

PHARMASCRIPT

NEWSLETTER OF THE MARYLAND SOCIETY OF HEALTH-SYSTEM PHARMACISTS

Presidential Perspective January 2000 VOL. 23 NO. 1

Thanks for a Great Year

Joseph T. Botticelli, MS, RPh
St. Joseph Medical Center

As I leave the office of President of MSHP, I am filled with a sense of accomplishment, joy at the friendships made and a little sadness at what we could have done for our membership and the practice of pharmacy in Maryland. Before I get too carried away, let me thank your Board of Directors and Committee Chairs:

Lieser Mayo-Michelson Chairman
James Trovato President-Elect
Annette Rowden Treasurer
Vince Pearson Secretary
Bob Feroli Board Member
Mari Kim Board Member
Kathleen Truelove Board Member
Alex Zarow Board Member
Howard Schiff MPhA Liaison
Judi Mellendick Administrative Director
Alex Zarow Annual Seminar
Louis Levenson Annual Seminar
Babette Duncan Finance
Lois Reynolds Industry Advisory
Darlene Gast Industry Advisory
David Moore Legal and Regulatory
Charles Twilley Legal and Regulatory
Mari Kim Membership
Larry Blandford Monthly Programs
James Trovato Nominating/ Pharmacist of the Year
Ken Walters Public Affairs
Vince Pearson Publications

All of these individuals gave of their precious time to help MSHP provide the best services possible to you the members. They did a great job. I would especially like to thank Larry Blandford and Mari Kim for going above and beyond in their roles as Chairs for the Monthly Programs and Membership Committees respectively.

Larry took the lead to create a monthly program schedule that is clear and consistent. All members can now be assured of monthly programs for months to come. He has outlined what it takes to sponsor a meeting in order that prospective sponsors have all they need to seek and obtain funding. The programs this year have been topnotch. Many thanks to Larry and the rest of his committee for their good work.

Mari led her committee in creating a membership plan for this upcoming year. It addresses many of our

membership categories from Active Pharmacists, Technicians, Industry and Students. We are planning to meet with area directors of pharmacy departments, students in the UM School of Pharmacy, around the state for nonmember pharmacists and in the boardrooms of the pharmaceutical industry. A lot of work still needs to be done. However, Mari and the Membership Committee did well.

Alas, I can't dwell on these feelings too long. After all, I am now charged with leading the MSHP Board of Directors. I hope to see all of you at our Monthly meetings and Annual Seminar. May the year 2000 bring continued success to you, your families and MSHP.

Election 2000 Results

President James A. Trovato

President-Elect Janet Mighty

Treasurer Annette M. Rowden

Secretary Morrell C. Delcher

Board Member at Large Bonnie Pitt

ASHP Delegates:

Joe Botticelli

David Moore

Bonnie Pitt

James A. Trovato

ASHP Alternate Delegate, David Arrington

Legislative Committee

David B. Moore, Chair

As the legislative season approaches there are four major issues that may be brought before the legislature:

1. Confidentiality/Privacy -- This is a hot topic both locally and nationally. The recent television report on the disposal of confidential information and the continuing concerns of the confidentiality of electronically stored and transmitted records are fueling the fires. It is important to keep track of what legislation may be proposed and the potential affect it may have on pharmacy practice.
2. Pharmacy Technicians -- Most likely the issues around the use of technicians will be kept at the regulatory level and not be introduced to the legislature. The Board of Pharmacy has issued a draft of proposed regulations regarding the use of technicians, which impact primarily on community pharmacy. If anyone would like a copy of the proposed regulations, they may contact me at (410) 402-7817.
3. Uniform Prescription Cards -- Once again, this will affect community more than health-system pharmacies. We will be monitoring any legislation to assure it will not have a negative impact on our practice sites.

4. Medication Management (Collaborative Practice) -- Due to the current political climate, it is unlikely that any legislation on collaborative practice, now being referred to as medication management, will be introduced this year. Legislative leaders have indicated that, without the backing of physicians, it would be impossible to get a bill passed. We are still looking at the regulations as a means to accomplish this goal.

There may also be a medical marijuana bill introduced. In addition to monitoring the bills as they are introduced, we hope to build our grassroots legislative network. This means identifying our members by legislative district and legislators, identifying the legislators on the committees considering pharmacy legislation, and encouraging members who are constituents of these key legislators to contact them. We would also have information and talking points available on the various bills.

ASHP/MSHP Student Chapter

Jared S. Calish, President

The fall semester continues the traditions of a successful ASHP Student Chapter. We have had incredible turnouts at student meetings, MSHP monthly meetings, and the ASHP Midyear Clinical Meeting.

