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A DEPARTMENT OF MEDICINE BULLETIN



UF UNIVERSITY of FLORIDA
College of Medicine
Jacksonville

CHAIRMAN'S MESSAGE

Dear colleagues:

It's that time again when a new crop of trainees are joining the Department. They will be joining a strong training program that recently received a five year approval from the Residency Review Committee. The strength of this program lies not only in the breadth of clinical experience the trainees receive but it also extends to developing the minds of these bright young physicians to think as scientists, educators and community leaders. Indeed, trainees are offered a wide range of research opportunities that accounts for the Department's continued success at our Annual Research Day with platform and poster presentations of fellows and residents.

On this year's Research Day, one quarter of platform and poster presentations of fellows and residents were made by members of the Department. Of the platform presentations, Dr. Tausef Qureshi was the second place prize winner and Dr. M. Kamran Aslam received the fourth place prize. In addition, among the poster presentations Dr. Senan Sultan received the third place prize and Dr. Abdul-Razzak Alamir received the 5th place prize. I am very happy to see that research productivity of the house staff is excellent. The challenge for all of us is to maintain this excellence.

Our faculty continue to receive the highest honors for teaching. This year, eight faculty members of the Department were recognized for their exceptional contributions to the teaching mission of the University of Florida.

It's been a wonderful and a productive academic year and we are looking forward for another year full of academic accomplishments.

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

Luis Guzman, M.D.

Assistant Professor of Medicine

Medical Director, Peripheral Program and Cath Lab

Division of Cardiology

Integrating Cardio-Vascular Care at Shands/UF Cardiovascular Center:

Lower Extremities Atherosclerotic Disease

Introduction

Atherosclerosis is a complex and systemic disease involving mainly medium and large arteries. Even though the most common clinical presentation of the disease affects the coronary arteries, multiple vascular beds are usually implicated, including the aorta, the carotid, the renal and the lower extremity arteries. For this reason, at UF/Shands Cardiovascular Center we have developed a comprehensive program to detect these patients early and offer a variety of diagnostics tests, created a vascular clinic and offer a state of the art technology in the interventional percutaneous treatment of these patients, including the newest technology in percutaneous revascularization of the lower extremities, renal stetting and the recently FDA approved stenting with cerebral protection to the carotid arteries.

Atherosclerosis affecting the lower extremities is the most common form of peripheral vascular disease (PVD). Its involvement appears to be an expression of a more advanced process associated with worse prognosis. The understanding of this process is critical for the development of preventive strategies, and institution of appropriate treatment.

Pathophysiology

Atherosclerosis is a heterogeneous and dynamic process. Even though initially described in a coronary arteries, recent advances have demonstrated similar process in all different territories. According to the plaque composition, atherosclerotic lesions have been classified in 7 different types.[1] The different lesion types develop as a consequence of a complex pathophysiologic mechanism at the cellular and molecular level with participation of multiple pro-inflammatory cytokines, growth factors, matrix metalloproteinase and coagulation factors. In the early phases, endothelial dysfunction is the main contributor. Endothelial exposure to multiple hemodynamic (shear stress, high blood pressure) and serum factors (high cholesterol, high glucose, etc), gradually leads to loss of its protective function and vessel wall homeostasis. Increased permeability to circulating lipoproteins and monocytes creates an intraplaque inflammatory state which stimulates the proliferation of smooth muscle cells, causes deposition of extracellular matrix, as well as development of a prothrombotic environment, leading to lipid accumulation, necrotic core and fibrous cap formation, characteristics of the more advance atherosclerotic process.

Epidemiology

Cardiac death represents 70% of the overall mortality of the disease.[2] Cerebrovascular diseases account for approximately 15% of mortality and an additional 10% mortality is related to aortic aneurysm and visceral infarction. Even though peripheral arterial diseases (PAD) represents only 1%-3% of the overall mortality in these patients, it is associated with a 3 fold increase in mortality due to cardiovascular diseases.[3, 4] The diagnosis of PAD (symptomatic or not) is associated with a 50% 10 years mortality due to cardiac and/or cerebrovascular disease. Approximately 60%-70% of patients with clinical manifestations of PAD will have associated coronary artery diseases.[2, 5, 6, 7] The incidence of asymptomatic lower extremity arterial disease in the 55- to 74-year-old age general population group is about 10%.[8] However, the incidence varies according to age with 2.5% incidence in < 60 years, 8.3% between 60-69 years and >19% in older than 70 years.[9] It is important to mention that smoking is a major risk factor, with 10 fold increase in symptoms as compared with non-smokers and the development of the disease appears approximately 10 years earlier.

