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CHAIRMAN'S MESSAGE

Dear Colleagues:

I hope you had an enjoyable summer and are now looking forward to the cooler weather of the fall.

I am pleased to report that the publication of the Academic Physician Quarterly (APC), the official newsletter of the Department of Medicine at the University of Florida-College of Medicine - Jacksonville, has been well received by many of our readers. I would like to encourage you all to send me your thoughts, comments and articles you would like see published in this venue.

The Department of Medicine and UF & Shands in general, are experiencing an unprecedented growth of faculty membership. As in the past we will be introducing some of our colleagues by highlighting their biography and areas of expertise in the current and future issues of the APC.

The Department of Medicine had an exceptional year of growth and productivity in FY 07. I am proud to report that faculty members of the Department have expanded the clinical productivity by 36% and were recognized for their exceptional contributions to the teaching mission of the University of Florida. In addition, the faculty members were engaged in high quality biomedical research that resulted in 77 publications in peer review journals along with numerous presentations in National and International conferences.

In this issue we highlight the Division of Infectious Diseases. This Division has a unique position, having a partnership with the Duval County Department of Health. It is a model for public health with an academic link to better serve the community and provide an educational resource to the UFCOM.

Also in this issue you will see the recent initiatives in enhancing cancer care resources at UF & Shands. The central piece of these initiatives is the proton beam facility that has put Jacksonville on the map of premier centers of excellence in cancer therapy.

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

FOCUS

Michael Sands, M.D.
Associate Professor of Medicine
Chief, Division of Infectious Diseases

UF Infectious Diseases Division, a model for public health-academic linkage and service to the community

The Division of Infectious Diseases of the Department of Medicine occupies a unique position in the Duval County community as a partnership between an academic division of infectious – communicable diseases and the department of public health. At the Shands Hospital – Jacksonville, the Division is primarily visible as a consultative and teaching service. In this capacity the Division provides Shands Hospital with infectious diseases consultative expertise in all areas of adult patient care. Consultations are done on request on both the teaching and non-teaching services. Consultations benefit not only patient care and potentially decrease patient length of stay but also provide a teaching benefit to the students, residents and fellows on both the consultative and the requesting services. A specialized area of infectious diseases consultation for transplant patients is also provided. Behind the scenes, the Division provides direction to the infection control activities of Shands Hospital.

Ten years ago, the Division Infectious Diseases and Duval County Health Department (DCHD) Communicable Diseases Division existed as two separate functionally disparate groups. Drs. Michael Sands, Robert Nuss, Ted Bass (then interim Chief of Medicine) and Jeffrey Goldhagen recognized the need to revamp the DCHD's Communicable Diseases Division into a professional group that could enhance the patient care and development needs of the Division. It was envisioned that collaboration between the University of Florida (UF) and DCHD would foster the recruitment and retention of highly qualified professionals, encourage the development of an academic linkage between the two divisions and create a growth environment that would benefit both parties and the community. Over the ensuing 10 years, the joint Infectious Diseases and Communicable Diseases Division has grown to 7 faculty members, 3 adjunct faculty, 2 fellows, 3 Physican Assistants, 1 travel medicine specialty nurse and 1 nurse research coordinator. The division continues to provide 24/7 consulting at Shands hospital, direction of hospital infection control, and outpatient travel medicine clinics. Members of the division have developed the administrative and area expertise to direct and/or provide consultative expertise in the areas of infection in transplantation, bioterrorism, tuberculosis, sexually transmitted diseases, HIV/AIDS, prison/institutional ID and communicable diseases epidemiology. The Division is currently supported through the UF Department of Medicine and consultative revenues. Communicable Diseases DCHD activities are supported through a contractual agreement with the UF Department of Medicine for services. The division has developed a research section that oversees research grants totaling approximately $250,000 and includes an NIH – CPCRA site grant for conduct of the SMART study, interim results of which have recently been published in the New England Journal of Medicine. A large component of the research conducted by the unit involves clinical trials in HIV/AIDS patients. These trials provide availability of investigational medications to the HIV/AIDS population of Jacksonville, advance the knowledge of efficacy, safety and utility of medication regimens, while also advancing the academic mission of the Division. The Division is also responsible for performance of components of federal and state categorical grants awarded to the DCHD for TB, HIV, refugee and STD care and epidemiologic services. These grants are in excess of $6.5 million. Additionally, the Division has been instrumental in acquiring and directing a federal Ryan White Title 3 grant of $300,000 annually for improved community based access to care, that provides HIV/AIDS care to 250 indigent patients not otherwise brought into care or previously known to health care or who had lost to follow up care.

