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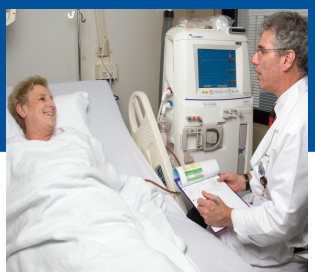
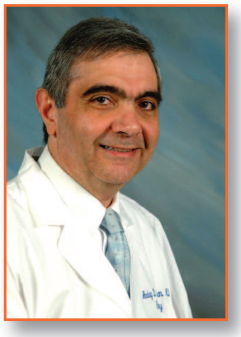


UF UNIVERSITY of FLORIDA
College of Medicine
Jacksonville

CHAIRMAN'S MESSAGE

Dear Colleagues:



On behalf of the Department of Medicine at the University of Florida, College of Medicine - Jacksonville, I would like to wish you a happy and prosperous 2008.

We are excited to be in our second year of publishing the Academic Physician Quarterly (APQ) newsletter. Although this vehicle of communication is still in its infancy, I am proud to say that the newsletter has been an invaluable tool to keep the physicians in our community abreast of the new services developed at the University of Florida and Shands Jacksonville.

We have made significant strides in developing our clinical units. We recently welcomed three new diabetologists and endocrinologists. These new members of the Division of Endocrinology, Diabetes and Metabolism are highlighted in the Meet your Colleagues section.

The Focus section gives a glimpse of the breadth of patient care offered by the faculty and staff of UF and Shands. The spectrum of this care spans from highly intensive critical care to more rehabilitative transitional care and everything in between. In the current issue, we highlight the activities of the Medical Intensive Care Unit. In the next issue, we will focus on the Transitional Care Unit.

We would like to see the APQ become a vehicle of dialogue with the community physicians. If you have any comments, interesting cases or observations to share with colleagues please e-mail them to me and I will be happy to include them in our future issues. My e-mail address is Arshag.mooradian@jax.ufl.edu.

Happy New Year to you all.

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

Kathryn Koch, M.D.

Associate Professor of Medicine
Division of Pulmonary and Critical Care Medicine

Critical Care Unit

The medical intensive care unit (MICU) is a very busy and dynamic service with high acuity. On the average, 10 patients are either admitted a day or require MICU consults. Through the heroic efforts of the staff, many patients in MICU survive despite the severity of their acute illness. A great example of a good outcome is the following case history.

In May, a 46-year-old man was found in his work van, in urine and vomit. He was flown to Shands Jacksonville where he was intubated for airway protection because of a Glasgow Coma Scale of 6. The patient was pink, diaphoretic, had a brisk capillary refill, blood pressure of 110/70 mm Hg, pulse of 130/minute, a sinus rhythm but there was no urine output. The arterial blood gas analysis on 100 percent oxygen showed pH 7.23, pO_2 302, pCO_2 45, measured O_2 saturation of 81.5 percent, calculated bicarbonate of 18.8 meq/l and carboxyhemoglobin was 17.9.

It turned out that the generator in his work van was three years old with no carbon monoxide monitor. He said that he, "felt funny" working in the back of the van, got out to see if he would feel better but found he could not walk well and went back inside the van to sit down. He was found about 2 hours later in the condition described above.

Carboxyhemoglobin was down to 8.4 after four hours on 100 percent oxygen, two hours later weaning off the ventilator was started and when carboxyhemoglobin was decreased to 1.6, he was extubated. The patient was discharged to the floor for a short period of recuperation and returned to work.

Despite the excellent outcome of patients in the MICU given the nature of injuries and organ damage the mortality rates are high. In 2006, there were 1,205 patients admitted to the MICU, of whom 237 subsequently died while still in the unit. This represents a mortality rate of 20 percent which is below the national average mortality rate of 30 percent for MICU patients. These statistics highlight the heroic work carried out by the UF Physicians and the Shands Jacksonville MICU staff.

Every death in the MICU is tragic for a family. Occasionally this tragedy may contribute to the miracle of life for another patient suffering from a fatal disease. This happens through the organ donation program.

Institutional policy mandates the referral of brain dead individuals or individuals with a Glasgow Coma Scale of 5 or less who are not expected to survive, to an organ donation program (Life Quest). Life Quest then evaluates these individuals and if deemed appropriate, approaches the family for consent. In 2006, there were 25 donors whose organs were retrieved. A patient who progresses to brain death is actually looked upon like eight patients. The donor patient and the seven people who would benefit from receiving transplanted organs.