Early Detection and Diagnosis

Although the clinical manifestations of the disease define a small subset of the population at risk, early detection of the sub-clinical forms is important. The PARTNERS study has demonstrated that there is a large proportion of patients who are without diagnosis.[10] More aggressive preventive measurement could be initiated if detected early, with the intended reduction in clinical events. Framingham risk score is most commonly used to define groups at higher risk. Multiple serum markers, also known as "emerging risk factors", like HS-CRP have been recently introduced as a potential screening tool. The most cost/effective, highly specific and sensitive diagnostic screening test for PAD is the Ankle/Brachial index (ABI) (Figure 1).

This test can be performed in the physician's office and

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provides valuable diagnostic and prognostic information. Patients with an abnormal ABI (<0.9) had a two fold increase in cardiovascular morbidity (myocardial infarction and stroke) and mortality.[11] In patients with abnormal ABI's and symptoms of limiting claudication or critical limb ischemia, further diagnostic modalities will be indicated if revascularization is considered. CTA and MRA are currently widely accepted as the preferred non-invasive imaging modalities. Angiography still remains the gold standard.

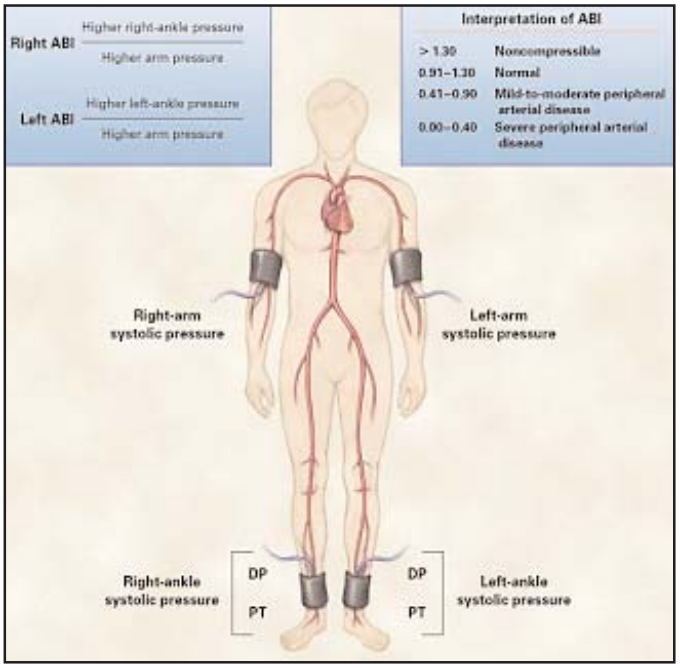

Figure 1: Ankle-Brachial Index

Clinical Presentation

Only a small proportion of patients complain of typical symptoms or claudication and the majority are either asymptomatic or present with atypical symptoms (Figure 2). [10] Even in the group of patients with known history of PAD, only 12% will complain of symptoms of claudications.

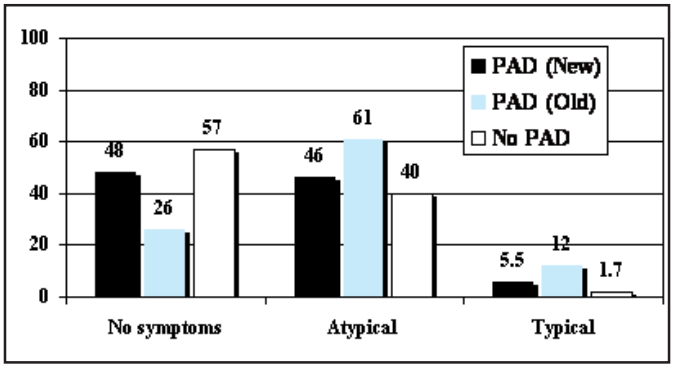

Figure 2: The clinical presentation of PAD as described in the PARTNERS study. The majority of these patients are either asymptomatic or present with atypical symptoms.

