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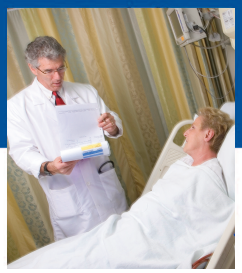
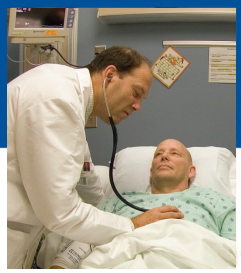
Academic Physician Quarterly

A DEPARTMENT OF MEDICINE BULLETIN

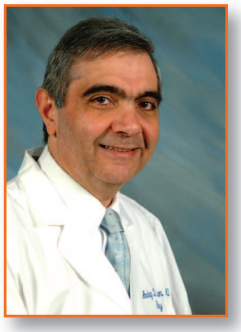




UF UNIVERSITY of FLORIDA
College of Medicine
Jacksonville

CHAIRMAN'S MESSAGE

Dear colleagues:



On behalf of the Department of Medicine at the University of Florida College of Medicine-Jacksonville I would like to wish you a happy and prosperous 2009.

We are in our third year of launching the Academic Physician Quarterly (APC) newsletter. I would like to invite you to look up our previously published issues of the APC on our website at http://hscj.ufl.edu/im/archives.asp. These archival issues give the reader a glimpse of the evolution of the Department over the last three years.

We have now completed the development of all subspecialties and have established training programs in each one. The last Division to come on board as a well rounded academic unit is the Division of Rheumatology. I am delighted that this deficiency is being rectified with the arrival of additional outstanding Rheumatologists. One of the new members of the Department is highlighted in the section on Meet your Colleagues.

The Focus section of the current issue of the APC is dedicated to the echocardiographic laboratory at Shands-Jacksonville. This is a state of the art facility that has thrived under the leadership of Dr. Steven Lavine.

As is traditional with the beginning of each new year the Department's pledge for this year is to make our training and educational programs patient centered, hypothesis driven, outcome focused and evidence based.

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

Steven Lavine, M.D.

Professor of Medicine

Program Director, Cardiology Fellowship

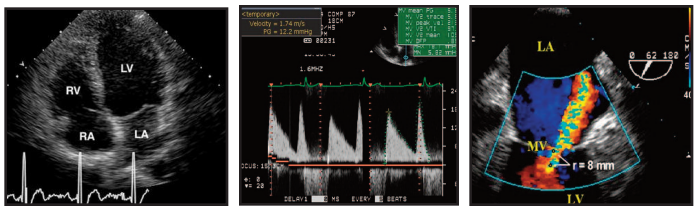
Director, Noninvasive Lab

Division of Cardiology

The Echocadriographic Laboratory at Shands-Jacksonville

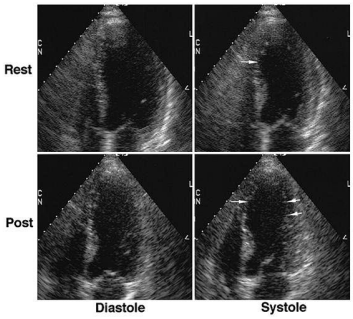
The Echocardiographic Laboratory at Shands-Jacksonville offers a variety of imaging studies that evaluate cardiac anatomy, cardiac function, and intracardiac flow. Although, echocardiography has not yet excelled in the area of evaluating myocardial perfusion, this aspect of cardiac evaluation may be imminently available. Echocardiography involves the use of high frequency ultrasound that is able to discern cardiac structures within a resolution of 1 mm. Furthermore, ultrasound may be emitted in pulses that may detect red blood cell movement and be able to characterize intracardiac flow. This has been termed the Doppler principle and serves as the basis for imaging intracardiac blood flood, detection of regurgitation, and characterization of the pressure gradients across valves. The Doppler principle has also been applied to the velocity of myocardial wall motion and has been useful in characterizing the timing of myocardial wall movement and increasing our understanding regarding myocardial mechanics. More recently, we have added the 3 dimensional imaging that will provide the busy clinician with a 3 dimension depiction of cardiac structure and function and will more accurately calculate ejection fraction, determine in severe mitral regurgitation which part of a mitral leaflet may need repair, and whether intracardiac shunts (atrial septal defects and the closely related patent foramen ovale) are repairable using closure devices deployed in the cardiac catheterization laboratory.

