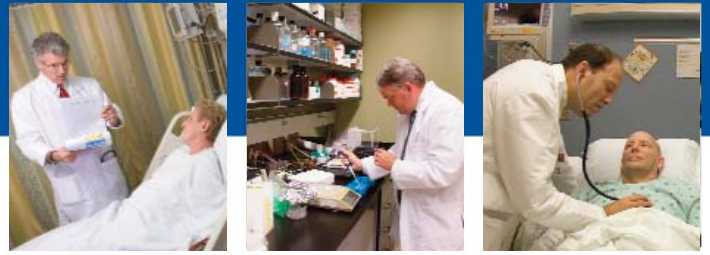


Academic Physician Quarterly

A DEPARTMENT OF MEDICINE BULLETIN



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Jacksonville

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CHAIRMAN'S MESSAGE

Dear colleagues:

I would like to share some good news that we had received recently. Our core residency program was reviewed by the Residency Review Committee (RRC) and it received five year full accreditation without any citations. Indeed, the letter of approval mentioned accolades for the training program. Specific quotes included were "enriched educational environment" and the program "generates significant enthusiasm among the residents." In addition, the subspecialty programs that were reviewed concomitantly namely, cardiovascular diseases, invasive cardiology, medical oncology and infectious diseases, all received the maximal 5 year approval. Subsequently, all these approved programs were given an unprecedented additional year of approval. This outcome was the result of the tireless efforts of our GME leadership, program directors, and most importantly our bright and talented trainees.



Since July 1st, the Cogent Healthcare became the hospitalist group covering the non-teaching services. This change was initiated to enhance efficiency of patient care and improve communications with referring physicians. In addition, this change will help our faculty focus their efforts in resident covered patient care areas.

The Department of Medicine continues to expand its repertoire of state-of-the-art technology. In this issue, Dr. Samir Habashi describes the role of endoscopic ultrasound (EUS) in the diagnosis of gastrointestinal and non-gastrointestinal diseases. This service is now available for the community.

Please let me know how we can improve the services we offer to meet your expectations.

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



Samir Habashi, M.D.
Assistant Professor of Medicine
Division of Gastroenterology

Endoscopic Ultrasound

Endoscopic Ultrasound (EUS) is an important and integral component in the diagnosis of gastrointestinal and non-gastrointestinal diseases. There is a relative underutilization of the technology. It has been demonstrated that EUS with and without FNA (Fine Needle Aspiration) has a clinical impact in the management of certain gastrointestinal disease processes and that FNA is cost-effective approach for staging of malignancy.

Here are some of the examples of the clinical utility of EUS:

ESOPHAGEAL CANCER

Choice of therapy and outcome in patients with esophageal cancer is stage dependent. One important role of EUS is the initial triage of patients to receive neoadjuvant therapy, undergo surgical resection or in very early stage undergo Endoscopic Mucosal Resection (EMR). EUS is superior to PET scan & CT in lymph node (LN) detection. The finding of celiac LN is considered an evidence of metastatic spread (M1).

Table 1: Comparison of accuracy of CT & EUS in the regional staging of esophageal cancer

| Technique | No. of pts | T Accuracy (%) | N Accuracy (%) |
|-----------|------------|----------------|----------------|
| CT | 1154 | 45(40-50) | 54 (48-71) |
| EUS | 1035 | 85(59-92) | 77 (50-90) |

(Rosch T. Endosonographic staging of esophageal cancer. A review of literature results. Gastrointest Endoscop Clin North Amer 1995; 5:537-547)

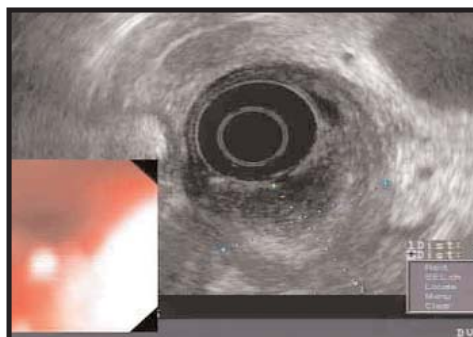


Figure 1: An example of a T3 N1 Esophageal tumor. The tumor (5 O'clock position) invaded the muscularis propria (T3) There is also an evidence of Lymph node invasion (N1) (12 O'clock position)

