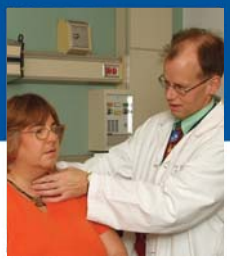
Volume 5, Issue 3, July 2011

Academic Physician Quarterly

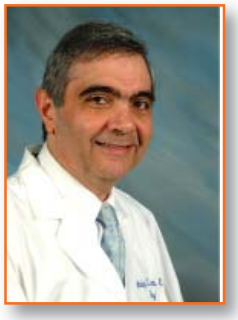
A DEPARTMENT OF MEDICINE BULLETIN


UF UNIVERSITY of FLORIDA
College of Medicine
Jacksonville

CHAIRMAN'S MESSAGE

Dear colleagues:



It is that time of the year when we say farewell to our graduating class and welcome a new crop of trainees. We are optimistic that the class of 2011 will be as good as the Class of 2010 who achieved 100% pass rate in their Internal Medicine Board examinations. Indeed we are very proud of our residents in the core training program. I am especially proud of their achievements at the annual meetings of the Florida Chapter of the American College of Physicians. Several of our residents made scientific presentations and our Medical Jeopardy Team had an exceptional year and won the competition. They will now go on to the regional competition in Fall.

The excellence of the faculty in the Department was also recently recognized as 19 faculty members were chosen to receive the 2011 University of Florida-College of Medicine's Exemplary Teachers Award. This award is given in recognition of outstanding teaching contributions of individual faculty member.

I am especially pleased to announce the appointment of Dr. James Scolapio as the new Chief for the Division of Gastroenterology. Dr. Scolapio is an internationally recognized thought leader who is entrusted with expanding of the Gastroenterology services we offer to the community.

We continue expanding the services we offer to our community. We recognize that wellness programs for adults are beneficial and indeed the recent changes in Medicare reimbursement rules encourages older adults to have wellness visits with their physicians. This is the time to invest in the health of our senior citizens through innovative geriatric care. In this issue we have a Focus topic by Dr. Kuo of the Division of General Internal Medicine who discusses the health care services we offer for older people with special needs. We now can offer the full array of Geriatric services including our senior Wellness program, home health care, rehabilitation and skilled nursing home care.

As always, if you have any suggestions on how to improve our services please feel free to contact me.

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

Hsiao-Yen Kuo, M.D.

Assistant Professor of Medicine

Division of General Internal Medicine (Geriatrics)

Annual Wellness Medicare Visit

Medicare's increased focus on prevention is extremely important for America's seniors who often are left without needed preventative care due to high costs and lack of coverage. Effective January 1 of this year, Medicare beneficiaries will no longer have any out-of-pocket expense for most preventative services. Medicare covers a one-time "Welcome to Medicare" physical examination, within the first 12 months of becoming eligible for Medicare if the patient has Medicare Part B. A new service provided is coverage of an annual wellness visit. This yearly wellness visit is an opportunity to review the patient's health, as well as educate and counsel them about preventative services that are available to them. During this visit, the health care provider and the patient will develop a personalized prevention plan that takes a comprehensive approach to improving patient's health. It is also an opportunity to make referrals for other needed care. This annual wellness visit will be provided once a year for the rest of every Medicare patient's life.

The annual Medicare wellness visit will cover the following services:

- Routine measurements such as height, weight, blood pressure, body-mass index (or waist circumference, if appropriate)
- Review of the patient's medical and family history, including all prescribed medications and any supplements, including calcium and vitamins
- Gather/update a complete list of all providers involved in the care of the patient
- A personal risk assessment (including any mental health conditions)
- A review of patient's functional ability and level of safety, including any hearing impairment, fall risk, home safety issues and the patient's ability to successfully perform "activities of daily living"
- An assessment of any cognitive impairment and screening for depression via direct observation and reports from family members and/or caretakers
- Screening for obesity, and counseling from the doctor and other health professionals to promote sustained weight loss
- Discussion of end-of-life planning including advance directives
- Set up a schedule for Medicare's screening and preventative services, in the form of a checklist, for the next 5 to 10 years of the patient's life
- Any other health advices or referral services that may help intervene and treat potential health risks including health education and counseling resources such as weight loss, smoking cessation, nutritional education programs

Based on the information gathered, the physician should review risk factors with the patient, including any primary, secondary and tertiary interventions that are indicated, along with their risks and benefits.