There are literally hundreds of indications for echocardiographic imaging of the heart. The growth of indications has been escalating to the point where the American Society of Echocardiography has now issued "appropriateness indications" in a recent publication. The use of digital acquisition utilized in echocardiographic imaging has shortened study time acquisition and allowed more sophisticated evaluation of cardiac function off-line. Presently, studies consist of 45-65 different imaging clips that are acquired by a cardiac sonographer who has passed a registry examination on cardiac anatomy, physiology, ultrasound physics, and knowledge of cardiac disease. Imaging begins from 4 separate ultrasound windows: parasternal, apical, subcostal, and suprasternal. Digital clips of anatomy and intracardiac blood flow using the Doppler principle are obtained from each cardiac chamber, each valve, and from the aorta, pulmonary artery, and great veins. More advanced imaging techniques are utilized to produce myocardial tissue velocity maps acquired from the 3 apical views.



Left: Apical 4 chamber view, Center: Continuous wave Doppler of patient with Mitral Stenosis, Right: Color flow jet of patient with moderate mitral regurgitation.

In addition to resting studies of cardiac function and intracardiac flow, patients may be stressed using either exercise or pharmacologic stress. Exercise modalities include treadmill exercise or bicycle. We favor supine bicycle as it lends itself to better imaging and the ability to obtain peak exercise images. Ischemia is better detected at peak exercise. To assist in the quality of imaging, we use an intravenous echo contrast agent that outlines the cavity producing images with detail comparable to MR imaging. Both endocardial wall motion assessment and wall thickening can be obtained. Sensitivities for detecting coronary disease by abnormal wall motion and thickening are nearly as robust as perfusion imaging. The greater strength of this technique lies in its specificity, as false positives are infrequent. Pharmacologic stress can be performed using dobutamine infusion to increase heart rate and myocardial contractility. Not only is the predictability for coronary disease strong but also both these testing modalities are exceptionally useful for preoperative noninvasive risk assessment of the pre-operative patient. Images are analyzed using a side-by-side format prior to and with peak stress.



Apical 4 chamber at rest and post exercise (treadmill) demonstrating apical akinesis immediate post exercise suggesting a significant stenosis in the left anterior descending artery.

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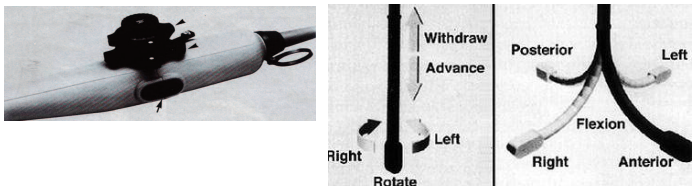
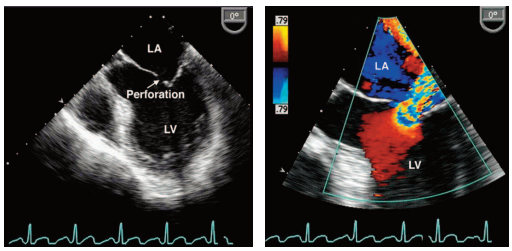
Focus continued from Page 2

An application of dobutamine stress echocardiography is the assessment of myocardial viability. Patients with heart failure most often have coronary disease as their etiology. Areas of the myocardium may be transmurally infarcted and akinetic or dyskinetic with others areas being hypokinetic and akinetic but capable of contracting with revascularization. Patients with viable myocardium are at increased risk for adverse events but at the same time have potential reversibility of heart failure and other serious adverse events including myocardial infarction and death. Low dose dobutamine increases blood flow to the myocardium resulting in hypokinetic and akinetic viable areas contracting. With greater stimulation by dobutamine, the myocardial wall may stop contracting demonstrating it is severely ischemic. Patients who respond to dobutamine in this fashion (biphasic response) have both the highest risk and greatest potential with revascularization to improving symptoms and survival.