GASTRIC TUMORS

EUS is useful for staging gastric cancer but is not an effective screening tool. Endoscopic Mucosal Resection can be applied to gastric cancer if the lesion is well differentiated and intramucosal (any size), or if ulcerative, with a diameter < 3 cm. EUS & CT scan are complementary rather than competitive. EUS is superior to CT scan in evaluating the structure of the gastric wall, but not accurate in assessing distant metastasis.

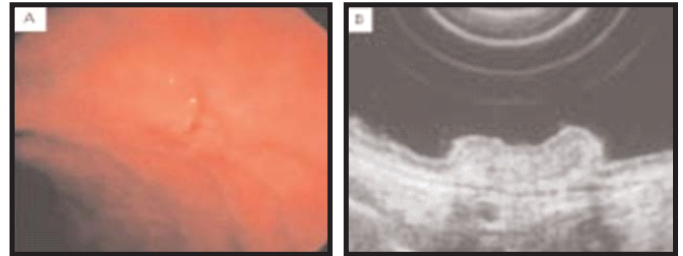


Figure 2: Malignant gastric ulcer where the tumor invades the muscularis propria

PANCREATIC CYSTS

The differential diagnosis of pancreatic cystic lesions is wide. The vast majority are pseudocysts. The detection of mucinous neoplasms is most important as these may be malignant or have malignant potential. The combination of EUS features, fluid cytology CEA and amylase levels can improve accuracy in detecting potentially malignant lesions.



Figure 3: Pancreatic pseudocyst: Radial EUS in a patient with a recent episode of pancreatitis reveals a 3-cm, thin-walled, anechoic cystic lesion in close to the gastric wall. Analysis of the cystic fluid showed a high amylase level and a low CEA level.

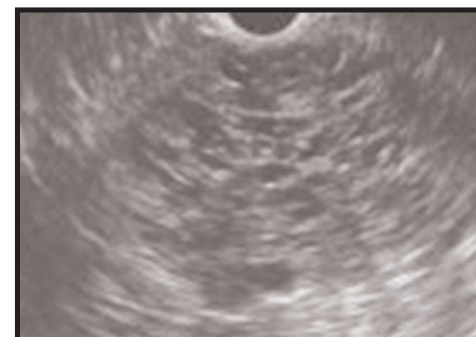


Figure 4: Serous cystadenoma: Typical honeycomb appearance of a 2.5 cm microcystic serous cystadenoma. There are multiple small anechoic areas.

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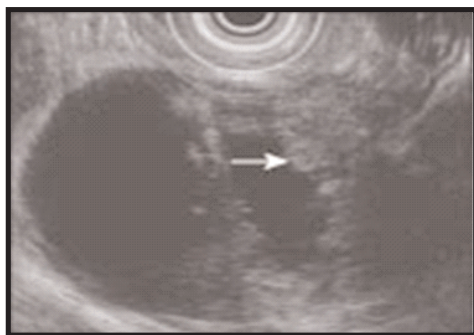


Figure 5: Mucinous cystadenoma. Numerous solid, papillary projections from the cyst wall are seen (arrow). FNA revealed mucin-positive cuboidal cells, and resection confirmed a benign mucinous cystadenoma.

PANCREATIC CANCER

EUS is the most sensitive imaging modality for the detection of pancreatic masses. It is particularly useful for the identification of tumors undetected by other methods such as CT. A normal-appearing pancreas without a mass would essentially r/o the possibility of pancreatic CA.



Figure 6: Pancreatic mass with cystic component FNA needle inside the mass

RECTAL CANCER

EUS is needed for accurate staging of rectal cancer. Patients with locally advanced disease should receive adjuvant therapy.

