

HRSA CARE ACTION



FEBRUARY 2009

Substance Abuse

Women's Issues

Medical Issues

Mental Health

THE GRAYING OF HIV

Older people need to be aware that there is no age limit for HIV.

—Hilda Morales, Nurse Practitioner
Montefiore Center for Positive Living, Bronx, New York

HIV/AIDS among older people is not something new. However, it is increasingly prevalent. The primary cause, which has been widely noted in the literature over the past decade, is that many HIV-positive people receiving appropriate care are living into middle and old age.

To deal with this most welcome development, the Health Resources and Services Administration and many other organizations, both public and private, have given a great deal of attention to the topic of how care needs evolve as people grow older. Many of the tools available for treating this population are listed in the table insert in this issue.

DID YOU KNOW?

----- According to the Centers for Disease Control and Prevention, 15 percent of new HIV/AIDS cases occur in people age 50 or older.¹

----- More than 25,000 people age 50 or older were diagnosed with HIV between 2003 and 2006.²

ONLINE RESOURCES

Centers for Disease Control and Prevention. *Persons aged 50 and over.* (2008) www.cdc.gov/hiv/topics/over50/index.htm

U.S. Administration on Aging. www.aoa.dhhs.gov

ART Cohort Collaboration. *Risk calculator for HIV-positive patients starting antiretroviral therapy.* (2007) www.art-cohort-collaboration.org/

See also the table insert for a complete list of online resources.

▶▶▶▶ Please visit our Web site at www.hrsa.gov

DIRECTOR'S NOTES

Aging often means coping with new concerns about health. For a growing number of older Americans, HIV is one of those concerns. Whether newly diagnosed or treatment experienced, thanks to the advent of highly active antiretroviral therapy, HIV-positive patients are living longer and healthier lives.

But we can do more. Unfortunately, older people often underestimate their risk for HIV—and so do providers. As a result, patients over age 50 are increasingly presenting in late “stage of disease” at diagnosis. In fact, this age group now accounts for 15 percent of all new HIV/AIDS cases. In 2005, among this population, one-half were diagnosed with HIV and AIDS simultaneously or given an AIDS diagnosis within a year of learning their HIV-positive status.

Compounding these challenges are others specific to the aging HIV-positive population—from HIV-related conditions such as lipodystrophy to age-related concerns such as hypertension. This issue of our newsletter is devoted to HIV and aging, because the more we understand about this population, the better we can treat older adults. That is, after all, what the Ryan White HIV/AIDS Program is all about.

*Deborah Parham Hopson
HRSA Associate Administrator for HIV/AIDS*

HRSA CAREAction

Publisher

U.S. Department of Health and Human Services
Health Resources and Services Administration, HIV/AIDS Bureau
5600 Fishers Lane, Room 7-05
Rockville, MD 20857
Telephone: 301.443.1993

Prepared for HRSA/HAB
by Impact Marketing + Communications

Photographs

Cover: An older woman consults her physician in a Midwestern clinic.
Page 5: An HIV-positive client outside a clinic in Albuquerque, NM.
Both clinics are funded in part by the Ryan White HIV/AIDS Program.
Photographs © See Change.

Additional copies are available from the HRSA Information Center, 888.ASK.HRSA, and may be downloaded at www.hab.hrsa.gov.

This publication lists non-federal resources in order to provide additional information to consumers. The views and content in these resources have not been formally approved by the U.S. Department of Health and Human Services (HHS). Listing these resources is not an endorsement by HHS or its components.

Increased longevity resulting from today's treatment is, however, only part of the story about HIV/AIDS among older adults.* The other part is related to new infections among this population, which are driven in part by social and biological factors. For example:

- ▶ Many older adults are newly single, widowed, or have grown children and have more time for sexual activity.
- ▶ New treatments for erectile dysfunction facilitate sex.
- ▶ Older adults may be unfamiliar with condom use or reluctant to use them because birth control after menopause is unnecessary, and condoms can make it difficult to maintain an erection.
- ▶ Vaginal dryness is common among menopausal women, making tiny cuts and tears during sex more likely.

When older adults have insufficient information about HIV transmission, the risks associated with the factors above are intensified.