Approximately 5% of patients will progress to clinical signs of critical limb ischemia (CLI), including pain at rest and/or the presence of skin lesions (ulcer, gangrene). An important concept to remember is that the majority of patients with CLI do not have symptoms of claudications prior to development of clinical signs of critical ischemia.

A smaller percent will present with clinical signs of acute limb ischemia. The classical 5 P's in a cold foot are helpful for the diagnosis (pallor, pulselessness, paresthesias, pain, paralysis). Appropriate and prompt recognition is vital for limb salvage.

Medical Management

The vast majority of the patients with PAD have a high risk for cardiovascular morbidity and mortality. Myocardial infarction and stroke will occur in 30% at 5 years, with an approximately 25% cardiovascular mortality. For this reason, the main target of treatment in this patient population is the prevention of cardiovascular events. All patients with PAD should achieve blood pressure control, antiplatelets treatment, lipid lowering, use of ACEI and participation in smoking cessation programs.[12]

Revascularization Modalities

Approximately 30% of this population will have symptoms or clinical situations in which revascularization modalities will be considered. It is important to emphasize that at the present time, no revascularization procedure has proven to prolong life. The main indication is to improve quality of life and/or to preserve limb viability. The recently published ACC/AHA guidelines give a Class 1 recommendation for revascularization for symptomatic patients with significant functional impairment.[12] Although surgical revascularization has been the treatment of choice for many years, in the last 15 years, several percutaneous interventions including balloon angioplasty, stent, cover stents, laser, atherectomy devices and other adjunctive modalities have offered less invasive treatment, rapid recovery, and outcomes comparable to surgery. Currently, percutaneous intervention is the first line of treatment for patients with critical limb ischemia.

Conclusion

As the population ages, and the new advances in preventive measures and treatment of coronary artery diseases continue to reduce the mortality, health care providers will increasingly face the problem of concomitant "non-coronary" arterial diseases. Atherosclerosis has a common systemic pathogenesis and simultaneously affects multiple vascular beds. Early diagnosis and preventive treatment is the main goal. For symptomatic patients, revascularization is appropriate with the incorporation of percutaneous alternatives as

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less invasive modalities. These patients currently seek consultation and care from multiple specialists. A team approach as used at UF/Shands Cardiovascular Center with an integrated management has clearly improved the care of these patients.

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GME CORNER

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

Assistant Professor of Medicine, General Internal Medicine

Associate Program Director, Internal Medicine Residency

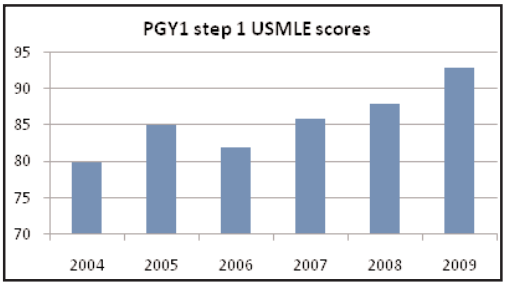
Maturation is a process of evolution and development over time and is very commonly studied in pediatrics. It is a complex interaction of personal wants and environmental wants interacting and resulting in personal growth. When I reflect on the last year for the Internal Medicine Residency Program this is the only term that came to mind. So here we go….the year in retrospect and how the program has MATURED.

The first three quarters were consumed in the following:

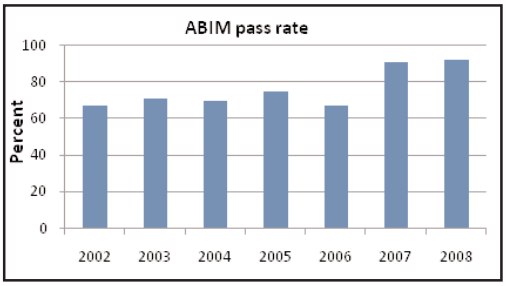
1. Finding reasonable associate program directors
2. Interviews
3. Board pass rate
4. Site visit

A lot of the internal and external wants for the program seemed like one and the same! The last quarter was really spent on waiting for the results of our actions from the first three.