A review of the number of patients clinically served by the Division gives some insight into the impact of this division on infectious and communicable diseases morbidity in the

A photograph of the faculty in the Division of Infectious Diseases. Christina Bailey, James Toomey, Nilmarie Guzman, Michael Sands, Levonne Mitchell-Sammon, Jeffrey Lauer

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community. In the 4 month period July 1 – Oct 31, 06, our ID specialists over saw the care for 3,546 HIV / AIDS clinical visits, 1,214 STD visits, 141 refugee visits and 653 TB visits at DCHD specialty clinics. During the 2005-2006 academic year the Division performed over 750 inpatient infectious diseases consultations at Shands Hospital.

The Division takes pride in its teaching and fellowship training program. Recently re-approved by the RRC for an additional 3 years, the Infectious Diseases fellowship program provides a 2 year clinical training program leading to board eligibility in adult infectious diseases as an internal medicine sub specialty. This program, in addition to providing extensive and diverse inpatient consultative experience at Shands Hospital, also provides outpatient experiences in HIV / AIDS, TB and STD management from a clinical and public health perspective through the DCHD communicable diseases specialty clinics, in clinical microbiology at Baptist Hospital and the State of Florida Laboratories, pediatric infectious diseases at Wolfson Children's Hospital and transplant infectious diseases at the Mayo Clinic and St. Lukes Hospital. Fellows leaving this program have gone on to diverse careers in academic ID, public health and community based infectious diseases consultation.

The Division has made remarkable strides in the past 10 years and hopes to continue its growth under the supportive leadership of UF administration and Dr. Robert Harmon, Director of Duval County Health Department.

GME CORNER

N. Stanley Nahman, Jr., M.D
Program Director, Internal Medicine Residency Program

Contemporary residency training includes more than just learning clinical medicine - it now mandates effective time management skills, a high dependence on teamwork, and free and open communication between trainees and program leadership. The core medicine residency program of the Department aspires to address each of these crucial training facets through a highly integrated and pragmatic training platform.

Time management skills are taught and reinforced by careful monitoring of duty hours on any rotation where the resident has primary patient care responsibility. These experiences include rotations through inpatient general medicine, nephrology, MICU, cardiology, and night float. All residents use a computerized card swipe system to clock in and out of each work day (or night). In this way, the program is assured that the 80 hour work week is never violated, that residents have at least 10 hours off between shifts, and that each resident receives one day off in 7. Violations of the policy are always inadvertent and usually due to over zealous residents starting too early in the morning or staying too late at night. As much as we appreciate this dedication, equally important is the development of effective time management skills to meet the stated duty hour restrictions. Duty hour monitoring with feedback is provided to each resident and if problems arise, appropriate steps are taken to improve time management skills.

Efficient time management ties directly to solid teamwork within the residency. Effective patient hand-offs are the most important way to assure quality patient care from day workers to night workers, or to cross covering colleagues on weekends and holidays. To facilitate quality hand-offs, the program adopted Dr. Robert Sullivan's (graduate of the residency and currently a 1st year fellow in Nephrology at UF-Jacksonville), unique computerized hands off system in the spring of 2005. As an intern Dr. Sullivan recognized the need for a computerized system for daily check-in and check-out. Using his unique skills in software development, he created the highly efficient system in use today by the program. A recent visiting professor from UF Gainesville remarked that he wished such a system was used in their program.