The semester started strongly as our membership grew during the "Tools for School¼Tools for Life" membership drive. This program was developed last year with the support of an ASHP grant. During 1998's membership drive, our student chapter placed third in the country for recruiting; however, in 1999 our chapter recruited over 100 student members (both new and returning) to become the largest ASHP student chapter. For these efforts, Jared S. Calish, the chapter president received an award for recruiting the most members as a first time recruiter during the opening session of the Midyear Meeting. In addition, he was given the opportunity to meet Dr. Bruce Scott, the ASHP president, and Dr. Henri Manasse, Chief Executive Officer of ASHP. This accolade could not of been achieved if it was not for the help of the chapter's executive board and Mary Zell, President-elect.

Furthermore, our chapter was elated for our clinical skills team, Melanie Ruane and Jeannie Rhee. Not only did they compete nationally at the ASHP National Clinical Skills Competition, but also our team finished as one of the top 10 finalists. By winning at the University of Maryland local competition, Melanie and Jeannie received airfare and hotel from our chapter, along with a pharmacy reference library for finishing in the top 10 teams among the 61 pharmacy school teams in the country. On a local note, our school competition increased to a record number of 8 competing teams; 2nd, 3rd, and 4th year students came out to our evening competition to detail their clinical pharmacy skills.

This fall we have had record turnouts for the student and state society meetings. At our first ASHP student meeting, Dr. James Trovato, chapter advisor, introduced MSHP as our guest speaker. The October meeting was another special and memorable meeting; Casey Thompson, Executive Resident for ASHP, detailed the benefits of ASHP and what ASHP can do in the community where we live. The September and November MSHP monthly meetings had a total of nearly 40 students in attendance. We wrapped up the year by helping Phi Delta Chi with their annual Thanksgiving Day dinner at the Ronald McDonald House. Special thanks go out to Mark Sellers and Jennifer Horn for their assistance in cooking the Thanksgiving Day turkeys!

Yet, the Student Chapter is not done exploring new territory. This spring we are planning the first ever *Interdisciplinary Patient Management Competition* (IPMC). In April, teams of three (medical student, a pharmacy student and a nursing student) will gather to analyze and assess a clinical case; they will place a special focus on developing a treatment plan incorporating all three of their specialty areas. ASHP and several drug companies are interested in turning the IPMC into a national program if it proves successful.

This spring is sure to be another record breaking and exciting year for the student chapter as we enter the next

millennium!

Jared S. Calish - President
Amanda Smith - Secretary
Mary Zell - President Elect
Jaja Teng - Treasurer
Clara Song - ASHP Liaison
Jeannie Rhee - MSHP Liaison
Dr. James Trovato - Chapter Advisor

Metabolic Complications Associated With the Use of Protease Inhibitors

Inna Kaplan, PharmD
University of MD Hospital

Introduction

There are currently 900,000 adults and children infected with the HIV virus.¹ Up through 1998, approximately 411,000 AIDS-related deaths have been reported to the CDC.² In addition, there are 40,000 new infections diagnosed each year.² However, this number has remained relatively constant throughout the 1990s.² In the U.S. the main modes of transmission of the HIV virus include intravenous drug use, homosexual and heterosexual transmission.¹ There has been an increasing number of women affected by the virus. Between 1985 and 1998 the number of women and adolescent girls has increased from 7% to 23%.² The economic burden of the HIV infection has been estimated at \$14 billion for costs associated with prevention and treatment alone in the U.S.²

Since 1996 the number of new AIDS diagnoses has decreased substantially for many reasons, such as, improved prophylaxis against opportunistic infections, increasing experience among health care professionals in caring for HIV-infected patients, improved access to health care for HIV patients, and prevention efforts.² The most influential factor, however, has been the increased use of combination potent antiretroviral drugs.² There are currently three classes of antiretroviral drugs which include nucleoside analogues, non-nucleoside reverse transcriptase inhibitors, and protease inhibitors (PIs).¹

Highly active antiretroviral therapy (HAART) describes the use of these three classes of potent antiretroviral drugs given in a combination of three or more agents which usually includes a protease inhibitor. This triple therapy regimen is expected to reduce the viral load to < 50 copies/ml in treatment-naïve patients.¹

The Swiss-HIV cohort study was designed to examine the progression of the HIV infection and survival among patients during 1988-1996 and to assess the influence of new antiretroviral combination therapies.³ This was a prospective multicenter study which included over 5,000 patients infected with HIV and over 15,000 patient-years of follow-up. The results of this study found that compared with no antiretroviral treatment, the risk of an initial AIDS diagnosis decreased by 42% with triple therapy. In addition, mortality was reduced by 65% in patients treated with triple therapy.

Despite the benefits of triple combination regimen, in 1996 specific side effects have been observed in an increasing number of patients treated with protease inhibitors. Although there is presently no case definition of these complications, the three main components of the lipodystrophy syndrome include an abnormal fat

distribution ("lipodystrophy"), insulin resistance, and hyperlipidemia.⁴ Patients may experience one or more of these three complications.