Transesophageal echocardiography (TEE) adds a unique window to imaging cardiac structure, function, and intracardiac flow. TEE requires conscious sedation in which the patient is attended by a team of health professionals including a cardiologist, nurse and sonographer to ensure safety. By placing a transducer on the end of a gastroscope and inserting the TEE probe into the upper, mid, lower esophagus, and the stomach, posterior views of the heart are available with high resolution unimpeded by the chest wall and the lung. Diagnosis of atrial clot, aortic dissection, prosthetic valve function, and delineation of endocarditis complications are only a few of the reasons why TEE is often performed.

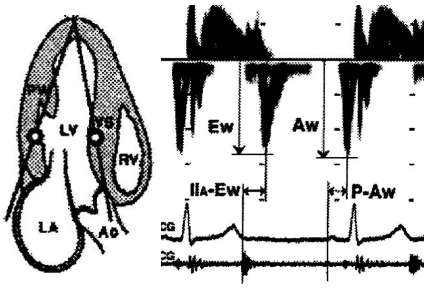


Transesophageal probe controls on the left and probe positions on the right



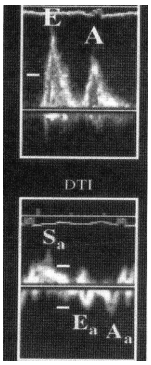
TEE apical 4 chamber view of anterior mitral leaflet perforation on the left and the severe mitral regurgitation on the right.

There are several recent developments in echocardiographic imaging. The first development was the application of myocardial tissue Doppler to the description of cardiac disease. Tissue Doppler is simply a refinement of the existing Doppler principle applied to myocardium. By altering the filters to show spectral traces of low velocity and high amplitude signals, myocardial Doppler can be demonstrated.



Apical 3 chamber view with sample volumes placed in both walls on the left with tissue Doppler signal from the posterior wall on the right (Ew=early peak lengthening velocity; Aw=late peak lengthening velocity).

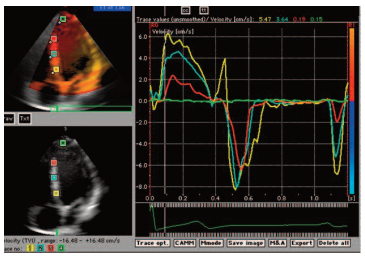
The sample volume can be placed in the mitral annulus and the peak rapid lengthening velocity can be obtained. The ratio of the mitral peak rapid filling velocity and the mitral annular peak rapid lengthening velocity can be used to predict LV filling pressures.



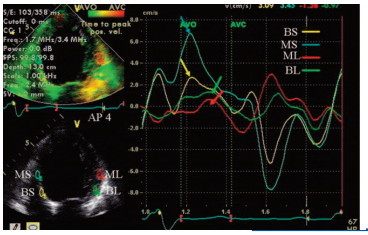
Transmitral velocity is shown on top and tissue Doppler (DTI) mitral annular velocities are shown on the bottom. The ratio of E/Ea can be used to estimate LV filling pressures by a simple formula (LV filling pressures=1.24*E/Ea+1.9 mm Hg).

Nagueh et al. JACC 1997;30:1527

Tissue Doppler can also be obtained as velocity maps superimposed on structural images of the left ventricle. Digital information can be extracted at a later time to evaluate the timing of contraction of the wall. This ability has been used to time the contraction of the base and mid-portion of all 6 walls of the heart. When the timing is not uniform, dyssnychrony is said to exist. Dyssnychrony occurs with LV dysfunction and heart failure and can be corrected by employing a biventricular pacemaker, which synchronizes LV contraction, and coordinates LV contraction with RV contraction and atrial systole. Echocardiography may be used to select patients more likely to respond to this therapy, and it also being used to determine changes in LV size and function, an important correlate of response and a predictor of survival.



Tissue Doppler color maps and derived spectral tracings demonstrating superimposition of systolic and diastolic peaks. All portions of the septal wall are synchronous in shortening and lengthening.



Myocardial dyssynchrony is demonstrated as the time from the R wave to peak shortening velocity occurs later on the lateral wall (red and green arrows) as compared to the septum (yellow and blue arrows). This delay was >65 milliseconds.