Now that I am one of the associate program directors along with Dr. House, I'd like to think that we had our best results in the first objective! As for the second objective, we want to make our program better each year and this year we achieved it. We filled all our categorical and preliminary positions and did not have to scramble. Our incoming class would have the highest USMLE step 1 scores of any class so far.



The program has done extremely well with the internal medicine boards as well. Over the last few years we have had an upward trend.



Finally the site visit - the pinnacle of accreditation would have to be a five year cycle. The IM program, along with all the fellowships that were visited, were awarded this status.

While we pause to gloat over the achievements of the last year we also realize the bar is now set high eternally. Look forward to the next year to move that bar just a tad bit higher still!! To all who have given us untiring support to make us a MATURE program – THANKS.

Joe M. Chehade, M.D.

Associate Professor of Medicine

Division of Endocrinology, Diabetes & Metabolism

Unusual Presentation of a Malignant Follicular Carcinoma of the Thyroid in Struma Ovarii

Case Presentation

A 58 year old woman was referred for evaluation of metastatic thyroid cancer. She presented initially to her primary care physician with symptoms of persistent cough. Chest x-ray revealed a 5.4 x 3.4 cm right upper lobe mass with adjacent rib and vertebral body erosion. A CT of the chest revealed a right upper lung mass and a 4.9 x 2.4 cm perivertebral mass in the right upper thorax; there was also some calcification noted in the right lobe of the thyroid with a possible cyst. CT guided biopsy of the mass confirmed metastatic follicular carcinoma of the thyroid. At that point she was referred to an oncologist for further evaluation. A PET/CT scan did not show any hypermetabolic activity in the thyroid bed area but there was a multiseptated mass in the pelvis measuring 16 x 9.9 cm arising from the left ovary and uptake identified in the soft tissue mass in the posterior right lung apex which appeared to be causing rib destruction. The decision was made to refer the patient to a gynecologic oncology surgeon to remove the ovarian mass. The pathology showed right ovary "struma ovarii with thyroid tissue that suggests a teratoma primarily composed of thyroid tissue, there was no evidence of vascular invasion. Some of the thyroid tissue was primarily composed of microfollicles and there was a component of malignant thyroid follicular carcinoma". Patient referred to Endocrinology for further evaluation.

Her past medical history was significant for hypertension, hyperlipidemia and depression. Family history was significant for mother with some ovarian or uterine cancer. The patient was married, never smoked and did not consume any alcohol..

Home medications consisted of fluoxitene 20 mg daily, alprazolam 0.25 mg as needed, valsartan/HCTZ 80/12.5 mg daily, ASA daily and loratidine 10 mg daily.

Physical examination: the patient appeared in no distress. Blood pressure 144/83, heart rate 80 beats/minute. There was no lymphadenopathy noted in the neck area and there was a 1.5 cm well defined right thyroid nodule. The rest of the physical was unremarkable.

A thyroid ultrasound completed during the physical examination confirmed the presence of a 1.9 x 1.3 x 1.6 cm hyperechoic nodule with little vascular flow by Doppler in the anterior right lobe (that was palpated on exam) along with another 1.2 x 1.8 cm hypoechoic nodule in the infero-posterior lobe (not palpated by physical examination). Laboratory data: Thyroglobulin level 400 ng/ml (<30); TSH 1.6 UIU/ml (0.27-4.6); Free T4 0.99 (0.7-1.85); Calcuim 10.6 mg/dl (8.2-10.2).

Review of the Literature

The most common germ cell tumor in the ovaries is the benign cystic teratoma (dermoid). 7% of theses tumors contain thyroid tissue, and 25% of these may be classified as struma ovarii (i.e. > 50% of the neoplasm consists of thyroid tissue).

Although the typical presentation is that of a pelvic mass, unusual clinical manifestations such as hyperthyroidism, ascites, and Meigs' syndrome have been recognized. In regard to the occurrence of follicular cell carcinoma in struma ovarii, there is a paucity of cases reported in the literature (<50 cases). The average age was 44. These patients predominantly presented with a pelvic mass (45%) and abdominal pain (40%). Patients also presented with menstrual irregularities (9%) and hyperthyroidism (5%). Papillary carcinoma was the most common (44%) malignant histopathologic finding followed by follicular carcinoma (30%), and follicular variant of papillary carcinoma (26%). Metastasis were seen in nine cases (23%)(1). Histologic malignancy in struma does not necessarily equate with biologic malignancy, and the majority of differentiated thyroid carcinomas do not spread beyond the ovary.