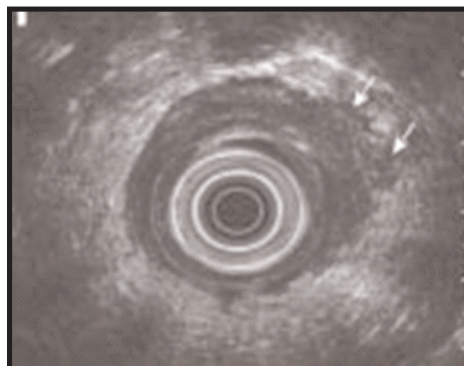


Figure 7: Figure 7 shows T3 rectal tumor with extension of tumor through muscularis propria (arrows)

CONCLUSION

- 1) The primary indications for EUS are cancer staging when there is potential additive value after CT or MRI has been performed, assessment (usually combined with EUS-FNA) of lymph nodes, and the evaluation of pancreatic disease and submucosal tumors.
- 2) Antibiotics are recommended for prophylactic use with EUS-FNA of a cystic lesion.
- 3) The risk of perforation with EUS is higher than for standard endoscopy.
- 4) EUS can play a role in endoscopic anastomosis & also for chemotherapy of pancreatic cancer.

GME CORNER



Jeffrey House, D.O.

**Assistant Professor of Medicine,
General Internal Medicine**

**Associate Program Director,
Internal Medicine Residency**

The beginning of the 2009 academic year is upon us and the new residents and fellows are in full swing. We are pleased to bring in another strong group of trainees who will surely contribute to what is now a very successful program. The end of the year was marked with a wonderful graduation dinner and accompanying send-offs to graduating residents and fellows. This year we had a first time winner of the Teacher of the Year Award. Dr. Laos continued the success

of the Pulmonary, Critical Care division by being this year's recipient. Intern of the Year went to Justin Federico and Resident of the Year went to Andrew Darlington, M.D., both well deserving of this recognition. We are very proud of these residents and teachers as well as all the new graduates.

After several anxious months, the core program and several fellowships finally heard the results of the RRC site visit and the news was great. First, the core residency program received the news that we were accredited for a 5 year cycle. Not only were there no citations, but the program received a few accolades; most notably that there was an "enriched educational environment" and the program "generates significant enthusiasm among the residents." Not to be out done, fellowship programs in medical oncology, infectious disease, cardiovascular disease, and interventional cardiology were also granted a 5 year accreditation cycle. On behalf of GME leadership, I would like to thank the faculty, staff, and trainees for their contribution to the success of the RRC site

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visit. This program has a genuinely strong foundation, built by hard work from everyone involved with the residency and fellowships. This is certainly the impression the site visitor took away after visiting the campus, the core program and the individual fellowships. All this said, one person in particular stands out when analyzing the success of this site visit as well as the overall achievements of the program. Dr. N. Stanley Nahman, Jr. has put countless hours of work into this program over the last five years, and I could not discuss the recent accomplishments without recognizing the person who is integral to all of these achievements. His devotion to the academic mission is quite unique, and he had the foresight to make changes to adapt to the evolving academic climate. The residency is particularly appreciative of Dr. Nahman and his work as program director.

Life moves pretty fast in the GME world and the upcoming year's accomplishments, as well as challenges, are right

around the corner. New graduates are currently taking their boards, and it won't be long before we begin the recruitment process again for the 2010 trainees. The Fall Florida ACP meeting is also coming up where three residents will be making presentations. The resident "Jeopardy" team will attempt to build on their prior success and go for their second victory. New regulations from the ACGME are being instituted this year and have already created changes within the teaching services. With the support of strong leadership and energetic residents, the program is prepared to take on the challenges these new requirements create. These are just a few of the recent events; the upcoming year certainly will be filled with many more.

Thanks to everyone who made last year so successful and we in the GME department look forward to working with you again this year.

