

HOSPITAL PHYSICIAN®

INFECTIOUS DISEASES BOARD REVIEW MANUAL

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The *Hospital Physician Infectious Diseases Board Review Manual* is a study guide for fellows and practicing physicians preparing for board examinations in infectious disease. Each quarterly manual reviews a topic essential to current practice in the subspecialty of infectious disease.

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Complications of Antiretroviral Therapy: Protease Inhibitors and New Antiretroviral Agents

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Complications of Antiretroviral Therapy: Protease Inhibitors and New Antiretroviral Agents

Risa M. Hoffman, MD, MPH, and Raphael J. Landovitz, MD

INTRODUCTION

Since protease inhibitors (PIs) were introduced in 1995, they have been the cornerstone of potent antiretroviral therapy (ART) combinations. Updated treatment guidelines from the International AIDS Society–USA Panel published in 2002 recommend a PI and 2 nucleoside reverse transcriptase inhibitors (NRTIs) as one of the first-line combination therapies for ART-naïve patients.¹ However, PI-based regimens can be difficult because of multiple times per day dosing regimens, pill burden, and toxicity, all of which can affect the utility of these regimens.

This review is the second of a 2-part series addressing common and emerging complications of ART. Part 1 reviewed antiretroviral mechanisms of action and discussed specific complications of NRTIs and non-nucleoside reverse transcriptase inhibitors (NNRTIs). Part 2 focuses on the metabolic toxicities of PIs, including fat redistribution, dyslipidemia, and insulin resistance. Potential etiologies, treatment options, and impact of metabolic toxicities on cardiovascular risk are explored. Complications associated with recently approved antiretroviral agents are briefly discussed. A section of sample board review questions is provided following the text.

PROTEASE INHIBITORS

FAT REDISTRIBUTION ASSOCIATED WITH PIs

Case Presentation

A 52-year-old man is seen for a routine visit in HIV clinic. He was diagnosed with HIV infection 8 years ago and has been on therapy since that time. He has been stable on combination therapy with zidovudine, lamivudine, and ritonavir-boosted indinavir for the past 2 years. His most recent CD4 cell count was 435/mm³ with a viral load of less than 75 copies/mL. He has been

feeling well but complains that despite his daily exercise routine at the gym and a low-fat diet, he has noticed increasing abdominal girth. He realizes that other HIV-infected acquaintances have had similar changes in body habitus and asks if this is the result of HIV infection. He also asks if there are treatments that can successfully reverse these changes.

- **What are the suspected causes of fat redistribution in HIV-infected patients?**
- **What treatment might you recommend for this patient?**
- **What additional testing would be warranted at this time?**

Adverse reactions associated with PIs are listed in **Table 1**. Recognition of body fat redistribution in HIV-infected patients on PI therapy dates to 1997, soon after these drugs were introduced.² In 1998, the first description of a syndrome associated with PIs, including lipodystrophy, dyslipidemia, and insulin resistance, was published.³ Since that time, the syndrome has been given a number of different names, but an established case definition has been elusive, making formal study difficult and the available data confusing.^{4,5} Lessons from clinical and research experience have clarified that fat redistribution occurs with both PIs and NRTIs. NRTI-related fat redistribution is associated more with lipoatrophy, weight loss, and lactic acidemia.⁶ PI-associated fat redistribution commonly manifests as central adiposity (including a dorsocervical fat pad—the so-called “buffalo hump”), dyslipidemias, and insulin resistance. Patients who have never been on ART have been described to have body morphologic changes similar to those seen in both of the above categories, suggesting at least a partial contribution of HIV infection itself.^{7,8} This section focuses on PI-associated body changes. The term *fat redistribution* is used to refer specifically to morphologic changes, whereas *lipodystrophy* refers to the entire syndrome of morphologic and metabolic derangements.