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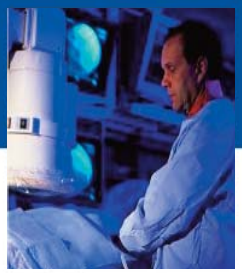
Academic Physician Quarterly

A DEPARTMENT OF MEDICINE BULLETIN



UF UNIVERSITY of FLORIDA
College of Medicine
Jacksonville

CHAIRMAN'S MESSAGE

Dear colleagues:

With this issue we are celebrating the five year anniversary of the launch of Academic Physician Quarterly (APQ). The significance of this landmark achievement becomes readily apparent when we review our archived issues available at http://hscj.ufl.edu/internal-medicine/archives.asp. Over the last five years the Department has grown in leaps and bounds and has achieved regional and national visibility. Nevertheless, we are aware that we cannot rest on our laurels. We will have to move forward to a new level of excellence in the next five years. As a first step, the Department had its one-day retreat on February 11, 2012, to draft a second five-year plan that will allow us to enhance our faculty, extend our service reach, expand our training programs and accelerate our scientific innovations.

The scientific inquiry has been steadily increasing on our campus. In this issue, we have a Focus topic by Dr. Michael Haas, Associate Research Professor, who describes some of the ongoing basic research activities within the Department.

A recent important development on our campus is the implementation of electronic medical records (EMR). Thanks to the dedication of scores of IT staff, nursing and medical staff and trainees, and the leadership of Dr. Joseph Tepas, the process has been very successful.

It is a wonderful experience to work in an environment where every day is better than the day before and yet it turns out to be worse than the day after. We have been blessed to have dedicated physicians, nurses and support staff who have chosen University of Florida & Shands Jacksonville as their employers.

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

Michael Haas, Ph.D.

Research Associate Professor

Director of Medical Research

Department of Medicine

Basic Science Research at the University of Florida College of Medicine–Jacksonville

Located behind the hospital north of 11th Street, the Medical Research Building is home to several Department of Medicine faculty members who are accomplished basic science researchers. Inaugurated in July 2007, the Medical Research Building is the flagship of our research efforts on campus. The current faculty including Steve Li (Division of Gastroenterology), Charles Heilig, Minghui Xiang, Leighton James (from the Division of Nephrology & Hypertension), and Michael Haas (Division of Endocrinology, Diabetes, and Metabolism) have active and productive research laboratories. They are also responsible for training many residents, fellows, and post-doctoral trainees in their fields of research.

Facilities

The basic science research space enjoyed by our faculty includes a core cell culture facility containing a biosafety cabinet sufficient in size for teaching cell culture techniques to trainees, and a glass-wear processing facility and steam autoclave. There are two large facilities that house common research equipment

The Medical Research Building

purchased by former Dean Robert C. Nuss and the Dean's office, including a PerkinElmer Tri-Carb 2800 TR Liquid Scintillation Analyzer and a Bio-Rad MyiQ Single Color Real-Time PCR Detection System: a PerkinElmer Victor3V Model 1420 Multi-label Counter; a Turner Biosystems luminometer for conducting enzyme and cell proliferation assays; a Coulter-Counter, an Eppendorf gradient PCR thermocycler; and an Eppendorf electroporator for introducing DNA and protein into both bacterial and eukaryotic cells. There is also a Sorvall RC3B high-speed centrifuge, a vacuum drying system, and access to -80ºC and -120ºC freezers. These resources allow the current laboratories to perform the highest quality experiments with both in vitro cell culture models and in vivo animal studies (utilizing the animal housing facilities in Gainesville), as well as store and process materials from investigator-initiated clinical studies.

Located in the darkroom, this is an inverted microscope with Hg lamp for fluorescence imaging of slides and cells in culture.

Research Laboratories

Steve Li, M.D., Ph.D. Dr. Li's laboratory conducts basic and clinical research on hepatitis C virus (HCV) to explore the interactions of human innate immunity and hepatitis C virus (HCV) replication to develop better therapeutic agents for treatment of HCV. His research is focused on the biological activities of interferons, including activation of the Jak/Signal Transducers and Activator of Transcription pathway, which regulates the expression of a large number of interferon-stimulated genes that are normally quiescent or expressed at low level. He is exploring two newly discovered genes, 1-8U and heterogeneous nuclear ribonucleoprotein M (hnRNP M), to determine how they modulate Cap-dependent and HCV-mediated translation. He is also elucidating the identity of several new cellular proteins that interact with oligodeoxynucleotides that inhibit HCV-mediated translation. By elucidating the molecular basis for HCV-mediated translation, a step that is essential for halting viral replication, he hopes to develop better anti-HCV therapeutic agents or better therapeutic strategies in the future.