Jesus Diaz, M.D.
Assistant Professor of Medicine,
Division of Pulmonary and Critical Care Medicine
Mayo Clinic - Jacksonville

Kathryn Koch, M.D.
Associate Professor of Medicine,
Division of Pulmonary and Critical Care Medicine

Pulmonary Hypertension In Pregnancy

Case Presentation

A 26-year-old African American woman, who had four normal pregnancies and deliveries, was admitted four-weeks after the last normal vaginal delivery complaining of shortness of breath which started two days post-partum. Her SOB had progressed to the point where it was persistent at rest. Chest pain had occurred for about a week post-partum but had subsided. There has been intermittent nausea and vomiting, particularly whenever she had to get up in the middle of the night, when coughing fits would stimulate emesis. Past medical, surgical and social history is otherwise negative.

Remarkable findings on initial evaluation were: Pulse 129/minute regular; respiratory rate of 32/minute; blood pressure of 113/72 mm Hg; O_2 saturation of 86% on room area and 93% on 10 liters via face mask. She was alert and oriented, no lymphadenopathy, neck veins were flat and a right ventricular heave was present. The breath sounds were decreased throughout all lung fields and a holosystolic murmur was heard on cardiac examination. Extremities were dry with good capillary refill, no clubbing cyanosis or edema but pedal and radial pulses were only 1+ and lower extremities were cool to touch.

Arterial blood gases on the second hospital day on 100% NRB revealed pH = 7.47, pCO_2 =22 and pO_2 =94. Electrolytes were normal, BUN =28, creatinine =1.7 mg/dl, Hb =16 gm/dl, Hct =46.4%, WBC =8.2K and platelets =353K. Chest X ray was clear with mild cardiomegaly. EKG showed sinus rhythm. Other tests included PT = 13.6, INR = 1.2, PTT =23.9, D-dimer =1.8. Urinalysis showed 4+ protein and large blood. CT scan of chest revealed no clots but changes consistent with pulmonary arterial hypertension were present. 2D-ECHO revealed PA pressures estimated 107 mmHg with EF55-60%. Differential diagnosis included pulmonary vasculitis, pulmonary arterial embolism and pulmonary veno-occlusive disease. Open lung biopsy was planned on the third hospital day but upon intubation, her condition deteriorated and aggressive resuscitation including nitric oxide and vasopressin treatment failed.

Discussion

This previously healthy young woman presented with dyspnea that developed two days after delivering a full-term healthy baby, which was followed by chest pain four weeks later. The differential diagnosis of a young woman with severe pulmonary hypertension in the absence of evidence of left-sided cardiac disease, congenital heart disease or diffuse pulmonary parenchymal disease is not broad. The current WHO classification of pulmonary hypertension lists five different groups. (Table):

TABLE : WHO classification of Pulmonary Hypertension.

- Group 1: Pulmonary arterial hypertension, in which there is proliferative obstruction of small, muscular arterioles. Causes include collagen vascular diseases (CVD), drugs (anorexigens), congenital heart disease (CHD) with left-to-right shunts and idiopathic form (formerly known as primary) which can be sporadic or familial.
- Group 2: Secondary to increased left-sided cardiac pressures.
- Group 3: Associated with bronchopulmonary disorders with hypoxemia (interstitial lung disease, COPD, hypoventilation syndromes).
- Group 4: Due to chronic pulmonary thromboembolic disease (CPTED)
- Group 5: Other causes, including fibrosing mediastinitis or sarcoidosis with extrinsic vascular compression.

Pulmonary hypertension of this severity could not have developed acutely. Therefore, it is admirable that this woman managed to bring a pregnancy to full term while dealing with her underlying cardiovascular illness. Case

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series of women with known pulmonary hypertension (idiopathic, due to CHD, CVD or CPTED) have shown that less than 25 percent are capable of carrying a pregnancy to term, with a neonatal mortality of 12 percent and a maternal mortality of between 30 and 56 percent, depending on the cause.[1,2]

Based on the data obtained pre-mortem, we can say that she did not have CHD, CVD, diffuse pulmonary parenchymal disease, left-sided cardiac disease or fibrosing mediastinits to explain her pulmonary hypertension. A CT angiogram did not reveal thromboembolic disease. However, this study may lack sensitivity in detecting segmental, well-endothelialized thrombi. Therefore, we suspect the cause of her pulmonary hypertension to have been either idiopathic PAH (WHO Group 1), but cannot rule out chronic thromboembolic disease.

Autopsy revealed features of primary pulmonary hypertension with plexiform lesions and marked congestion. There were intra-acinar arteries with concentric laminar intimal thickening, medial hypertrophy, plexiform lesions and dilatation lesions. There was a hypertrophic right ventricle with a transmural infarction of the posterior wall of approximately 10 days of age. The cause of death was determined to be primary pulmonary hypertension with right ventricular myocardial infarction.

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GME CORNER

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

The annual identification and recruitment of strong PGY-1 (intern) trainees is a crucial facet of every successful residency training program. The residency program leadership, Departmental leadership, and all members of the faculty recognize this fact and each year work as a cohesive team to attract the strongest candidates to the program.