A CLINICAL CASE

Manish Relan, M.D., Department of Medicine

Pramod Reddy, M.D., Department of Medicine

Robert Booth, M.D., Department of Radiology

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

Wernick's Encephalopathy Secondary to Nutritional Thiamine Deficiency

CASE REPORT

A 45 year old woman presented to the emergency room with the chief complaint of left sided chest pain. Patient had a significant medical history of depression for which she was being managed by an outpatient psychiatrist. Her chest pain was described as intermittent, lasting for ten to fifteen minutes, moderated intensity and had no radiations. The pain started 5 days ago and the patient could not describe any aggravating or relieving symptoms.

The patient had lost close to twenty pounds over the last one month and had been experiencing weakness, shortness of breath, palpitations and was having difficulty at times understanding other people.

On admission she was alert but slow to respond to questions and had difficulty understanding commands and she appeared malnourished. Her heart rate was 78 beats per minute with a blood pressure of 90/74 mmHg. No ortho-

static pressures were recorded at that time. On examination she was found to have bilateral lateral nystagmus and left sixth nerve palsy. Her speech was fluent and clear and there was no dysarthria. The patient had difficulty following three step commands properly although she was able to perform one step commands without much difficulty. There was no facial asymmetry, no weakness of the tongue, no bulbar symptoms and there was no motor deficit but she had dysmetria in both upper and lower extremities with the reflexes normal and symmetrical in upper extremity and absent at both knees and ankles. The rest of her physical examination was unremarkable.

Laboratory markers of cardiac injury were not elevated. The results of the lumbar puncture showed an opening pressure of 8ml of water, cerebrospinal fluid (CSF) protein was elevated to 94 mg/dl with no xanthochromia with only three red blood cells and no white blood cells. The CSF was negative for cryptococcal antigen, arbovirus antibody panel, herpes simplex virus 1/2 DNA PCR and for VDRL. The serum concentration of thiamine was 1.2 µg/l (normal range 4.0-20.0). Vitamin B12 and folate were within normal range.

Wernicke's encephalopathy was suspected and patient was treated with thiamine. A magnetic resonance imaging of the head two days after admission showed multifocal areas of scattered abnormalities with Wernicke's encephalopathy (Figures 1).

Two-dimensional echocardiogram showed severe global

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left ventricular dysfunction with an estimated ejection fraction of fifteen to twenty percent with a normal left ventricular size and thickness.

The patient continued to improve with her intravenous thiamine therapy and at the time of discharge her mental condition had markedly improved.

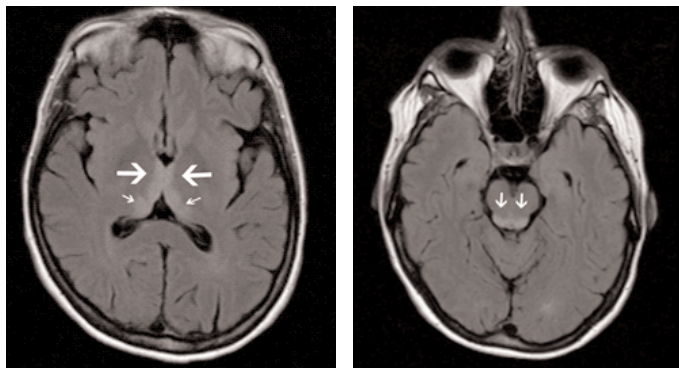


Figure 1: Axial magnetic resonance FLAIR images of the brain demonstrate striking focal areas of increased signal on T2 sequences noted in the periaqueductal grey matter (large arrows) and medial thalamic nuclei and tectal plate of the midbrain (small arrows). The findings are consistent with a toxic/metabolic encephalopathy notably Wernicke's encephalopathy.

DISCUSSION

Most cases of thiamine (or vitamin B1) deficiency worldwide are the result of poor dietary intake (1). In the United States, the primary cause of thiamine deficiency is alcoholism. Thiamin triphosphate plays a key role in integrity of the peripheral and the central nervous systems (2). The case illustrates the insidious nature of the clinical course of nutritional thiamine deficiency. It is not clear whether the depression was the primary event causing anorexia, malnutrition and gradual thiamine deficiency while the latter in turn aggravated the depression and further contributed to the emergence of the encephalopathy. Many of the symptoms were readily reversible with thiamine supplementation.