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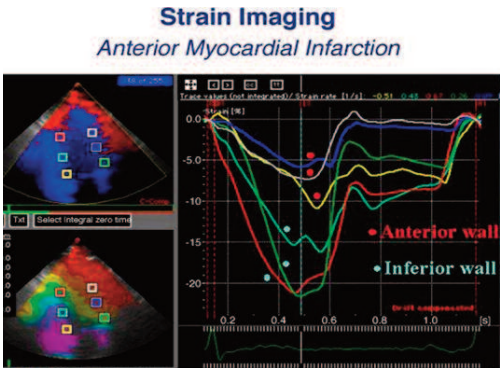
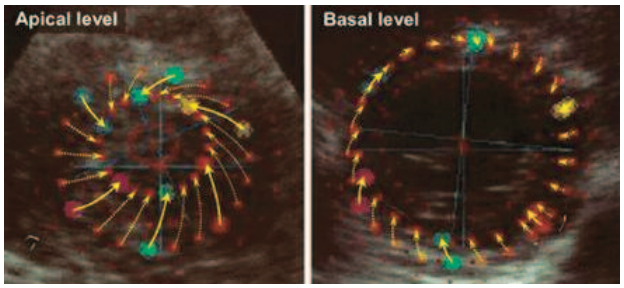
Focus continued from Page 3

Myocardial tissue velocity images can be mathematically manipulated to demonstrate myocardial strain in all segments of the heart. Myocardial strain refers to the deformation of tissue that occurs during active contraction and during diastolic lengthening. It is unaffected by cardiac motion which makes it more robust than velocity measurements which may be affected both by myocardial contraction and cardiac motion. Strain may be measured in the longitudinal and radial directions using tissue Doppler imaging.



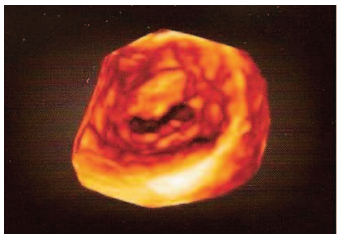
Apical 2 chamber view with tissue Doppler image on the upper right and myocardial displacement on the bottom right. Strain curves are shown demonstrating reduced longitudinal systolic strain (negative) in the anterior wall.

Myocardial velocity and strain measurements can also be derived directly from the two dimensional images using a process called speckle tracking. The computer tracks various amplitude signals called speckles of the various myocardial walls. The change in the position of the speckles at each frame of studied can be calculated. Myocardial velocity and strain can be assessed as with tissue Doppler. However, with this technique, myocardial strain can be assessed longitudinally, radially, and circumferentially. This technique allows us to note circumferential strain at the apex, which is in the opposite direction to the base. This difference is called twist or torsion and represents the "wringing" motion of the heart. Abnormalities in pump function can be accentuated by reduced apical rotation. Diastolic dysfunction may be evident when the rate of untwisting is reduced. Normally, marked untwisting allows suction to fill the heart at lower pressures.



Left ventricular rotation at apical and basal levels during systole from speckle tracking images. End-systolic speckle tracking imaging acquisitions are overlaid on the end-diastolic image with corresponding local trajectories. Normally, at apical level, the left ventricle rotates counterclockwise as viewed from apex, whereas the base rotates clockwise. This gradient of LV rotation between the two levels creates a "wringing" motion of the left ventricle.

Finally, the most recent addition to advanced echocardiographic imaging is 3 dimensional echocardiography. Images are most often acquired from the apical and parasternal windows. A single apical and parasternal view are acquired as a composite of 4 beats. Images are acquired volumetrically and can be displayed with any degree of rotation or as any view. Images may be viewed en face as a surgeon might visualize in the operating room. Three-dimensional imaging has found use in calculating ventricular volumes and ejection fraction with an accuracy comparable to MR imaging. It has utility in characterizing masses, valve disease, and how much the aortic or mitral valve regurgitates. It may have use in identifying prosthetic valve abnormalities possibly saving a patient the need for TEE. Recently, using 3 dimensional echocardiography, we were able to differentiate prosthetic valve infection from a torn bioprosthetic leaflet. The time of 3D imaging has now arrived bringing echocardiography closer to other volumetric imaging techniques especially MRI and CT angiography.