HIV/AIDS prevalence among older adults is driven by many factors, not one. Therefore, full comprehension of the HIV/AIDS-related needs of this population requires an understanding of care as well as prevention needs. This issue of the newsletter highlights both kinds of needs.

Late Diagnosis

In 2005, among HIV-positive older adults, one-half were diagnosed with HIV and AIDS simultaneously or diagnosed with AIDS within 1 year of their HIV diagnosis.³ HIV often goes undiagnosed in older adults for several reasons:

- ▶ Clinicians may underestimate the risk for HIV among older adults and not discuss HIV transmission or perform testing.

*For simplicity, in this article we use the term “older adults” to refer to people age 50 and older.

ESTIMATED NUMBER OF HIV/AIDS CASES, 2003-2006

Age at HIV Diagnosis	No. of Cases 2003	No. of Cases 2004	No. of Cases 2005	No. of Cases 2006	Total Cases by Age at Diagnosis 2003–2006
50–54	2,451	2,401	2,547	2,718	10,117
55–59	1,279	1,363	1,455	1,438	5,535
60–64	655	702	692	714	2,763
≥65	570	624	613	618	2,425
Total	4,955	5,090	5,307	5,488	20,840

Source: Centers for Disease Control and Prevention. *HIV/AIDS Surveillance Report*. 2006;18.

- ▶ Common, nonspecific HIV symptoms, such as fatigue, may be mistaken for signs of aging or other conditions.
- ▶ Older patients may not perceive themselves as at risk for HIV because of a lack of information on HIV prevention and transmission.

A prompt HIV diagnosis is important for older adults, because HIV may accelerate aging, and aging may speed up HIV progression. Studies conducted before the advent of highly active antiretroviral therapy (HAART) reported that aging was associated with rapid progression to AIDS, particularly among people who were age 40 or older at seroconversion.⁴⁻⁶ Some studies report that older adults tend to have better virologic responses to antiretroviral therapy (ART) but have more blunted immune responses, more AIDS-defining events, and higher mortality than younger patients.^{7,8} Immune restoration may simply take longer in older adults.⁹

Several culprits may cause discordant responses to treatment in older patients (e.g., poor CD4 recovery despite undetectable HIV viral load). Virologic response may be attributed in part to higher adherence rates among older patients. Delayed or partial immune restoration may be caused by late presentation, low CD4 cell count, reduced thymic output, long-term immune activation from untreated HIV, and other factors.

Injection Drug Use

Injection drug use accounts for more than 16 percent of AIDS cases among older adults.¹ In the United States,

more than 3 million people have injected drugs; most of them are over 40 years old.¹⁰ Factors contributing to late diagnosis in this group are that former injection drug users (IDUs) may be reluctant to disclose past behavior, and that current users may shy away from or not have access to health care. Thus, many people remain undiagnosed for years.

Aging and injection drug use can lead to poorer health outcomes among people with HIV. Even in the HAART era, survival after an AIDS diagnosis is poorest among IDUs and older adults.^{2,6,11,12}

Women

HIV incidence has been increasing in women over age 50. Older women are less likely than their younger peers to have accurate information on HIV transmission, to see themselves as at risk, or to undergo HIV testing.¹³⁻¹⁵

Medical care for older HIV-positive women should include an annual gynecological exam, cervical and anal pap smears (repeated 6 months after initial screening, then annually), bone mineral density assessment (at age 50 and at menopause, no current recommendation thereafter), yearly mammography, and STI screening (repeated annually or more often for ongoing risk).

Medical and Mental Health Issues

Many older adults have been living with HIV/AIDS for years or even decades; others are recently infected or diagnosed. Although medical and psychosocial issues may differ for newly diagnosed and for treatment-experienced patients, both groups may be at higher risk

for age-associated comorbidities (e.g., cardiovascular disease, cancer, liver and kidney disease, bone loss, and dementia) than their HIV-negative peers. “Many of our older HIV-positive patients are already diabetic and have high blood pressure . . . with HIV plus aging, we do a lot of primary care,” explains Hilda Morales, a nurse practitioner at the Montefiore Center for Positive Living in Bronx, New York.

As HIV-positive people live longer, researchers are working to understand interactions among HIV disease, drug toxicity, and aging and how best to treat the increasing number of HIV-related conditions.