The exact mechanism by which the syndrome occurs is not well understood. However, there have been several proposed hypotheses regarding the pathophysiology of these complications. The most widely discussed hypothesis is proposed by Carr et al. which suggests that protease inhibitors bind to the region of the HIV protease enzyme.^{4,5} This enzyme is structurally similar to regions on two human proteins which regulate the breakdown of lipids. These proteins include cytoplasmic retinoic-acid binding protein type 1 (CRABP-1) and lipoprotein-receptor-related protein (LRP). Therefore, the authors hypothesize that in addition to protease enzyme inhibition, protease inhibitors also inhibit CRABP-1 and LRP. CRABP-1 presents retinoic-acid to cytochrome P450 3A where it is synthesized into cis-9-retinoic acid which helps regulate cell differentiation and is responsible for programmed cell death in peripheral fat cells. Inhibition of retinoic acid binding to CRABP-1 could lead to decreased cis-9-retinoic production, thereby leading to reduced differentiation and increased death of peripheral fat cells. LRP is important for postprandial chylomicron clearance and consequently for clearance of TG from the circulation. Therefore, inhibition of LRP by protease inhibitors would contribute to hyperlipidemia which could subsequently lead to central fat deposits, insulin resistance, and in susceptible individuals, frank diabetes (DM). In addition, the altered fat metabolism may be proportional to the degree of cytochrome P450 3A inhibition of each protease inhibitor.⁴ For instance, patients receiving the most potent of the inhibitors, ritonavir, would be most likely to develop these metabolic abnormalities.⁴ Carr et al. found that these metabolic complications were more frequent in patients taking ritonavir-saquinavir combination than in those patients taking indinavir.⁶

Others have argued against the hypothesis that protease inhibitors directly cause metabolic abnormalities. Although these complications have been most closely associated with protease inhibitors, they have also been observed, to a much lesser extent, in patients whom have not been treated with protease inhibitors.^{4,6,7}

Lipodystrophy

Lipodystrophy may present with any of the following symptoms such as, an increased waist-to-hip ratio or "truncal obesity," increased visceral fat and decreased subcutaneous fat, the development of a fatty mass at the back of the neck or "buffalo hump," thinning of extremities, prominent veins, loss of facial fat, and breast enlargement especially in women.^{4,8} The incidence of lipodystrophy varies between 5-75% of patients taking triple therapy.⁴ Such a divergent range may be explained by two reasons. First, there are currently no objective criteria for the diagnosis of lipodystrophy. Therefore, physicians have used patient self-reporting as a major criterion for the diagnosis.⁴ Second, different studies have used different follow-up periods and those studies with a longer follow-up period have found higher prevalence rates.⁶

In the study by Carr et al, the authors evaluated two risk factors for developing lipodystrophy which include increased duration of protease inhibitor use and the use of specific protease inhibitors.⁶ This cross-sectional analysis included 116 patients on at least one protease inhibitor for an average 13.6 months, 32 protease inhibitor-naïve patients, and 47 control patients without a diagnosis of HIV. Lipodystrophy was observed in 64% of patients receiving a protease inhibitor and 3% of protease inhibitor-naïve patients. Of the 116 patients who were on at least one protease inhibitor, 74 were found to have lipodystrophy and were taking a protease inhibitor for a mean of 15.2 months. The 42 patients who did not develop lipodystrophy had been on PI therapy for only 10.9 months (P=0.0001). Lipodystrophy was attributed to indinavir in 41 patients and to ritonavir+saquinavir combination in 25 patients. The time to lipodystrophy was eight months in patients who

received combination of ritonavir and saquinavir as compared to patients on indinavir which took 12 months to develop lipodystrophy. Therefore, the time to develop lipodystrophy was shorter in patients who took the ritonavir+saquinavir combination. Lipodystrophy was attributed to nelfinavir in three patients and to saquinavir in one patient, however, the patient numbers were too small in these two groups to make any conclusions.

Carr et al. concluded that patients who were treated with protease inhibitors were more likely to develop lipodystrophy. In addition, those patients with protease inhibitor-induced lipodystrophy had significantly longer duration of PI therapy than those without lipodystrophy. Lipodystrophy was also more common in patients receiving ritonavir+saquinavir than in those receiving indinavir.

Insulin Resistance

Insulin resistance occurring in patients treated with protease inhibitors appears to similar to insulin resistance occurring in patients with type 2 diabetes mellitus (DM). The proposed similarities include the absence of ketosis, increased fasting plasma insulin, increased C-peptide levels, peripheral insulin resistance, impaired glucose tolerance, and a therapeutic response to sulfonylureas. The incidence of overt type 2 DM is < 6%.^{4,9} If it occurs, it usually occurs within 1-6 months.⁴ In addition, protease inhibitor-induced insulin resistance is more likely to develop in patients with a predisposition to DM (ie. family history).

**Maryland Society of Health-System Pharmacists
3525 Ellicott Mills Drive, Suite N
Ellicott City, MD 21043-4547**

Return to the [MSHP home page](#)