The eight-month process begins in August of each year when the Electronic Residency Application Service (ERAS) begins accepting applications from over 20,000 prospective interns. ERAS provides a vital service by offering a standardized, online application platform. The ERAS database contains a file on each applicant and allows training programs to screen for desirable candidates. From this pool, candidates are invited for an interview. After all interviews are conducted (late January) candidates rank their programs in order of preference and programs rank their applicants in the same manner. In mid-March, the National Residency Match Program (NRMP) uses a computer algorithm to match applicants and training programs according to the highest ranked preferences by each party. The result of this computation is termed "the match" and is one of the most important days of the year for the program.

It is highly desirable to fill all open slots with candidates from the rank list submitted by the program. Unfilled positions result in a "scramble" for applicants. The scramble is a gamble for both applicants and programs —a professional blind date, if you will— and most programs (including the University of Florida at Jacksonville) prefer to avoid scrambling.

A key strategy to a successful match is to submit a rank list with a sufficient number of candidates.

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According to the NRMP, programs that match successfully rank ~ 9 candidates for every position. Programs that scramble rank about half that number (~ 4.8 candidates per position).

In 2007, our program was seeking 13 categorical trainees. This final number translated to a desired active rank list of ~ 117 candidates (9 candidates per position). In fact, we ranked 100 candidates (~ 7.7 candidates per position). The rank list was based upon interviewing 118 applicants. To identify the 118 interviewees, the program used ERAS to screen more than 1,600 applicants.

The interview days were conducted between November and January. The interview itinerary included an ice-breaker with current residents the night before the interview and a one night stay at the Hyatt (both at the program's expense), followed the next day by a morning of interviews with faculty and interaction with the residents. By 1 p.m., the typical interview day had concluded and preparation for the next group began.

The interview season is a scheduling nightmare capped with frantic days of interviews but well worth the effort for a successful match. We did match last year, managing to recruit a delightful group of bright, energetic professionals all derivative of the top end of our rank list. No blind dates here, just another suc-

RX UPDATES

Luis Laos, M.D.
Associate Professor of Medicine
Division of Pulmonary and Critical Care Medicine

Drotrecogin alfa (XIGRIS[fi])

Drotrecogin alfa (activated) is a recombinant form of human activated protein C, an endogenous protein that promotes fibrinolysis and inhibits thrombosis and inflammation. It appears to be an important modulator of the coagulation and inflammation associated with severe sepsis.

Drotrecogin alfa is approved by the FDA for adults with severe sepsis who have a high risk of death as determine by an APACHE II score greater than 25. This approval is based on a large multicenter, randomized, placebo-controlled trial (PROWESS) that showed that treatment with drotrecogin alfa was associated with a 6.1% absolute reduction in 28-day mortality in patients with severe sepsis, compared with placebo (24.7% vs. 30.8%)[1]

Patients included in PROWESS had a known or suspected infection, three or more signs of systemic inflammation (temperature >100.4°F or <96.8°F; heart rate >90 beats/min; respiratory rate >20 breaths min, $PaCO_2$ <32 mmHg, or need for mechanical ventilation; and white blood count of >12,000/mm3, <4,000/mm3, or > 10% immature neutrophils), and sepsis-induced dysfunction of at least one organ system for less than 24 hours. Patients were primarily excluded if they had any condition that increased the risk of bleeding.

The mortality benefit of drotrecogin alfa was largest in the sickest patients, such as those with an APACHE II score of more than 25. In this group there was a 13 percent absolute risk reduction in 28-day mortality compared with placebo. This represents a 29 percent relative risk reduction.

Since PROWESS, a follow-up study has confirmed a large, sustained benefit in sicker patients with an im-

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provement in survival that remains highly significant over a follow-up period of more than two and half years.[2]

The ADDRESS trial was an FDA required study to evaluate the efficacy of drotrecogin alfa for adults who had severe sepsis and a low risk of death[3]. Enrollment was terminated early because of a low likelihood of meeting the prospectively defined objective of demonstrating a significant reduction in the 28-day mortality rate with the use of drotrecogin alfa. The absence of a beneficial treatment effect indicates that drotrecogin alfa should not be used in patients with severe sepsis who are at low risk for death, such as those with single-organ failure or an APACHE II score less than 25.

Drotrecogin alfa does have anti-coagulant properties and there was a trend to an increased incidence of serious bleeding in the therapy arm in PROWESS (3.5% vs. 2.0%, p=0.06). However, serious bleeding occurred primarily in patients with an identifiable predisposition to bleeding, and blood-transfusion requirements were similar between groups after adjustment for duration of survival. Several large uncontrolled series since PROWESS have reported similar bleeding rates. The elimination half-life is 13 minutes, indicating a rapid inactivation of drotrecogin alfa after stopping infusion. Approximately 80 percent of the drug is eliminated in 30 minutes. The above-mentioned pharmacokinetic data is based on healthy subjects. Plasma clearance of drotrecogin alfa in patients with severe sepsis is approximately 50 percent higher.