Metabolic Syndrome and Cardiovascular Disease

Metabolic syndrome—a cluster of metabolic abnormalities including abdominal fat accumulation, elevated triglycerides and cholesterol (also called *dyslipidemia*), hypertension, and glucose intolerance—has been observed in people living with HIV. HIV disease, aging, genetics, lifestyle, and ART contribute to these metabolic abnormalities.

Clinicians use several strategies to treat metabolic syndrome, such as switching antiretroviral agents, pharmacotherapy, and lifestyle changes. Stavudine (Zerit or d4T) and zidovudine (Retrovir or AZT) are associated with increased risk for lipoatrophy and diabetes; if possible, those drugs should be avoided.^{16,17} Dyslipidemia has been linked to protease inhibitors (PIs), including stavudine and efavirenz. Dyslipidemia can be treated with drugs that do not have significant interactions with PIs or nonnucleoside reverse transcriptase inhibitors and through exercise and diet. Glucose intolerance is associated with hepatitis C virus (HCV)-HIV coinfection and use of indinavir and lopinavir/ritonavir.¹⁷

Cardiovascular disease (CVD) is also related to metabolic abnormalities. Aging is a significant risk factor, especially for HIV-positive men.¹⁸ Some major risk factors, such as genetics, sex, and prior cardiovascular events, cannot be changed, but others may be modifiable. To address CVD, clinicians can treat hypertension, dyslipidemia, elevated triglycerides, obesity, insulin resistance, and diabetes and promote lifestyle changes (e.g., quitting smoking, exercising, and healthy eating).

In recent years, clinicians and researchers have speculated about whether HIV increases risk for CVD. Recent research has identified an association between untreated HIV disease and markers of increased risk for CVD in two treatment interruption trials: Strategies for Management of Anti-Retroviral Therapy (SMART) and Staccato.^{19,20}

Although the benefits of HIV treatment far outweigh the risks, the duration of ART and the use of PIs, abacavir, and didanosine have been linked with an increased risk for cardiovascular events, especially in people with other risk factors.²⁰⁻²²

Cancer

Non-AIDS-defining malignancies (nADM)—cancers that are not associated with AIDS, such as lung, anal, and gastrointestinal malignancies—are becoming increasingly common among people living with HIV. HIV doubles—and may even triple—cancer risk, even in the HAART era.²³ In fact, mortality from nADM has outpaced deaths from AIDS-defining malignancies (ADM); that is, non-Hodgkins lymphoma, cervical cancer, and Kaposi's sarcoma. Immunodeficiency increases the risk of cancer and death from both nADM and ADM.^{24,25}

Although the CDC and other government agencies have not issued specific recommendations for optimal initiation and frequency of cancer screening in people who are HIV positive, the American Cancer Society recommends that “people who are at increased risk for certain cancers may need to follow a different screening schedule, such as starting at an earlier age or being screened more often.”²⁶

Early detection is critical for HIV-positive people because cancer can be more aggressive in this population and treatment is complicated by additive toxicities and immunosuppression from chemotherapy and drug interactions.^{27,28} “The fact that we take these very demanding, complex regimens of chemotherapeutic drugs means that we need our doctors to keep an eye on our kidneys and livers,” explains Ron, who at age 60 has been HIV positive for more than 20 years.

Renal Disease

Glomerular filtration rate, a measure of kidney function, decreases with age and is a sign of kidney disease.²⁹ Traditional risk factors for renal disease are diabetes, coronary artery disease, and hypertension. HIV infection increases the risk for renal disease because the kidney is an HIV reservoir. Low CD4 cell count, HIV ribonucleic acid (RNA; commonly referred to as “viral load”) of >10,000 copies/mL, HIV-HCV coinfection, and duration of ART are associated with a greater risk for acute kidney failure.³⁰

HIV-associated nephropathy (HIVAN) is prevalent among HIV-positive African-Americans, and HIVAN progresses more rapidly to end-stage renal disease in African-Americans than in Whites.^{31,32} All HIV-positive



RESOURCES FOR HIV AND AGING

TOPIC

DOCUMENTS

MEDICAL CARE FOR OLDER WOMEN

New York State Department of Health AIDS Institute and Johns Hopkins University Division of Infectious Diseases. *Medical Care for Menopausal and Older Women With HIV Infection* (2008) www.hivguidelines.org/GuideLine.aspx?pagelD=259&guidelineID=134