The following preventative services are covered at no cost to the patient:

- Annual Mammogram
- Colorectal cancer screening, including flexible sigmoidoscopy or colonoscopy
- Cervical cancer screening, including a Pap smear test and pelvic exam
- Cholesterol and other cardiovascular screenings
- Diabetes screening including diabetes self-management training
- Medical nutrition therapy to help people manage diabetes or kidney disease
- Prostate cancer screening
- Annual influenza vaccine, pneumococcal vaccination, Herpes zoster and hepatitis B vaccination
- Bone mass measurement
- Abdominal aortic aneurysm screening in men patients 65-75 who smoke or have smoked
- HIV screening tests for people of who are at increased risk or who ask for the test
- Smoking cessation
- Annual eye exam including glaucoma testing and vision testing

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Preventative services are routine health care services that include screening tests, check-ups, and patient counseling to prevent illness, disease, or other health problems.

Preventative services include:

a) Primary prevention: : Aims to prevent disease from occurring. Immunizations, life style modifications (smoking cessation, promoting physical activity) and chemoprophylaxis (aspirin for primary prevention of heart disease);

b) Secondary prevention: Focuses on early detection and treatment of asymptomatic disease. Screening for cancer, hearing or vision impairment, osteoporosis, hypertension, abdominal aortic aneurysm (AAA) are examples of secondary prevention;

c) Tertiary prevention: Identifies established symptomatic disease to prevent further morbidity or functional decline. Examples of tertiary prevention include diabetes and lipid management, identification of cognitive problems, assessment of disorders of gait and balance, assessment for malnutrition and urinary incontinence as well as assessment of driving skills.

When to stop screening?

Important questions to be considered include "what is the patient's life expectancy" and "what is the time to benefit from the intervention". For example, whether to screen if the time to benefit is more than ten years but the life expectancy is only five years (e.g. prostate cancer) or screen if the time to benefit is 5 years and the life expectancy is 10 years (e.g. Breast Cancer).

The provision of coverage by Medicare for preventative services for which there is strong evidence of a benefit to an individual's health demonstrates Medicare's commitment both to keeping beneficiaries healthy and using evidence to drive coverage decisions.

RESOURCES: United States Preventive Services Task Force (USPSTF), American Geriatric Society (AGS), American Cancer Society (ACS), Medicare.gov, Guide to Medicare's preventive Service, Centers for Disease Control and Prevention Preventive Health Guidelines, Disease Management Guidelines, American College of Physicians

GME CORNER

Christina Bailey, M.D.

Assistant Professor of Medicine, Division of Infectious Diseases

Associate Program Director, Internal Medicine Residency

Milestones: Going beyond the competencies

Top 10 Things You Need to Know About the Milestones Project

1) **What are milestones?**
They are specific developmental progressions of behaviors and accomplishments within each of the 6 general competencies

2) **Milestones will provide objective, measurable standards for each competency.**
Each of the 26 specialties will be tasked with defining the outcomes expected for that specialty and the core methods for their assessment. Internal medicine is the first specialty to complete a proposed list of milestones. (Journal of Graduate Education, September 2009)

3) **Who creates the milestones?**
A team of experts within each specialty will develop the milestones, not the ACGME. This team will include representatives from the ABMS Board, program directors, RRC, and residents.

4) **Clarification of outcome assessment.**
Each specialty team will not only define the milestones, they will also define the assessment methods for objective evaluation of achievement of each one.

5) **Promotion criteria will be defined by milestones.**
Once established, the milestones will provide a national performance standard. Resident advancement for year-to-year will be based on objective outcomes, rather than subjective ones.

6) **Individual learning plans will be possible.**
By having defined milestones, residents may progress at different rates within each competency while remaining on track for graduation.

7) **Normative data for each resident will be available for the program.**
For residents who are marginal performers, documentation of deficits is clear and provides a

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basis for remediation and/or academic probation.

8) **Standardized markers for entry and exit will be developed.**
Tools for assessment of resident skills will be available at both entry and exit from the program. The final milestones will be attained prior to graduation. These skills are needed to practice medicine unsupervised within that specialty.

9) **"Outcomes to improvement"**
Milestones within each competency will provide aggregate outcome data for annual evaluations of each program. The information can be used to identify areas/rotations needing improvement.

10) **Learning portfolio**
The ACGME learning portfolio will be implemented and will provide an additional means of collecting outcome data of the defined milestones within each program. This information will be used in for accreditation of programs and institutions.

Welcome to the next step towards outcome-based accreditation.