The laboratory diagnosis of thiamine deficiency is usually made by functional enzymatic assay of transketolase activity and measurements of serum thiamine level (2).

Thiamine deficiency can present with a wide spectrum of clinical symptoms and signs. Early manifestations of thiamine deficiency include anorexia, muscle cramps, paresthesias, and irritability (1). Advanced thiamine deficiency can result in lactic acidosis, chronic peripheral neuritis, gastrointestinal beriberi manifesting as abdominal pain, vomiting and lactic acidosis, wet beriberi (shoshin beriberi) characterized by marked peripheral vasodilation resulting in high-output heart failure (6) and dry beriberi that involves both the

peripheral and the central nervous systems. The peripheral nervous system disease presents as symmetric motor and sensory neuropathy associated with pain, paresthesias, and loss of reflexes while the central nervous system involvement results in Wernicke's encephalopathy, consisting of horizontal nystagmus, ophthalmoplegia due to weakness of one or more extraocular muscles, cerebellar ataxia, and mental impairment. When there is an additional loss of memory and a confabulatory psychosis, the syndrome is known as Wernicke-Korsakoff syndrome.

Thiamine has a central role in the metabolism of carbohydrates and the daily requirement of thiamine depends on carbohydrate consumption. The DRI for thiamine is 1 to 2 mg per day. Since the liver stores only about 30 to 50 mg of thiamine, inadequate intake can cause symptomatic deficiency by depleting body stores in 4 to 6 weeks. Generally, because of the renal excretion of thiamine, there is no known toxicity associated with the ingestion of large doses of vitamin B1 over prolonged periods of time.

In acute thiamine deficiency with either cardiovascular or neurologic signs, 100 mg/d of thiamine should be given parenterally for 7 days, followed by 10 mg/d orally until there is complete recovery. Patients with Wernicke's encephalopathy require immediate treatment with 100 mg of intravenous thiamine, with titration of additional doses until the ophthalmoplegia resolves. Resistance to thiamine may result from hypomagnesemia because magnesium is a cofactor for thiamine transketolase. Eye movements sometimes begin to improve within a few hours and, except for residual nystagmus, may be normal within 1 or 2 weeks. Cardiovascular improvement occurs within 24 hours. Ataxia tends to improve less completely and more than half of patients are left with a broad-based, unsteady gait. Drowsiness, inattentiveness, and apathy tend to clear with treatment, but Korsakoff's syndrome often persists. Once established, the memory disorder is permanent in the majority of patients.

The case highlights the need for a high index of suspicion to identify thiamine deficiency in high risk patients. The MRI findings of the brain are helpful in alerting the clinician to this diagnosis.

REFERENCES

1. Harper C. Thiamine (vitamin B1) deficiency and associated brain damage is still common throughout the world and prevention is simple and safe! *Eur J Neurol.* 2006; 13(10):1078-82.
2. Reuler JB, Girard DE, Cooney TG: Wernicke's encephalopathy. *N Engl J Med* 1985; 312(16):1035-9

Endocrine Society Statement addressing the concerns of insulin glargine (Lantus®) and neoplasia:

Recently, the press has reported a potential relationship between malignancy and the use of insulin glargine. These reports are based on a series of five retrospective observational studies (4 papers and one letter) published on-line in *Diabetologia*. The studies differ considerably in patient populations, confounding variables, and analytic methods, as well as in conclusions. Certain factors should be kept in mind as one considers this new information. Obesity, diabetes (particularly Type 2), and insulin resistance all appear to be associated with occurrence of malignancy (especially breast, colon, and pancreas). Insulin is a dose-dependent mitogen under various experimental paradigms, and there appears to be a positive correlation between insulin dosage and occurrence of malignancy in diabetic patients. Genetic modification of the insulin amino-acid sequence can alter hormonal conformation and interaction with receptors, potentially leading to changes in insulin's hypoglycemic and/or mitogenic activity, or the ratio between these two.