METABOLIC and CARDIOVASCULAR SYSTEMS

AIDS Education and Training Centers. *Management of Dyslipidemia and HIV* (2006) www.aidsetc.org/pdf/p02-et/et-03-00/dyslipidemia.pdf

American Diabetes Association. *2008 Clinical Practice Recommendations (Diabetes Care. 2008;31)* http://care.diabetesjournals.org/content/vol31/Supplement_1/

European AIDS Clinical Society. *Guidelines on the Prevention and Management of Metabolic Diseases in HIV* (2008) www.eacs.eu/guide

National Heart, Lung, and Blood Institute. *Risk Assessment Tool for Estimating 10-Year Risk of Developing Hard CHD (Myocardial Infarction and Coronary Death)* (n.d.) <http://hp2010.nhlbihin.net/atp/iii/calculator.asp?usertype=prof> (not validated in HIV-positive people; based on Framingham Heart Study data)

CANCER

American Cancer Society. *Guidelines for the Early Detection of Cancer* (2008) www.cancer.org/docroot/PED/content/PED_2_3X_ACS_Cancer_Detection_Guidelines_36.asp?sitearea=PED

National Cancer Institute. *Screening and Testing to Detect Cancer* (n.d.) www.cancer.gov/cancertopics/screening

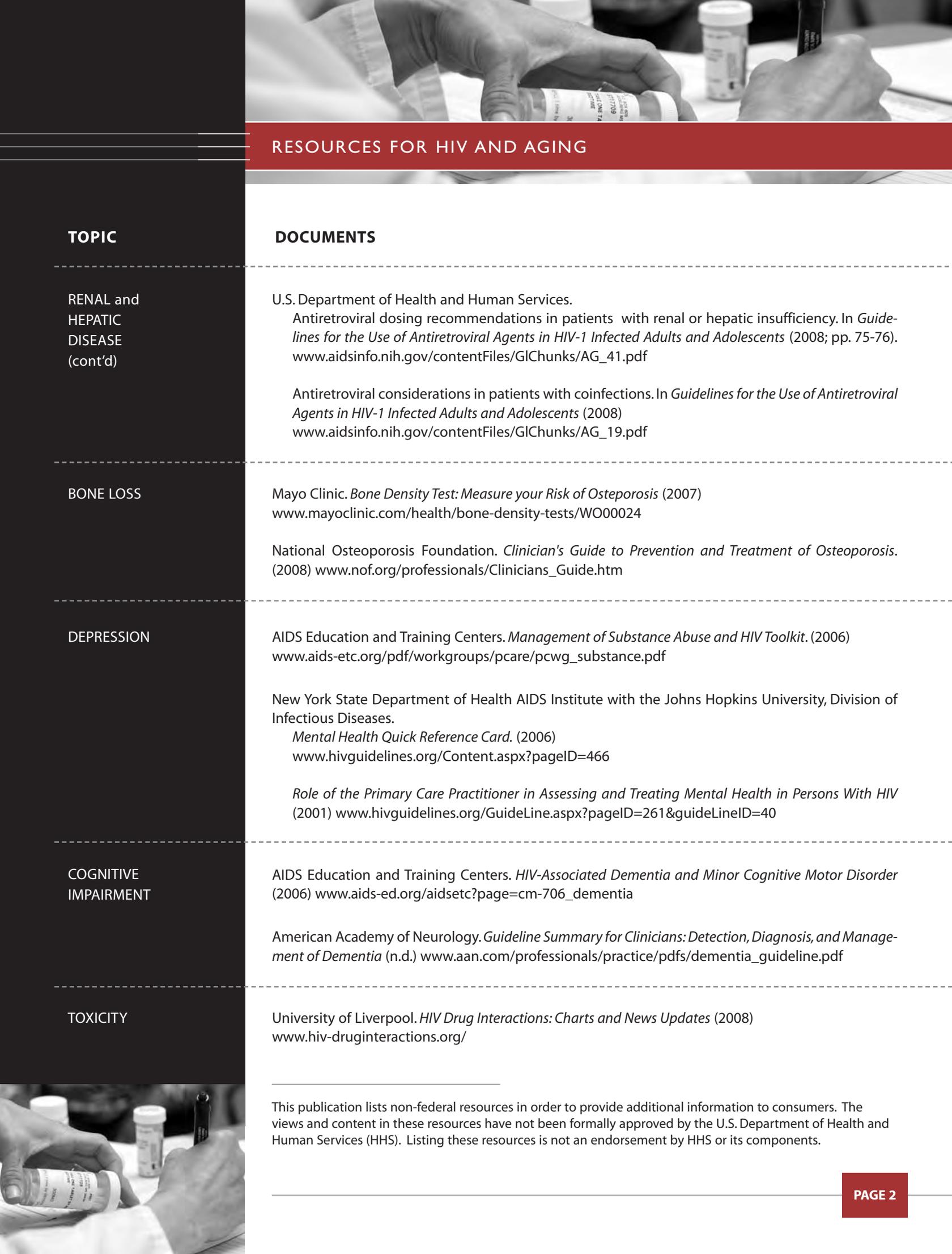
RENAL and HEPATIC DISEASE

Gupta SK, Eustace JA, Winston JA, et al. *Guidelines for the management of chronic kidney disease in HIV-infected patients: recommendations of the HIV Medicine Association of the Infectious Diseases Society of America (Clinical Infectious Diseases. 2005;40:1559-85)* www.journals.uchicago.edu/doi/pdf/10.1086/430257

Soriano V, Puoti M, Bonacini M. *Care of patients with chronic hepatitis B and HIV co-infection: Recommendations from an HIV-HBV International Panel (AIDS. 2005;19:221-240)* www.aidsonline.com (search on "Soriano")

Tien PC, Veterans Affairs Hepatitis C Resource Center Program, National Hepatitis C Program Office. *Management and treatment of hepatitis C virus infection in HIV-infected adults: recommendations from the Veterans Affairs Hepatitis C Resource Center Program and National Hepatitis C Program Office (American Journal of Gastroenterology. 2005;100:2338-54)* www.hepatitis.va.gov/vahep?page=prtop06-gd-01





RESOURCES FOR HIV AND AGING

TOPIC

DOCUMENTS

RENAL and
HEPATIC
DISEASE