The dynamic nature of today's training environment necessitates free and open communication with the program leadership. The residency has two fourth-year chief medical residents (CMR) who are the primary liaisons between the residents and the program directors. The CMR are chosen by the program leadership 18-20 months in advance and selection is based on demonstrable quality leadership, outstanding clinical skills, and the strongest of scholastic abilities. The CMR provide the program director group with open feedback on what is working and what is not, and frequently devise solutions to recognized operational problems.

Free communication with the program leadership is also encouraged through the House staff council for education - a twelve member elected body of residents (4 per class) who meet on a regular basis with the program leadership to review the functional quality of the training platform. The House staff council (HSC) has played a crucial role in helping to make good ideas workable ideas. For example, our highly successful night float system was converted from a 4 week to a 2 week rotation in 2006. The leadership conversion plan proved unrealistic, and was successfully reformatted by the HSC into a workable plan. The positive relationship between the HSC and the program leadership allows the leadership to vent new ideas with an engaged resident group and provides an effective means for residents to bring issues to the

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Annual Chief Medical Resident Dinner, June 2007

leadership in a formal and non-confrontational way. The HSC is a key component to our recent and ongoing successes in keeping our program educationally relevant and effective.

Taken together, the successful training program in medicine today emphasizes strong training in clinical medicine that is integrated into a balanced work environment of teamwork and free communication, with an open eye to steady improvement. We believe our residency program aspires to meet these needs and through this process will continue to offer the highest quality educational experiences for our residents.

A CLINICAL CASE

Carlos Palacio, M.D. (Adapted from South Med J. 2005 Jan; 98(1):129-30).

Hypercalcemia Complicating Infection with Mycobacterium Avium-Intracellulare Complex

CASE REPORT:

A 35 year-old woman with the diagnosis of AIDS of one month duration and a CD4 count of 25, presented to the emergency department with nausea and vomiting for two days, a constant sharp pain under her diaphragm that was pleuritic in nature. It radiated to her back and decreased with lying on her right side. She reported constipation and a feeling of fullness in her abdomen for two days with fevers of 102.9∞F.

She denied any drugs of abuse or alcohol. She acquired HIV from unprotected heterosexual activity. She denied exposure to tuberculosis, and had started trimethoprim/sulfamethoxazole, azithromycin and HAART (lamivudine, zidovudine and nelfinavir) in the preceding month.

She was thin and appeared her stated age. She was tachycardic with clinical signs of dehydration. Abdominal exam showed bowel sounds, diffuse tenderness without peritoneal signs or organomegaly.

Admission labs included: BUN-29 mg/dl, creatinine-1.7 mg/dl, and calcium-15.2 mg/dl. Calcium corrected to 16.2 mg/dl when albumin of 2.7 gm/dl was taken into account. Ionized calcium was 1.91 (1.09 – 1.31). Fractional excretion of sodium was consistent with pre-renal insufficiency. White blood count was 3,900/mm3, hemoglobin was 7.3 gm/d, and platelet count was 97,000/mm3. Reticulocyte count was 1.2%. Alkaline phosphatase was 183 U/L with a normal AST, ALT and gamma-GT. Lipase was 1047 U/L. Triglycerides were 354 mg/dl and the chest x-ray was normal.

The patient was admitted with a diagnosis of pancreatitis secondary to hypercalcemia, severe dehydration, and pancytopenia. Her hypercalcemia resolved with IV saline. After fluids, creatinine was 0.6 mg/dl. An ultrasound of her abdomen showed mild to moderately enlarged liver and spleen that were homogenous in appearance, sludge in the gallbladder and a normal pancreas. A bone marrow biopsy showed a hypercellular bone marrow with trilinear

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hematopoiesis and normal maturation with multifocal granulomas that were positive for numerous acid-fast bacilli. Blood cultures and bone marrow culture grew mycobacterium avium-intracellulare complex. 1,25-dihydroxyvitamin D level was 56.8 (normal range 15.9-55.6). PTH Intact (pg/ml) was 2.57 (normal range 16-65). 25-hydroxyvitamin D level was 28.5 (normal range 8.9- 46.7). PTH-related peptide was not detectable.