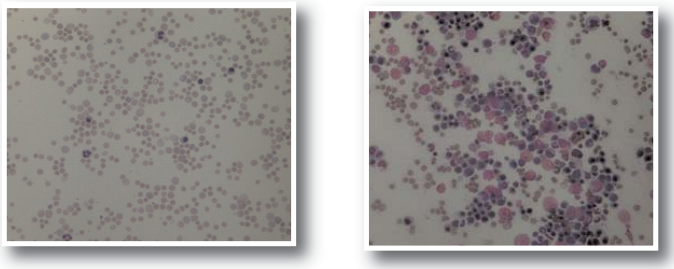
A CLINICAL CASE

Hasan Riaz, MD, Naeem Latif, MD, Fauzia Rana, MD
Department of Medicine, Medical Oncology, University of Florida College of Medicine, Jacksonville

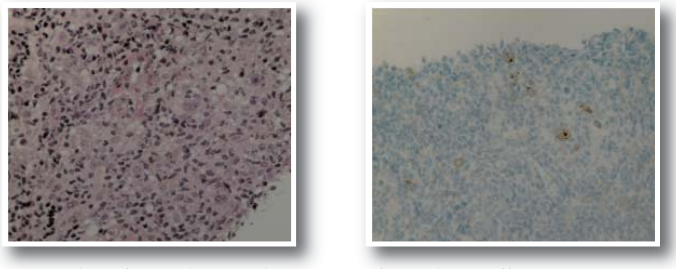
Auto-immune Hemolytic Anemia Associated with Hodgkin's Disease

Introduction

Auto-immune hemolytic anemia (AIHA) is an immune mediated disorder caused by antibodies directed against unmodified autologous red blood cells. It can be primary (idiopathic) or secondary to an underlying disease such as lympho-proliferative disorders like Hodgkin's disease. The incidence of AIHA with Hodgkin's disease in adults has been reported between 1.5 to 2.7% which is higher than the general population.



A-Peripheral blood showing: nucleated RBCs, B- Bone marrow aspirate smears showing erythroid hyperplasia (increased erythroid precursors compared to myeloid ones, reversed myeloid : erythroid ratio)



C-Lymph node core biopsy showing Reed sternberg cell, D- Positive CD30 stain

Case Reports

A 52 year old female with history of stage IV Hodgkin's lymphoma was treated with ABVD chemotherapy and was in remission. She presented with symptoms of fatigue and chest pain with hemoglobin of 5.8 g/dl. She had no GI symptoms like blood per rectum or hematemesis and her GI evaluation with endoscopy and colonoscopy was normal.

Physical examination revealed scleral icterus, left axillary and inguinal lymphadenopathy as well as splenomegaly. Initial laboratory data showed Hb 5.8 g/dl, hematocrit 18.9, WBC cell count of 8.9, platelets 33. Direct Coombs test was positive, haptoglobin was less than 20 and LDH was 341. LFT's showed albumin 3.1, total protein 5.1, total billirubin 2.5 with indirect billirubin of 1.8. The diagnosis of hemolytic anemia secondary to relapsed Hodgkin's disease was made. Patient was treated with steroid and ABVD chemotherapy and her anemia improved after receiving treatment.

Discussion

Various immunologic disorders, such as immune thrombocytopenia (ITP), auto-immune hemolytic anemia (AIHA), immune neutropenia, and antibodies to insulin receptors have been reported with Hodgkin's disease.

The pathogenesis of auto-immune hemolytic anemia (AIHA) in relation with lympho-proliferative disorders seems to be multifactorial. Patients with Hodgkin's disease shown to have impairment in their immune system particularly the cell mediated immunity. Thus the decreased number of cytotoxic T cells is what possibly leads to an increased auto-antibody production.

AIHA is associated with all stages of Hodgkin's disease and usually suggests active or advanced disease and may precede a relapse. So the development of a positive DAT

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in a patient with history of Hodgkin's disease or other lymphproliferative disorder warrants further investigations regarding the possibility of an underlying active lymphoma. The treatment for AIHA associated with Hodgkin disease is to treat the underlying disease with chemotherapy. However the therapy for warm antibody AIHA is glucocorticoids with or without immunoglobulins and also splenectomy as second line therapy. The efficacy of standard therapy i.e. steroids and immunoglobins is low in secondary AIHA associated with lymphoma. Other immunosuppressive treatments, i. e rituximab an anti-CD20 antibody seems to be highly effective in patients with warm antibody AIHA refractory to standard therapy. Mycophenolate mofetil is also quite effective in AIHA patients with an underlying autoimmune disease.

In conclusion; A possible relapse of an underlying lympho-proliferative disorder i. e Hodgkin's disease should be considered in patients presenting with AIHA and having history of the disease. The recognition of this picture as one of the complications of Hodgkin's disease has important implications regarding treatment because treatment of underline Hodgkin's disease will improve AIHA.