Several studies have demonstrated that despite the initial acquisition cost, drotrecogin alfa has a very acceptable cost-effectiveness profile similar to, or better than, many well-adopted healthcare interventions. [4-6]

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NEWS & NOTES

- During the last six months, several faculty members in the Department of Medicine received prestigious awards and grants. Four faculty members were the recipients of 2007 Dean's Fund Faculty Research Awards. The awardees were Dr. Arpitha Ketty (General Internal Medicine), Dr. Fauzia Rana (Hematology and Oncology), Dr. Kenneth Vega (Gastroenterology) and Dr. Kent Wehmeier (Endocrinology).

These competitive awards provide seed money to enable the faculty to develop a research idea into a publishable manuscript and use the information generated as preliminary data when seeking additional extramural funding.

- Dr. Martin Zenni, Division of Cardiology, is the recipient of the 2007 Rear Admiral Paul Kaufman Award. The award is given annually by the Medical Staff of Naval Hospital Jacksonville in appreciation of a healthcare provider's selfless support of the Naval Hospital staff and care of its patients. Congratulations to Dr. Zenni for this honor.

MEET YOUR COLLEAGUES

Three Endocrinologists and Diabetologists Join the Department.

Kent Wehmeier, M.D., Associate Professor of Medicine and Division Chief.
Dr. Wehmeier completed his residency in internal medicine at Washington University and a fellowship in endocrinology, diabetes & metabolism at St. Louis University both located in St. Louis, Missouri. His areas of clinical expertise include metabolic bone disease and hyperlipidemia. His research interests include vitamin D, lipid metabolism and non-alcoholic fatty liver disease. Current projects include osteoporosis epidemiology, lipoprotein metabolism and the actions of vitamin D.

Joe Chehade, M.D., Associate Professor of Medicine.
Dr. Chehade completed his residency in internal medicine at Staten Island University in Staten Island, New York and a fellowship in endocrinology, diabetes and metabolism at St. Louis University in St. Louis, Missouri. His areas of clinical expertise include thyroid disease, diabetes mellitus and intensive insulin therapy. His research interests include thyroid disease and the evaluation of thyroid nodules.

Mae Sheikh-Ali, M.D., Assistant Professor of Medicine.
Dr. Sheikh-Ali completed her residency in internal medicine at Drexel University College of Medicine in Philadelphia, Pennsylvania and a fellowship in endocrinology, diabetes and metabolism at Mayo Clinic - Jacksonville. Her areas of clinical expertise include diabetes mellitus, insulin pump therapy, thyroid disease, metabolic bone disease and vitamin D metabolism. Her research interests include metabolic syndrome (a syndrome linking diabetes, hypertension and hyperlipidemia which results in higher risk of cardiovascular disease) as well as vitamin D metabolism.

UF&Shands Jacksonville

Ann Harwood-Nuss, M.D.,
Assistant Dean for Program Development.

Shands Jacksonville Debuts Redesigned Web Site

Shands Jacksonville and the University of Florida College of Medicine-Jacksonville have formed a collaborative Web Development Team in order to grow our Internet presence. The initial efforts were directed toward the development of a comprehensive clinical services Web site. This required the acquisition of additional web developers, equipment and software in order to redesign, enhance and present the clinical services provided on our campus. The Web Team has also purchased a Google server for searching the site.

A template was developed so that information provided by the academic departments would be organized in an informative, comprehensive manner to serve as a marketing tool for the public, patients and referring physicians. All departments were asked to provide information about their

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clinical services and faculty. The ultimate goal is to have an interactive Web site with online appointments, podcasts, featured faculty, on-line health surveys and other patient-friendly features.

Thanks to the response of the University's departments and divisions, the redesigned site was launched in September.

Successful Web sites are dynamic, consistently updated with new information. The great value of Web-based information is obvious; however, its success is dependent upon the integrity of the information. There is a Web site feedback link on the home page for the purpose of obtaining customer impressions. This link can also be used by you and your staff to send comments or suggestions to the Web Team.

Take some time to review the new Web site at jax.shands.org and click on the Healthcare Services link. You'll see there are now several ways for visitors to find the information they're looking for: by centers and institutes, departments and divisions, and alphabetically by topic. The pages for each department include more detailed descriptions of medical conditions and the services we provide—something consumers have come to expect from an academic medical center.

UF UNIVERSITY of FLORIDA
College of Medicine
Jacksonville

653-1 West 8th Street
Department of Medicine, L20
Jacksonville, FL 32209-6511
904-244-8846; fax: 904-244-8844

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