Discussion:

The association of hypervitaminosis D is documented in many granulomatous diseases. These include sarcoidosis, Wegener's disease, fungal infections, tuberculosis and, a typical mycobacteria[1-4]. The mechanism of hypercalcemia is unregulated, constitutive production of dihydroxyvitamin D by macrophages. Theoretically, any granulomatous disease may lead to the constitutive production of 1, 25-vitamin D through dysregulation by cytokines[5]. Vitamin D increases the gut absorption of dietary calcium and this suppresses the secretion of parathyroid hormone.

This patient's pancytopenia and hypercalcemia resulted from MAC infiltrating her bone marrow. Hypercalcemia can cause pancreatitis, and nephrogenic diabetes insipidis manifesting as polyuria.

The initiation of HAART likely precipitated an immune reconstitution syndrome. The increase in production of a cytokine such as gamma-interferon led to constitutive vitamin D production. We may well see more similar cases with initial HAART in severely immunocompromised HIV disease.

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RX UPDATES

Patrick Aaronson, Pharm.D., PGY1 Pharmacy resident, reviewed by Amy Rockwell, Pharm.D.

Fluoroquinolones are no longer recommended for the treatment of gonococcal infections

The Centers for Disease Control (CDC) recently revised the treatment recommendations for gonococcal infections, due to a steady increase in reports of quinolone resistant Neisseria gonorrhoeae (QRNG). Fluoroquinolones are no longer recommended for the treatment of gonococcal infections caused by *Neisseria gonorrhoeae*.[1] This recommendation was based on analysis of data from the CDC's Gonococcal Isolate Surveillance Project (GISP), system that monitors antimicrobial susceptibilities of strains of N. gonorrhoeae from approximately 26 sexually transmitted diseases (STD) clinics throughout the country.[2] Intermediate and resistant isolates have increased from less than 1% of clinical isolates in 1990 to approximately 15% in 2006.

The CDC's most recent sexually transmitted disease treatment guidelines recommend the following regimens[3]:

- *Uncomplicated Gonococcal Infections of the Cervix, Urethra, and Rectum:*

First line treatment includes: ceftriaxone 125 mg IM in a single

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dose or cefixime 400 mg orally in a single dose plus treatment for chlamydia if chlamydial infections are not ruled out.

- *Uncomplicated Gonococcal Infections of the Pharynx:*

First line treatment includes: ceftriaxone 125 mg IM in a single dose plus treatment for chlamydia if chlamydial infections are not ruled out.

- *Disseminated Gonococcal Infection (DGI):*

First line treatment includes: ceftriaxone* 125 mg IM or IV every 24 hours. Alternative regimens includes: cefotaxime* or ceftizoxime* 1 g IV every 8 hours (non-formulary at Shands Jacksonville).

* All of the preceding regimens should be continued for 24-48 hours after improvement begins, at which time therapy may be switched to one of the following regimens to complete at least 1 week of antimicrobial therapy, which includes: cefixime 400 mg, cefixime suspension 500 mg, or cefpodoxime 400 mg orally twice daily.

- *Parenteral treatment of Pelvic Inflammatory Disease (PID):*

Parenteral regimen A includes: cefotetan 2 g IV every 12 hours or cefoxitin 2 g IV every 6 hours (non-formulary at Shands Jacksonville) plus doxycycline 100 mg orally or IV every 12 hours. Parenteral regimen B includes clindamycin 900 mg IV every 8 hours plus gentamicin loading dose IV or IM (2 mg/kg of body weight), followed by a maintenance dose (1.5 mg/kg) every 8 hours. Single daily dosing of gentamicin may be substituted. An alternative parenteral regimen includes: ampicillin/sulbactam 3 g IV every 6 hours plus doxycycline 100 mg orally or IV every 12 hours.