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Focus continued from Page 2

Charles Heilig, M.D. Dr. Heilig is interested in the molecular pathways that give rise to glomerular sclerosis. Using cultured mesiangial cells as well as various mouse models, he is investigating how hyperglycemia, vascular endothelial growth factor, transforming growth factor beta, and glucose transporter 1 impact extracellular matrix deposition and fibrosis. Currently, he is investigating the role of mechanogrowth factor in mediating induction of GLUT-1 expression in various models of type 2 diabetes.

Leighton James, M.D. Dr. James is the newest member of the research community on campus and has been actively investigating the roles of hyperglycemia and hexosamine flux in mediating mesiangial cell toxicity.

Minghui Xiang, Ph.D. Dr. Xiang's laboratory is currently investigating the roles of novel sodium hydrogen antiporters (NHA) in hypertension and diabetes. He works on two human isoforms, HsNHA1 and HsNHA2, which belong to a superfamily of monovalent cation/proton antiporters. He is characterizing the transport properties of HsNHA2 using yeast expression system. He recently found that expression of this gene conferred robust tolerance to Li+ and Na+. The gene locus of human NHA (4q24) is within a chromosomal region associated with essential hypertension in several genome-wide linkage studies. He localized NHA1 and NHA2 among the 300 genes within this region and found no obvious Na+ transporter candidate, suggesting that the NHA genes may be linked to hypertension. Relevant to diabetes, both NHA1 and NHA2 are highly expressed in mouse insulin producing pancreatic β-cells, consistent with evidence linking Na+-Li+ countertransport (SLC) to diabetes. The electrogenic property of NHA may regulate the β-cell's membrane potential that is important for insulin secretion.

Michael Haas, Ph.D. Research in Dr. Haas's laboratory is focused on characterizing the expression of cholesterol transport proteins in the liver. Apolipoprotein A-I (apo A-I) is the primary protein component of high-density lipoprotein (HDL) and confers many of the atheroprotective properties of the particle. He is currently developing a novel high-throughput screening method to test drug candidates for their ability to raise HDL and is investigating how environmental toxins and cigarette smoke lead to low HDL. He is also conducting experiments to examine how HDL and vitamin D inhibit endothelial cell stress associated with hyperglycemia, a process that predisposes to atherosclerosis.

The Future

Although basic science research currently constitutes a small portion of the research being conducted on the UF-Jacksonville campus, it is well supported and expanding. Since the Accreditation Council for Graduate Medical Education (ACGME) has consistently affirmed that graduate medical training programs should have a strong research component, basic science on this campus provides ample opportunities for trainees to expand their horizons and participate in research programs they may have never considered before. This resource also provides ample opportunities for scientists to pair with clinicians in formulating exciting partnerships to expand the clinical research enterprise.

GME CORNER

Christina Bailey, M.D.

Assistant Professor of Medicine, Division of Infectious Disease

Associate Program Director, Internal Medicine Residency

Epic-Isn't there an app for that?

As you are well aware, Epic launched Jan. 21, 2012. The transition overall has been relatively smooth, but not surprisingly there have been a few glitches and growing pains. The most immediate need was for additional computers. The administration was quick to respond to our request for iPads for the inpatient core services for which we at GME are grateful. User use agreements and attestations are forthcoming.

Here is a quick summary of what's going on administratively with Epic:

1. The physician champions will continue to meet monthly to optimize our clinical care. Tricks, tips and interesting shortcuts that emerge will be shared with other departments at this meeting. The core managers

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GME Corner continued from Page 3

who helped build and launch all of the components of this system will continue to meet on a weekly basis. It is vital, therefore, that we physicians, who are

ultimately responsible for assuring that all these efforts yield optimal patient care continue to interact productively, provide insight and give guidance to this project as it moves forward. In other words, this group of physician champions will now evolve into the physician IT advisory group.

2. Tracking problems will continue to be a priority.

3. Change is not always pretty or pleasant, but it is inevitable. Use of an electronic medical record is mandated. Do not forget about medicine reconciliation, which is a component of every navigator. This whole process is new to us in Epic and still has some frustrating extra steps. With time, the system will become smoother and faster. Until then, stay mindful of this change, which has annoyed more than it has pleased. Remember, personal attempts at workarounds may do nothing more than make the problem worse.