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RX UPDATES

By Matthew Hinton, Pharm.D.
PGY1 Pharmacy Practice Resident

Pharmacogenetics - The Role of Genetic Factors in Drug Therapy

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Pharmacogenetics is a field of study that investigates how genetic factors affect drug response. While the field of pharmacogenetics is not new, recent discoveries have generated an increased amount of public interest.

One major area being studied is the genetics of drug metabolism. The cytochrome P450 (CYP450) enzymes are the most important group of phase I metabolizing enzymes for medicinal drugs. It is estimated that 80% of all prescribed drugs undergo oxidation reactions catalyzed by CYP450 enzymes [(1)]. The prevalence and effects of genetic polymorphisms among these enzymes are of particular interest to researchers.

One polymorphic enzyme that has been well described is CYP2D6. Genetic variance in the expression of CYP2D6 affects the efficacy of many drugs. For example, it is known that the opioid analgesic codeine is a pro-drug that must be metabolized to its active form (morphine) by CYP2D6 [(1)]. Polymorphisms exist that lead to the production of multiple copies of CYP2D6 resulting in an ultra-rapid metabolizer phenotype. Other polymorphisms code for a non-functional CYP2D6 enzyme. Therefore, some patients may experience exaggerated effects while others may experience minimal to no analgesic effect with codeine.

Tamoxifen (Nolvadex®) is another pro-drug that requires similar activation by CYP2D6 and CYP3A4 to produce the active metabolites endoxifen and 4-hydroxy-tamoxifen [(2)]. The metabolites of tamoxifen are 30 to 100 times more potent than the parent drug at suppressing estrogen-dependent cell proliferation. While CYP2D6 phenotype is important in determining tamoxifen response and disease recurrence, there is conflicting information on whether or not phenotype status affects overall survival. Therefore, to date, no genetic testing recommendations have been formally introduced for tamoxifen.

Many other CYP enzymes have been studied as well. Studies show that proton pump inhibitors are affected by CYP2C19 polymorphisms. One study demonstrated that the area under the concentration time curve (AUC) was 12-times higher in patients with a non-functional CYP2C19 enzyme compared to the typical wild-type genotype [(3)]. Another study showed that H. pylori-positive peptic ulcer disease cure rates in patients treated with omeprazole (Prilosec®) and amoxicillin (n=62) were much higher (100% vs. 28.6%) in the patients with the non-functional enzyme [(4)].

Metabolic pathways outside of the cytochrome system have also been investigated. The genetics of response for some drugs are so well described that it has led to changes in product labeling. For example, irinotecan (Camptosar®) used in the treatment of several different cancers is metabolized by the enzyme UDP-glucuronosyl transferase 1A1 (UGT1A1). Patients with the UGT1A1*28 allele have lower amounts of UGT1A1 produced. Therefore, irinotecan levels accumulate and put patients at higher

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risk for serious adverse events. This discovery prompted the FDA to include UGT1A1 genetic testing in the package labeling [5].

Another drug that has had labeling information changed is warfarin (Coumadin®). In 2007, the FDA approved updated labeling for warfarin that explained more fully how genetic factors may affect metabolism (6). The more potent S-isomer of warfarin is metabolized by CYP2C9. Well studied variant alleles of CYP2C9 reduce the metabolism of warfarin by 50% to 90%. This decrease in enzymatic activity increases the anticoagulant effects of warfarin. It is estimated that 18% of the US white population carry the mutation, whereas Asian and black patients exhibit these mutations at a rate of only 1 to 4% [2, 7].

Another mechanism for variability of warfarin response is genetic variation of vitamin K epoxide reductase complex subunit 1 (VKORC1). VKORC1 variant phenotypes differ in the amount of vitamin K recycled, and therefore, the amount of vitamin K dependent clotting factors produced. Phenotypes of VKORC1 that correlate to decreased warfarin dosing are very common among Asian patients (89%) and less common in white (37%) and black patients (14%). Phenotypes necessitating a higher therapeutic dose are higher in white patients (58%) than in black (49%) or Asian patients (10%) [2].

Another good example of how genetic testing can alter practice is the case of abacavir (Ziagen®). Abacavir is a nucleoside reverse transcriptase inhibitor used in the treatment of HIV. Abacavir is associated with a unique hypersensitivity reaction that can limit its use. Recent studies have revealed that patients with a known polymorphism in the human leukocyte antigen (HLA-B*5701) gene are more likely to develop a reaction [2, 9]. In these studies, hypersensitivity reactions were greatly reduced when patients were screened for HLA-B*5701. The reduction was so great that it lead to the manufacturer recommending screening for all patients who are naive to abacavir treatment or those restarting therapy.[2]

Pharmacogenetics is an evolving field and important discoveries are being made every day. Currently the high cost and limited accessibility of genetic testing are prohibitive factors to broader acceptance and use in clinical practice.