3 dimensional imaging of the mitral valve providing a surgical like view.

The Echocardiography Laboratory also performs and supports a number of clinical investigations. Echocardiographic imaging of the left ventricle is performed following bone marrow stem cell instillation into the myocardium by catheter techniques to determine the contractile status of the myocardium at regular intervals following the experimental procedure. Our electrophysiology section is investigating whether earlier use of cardiac resynchronization therapy is helpful in patients with heart failure using tissue Doppler indices of systolic dyssynchrony for both selection and optimization of biventricular pacing. The echocardiography laboratory has also developed a registry for patients with various heart diseases to determine the importance of myocardial dyssynchrony. Of interest, patients with diastolic dysfunction and aortic regurgitation are being evaluated. Finally, using tissue Doppler optimization parameters following resynchronization therapy as selection criteria prior to CRT is also being investigated.

The Echocardiography laboratory cardiologists include Steven J. Lavine, M.D. (Medical Director and Cardiovascular Fellowship Director), Donald A. Conetta, M.D., and Robert F. Percy, M.D.

GME CORNER

Senthil Meenrajan, M.D., M.B.A.

Assistant Professor of Medicine, General Internal Medicine

Associate Program Director, Internal Medicine Residency

"Either write something worth reading or do something worth writing" - Benjamin Franklin

This fall the residents & the GME office has a lot worth writing and hopefully I will make it worth reading too! The Internal Medicine Residency continues to march forward, building on the successes from the end of the last academic year. The excitement of the 'new' interns, fellowship match are all behind us now and a new set of familiar and some unfamiliar issues are at our forefront.

First, ABIM results- at this year's Internal Medicine Board exams our residents secured a 92% pass rate. This is almost identical to the good showing from last year and we now cannot wait for next year, so our 3 year rolling average will be one of the best in the state. Kudos to all residents, faculty and staff who worked so hard to make this happen. Our Board Review course and quizzes help ensure all residents stay focused toward this goal.

Second, success breeds success. Our awesome performance in the fellowship match and the Boards seems to weave it's magic on the interviewees. The interviews could not be going better. The whole routine starting with a dinner with residents the previous night, tour of facilities, morning report and the interviews seem to hit a perfect vibe with all the candidates. All indicators point to a very positive experience for everyone involved and we are interviewing truly desirable candidates for the program.

Third, its everything else! Dr. Petrucelli made the very difficult (and saddening) decision to leave the GME program and we wish her the very best in everything she pursues. The silver lining to that though is the fact that Dr. House will be joining as the Associate Program Director. If there is an emotion that is 'sad-happy', that's what I feel now!! The program never seems to run out of motivated and talented residents who want to serve it's ranks, as exemplified by Drs. Tauseef Qureshi and Naveen Seecharan who will be the Chief Medical Residents in 2010.

Finally, the big one – SITE VISIT. The core program with a number of the subspecialties will have it's site visit in January of 2009. This has become the singular focus of the GME at this point in time and hopefully the next time we have the GME update our site visit success will be the first, biggest and proudest item on the list. Until then……keep your fingers crossed and stay tuned.

RX UPDATES

By Lauren Stafford, Pharm.D.

FDA Proposes Eliminating Pregnancy Letter Categories for Safety of Drugs

In 1979, the FDA established the current "letter category system" for rating the risks of drug use during pregnancy. This system was initially praised as being easy for providers to understand and for encouraging drug prescribing; when necessary, in pregnant women. [1,2] Over the past ten years, criticism of this system has increased because the current system does not provide practitioners with enough information to make informed decisions about appropriate therapy in this vulnerable population.

The current lettering system (Table 1) does not take into account variations in safety in different trimesters of pregnancy or provide information regarding the data from which the letter category is derived. The A through X system also indicates a gradient of safety rather than indicating the true benefit to risk ratio, which may be patient specific. It also leads practitioners to believe that all drugs within one category carry the same level of risk.

