH FOR MALES AND FEMALES 2008



A indicates cardiovascular disease plus congenital cardiovascular disease (ICD-10 I00-I99, Q20-Q28);
 B indicates cancer (C00-C97);
 C indicates accidents (V01-X59, Y85-Y86);
 D indicates chronic lower respiratory disease (J40-J47);
 E indicates diabetes mellitus (E10-E14);
 F indicates alzheimer disease (G30 Source: NCHS).

CARDIOVASCULAR DISEASE MORTALITY TRENDS FOR MALES AND FEMALES UNITED STATES: 1979-2008



CVD excludes congenital cardiovascular defects (ICD-10 I00-I99). The overall comparability for cardiovascular disease between the ICD, 9th Revision (1979-1998) and ICD, 10th Revision (1999-2008) is 0.9962. No comparability ratios were applied. (Source: NCHS)



Nilmarie Guzman, MD

**Assistant Professor of Medicine
Division of Infectious Disease**

**Associate Program Director
Internal Medicine Residency**

Research Activity in our Residency Program

As the incoming Associate Program Director for the Internal Medicine Residency, I would like to preface this message by expressing my gratitude to the GME leadership and administrative staff for your warm welcome and assistance during this transition.

One of the main goals of the Internal Medicine Residency Program is to motivate and assist our trainees in research and scholarly activities. Our residents have been striving to achieve academic excellence and be prolific in research activity.

During this year's Southern Regional Meeting, our program was well represented by three of our residents. Jason D. Hew, MD, had an abstract presentation titled: "Secondary Cutaneous Diffuse Large B Cell Lymphoma Initially Described as a T cell Histiocyte Rich B Cell Lymphoma." Jean Touchan, MD, had a poster presentation on "First Case of Hafnia Alvei Urosepsis in the United States." Bilkisu Saye, MD, presented a poster on rapidly reversible cardiomyopathy. Our second year resident Paul Maraj, MD, had an oral abstract presentation on *Coccidioides immitis* meningitis.

Research and scholarly activity continues gaining momentum among our residents. Aisha Khan, MD, had an electronic publication for the Duval County Medical Society, about an interesting case of keratoacanthoma. She also presented an oral abstract during the Florida ACP meeting held in March. Dr. Khan presented the data obtained so far on a quality improvement project titled: "Institution of a Sustainable Chart Review Process at an Internal Medicine Residency Program." This project has been carried out at the internal medicine continuity clinic and focuses on preventative measures. It can potentially be a model for other training programs in the future. During the same meeting, our program was also represented by Sharica Brookins, MD, and Wesley Thompson, MD, who had poster presentations and Ke Ning, MD, who presented an oral abstract. The Doctor's Dilemma team this year included Paul Maraj, MD, Kaitlin McCurdy, MD, and Jean Touchan, MD.

Our residents are highly motivated in continuing research projects in various areas of interests. Topics range from general internal medicine to subspecialties or quality improvement projects. Our program focuses on assisting and mentoring our trainees with their research interests and providing the tools needed.

Witnessing our residents' research accomplishments is one the most rewarding experiences we can have in our career as a faculty member or mentor. We are extremely proud of our trainees and exhort them to continue pursuing excellence in clinical practice and research activity.

Please join me in congratulating our residents for their excellent representation of our program.

A CLINICAL CASE

Cristian Landa, MD, Assistant Professor

Division of General Internal Medicine, Department of Medicine, University of Florida COM, Jacksonville

Asymmetric Arthritis in a Patient with Hidradenitis Suppurativa

CASE HISTORY

A 47-year old African-American man, who is a former Massachusetts resident with a medical history of hidradenitis suppurativa and rheumatoid arthritis, presented with pain and swelling of the left wrist, left knee and both ankles. The onset was six days ago, initially

involving swelling of the left knee progressing to his ankles and, lastly, the left wrist. Three days later, he developed redness of the left eye and purulent discharge from the cutaneous lesions involved by HS. He denied any fever, weight loss, night sweats, back stiffness or pain, recent outdoor activity, rash, urethral discharge, or intercourse with multiple sexual partners. On physical examination he was a thin, middle-aged male in no acute distress. He had injected left conjunctiva without discharge and had bilateral ankle, left knee, and left wrist swelling with tenderness to palpation. He also had fibrous skin gluteal folds, axillae, genitalia, and inguinal region with active purulent discharge. The rest of the physical

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examination was normal. The labs included CBC: normal; ESR 108; C-reactive protein 114; RF (+) 1:8 titer, anti-CCP (-); ANA (-), HLA-B27 (-), HIV (-), Lyme titers (-); complement levels: normal.