(cont'd)

U.S. Department of Health and Human Services.

Antiretroviral dosing recommendations in patients with renal or hepatic insufficiency. In *Guidelines for the Use of Antiretroviral Agents in HIV-1 Infected Adults and Adolescents* (2008; pp. 75-76).
www.aidsinfo.nih.gov/contentFiles/GlChunks/AG_41.pdf

Antiretroviral considerations in patients with coinfections. In *Guidelines for the Use of Antiretroviral Agents in HIV-1 Infected Adults and Adolescents* (2008)
www.aidsinfo.nih.gov/contentFiles/GlChunks/AG_19.pdf

BONE LOSS

Mayo Clinic. *Bone Density Test: Measure your Risk of Osteoporosis* (2007)
www.mayoclinic.com/health/bone-density-tests/WO00024

National Osteoporosis Foundation. *Clinician's Guide to Prevention and Treatment of Osteoporosis*. (2008) www.nof.org/professionals/Clinicians_Guide.htm

DEPRESSION

AIDS Education and Training Centers. *Management of Substance Abuse and HIV Toolkit*. (2006)
www.aids-etc.org/pdf/workgroups/pcare/pcwg_substance.pdf

New York State Department of Health AIDS Institute with the Johns Hopkins University, Division of Infectious Diseases.

Mental Health Quick Reference Card. (2006)
www.hivguidelines.org/Content.aspx?pageID=466

Role of the Primary Care Practitioner in Assessing and Treating Mental Health in Persons With HIV (2001) www.hivguidelines.org/GuideLine.aspx?pageID=261&guidelineID=40

COGNITIVE
IMPAIRMENT

AIDS Education and Training Centers. *HIV-Associated Dementia and Minor Cognitive Motor Disorder* (2006) www.aids-ed.org/aidsetc?page=cm-706_dementia

American Academy of Neurology. *Guideline Summary for Clinicians: Detection, Diagnosis, and Management of Dementia* (n.d.) www.aan.com/professionals/practice/pdfs/dementia_guideline.pdf

TOXICITY

University of Liverpool. *HIV Drug Interactions: Charts and News Updates* (2008)
www.hiv-druginteractions.org/

This publication lists non-federal resources in order to provide additional information to consumers. The views and content in these resources have not been formally approved by the U.S. Department of Health and Human Services (HHS). Listing these resources is not an endorsement by HHS or its components.