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NEWS & NOTES

UF COM Jax win big at Florida ACP

The Medical Jeopardy Team members Drs Ramlal, Chandrasekharan, and Jaikaransingh faced stiff competition but ultimately won their bracket in the Florida Chapter of American College of Physicians meeting last winter. They will now go on to the regional competition in Fall. Please join me in congratulating them on this remarkable accomplishment.

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Exemplary Teachers Awards to the Faculty

19 faculty members in the Department of Medicine were chosen to receive the 2011 University of Florida-College of Medicine's Exemplary Teachers Award. This award is given in recognition of outstanding teaching contributions of individual faculty member.

The awardees include (arranged alphabetically): **Drs. Irene Alexandraki, Abubakr Bajwa, Theodore A. Bass, Lyndon C. Box, James D. Cury, Malcolm T. Foster Jr., Luis A. Guzman, Jeffrey G. House, Steven S. Hsu, Steven J. Lavine, Alan B. Miller, Fauzia N. Rana, Pramod K. Reddy, Manish Relan, Mae Sheikh-Ali, Adil Shujaat, Kent R. Wehmeier, Robert A. Zaiden and Martin M. Zenni II.**

The awardees were recognized on April 14th during the proceedings of Advances in Medical Education held in the LRC Auditorium/Atrium.

Congratulations to the awardees.

MEET YOUR COLLEAGUES

Lisa Jones, M.D., Assistant Professor, Division of Pulmonary, Critical Care & Sleep Medicine

Dr. Jones earned her medical degree from the University of Cincinnati College of Medicine in Ohio. She completed her residency in Internal Medicine at University of Hospital Cincinnati and her fellowship in Pulmonary/Critical Care at Naval Medical Center San Diego.

Emad Naem, M.D., Assistant Professor, Division of Endocrinology, Diabetes & Metabolism

Dr. Naem earned his medical degree at Damascus University School of Medicine in Syria. He completed his internship in Preliminary Surgery at MCP Hahnemann University in Philadelphia, his residency in Internal Medicine at Northwestern University in Chicago and his fellowship in Endocrinology at the University of Florida College of Medicine, Jacksonville.

James Scolapio, M.D., Professor and Chief, Division of Gastroenterology

Dr. Scolapio earned his medical degree from Marshall School of Medicine in West Virgina. He completed his residency in Internal Medicine at Mayo Graduate School of Medicine in Minnesota and his fellowship in Gastroenterology at Mayo Graduate School of Medicine in both Minnesota and Florida. In addition to serving as Chief for the Division of Gastroenterology, Dr. Scolapio will also serve as Program Director of the Gastroenterology Fellowship.

Faisal Usman, M.D., Assistant Professor, Division of Pulmonary, Critical Care & Sleep Medicine

Dr. Usman earned his medical degree from King Edward Medical College in Pakistan. He completed his residency in Internal Medicine at Queens Hospital Center - Jamaica, NY and his fellowship in Pulmonary/Critical Care Medicine at the University of Florida College of Medicine - Jacksonville.

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UF & SHANDS BRAND

Miller, Vukich Appointed to New Roles at Shands Jacksonville

Greg Miller has been promoted to senior vice president of hospital operations. Miller is responsible for planning and directing all operational aspects of a number of hospital business units. He develops hospital policies and procedures in order to ensure optimization and compliance with established standards and regulations. He exercises management responsibility over the hospital, ensuring efficient services that are designed to meet the needs of patients, physicians, the public and staff.

Miller has more than 20 years of management experience, about 18 of those at Shands Jacksonville. For nearly 12 years he has served as an operational vice president and prior to that he was director of managerial accounting. He received his bachelor's degree in hospitality administration from Florida State University and an MBA from the University of North Florida.

University of Florida College of Medicine professor David Vukich, MD, has been selected as UF Senior Associate Dean for Hospital Affairs and Senior Vice President and Chief Medical Officer/Chief Quality Officer at Shands Jacksonville. Dr. Vukich had been serving as Chair of the Department of Emergency Medicine and Senior Vice President for Medical Affairs at Shands Jacksonville since 2001.

Some of Dr. Vukich's new duties as CMO/CQO include directing and overseeing medical staff within Shands Jacksonville; facilitating interactions between Shands and Jacksonville-based medical staff; developing a quality and performance improvement program for the hospital and UF Jacksonville clinics; and developing medical staff policies and procedures. Dr. Vukich will be a key representative for Shands Jacksonville in physician recruitment, credentialing, discipline and continuing medical education.