DISCUSSION

Hidradenitis suppurativa is a chronic inflammatory process involving sebaceous and apocrine glands and is generated at the level of the hair follicle. Follicular contents spill into the surrounding dermis, producing a chemotactic response. The condition is characterized by comedo-like follicular occlusion, relapsing inflammation, fistulization, scar production, and mucopurulent



Figure 1: Radiography of left foot. Periosteal reaction involving the proximal phalanges of 2nd, 3rd, 5th digits with periarticular osteopenia 2nd-5th metatarsal-phalangeal joints



Figure 2: Radiography-left hand. Periarticular soft tissue swelling with erosions at 4th and 5th proximal interphalangeal joints.

discharge. Bacteria play a secondary pathogenic role. The disease affects approximately 1% of the population with a predilection in African Americans with women>men in 3:1 ratio.

Reactive arthritis, formerly known as Reiter's syndrome, is a non-purulent joint inflammation associated with GI

or GU bacterial infections. The triad of clinical symptoms includes conjunctivitis, arthritis and urethritis. Conjunctivitis is usually mild and transient, and urethritis usually involves mucopurulent discharge in men with variable presentation in women

The association of reactive arthritis and hidradenitis was first described in 1982 at which time only 10 cases had been reported in the literature. Most patients afflicted are in their third and fourth decade of life. The onset of reactive arthritis follows the cutaneous manifestations of hidradenitis suppurativa by 10-20 years. Classic reactive arthritis triad does not occur in all patients. There are no specific diagnostic tests. ESR and C-reactive protein usually elevated, WBC normal to mildly elevated are normocytic and normochromic anemia. Synovial fluid analysis is commonly sterile and non-inflammatory.

NSAIDs are mainstay first-line therapy. Initial infections can be treated with antibiotics, but long-term antibiotics are not recommended. Response to corticosteroids is variable and methotrexate is occasionally used in refractory cases but also has variable efficacy.

The patient described here was initiated on an NSAID and the cutaneous lesions with active discharge were treated with clindamycin. He made rapid improvement after institution of prednisone and was discharged home on tapering course.

CONCLUSION

Recognition of reactive arthritis associated with HS remains a challenging diagnosis. The combination of clinical presentation, asymmetric oligoarthropathy, typical radiographic findings and laboratory data discarding other potential disease presentations aids in the definitive diagnosis of reactive arthritis. Most patients commonly do well with NSAIDs but other patients with more aggressive disease may benefit from immunosuppressive therapy with variable outcomes.

RX UPDATES

Joe M. Chehade, MD, Margaret Gladysz, MD, and Arshag D. Mooradian, MD - Department of Medicine

Drug Therapy of Diabetic Dyslipidemia

Excerpted with some editing from "Dyslipidemia in Type 2 Diabetes," published in DRUGS 2013.

There are a large number of lipid modifying agents in various formulations available for the management of dyslipidemia. The fundamental role of LDL-c in atherogenesis and utility of statins in reducing CVD risk is well established in clinical trials.

The current consensus is to recommend the following targets for therapy for highest-risk individuals, including those with known CVD or those with one or more additional CVD risk factor: LDL-c < 70 mg/dL, non HDL-c < 100 mg/dL and apo B < 80 mg/dL. For low-risk individuals who are less than 40 years of age, with no other major CVD risk factors, the recommended target LDL-c is < 100 mg/dL, non HDL-c < 130 mg/dL and apo B < 90 mg/dL.

In recent years, the increased risk of new onset T2DM has emerged as a safety concern among longtime statin users.

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When compared with the potent cardioprotective effects of statins, the marginal increase in the risk of new onset diabetes should not be a deterrent to prescribing these drugs to high-risk individuals.

Ezetimibe, is a selective cholesterol absorption inhibitor that has been a valuable addition to the lipid lowering drug armamentarium in patients who are unable to tolerate statin therapy. It is also an adjunct to statin therapy for a greater cholesterol-lowering efficacy. To date, despite its LDL-c lowering effect, there are no conclusive data to document that ezetimibe decreases cardiovascular events or slows atherosclerosis progression in people with or without diabetes.

Traditionally, bile acid sequestrants (BAS) were considered as second-line therapy for lowering LDL-c and have been used in patients who are unable to tolerate statin therapy or in specific populations, such as women of reproductive age or children where safety of statins is a concern. Aside from the well known gastrointestinal side effects and an increased prevalence of cholelithiasis, BAS can also aggravate hypertriglyceridemia. Colesevelam has a better gastrointestinal side effects profile and has favorable effects on glucose metabolism.