The index paper from Germany by Hemkens et al examined records of 127,000 individuals who began monotherapy with a single type of insulin (native, lispro, aspart, or glargine) and were followed retrospectively over an average time of 1.6 years for the development of malignancy. The key finding, determined with a Cox multiple regression model, was that use of insulin glargine monotherapy was associated with a statistically higher chance of malignancy, for any given dose of insulin, than use of native insulin monotherapy; the adjusted hazard ratio increased from 1.09 for daily insulin doses of 10 units up to 1.31 for daily insulin doses of 50 units.

In considering these results, there are several aspects of this study that should be kept in mind:

- 1) The follow-up period was very short in terms of development of malignancy, so that the investigators were probably examining growth of pre-existing cancers rather than initiation of de-novo malignancy;
- 2) The results were not adjusted for differences in weight or BMI, factors known to be associated with malignancy;
- 3) There was no breakdown of the malignancy occurrence by site of cancer.

Furthermore, it should be emphasized that this paper's conclusion of an association between insulin glargine and malignancy was the result of a complicated statistical analysis in which insulin dosage played a key role. Analysis of the raw data, reflecting the real-life situation rather than the prediction of a statistical model, showed that absolute cancer incidence was actually 15% lower with insulin glargine monotherapy. Furthermore, the gross all-cause mortality was considerably lower with insulin glargine (hazard ratio 0.68; CI 0.65-0.72). Consequently, it is difficult to assess, from this study alone, whether insulin glargine is helpful or harmful, compared to native insulin, in a clinical practice environment. The other papers reported in *Diabetologia*, considered as a whole, did not support a clear-cut answer to the question of potential harm from insulin glargine, and these studies also came to a series of perplexing conclusions. For example, a Swedish study reported an increased risk of breast cancer with insulin glargine (relative risk 1.99), but also showed that women using insulin glargine had lower all-cause mortality (relative risk 0.83). A Scottish study suggested that insulin glargine monotherapy was associated with cancer occurrence, but that insulin glargine combined with other insulins seemed to be beneficial as far as cancer incidence. One surprising finding was that metformin use seemed to be strongly protective against cancer, another plus in favor of this popular medication.

A particular concern in all of these studies is the possibility of "allocation bias": differences in underlying cancer-predisposing factors (especially weight and age) between the insulin glargine group and the comparator group that may not have been corrected for by the statistical methods used and which might account for some or all of the differences noted in purported cancer incidence.

Taken together, these studies do not clearly indicate that inclusion of insulin glargine in a treatment regimen for diabetes leads to worse overall health or, for that matter, better overall health. Nevertheless, the possibility of increased cancer occurrence with insulin glargine use under some circumstances does raise concern. Practitioners who treat diabetes have a variety of potential treatment regimens in their armamentarium, and they should continue to individualize their recommended therapy based on each patient's situation.

References

1. <http://www.endo-society.org/media/press/2008/SocietyRespondstoRecentInsulinGlargineLantusStudy.cfm>

NEWS & NOTES

- **Dr. Andrew Darlington** was the recipient of the 2009 Outstanding Resident Clinician Award. The award was presented to him at the resident graduation ceremonies on June 17, 2009. The Edward Jelks Outstanding Resident Clinician Award is given annually to the resident who through dedication, diligence and compassion, or through innovation in patient care, is considered to have contributed the most to the improvement of patient care at Shands Jacksonville.

Dr. Darlington is currently one of the two Chief Residents in the Department and he is planning to stay on as a fellow in Cardiology starting July 1st, 2010.