The FDA has proposed a rule, currently open for public comment, to abolish the letter categories and provide more comprehensive information in a standardized format (Table 2) within the drug's prescribing information, allowing practitioners to make prescribing decisions based on a review of all available data of the drug's use in pregnancy. This rule will also give drug manufacturers incentives to develop pregnancy registries and publish both positive and negative data from these registries, adding to the knowledge base of drug use in pregnancy, associated safety factors, and outcomes.

Once the proposed rule is approved, all newly approved drug labeling will be required to conform to the above format. The proposed rule for these changes is currently open for comment to the FDA, but is expected to take effect before the end of 2008.[3]

Continued on Page 6

RX Update continued from Page 5

Table 1: Review of Current FDA Pregnancy Categories[1]		
Category	**Definition**	**% of Drugs**
A	Well-controlled, adequate studies in pregnant women have failed to demonstrate risk to the fetus.	0.7%
B	Either animal study shows risk, but human studies do not support the identified risk, or if no human studies have been performed, animal studies do not demonstrate risk	19%
C	Human studies are absent or inadequate and animal studies either show fetal risk or are absent. Potential benefits may justify the risks	66%
D	Studies or post-marketing data demonstrates risk to the human fetus. Potential benefits to the patient may still outweigh the known risks.	7%
X	Studies in humans or animals or post-marketing data show risk to the human fetus which clearly outweighs all possible benefits. Drug is contraindicated in pregnancy.	7%

Table 2: Summary of Proposed Changes to Pregnancy Labeling in Prescribing Information (PI)		
1)	**Eliminate all current pregnancy category listings from PI**	This change will affect all new drugs upon approval, and all existing drugs whenever changes to labeling are made
2.)	**New Pregnancy Labeling Sections**:	
	• *Fetal Risk Summary*	One sentence describing likelihood of abnormalities (i.e., structural, fetal and infant mortality, impaired physiologic function, alterations to growth). This section will also describe: 1) Incidence, seriousness, reversibility, & correct-ability of the abnormality 2) Effect of dose, duration of exposure, and gestational timing of exposure 3) Evidence (animal vs. human data)
	• *Data*	Will provide information on: 1) Inadvertent exposure in pregnancy 2) Prescribing decisions in pregnant women 3) Drug effects on labor and delivery
	• *Pregnancy registry exposures*	Will provide phone # and other information to enroll patients
	• *General Statement of Background Risk*	Will include a statement that all pregnancies have a background risk of birth defects, loss, or other adverse outcome regardless of drug exposure
3.)	**Lactation**	
	• *Risk Summary*	If appropriate, include a statement that the use of the drug is compatible with breast-feeding. 1.) Effects of the drug on milk production 2.) Whether the drug is present in human milk (and if so, how much) 3.) The effect of the drug on the breast-fed child
	• *Clinical considerations*	1.) Ways to minimize exposure to the breast-fed child, such as timing or pumping and discarding milk. 2.) Potential drug effects in the child and recommendations for monitoring or responding to these effects. 3.) Dosing adjustment during lactation.
	• *Data*	Overview of data on which risk summary and clinical considerations are based.

References

1) Doering PL, Boothby LA, Cheok M. Review of pregnancy labeling of prescription drugs: Is the current system adequate to inform of risks. Am J Obstet Gynecol. 2002;187:333-9

2) Public Affairs Committee of the Teratology Society. Teratology public affairs committee position paper: Pregnancy labeling for prescription drugs: Ten years later. Birth Defects Res A Clin Mol Teratol. 2007 79 (9):627-30

3) Food and Drug Administration (FDA)Center for Drug Evaluation and Research (CDER) homepage. Pregnancy and lactation labeling. Available at http://www.fda.gov/cder/regulatory/pregnancy_labeling/default.htm. Accessed June 8th 2008

NEWS & NOTES

Dr. Dominick Angiolillo receives "William Harvey" award from the Italian Society of Cardiology

This year, Dr. Dominick Angiolillo is the recipient of the "William Harvey" award from the Italian Society of Cardiology. This award is in recognition of an Italian investigator who has made contributions to cardiovascular research over the past 3-5 years and representing "Italian Cardiology" internationally.

Congratulations to Dr. Angiolillo for this exceptional honor.