- *Oral Treatment for mild-to-moderately severe acute PID:*

First line oral regimen includes: ceftriaxone 250 mg IM, cefoxitin 2 g IM and probenecid, 1 g orally administered concurrently in a single dose, or other parenteral third-generation cephalosporin (e.g., ceftizoxime or cefotaxime). The preceding regimen also includes doxycycline 100 mg with or without metronidazole 500 mg orally twice a day for 14 days.

Since there are limited data regarding alternative regimens for treating gonorrhea among persons who have documented severe cephalosporin allergy, infectious diseases consultation is recommended. The best available treatment option is cephalosporin treatment following desensitization. If desensitization is not an option, azithromycin may be considered. Azithromycin 2 grams orally is effective against uncomplicated gonococcal infection, but concerns with emerging antimicrobial resistance to macrolides should limit its use.[1]

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Mark Schreiber, Pharm.D.
Clinical Toxicology Fellow
Florida Poison Information Center/Jacksonville

Hydroxocobalamin for Cyanide Toxicity

Cyanide is an extremely lethal poison. As a concentrated aerosol, it has the ability to cause death within seconds. Concerns over terrorist activity and expanded use of synthetic products which release cyanide in smoke when burned have increased awareness of cyanide toxicity. Until recently, the Taylor Cyanide Antidote Kit (previously the Lilly Cyanide Antidote Kit) was the only cyanide antidote available in the United States. However, the methemoglobin produced by the nitrite portions of the kit can dangerously lower the oxygen carrying capacity in patients with an elevated carboxyhemoglobin level. As a result, it is generally unsafe to administer these kits in a prehospital setting. On December 15, 2006, hydroxocobalamin was approved by the Food and Drug Administration as a cyanide antidote.

Hydroxocobalamin is vitamin B12a, the precursor to cyanocobalamin (vitamin B12), which had previously been approved in a more dilute formulation in the United States for the treatment of pernicious anemia. It has been approved for cyanide toxicity in France since 1996. Hydroxocobalamin functions as a cyanide antidote by binding cyanide in a 1 mol:1 mol ratio. This reaction converts hydroxocobalamin and cyanide to cyanocobalamin, which is then excreted safely in the urine. It is now distributed by Dey®, L.P. in the United States as the Cyanokit® which consists of two vials, each containing 2.5 g hydroxocobalamin.[2] Each vial must be diluted with 100 mL normal saline and then individually infused intravenously over 7.5 minutes.[2] The starting dose is 5 g for adults and 70 mg/kg for pediatric patients.[2] Depending on the severity and clinical response, a second dose may be administered.[2]

An efficacy trial utilizing adult beagle dogs poisoned with potassium cyanide compared mortality of those treated with 150 mg/kg hydroxocobalamin, 75 mg/kg, and placebo.1 Fifteen day survival rates of the three groups were 100%, 79%, and 18%, respectfully.[1] A safety trial for hydroxo-

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cobalamin compared the effects of 2.5 g, 5 g, 7.5 g, and 10 g of hydroxocobalamin given to healthy volunteers.[4] Due to the red color of hydroxocobalamin, all patients should be expected to develop chromaturia and skin redness which requires several days to subside.[4] Elevation of blood pressure and a compensatory decrease in heart rate are also to be expected, both of which return to baseline within 4 hours of treatment completion.[4] Two of the 136 volunteers in the study developed an allergic reaction, which responded to antihistamine treatment and resolved within 2.5 hours of onset.[4]

Due to the deep red color of hydroxocobalamin, interference of colorimetric dependent laboratory tests is to be expected.[2] The extent and duration of laboratory interference is dependent on several factors such as dose, analyte, methodology, and analyzer.[2] Therefore, it is imperative to use caution when reporting and interpreting laboratory results following the administration of hydroxocobalamin.