- **Dr. Linda R. Edwards** was the recipient of the 2009 Russo Professionalism Award. The award was presented to her at the resident graduation ceremonies on June 17, 2009. The Louis S. Russo Award for Outstanding Professionalism in Medicine is presented annually to an individual with the highest standards of medical

professionalism, substantiated by a commitment to personal behavior that reflects the core values of the consummate physician.

Dr. Edwards' contributions to the clinical excellence in this institution are widely recognized. She has effectively led the Division of General Internal Medicine for many years and has served the Department and the Institution in multiple capacities. Her academic achievements have earned her a national recognition. She is a dedicated educator and a role model for our faculty and trainees.

- **Department of Medicine Awards:** Dr. Luis Laos of the Division of Pulmonary, Critical Care & Sleep Medicine was the winner of Teacher of the Year Award. Intern of the Year recognition was given to Dr. Justin Federico and the Resident of the Year was Dr. Andrew Darlington. Congratulations to all awardees.

MEET YOUR COLLEAGUES



Chrysoula Pappa, M.D., Assistant Professor of Medicine, Division of Rheumatology

Dr. Pappa earned her medical degree from Aristotle University of Thessaloniki in Greece. She completed her residency in Internal Medicine and her fellowship in Rheumatology at Albany Medical College in Albany, NY. Dr. Pappa is board certified in Internal Medicine and her clinical interests include general rheumatology.



Robert Zaiden, M.D., Assistant Professor of Medicine, Division of Hematology/Oncology

Dr. Zaiden earned his medical degree from St. Matthews University School of Medicine. He completed his residency in Internal Medicine and his fellowship in Medical Oncology at the University of Florida College of Medicine - Jacksonville. Dr. Zaiden is board certified in Internal Medicine and his clinical and research interests are GI oncology to include esophageal, gastric and colorectal cancers.

SHANDS BRAND

Shands Jacksonville on Social Networking Scene

Facebook and Twitter began as a way for individuals to connect with one another. It is also quickly becoming a place for companies to communicate with various audiences. Shands Jacksonville has recently joined the social media scene with organizations such as Motrin, Baskin-Robbins,

Coca-Cola, and even the White House.

Social networking sites like these are rapidly changing the way businesses market and advertise their products and services to potential consumers. Healthcare organizations, including Shands Jacksonville, are no different than the organizations mentioned above. Our environment is becoming increasingly competitive, and for hospitals to survive, we

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must consider non-traditional means of reaching our audiences.

A good Web site provides in-depth information about a company's products and services and it is continually updated with new content. Using social networking sites enables us to share updates on jax.shands.org with fans on Facebook and followers on Twitter and pushes them to our Web site. In addition to updates on service line pages, fans and followers are informed of new patient spotlights as well as healthcasts with physicians. Recent healthcasts include interviews with Christopher Williams, MD, about prostate cancer, and Scott Silliman, MD, on stroke.

Social networking is not a trend—it is here to stay. It is estimated that two-thirds of all Internet users visit social networking or blogging sites. Last year, Facebook recorded 1.2 billion visits a month, making it the top-ranked social network site. Twitter ranked third with 54.2 million visits.

And it's not just for teens and young adults. The audience has become broader and older. This shift has primarily been driven by Facebook, whose greatest growth has come from people aged 35-49 years of age (+24.1 million). From December 2007 through December 2008, Facebook added almost twice as many 50- to 64-year-old visitors (+13.6 million) than

it added under 18-year-old visitors (+7.3 million).

For Shands Jacksonville, the future of social networking will be to continue offering pertinent information (latest news, breakthroughs in treatment and clinical trials) to existing and potential customers that will keep them informed and returning to the site. Healthcare organizations maximize their social networking sites by allowing patients from the community and around the globe to connect with others living with the same illnesses, while physicians can share information with one another and learn about the latest treatment options and research. The site incorporates the existing brand and marketing strategy, as well as serves as an extension of the organization's outreach programs.



If you're interested in following us on these sites, go to Facebook.com or Twitter.com and type Shands Jacksonville Medical Center in the search box to find the official page, or visit jax.shands.org/news and click on the Facebook or Twitter links.

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