Malignant struma ovarii is a medical rarity. This paucity of published cases and the difficulty in distinguishing between benign and malignant strumas make it difficult for a physician to discern the natural progression of disease and its best treatment modality. Should fertility not be a desired option, and the physician knows the diagnosis beforehand, total abdominal hysterectomy, bilateral salpingo-oophorectomy, pelvic washings, and pelvic lymph node sampling should be

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A Clinical Case continued from Page 5

performed and followed by total thyroidectomy and I^{131} ablation. For women of child-bearing age, a thorough understanding of the disease both by the patient and physician must be undertaken to discern the best treatment options. Despite its complications, thyroidectomy has an important role in the treatment of malignant struma ovarii. First, it confirms normal thyroid histology and excludes a primary thyroid carcinoma with subsequent metastasis to the ovary. Second, large amounts of retained thyroid tissue when treated with radioactive iodine incite an inflammatory response that may cause the patient significant pain and disability. Thirdly, less ^{131}I is available to destroy malignant cells. Finally, serum thyroglobulin levels provide accurate information on recurrence only after thyroidectomy. However, the rarity of this tumor will make it difficult for prospective trials to validate this assertion.

Diagnosis

In general patients presenting with a thyroid nodule ≥ 10 mm and normal TSH, fine needle aspiration biopsy (FNA) should be performed as an initial evaluation to differentiate malignant from benign nodule (4-5). Some thyroid nodule ≤ 10 mm with capsular invasion or other suspicious finding by ultrasound, by history or on clinical examination should also undergo FNA. In our case study the patient already presented with a metastatic follicular thyroid carcinoma based on her CT guided lung biopsy. Usually the primary lesion is in the thyroid and total thyroidectomy followed by ^{131}I ablation is the standard of care. Any other metastatic lesion amenable to surgical debulking should be performed and patient should be followed by periodic thyroglobulin level and ^{131}I whole body scan to monitor for any recurrence. For our patient the large asymptomatic pelvic mass (16 x 10 cm) with hypermetabolic activity on PET scan was an unexpected finding. The question at this point: Is this another metastatic lesion (in the ovary) or ectopic thyroid tissue from the ovary (struma ovarii) is the source of metastasis? She underwent exploratory laparotomy, total abdominal hysterectomy, bilateral salpingo-oophorectomy, staging peritoneal biopsies, selective pelvic periaortic lymphadenectomy and partial omentectomy. The pathology report was consistent with features of teratoma with thyroid microfollicules that are mostly seen with thyroid follicular carcinoma.

The patient and was found to have two thyroid nodules and the best approach would have been to refer for thyroidectomy and followed by ^{131}I ablation.

In conclusion, this patient had a metastatic follicular thyroid carcinoma most likely arising from an ectopic thyroid tissue in the left ovary "struma ovarii" although a total thyroidectomy was needed to confirm the ectopic origin.

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RX UPDATES

Bernadette S. Belgado, Pharm. D.

Methadone - Not Your Average Controlled Substance

Methadone is a long-acting opiate agonist used for the treatment of chronic pain and withdrawal symptoms related to opioid-addiction. Methadone is a Schedule II controlled substance strictly regulated under federal law. When used as a treatment for withdrawal, patients must be enrolled in a Narcotic Treatment Program (NTP) to receive methadone.

No physician, even those registered as a NTP, can write a methadone prescription for treatment of addiction. Only when methadone is being used for analgesic purposes can a physician prescribe methadone.

Although they cannot write a prescription, physicians who are registered with the Drug Enforcement Agency (DEA) as a NTP can administer or directly dispense methadone for treatment of addiction. When arrangements are being made to enter the patient into a treatment program, physicians who are NOT registered as a NTP may administer or directly dispense methadone for the purpose of alleviating withdrawal symptoms ONLY under the following conditions:

- No more than a one-day supply of medication may be administered or directly dispensed to a patient at one time
- Treatment may not be carried out for more than

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three days

- This three-day period cannot be renewed or extended.

If a patient is enrolled in a NTP and is admitted to the hospital for a reason other than addiction, an unregistered physician may order methadone for the patient. At Shands Jacksonville the pharmacist will verify the maintenance dose with the methadone treatment facility before methadone is dispensed for this purpose.