Dr. Senthil Meenrajan receives Philip H. Gilbert Young Physician Award

Dr. Senthil Meenrajan is the recipient of the 2008 Philip H. Gilbert Young Physician Award. This award is given annually by the Duval County Medical Society (DCMS) to recognize young physicians with leadership traits. The award will be presented to Dr. Meenrajan at the 2009 DCMS Annual Meeting on Thursday, January 15, 2009.

Congratulations to Dr. Meenrajan for this honor.

JaxHATS is recognized as one of seven programs in the country

The Maternal and Child Health Bureau (MCHB) Division of Services for Children with Special Healthcare Needs (DSCSHN) is charged with achieving a community-based service system for all children and youth with special health care needs and their families. The MCHB has recognized only seven programs addressing transition issues for children and youth with special health needs (CYSHN). One of those seven programs was the JaxHATS program under the leadership of Dr. David Wood (Pediatrics) in collaboration with Dr. Linda Edwards (Internal Medicine). JaxHATS was also named one of Jacksonville Business Journal's Health Care Heroes for 2008.

Congratulations to this unique program and the team that makes is a success.

Dr. Malcolm Foster is recognized as a Health Care Hero

I am proud to inform you that Dr. Malcolm Foster was selected as an honoree by the Jacksonville Business Journal's Health Care Heroes Program 2008. This program honors top medical professionals in Northeast Florida who have improved healthcare and saved lives, especially in the past few years.

Congratulations to Dr. Foster.

MEET YOUR COLLEAGUES

Editor's note: Periodically the "Academic Physician Quarterly" will introduce our readership to new faculty members who have exceptional clinical skills. In this issue we highlight a new member of the Division of Rheumatology and Clinical Immunology who will also serve as Director of Musculoskelatal Ultrasound.

Gurjit Kaeley, M.D., Assistant Professor of Medicine
Division of Rheumatology and Clinical Immunology
Director of Musculoskeletal Ultrasound

Dr. Kaeley earned his medical degree from the University of London in London, England and completed his residency in Internal Medicine and his fellowship in Rheumatology at the University of Tennessee in Memphis, TN. Dr. Kaeley also holds an International Society of Clinical Densitometry Certification in Clinical Densitometry. He is a pioneer and national expert in the utilization of musculoskeletal ultrasound in rheumatology.

Shands Jacksonville Program Used as System Model

In October 2007, Shands Jacksonville initiated patient and family activation of the Rapid Response Team in emergency situations. This program, called Partners in Care, was used as the model for other hospitals in the Shands HealthCare system.

The RRT responds to the patient's bedside at the first sign of trouble or deterioration. The team is comprised of critical-care trained respiratory therapists and registered nurses who provide detailed assessments and resources to the patients and nurses in the Med/Surg and Progressive Care units. They also collaborate with the primary nurse, physician team and other disciplines to stabilize the condition or assist in transferring the patient to a higher level of care.

The goal of the RRT is to decrease Code Blues that occur outside of the Intensive Care setting. The team rescues or stabilizes the patient before the patient deteriorates to the point of cardiopulmonary arrest. Additionally, RRT nurses make rounds on patients during their first 24 hours out of the ICU and respond to Code Blue calls.

So far, the team has helped decrease the number of Med/Surg Code Blues by 27 percent and survival to discharge after Code Blues has increased from 21.05 to 38.6 percent.

"By providing a dedicated RN 24 hours a day, we are proactively assessing and intervening as opposed to responding only when there are signs of trouble," said Kelly Miles, vice president and chief nursing officer. "By doing so, we are giving our patients the best chances of survival and the highest level of quality care possible."

Patients and their families are educated about the Partners in Care program and RRT process at the time of admission. Signs have been posted in all patient rooms, and patient phones are labeled with instructions for accessing the 4-CARE hotline. There have been fourteen calls since implementing the program and all but two were clinically indicated as necessary. Two patients called because visitors in their rooms became ill and one patient called because another patient in the room was exhibiting signs of a stroke.

In addition to responding to patient emergencies, the RRT also responds to employee and visitor medical emergencies in the Clinical Center, LRC and ACC buildings. To access the Rapid Response Team, call extension 4-2222. For non-emergent ICU consults, page the team at 306-4049. For the Pavilion, page 393-0178.

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