Niacin has the potential to target the triad of diabetic dyslipidemia as it lowers triglyceride and LDL-c levels and raises HDL-c. While niacin is known to be a potent agent for raising HDL-c levels, at the high doses usually needed to achieve a significant increase in HDL-c it can aggravate hyperglycemia. The use of niacin has been limited by its side effects, mostly flushing and, to a lesser extent, itching, gastrointestinal upset, tachycardia and hypotension. Flushing is induced by releasing prostaglandin D2 from skin cells and when niacin is combined with laropiprant—a prostaglandin D2 receptor antagonist, the niacin-related flushing is significantly reduced. This combination product was approved in Europe in 2008. However, in January 2013, The European Medicines Agency (EMA) recommended that the marketing of three identical niacin/laropiprant products, Tredaptive, Pelzont, and Trevaclyn, be suspended across the European Union. The decision was in response to the failure of the Heart Protection Study 2 Treatment of High-Density Lipoprotein to Reduce the Incidence of Vascular Events (HPS-2 THRIVE) to show any clinical benefit of adding extended-release niacin/laropiprant to statin therapy. Until more data are available, the combination of statins and niacin in T2DM should probably be limited to patients with high risk of hypertriglyceridemia-related pancreatitis.

Although the combination of fibrate and statins in the ACCORD trial failed to improve the primary endpoint, in the subgroup of patients with moderate dyslipidemia (high TG \geq 200 mg/dL and low HDL-c $<$ 35–40 mg/dL) fenofibrate treatment compared to placebo was associated with

fewer cardiovascular events (12.37% vs. 17.32%, respectively). Fibrate monotherapy, along with dietary modification and improving glycemic control, is recommended in diabetics with elevated TG level $>$ 500mg/dL with the intention of preventing chylomicronemia and the associated risk of pancreatitis. Whereas the combination of statins with either fenofibrate or bezafibrate seems to convey a minimal risk of rhabdomyolysis, the combination with gemfibrozil should be avoided whenever possible.

Daily supplements of 3-5 g of eicosapentanoic acid (EPA) and docosahexanoic acid (DHA) reduce serum triglyceride levels by an average of 28%. The Combination of Prescription Omega-3 Plus Simvastatin (COMBOS) trial in statin-treated patients who have persistent triglyceride levels between 200 to 499 mg/dL after achieving their LDL-c goal found that omega-3 fatty acid supplementation reduced non-HDL-c by 9% compared with 2.2% with placebo, triglycerides by 30% compared to 6% with placebo and increased the HDL-c by 3.4%. At the present time there are no conclusive clinical end-point data on omega-3 fatty acids. In a subgroup analysis of the Gruppo Italiano per lo Studio della Infarto Miocardico (GISSI-Prevenzione) trial, mortality was reduced by 28% in diabetics and by 18% in nondiabetics randomized to omega-3 fatty acid supplementation. Similarly, in a study of Japanese hypercholesterolemic patients, daily supplementation with 1800 mg EPA was associated with a significant reduction in non-fatal coronary events. However, in a recent trial of a large cohort of diabetic patients, fish oil supplementation was not associated with any beneficial outcomes. Thus, at the present time, the only justification of prescribing omega-3 fatty acids in people with diabetes is to treat hypertriglyceridemia in order to reduce the risk of pancreatitis.

CONCLUSIONS

Managing hyperlipidemia in people with diabetes should include therapeutic agents with an established ability to reduce cardiovascular events. The choice of what statin to use and when to initiate drug therapy must be individualized. In general, individuals with diabetes over the age of 40, or those who are younger but have established CVD or have multiple risk factors are candidates for statin therapy, regardless of their basal plasma cholesterol levels. The residual cardiovascular risk, despite proper management of the hyperlipidemia, should prompt the clinician to focus on treating the other risk factors frequently associated with diabetes, such as hypertension, obesity, smoking cessation and hyperglycemia.

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- 1) Mooradian AD. Dyslipidemia of type 2 diabetes mellitus. *Nature Clinical Practice Endocrinology & Metabolism*. 5:150-159, 2009.
- 2) Chehade JM, Gladysz M, Mooradian AD. Dyslipidemia in type 2 diabetes. Prevalence, pathophysiology and management. *Drugs* (2013) in press.
- 3) Mooradian AD. Cardiovascular disease in type 2 diabetes mellitus: Current management guidelines. *Arch. Intern. Med.* 163:33-40, 2003.

Exemplary Teachers Awards

Fourteen faculty members in the Department of Medicine were chosen to receive the 2013 University of Florida College of Medicine's Exemplary Teachers Award.