The Paris Fire Brigade has reported their experience with hydroxocobalamin from 1995-2003.[3] They reported treating 101 patients with a survival rate of 42%.[3] Of the thirty-eight patients found in cardiac arrest, 21 had a return of circulation; however, 19 of those patients expired within 8 days.[3] Hemodynamic instability was reported in 12 patients and improvement was observed in 9.[3]

Until recently, the United States lacked a cyanide antidote suitable for prehospital administration. Hydroxocobalamin is now commercially available and potentially fills this need. The availability of Cyanokit® better prepares the United States and its health care providers with the best available treatment for cyanide victims of potential terrorist attack or smoke inhalation. The Cyanokit® was approved for addition to the Shands Jacksonville Formulary by the Pharmacy and Therapeutics Committee in May. If you have any further questions regarding hydroxocobalamin, its administration, or cyanide toxicity in general, please contact your local poison information center at 1-800-222-1222.

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UF & SHANDS BRAND

By Erin VanWey

Shands Jacksonville, UFPTI offer world's most advanced forms of radiation in one setting

UNIVERSITY OF FLORIDA PROTON THERAPY INSTITUTE

Shands Jacksonville and the University of Florida Proton Therapy Institute (UFTPI) began offering consolidated radiation oncology services in August. With the latest conventional radiation equipment and proton beam, the two organizations together offer patients the most advanced forms of external beam radiation therapy in the world in one setting.

This partnership gives patients access to more treatment options. Every patient referred for radiation therapy will be evaluated to identify whether they are a candidate for conventional treatment, proton therapy or both.

Situated on the Shands Jacksonville campus, UFPTI is one of only several proton therapy facilities operating in the nation and the only proton therapy facility in the Southeast.

On average, 65 patients receive proton therapy in the 98,000-square-foot facility each day. With the addition of conventional therapy services, the number of patients receiving radiation treatment will grow to 150.

UFPTI has been treating adult patients with prostate, head and neck, breast and brain cancer, as well as pediatric patients, with proton therapy since August 2006. Proton therapy is a precise radiation treatment that destroys cancer cells and minimizes damage to healthy tissue. This results in higher cure rates, a low incidence of side effects and fewer long-term effects. UFPTI has future plans to expand proton therapy treatment to cancers of the eye, lung and gastrointestinal tract.

Making this facility even more unique is the addition Shands Jacksonville's conventional external beam equipment: LINAC, IMRT, IGRT and stereotactic radiosurgery.

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The linear accelerator (LINAC) is the device most commonly used for external beam radiation treatments for cancer patients. The LINAC can also be used in stereotactic radiosurgery similar to that achieved using the gamma knife on targets within the brain. Its delivery of a uniform dose of high-energy x-ray to the region of the patient's tumor destroys the cancer cells while sparing surrounding normal tissue.

Intensity-modulated radiation therapy (IMRT) uses computer-controlled x-ray accelerators to deliver precise radiation doses to a malignant tumor or specific areas within the tumor. The radiation dose is designed to conform to the 3D shape of the tumor by modulating the intensity of the radiation beam to focus a higher radiation dose to the tumor. Because the ratio of normal tissue dose to tumor dose is reduced to a minimum with IMRT, higher and more effective radiation doses can safely be delivered to tumors with fewer side effects.

Tumors can shift and move slightly between treatments, and even during treatments, because of normal physiological processes. Image-guided radiation therapy (IGRT) verifies the tumor's exact location at the moment of treatment. The accuracy results in higher radiation doses to the tumor, thereby increasing the likelihood of controlling or eliminating the cancer. IGRT is well suited to treating tumors virtually anywhere in the body, including those areas affected by respiratory motion.

Stereotactic radiosurgery involves the delivery of a single high-dose—or sometimes smaller, multiple doses—of radiation beams that converge on the specific area of the brain where the tumor or other abnormality resides. Stereotactic radiosurgery is an important alternative to invasive surgery, especially for tumors and blood vessel abnormalities located deep within or close to vital areas of the brain. Radiosurgery is also used to treat arteriovenous malformations.

In determining the most effective therapy, the patient's treatment team conducts a simulation using CT, MRI, PET/CT or a combination of the modalities to localize the tumor and get the most accurate representation of treatment volume.

For more information or to make a referral, call 244-7810.

Reference: Radiological Society of North America (rsna.org).

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