4. SMART Text: Many users are customizing common clinical statements as Smart phrases to make their work easier is absolutely appropriate. Unfortunately, some have daisy chained multiple Smart phrases into a variant of Smart text that are then used to replace a note template. These may be great shortcuts, but may also make a note out of compliance or jeopardize it in other ways. The templates that exist (SH IP --------) have been vetted by compliance and others. They represent the "ideal" starting point, then add specific data by Smart phrases. Stick with templates whenever possible.

Thank you for your patience during this transition!

A CLINICAL CASE

University of Florida College of Medicine – Jacksonville
Laurie Ann Ramrattan, M.D., PGY-2 Resident, Department of Medicine
Raafat Makary, M.D., Ph.D., Associate Professor, Department of Pathology
William J. Salyers Jr, M.D., M.P.H., Fellow, Division of Gastroenterology
Juan Carlos Munoz, M.D., Associate Professor, Division of Gastroenterology

Malignant Duodenal Melanoma Presenting as Iron Deficiency Anemia

Malignant duodenal melanomas may be primary lesions but the vast majority are metastatic from cutaneous or ocular sources. They can precede the onset of seemingly benign gastrointestinal symptoms including iron deficiency anemia by an average of > 4 years.

Case Report

A 48 year-old male presented with altered mental status due to an acute overdose of opiods and benzodiazepines and was found to be anemic. He admitted to chronic narcotic use for lower back pains and generalized malaise and weight loss of 26 pounds over the past two months. He was found to have anemia with hemoglobin of 6.4mg/dl and MCV of 72.3 fl. The patient was transfused with two units of packed red blood cells and underwent endoscopic evaluation. Upper GI endoscopy revealed a large fungating, ulcerated mass (Fig. 1&2) with no bleeding in the third portion of the duodenum.

Microscopically HE stains revealed duodenal mucosa focally ulcerated by infiltrating sheets of large polygonal cells with large prominent nucleoli and finely vacuolated cytoplasm showing focal sparse melanin pigmentation (Fig. 3) with immunostains (Fig. 4) consistent with melanoma.

Discussion

Malignant melanomas can originate in, as well as metastasize to, the gastrointestinal tract. Primary malignant duodenal neoplasms are relatively rare and the diagnosis is often delayed because of their vague and nonspecific symptoms which may include weight loss, symptomatic anemia, or an upper or lower gastrointestinal bleed.

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Figure 1: Endoscopic view from the second portion of the duodenum demonstrates a mass (white arrow) in the distance in the third portion of the duodenum.

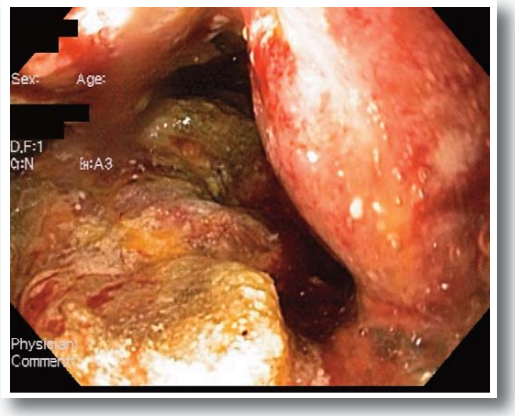

Figure 2: Endoscopic view of the large mass (white arrow) found in the third portion of the duodenum.

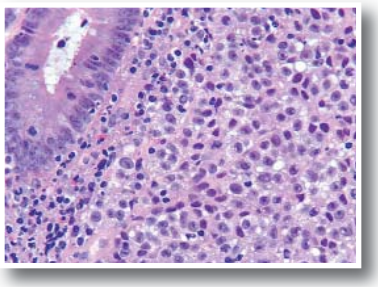

Figure 3a: HE stain showing mucosal infiltration of melanoma (A) with focal melanocytic pigmentation (B).

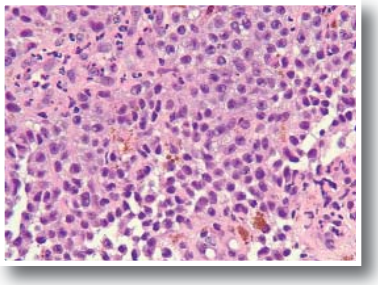

Figure 3b: HE stain showing mucosal infiltration of melanoma (A) with focal melanocytic pigmentation (B).

The criteria for the diagnosis of primary duodenal melanoma includes lack of concurrent or previous removal of a melanoma or atypical melanocytic lesion from the skin, lack of other organ involvement, and in situ change in the overlying or adjacent gastrointestinal epithelium.