The awardees include (alphabetically): **Drs. Abubakr A. Bajwa, James D. Cury, Linda R. Edwards, Jeffrey G. House, Leighton R. James, Gurjit S. Kaeley, Naem Latif, Alan B. Miller, Dat C. Pham, Fauzia N. Rana, Pramod K. Reddy, Michael L. Sands, Adil Shujaat, and Robert A. Zaiden, Jr.**

This award is given in recognition of outstanding teaching contributions of individual faculty members. The recipients each received a lapel pin and a financial award determined by the compensation plan's incentive for outstanding teaching.

The awardees were recognized on April 11, during the proceedings of Advances in Medical Education held in the LRC Auditorium/Atrium from 12-2:30 p.m.

Please join me in congratulating the awardees.

Update in Nephrology

This half-day annual conference will include relevant topics such as hypertension and diuretics, diabetic nephropathy, hyponatremia, metabolic bone disease, anemia and the ADH receptor blockers.

When: April 27, 2013 at 8am

Where: Hyatt Regency Jacksonville Riverfront

For more information please contact Kai Woods at 904-244-3158 or kai.woods@jax.ufl.edu.

UF&SHANDS JACKSONVILLE

New Shands Jacksonville Chief Executive Officer



Russell E. Armistead, MBA, joined Shands Jacksonville as chief executive officer of Shands Jacksonville Jan. 7. He replaces Jim Burkhart, D.Sc., who resigned to become president and CEO of Tampa General Hospital.

Armistead has broad experience in academic health center and medical school administration. Since 2004, he has served as associate vice president for finance and planning for the University of Florida Health Science Center in both Gainesville and Jacksonville, working directly under David S. Guzick, MD, PhD, senior vice president for health affairs at the University of Florida and president of UF&Shands, the University of Florida Academic Health Center. The Health Science Center includes the colleges of Dentistry, Medicine, Nursing, Pharmacy, Public Health and Health Professions, and Veterinary Medicine. The HSC, which is part of UF&Shands, generates approximately \$1 billion in annual revenue, with more than 6,000 students and 1,700 full-time faculty across both campuses.

Since March 2012, Armistead has worked closely with

Daniel R. Wilson, MD, PhD, vice president for health affairs at the University of Florida and dean of the UF College of Medicine-Jacksonville, on matters pertaining to the faculty practice in partnership with Shands hospital leadership. He has led initiatives to improve profitability, managing financial and planning projects affecting the Jacksonville campus.

"Russ has a long history of effecting change that has led to positive results for our patients and our employees. He was instrumental in leading the recent strategic planning process for the UF&Shands system, which we call 'Forward Together.' Our plan sets the vision for our organization as a place where the patient comes first, and where we make careful use of our resources in support of that goal," said Guzick.

According to Lawrence J. DuBow, a member of the Shands Jacksonville Board of Directors, Armistead is the right choice to lead the organization.

"The Board of Directors believed we needed someone who could step in immediately in order to further efforts that have already led to significant accomplishments for Shands Jacksonville in the last two years," DuBow said. "We are confident that his combination of business savvy and experience working in an academic health care setting will help us achieve our financial goals as well as plans for

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UF&Shands Jacksonville continued from Page 7

future growth.”

Fellow board member Beth McCague agrees, adding that Armistead’s commitment to the success of UF&Shands Jacksonville is also a benefit to the community.

“UF&Shands Jacksonville is one of this city’s most valuable assets. We are one of the largest employers in the area, creating a substantial positive economic impact here and in surrounding areas,” McCague said. “But more importantly, we bring something unique to our community – high-quality health care for everyone in one of the region’s most acclaimed academic health centers by some of the country’s best physicians.”

Wilson, who began his leadership of UF’s Jacksonville medical campus a year ago, said he is looking forward to working side-by-side with Armistead.

“I am truly pleased Russ has accepted this position. He is familiar with all facets of UF&Shands Jacksonville – from finance to clinical operations, patient care, education and research,” Wilson said. “Russ also has the right temperament to be a great CEO. He has consistently good

judgment and a quiet wisdom that will lead us well. Russ is a direct, honest and very thoughtful person. I am confident he is the right person for this position of such consequence for UF, Shands and, indeed, the entire region.”

Prior to joining UF, Armistead was president of Armistead Consulting LLC, a North Carolina firm that provided management and consultation services to academic health centers, hospitals and other health care organizations. During this time, he served dual roles at the Medical College of Ohio in Toledo – interim executive director of MCO Hospitals and vice president for finance and chief financial officer/treasurer. Efforts focused on revenue enhancement, consolidation and cost reduction, including efficiency and productivity of staff, resulting in the hospitals becoming profitable within a year.

Before starting his consulting firm, Armistead held leadership positions at Wake Forest University School of Medicine over the course of 24 years, including vice president for health services administration and associate dean for administrative services.