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NEWS & NOTES

Exemplary Teachers Awards

Eight faculty members in the Department of Medicine were chosen to receive the 2009 University of Florida-College of Medicine's Exemplary Teachers Award.

The awardees include (arranged alphabetically): Drs. Irene Alexandraki, Dominick J. Angiolillo, Linda R. Edwards, Malcolm T. Foster, Jeffrey G. House, Senthil R. Meenrajan, N. Stanley Nahman Jr., and Elisa M. Sottile.

This award is given in recognition of outstanding teaching contributions of individual faculty member. The awardees will receive a plaque, a lapel pin and a financial award determined by the compensation plan's incentive for outstanding teaching.

Congratulations to the awardees.

UF COM Jacksonville Oncology Group Joins NCCTG

The University of Florida College of Medicine-Jacksonville has been approved by the Executive Committee of North Central Cancer Treatment Group (NCCTG) as an affiliate site of Mayo Florida. It was announced at the General Session of the NCCTG Spring Meeting last week.

Last year the UF College of Medicine's Hematology/Oncology Department evaluated over 1000 new cancer cases. They have solid experience in clinical trial participation and over the years have established productive relationships with Mayo physicians and researchers.

SHANDS BRAND

TraumaOne Rebranded

Mayor John Peyton, Jacksonville City Councilman Johnny Gaffney and members of the media attended a special event in May to reintroduce TraumaOne to the community.

While part of Shands Jacksonville, TraumaOne has been branded as a distinct program. The Trauma Center, Flight Services, Communications/Dispatch, Trauma Prevention and Education, and Emergency Preparedness are all part of TraumaOne rather than the hospital.

TraumaOne was the first trauma program in the state of Florida. Twenty-six years later, it is still the only adult and pediatric Level I trauma program in Northeast Florida and Southeast Georgia.

"TraumaOne is the only trauma program in this area, and we invest a significant amount of resources to ensure we maintain our Level I status," said Wayne Marshall, division director of Emergency/Trauma Services. "Nobody else does what we do. Nobody."

Trauma Center

The Trauma Center is staffed 24 hours a day, seven days a week with specialty trained healthcare providers in emergency, trauma and critical care. More than 4,000 patients came through the doors of the Trauma Center in 2008. On each of its four busiest days, 24 patients were treated by the team. Motor vehicle crashes, motorcycle crashes, falls, pedestrian and other accidents accounted for 74 percent of trauma cases last year.

Flight Services

TraumaOne flight nurses and paramedics have extensive training and years of experience in caring for trauma patients. Interestingly, the pilots have no medical background at all. Their decisions must be made purely on their aviation experience. They are not given details of an accident until after they have accepted the call and determined it is safe to fly to the scene based on FAA regulations; this practice prevents pilots from making emotional decisions.

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Communications/Dispatch

The communications staff in TraumaOne dispatches four helicopters within a 100-mile service area. They accept all rescue calls for the hospital and notify the trauma, emergency or pediatric emergency teams of incoming patients. The team also plays a vital role in mass casualty incidents, serving as a link between the Emergency Preparedness team, Trauma Center and Emergency Department, city government and local agencies, such as police and fire rescue departments.

Trauma Prevention and Education

Shands Jacksonville's Trauma Prevention Program began 20 years ago to educate children and parents in our community on important safety topics in an effort to reduce the number and severity of injuries. Each year, 15,000-20,000 people learn about injury prevention through lectures, mock simulations, health fairs, hands-on activities and general distribution of educational materials, helmets and car seats.

Emergency Preparedness

TraumaOne's emergency preparedness staff is responsible for the safety of patients, visitors and staff throughout Shands Jacksonville's 65-acre campus during natural and man-made disasters—from hurricanes to terrorist threats. The team is also responsible for coordinating the hospital's response to any MCI with the potential to bring in a large number of patients with serious injuries.

"The community at large would see a significant increase in the mortality rate of victims of traumatic injuries if TraumaOne was not available," said Julia Paul, MSN, RN, Trauma Program manager.

Mayor John Peyton discussed the significance of TraumaOne in Jacksonville and surrounding counties before helping to unveil the new logo for the trauma program.

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