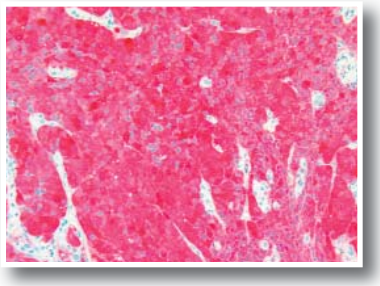

Figure 4a: The tumor cells were diffusely and densely positive for S100 (A), HMB-45 (B), and focally positive for Melan-A (C) immunostains consistent with melanoma.

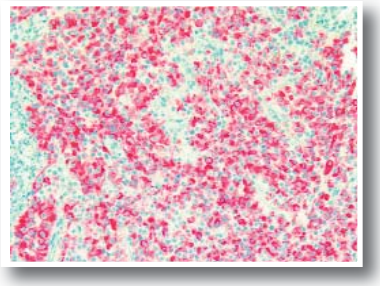

Figure 4b: The tumor cells were diffusely and densely positive for S100 (A), HMB-45 (B), and focally positive for Melan-A (C) immunostains consistent with melanoma.

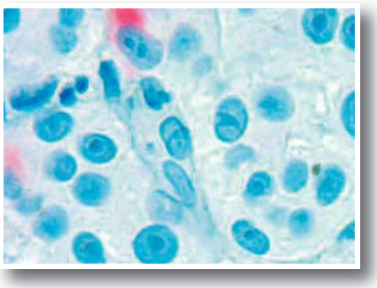

Figure 4c: The tumor cells were diffusely and densely positive for S100 (A), HMB-45 (B), and focally positive for Melan-A (C) immunostains consistent with melanoma.

Malignant melanomas are the most common source of metastatic cancers to the gastrointestinal tract and between 1% and 4% of all patients with malignant melanomas will have clinically apparent GI involvement diagnosed antemortem with up to 60% found to have GI metastases at autopsy. Metastatic melanomas can occur in the gastrointestinal tract many years after regression of a diagnosed or undiagnosed primary melanoma. Early detection of gastrointestinal metastases using abdominal CT scan has been shown to be useful in asymptomatic melanoma patients and those with nonspecific symptoms.

Aggressive surgery remains the treatment of choice offering both symptom palliation and long-term survival for patients, with the median survival after curative resection in the small intestine being 49 months and the longest reported survival being 21 years.

Conclusions

This case is presented to increase the awareness of considering malignant melanomas in the differential of iron deficiency anemia and the importance of investigating primary skin and ocular lesions since early detection and management can improve patient outcome.

A New Option for Treatment of Latent Tuberculosis

Reprinted from Drug Update Volume 28, Number 5; November-December 2011 with permission.

On December 9, 2011, the Centers for Disease Control and Prevention's (CDC) Morbidity and Mortality Weekly Report outlined recommendations for a new 12-dose weekly treatment regimen for latent tuberculosis (TB) infection [1]. This new 12-dose regimen reduces the duration of treatment with isoniazid (typically given daily over nine months for 270 doses) to 12 doses of isoniazid + rifapentine (Priftin®) given once-weekly over three months (total of 12 doses).

The CDC reports that more than 11 million people in the United States have latent TB infection and 5 to 10% of these will convert to active TB. Although 300,000 to 400,000 patients begin treatment for latent TB infection each year, only about 60% typically complete the nine-month standard self-supervised isoniazid regimen [1, 2].

The new regimen was studied in a randomized, controlled, 33-month trial of 7,731 patients with latent TB infection. The trial found a combination of isoniazid (INH) and rifapentine (RPT) administered as directly observed therapy (DOT) in 12 once-weekly doses was as effective in preventing TB as the nine-month daily self-supervised INH regimen, with the benefit of improved compliance (82% vs. 69%, $p<0.01$). Drug discontinuation for any reason was more common in the isoniazid-only arm, but hypersensitivity reactions and drug discontinuation due to adverse events were more common in the combination therapy arm. Two smaller studies also found the 12-dose INH and RPT regimen effective.

The 12-dose weekly regimen consists of isoniazid 15 mg/kg (rounded to nearest 50 mg to 100 mg; maximum dose of 900 mg) and rifapentine (weight-based dosing; maximum once-weekly dose is 900 mg). It should be administered under DOT to ensure the completion of all doses.

Clinical monitoring should include:

- Baseline liver function tests (LFTs) especially for patients with HIV, alcohol use, liver disorders, those in the immediate postpartum period (≤ 3 mo), and the elderly (e.g., those with complicated medication or medical histories).

- Monthly assessment for toxicity (e.g. icterus, tenderness of liver, rash) and hepatic tests for those at risk for liver disease. Clinical assessment at first sign of toxicity.

- Discontinuation of therapy if LFTs exceed 5x normal in patients without symptoms or 3x normal in patients with symptoms of toxicity.

- Monitoring for hypersensitivity (e.g., hypotension, thrombocytopenia) and drug discontinuation where needed.

The 12-dose regimen does not replace existing treatment options for latent TB infection, but it provides another option for treatment in healthy patients (older than 12 years) who are recent contacts of a TB patient, who have recently converted via PPD testing, or who have radiographic evidence of healed pulmonary TB. Currently, this regimen is not recommended for children younger than 12, or HIV patients who are taking antiretroviral therapy.

References

1. Centers for Disease Control & Prevention. Recommendations for Use of an Isoniazid-Rifapentine Regimen with Direct Observation to Treat Latent Mycobacterium tuberculosis Infection. MMWR 2011; 60:1650-1.

2. Centers for Disease Control & Prevention. "CDC Issues Recommendations for Shorter Treatment Regimen for Latent TB Infection." Available at: http:// www.cdc.gov/tb/publications/matte_articles/12Dose_HCP.pdf Accessed: 12/19/11.

Jacksonville Training Program at the 2012 Southern Regional Meeting of the American Federation for Medical Research

This year several of the trainees in our Internal Medicine Program have been accepted for presentations at the 2012 Southern Regional Meeting of the American Federation for Medical Research held February 9-11 at the InterContinental Hotel in New Orleans, Louisiana.

Oral presentations included:
1) "Asymmetric arthritis in a patient with hidradenitis suppurativa" by Dr. Cristian Landa (PGY 3);
2) "Thyrotoxic periodic paralysis in an African American male" by Dr. Hammad Jafri (Chief Resident)

Poster presentations included:
1) "Non-genomic signaling by 24,25-Dihydroxyvitamin D3 in HepG2 cells" by Dr. Jaisri Maharaj (PGY 2);
2) "A fatal case of Dress syndrome" by Dr. Reshma Ramlal (PGY 3)

Congratulations to all involved in these research efforts.

Dr. Abubakr Bajwa elected as the vice president of the Southeast Thoracic Association

Dr. Abubakr Bajwa, Chief of the Division of Pulmonary, Critical Care and Sleep Medicine, has been elected to serve as vice president of the Southeast Thoracic Association for the 2012-2014 term. He was nominated for this post by Dr. Bruce Krieger and he was elected with a unanimous vote.

Dr. Bajwa's fellow officers include President, David Schulman, MD, MPH, Emory University and Secretary, Jason Spires, MD, University of South Carolina.

Please join me in congratulating Dr. Bajwa for this honor.

Dr. Syed Jafri receives Edward AFMR Award

One of our Chief Residents Dr. Syed Jafri has received Young Trainee Research Award for his presentation on February 11, 2012 at the Annual Meetings of the American Federation for Medical Research (Southern region) in New Orleans, Louisiana. The title of his presentation was "Inhibition of Endoplasmic Reticulum Stress by Vitamin D in Endothelial Cells".

Congratulations to Syed for this honor.

Exemplary Teachers Awards to the Faculty

Fourteen faculty members in the Department of Medicine were chosen to receive the 2012 University of Florida College of Medicine's Exemplary Teachers Award.

The awardees include (arranged alphabetically): **Drs. Irene Alexandraki, Linda Edwards, Malcolm T. Foster Jr., Ashwani Gupta, Nilmarie Guzman, Michael Haas, Jeffrey G. House, Alan B. Miller, Arshag Mooradian, Juan Munoz, Dat Pham, Fauzia N. Rana, Michael Sands and Robert A. Zaiden.**

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

The awardees will be recognized on April 12 during the proceedings of Advances in Medical Education held in the LRC Auditorium/Atrium from 12 p.m. to 4:30 p.m.

Please join me in congratulating the awardees.

Internal Medicine Update

The Internal Medicine Update conference is offered annually to provide primary care physicians and allied health professionals with an in-depth overview of current healthcare issues, and the latest treatment modalities relevant to the clinical practice of general medicine.

When: June 8-10, 2012

Where: Sawgrass Marriott, Ponte Vedre Beach

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

UF UNIVERSITY of FLORIDA
College of Medicine
Jacksonville
653-1 West Eighth St.
Department of Medicine
Jacksonville, FL 32209-6511
904-244-8846; fax: 904-244-8844

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