Many older adults have been living with HIV/AIDS for years or even decades; others are recently infected or diagnosed. Although medical and psychosocial issues may differ . . . both groups may be at higher risk for age-associated comorbidities.



In contrast with the general population, rates of depression and substance abuse among HIV-positive people do not decrease with age.

patients should undergo initial screening for renal disease. Annual screening is recommended for patients who have the following characteristics or conditions, because they are at higher risk for HIVAN:³³

- ▶ African-American ethnicity
- ▶ Diabetes
- ▶ High blood pressure (hypertension)
- ▶ HIV-HCV coinfection
- ▶ CD4 count of <200 and/or HIV RNA >4,000 copies/mL.

ART is used to treat HIVAN, although certain antiretroviral agents (i.e., indinavir and tenofovir) can cause renal toxicity.³⁴ Dosage of some antiretroviral agents may require adjustment in people with renal insufficiency.

Hepatic Disease

HCV is prevalent among HIV-positive IDUs; up to 90 percent are HCV coinfecting.³⁵ HIV accelerates HCV disease progression and doubles the risk for cirrhosis.³⁶ End-stage liver disease from HCV has become a leading cause of death among people with HIV in regions where HAART is readily available.^{37,38} Although HCV is treatable, regardless of HIV status, HCV treatment is less effective for HIV-positive people.³⁹⁻⁴¹

Approximately 10 percent of all people living with HIV are coinfecting with hepatitis B virus (HBV). Liver damage from HBV develops more rapidly in people with HIV, and HBV coinfection increases the risk of liver-related mortality.^{42,43}

HBV treatment is recommended for people with HIV who have liver damage, regardless of CD4 cell count. Some antiretroviral agents, including lamivudine, tenofovir, and emtricitabine, are active against HIV and HBV; they should be used as part of ART. For people with HIV-HBV coinfection who do not require ART, drugs that are active against HBV—but not HIV—should be used. HIV-HBV coinfecting patients who receive treatment for both conditions should be monitored for immune-mediated flares of HBV and evidence of HBV drug resistance.⁴²

Viral hepatitis coinfection complicates HIV treatment by tripling the risk of antiretroviral-associated hepatotoxicity.⁴⁴ Hepatotoxicity can be avoided by careful selection of antiretroviral agents. Dose modification

of certain antiretroviral agents may be necessary for coinfecting people with advanced liver disease.

Bone Loss

Osteopenia (decreased bone density) and osteoporosis (decreased bone mass and density) are often associated with aging, White race, female sex, family history, smoking, heavy alcohol consumption, poor nutrition, and physical inactivity. Osteopenia and osteoporosis are 3 times more prevalent among people with HIV than among the general public.^{45,46} Factors contributing to accelerated bone loss in people who are HIV positive may include immune activation, HAART use, abnormal vitamin D metabolism, and premature menopause.

Aging and ART—especially protease inhibitors—have been associated with loss of bone density in HIV-positive men and women. In HIV-positive men, bone loss has also been linked with HIV RNA of <500 copies/mL and low body mass index (BMI); in HIV-positive women, it has been linked to low CD4 count.⁴⁶⁻⁴⁸ Experts suggest screening for loss of bone density in people living with HIV who have traditional risk factors.

Weight-bearing exercise, adequate daily intake of calcium and vitamin D, smoking cessation, and reducing alcohol intake to a moderate level may help stave off bone loss. Once it manifests, bone loss can be treated with alendronate.⁴⁹ Monitoring for treatment-limiting side effects (e.g., severe bone, joint, or muscle pain) from alendronate is crucial.

Mental Health Issues

Untreated depression is associated with decreased HAART initiation and poor drug adherence.⁵⁰⁻⁵² In contrast with the general population, rates of depression and substance abuse among HIV-positive people do not decrease with age.^{53,54} Older HIV-positive men and women face some psychosocial issues that are unique to their demographic group, yet few programs are tailored to their needs. Many older adults with HIV experience bereavement, stigma, loneliness, and isolation.

Mental health care and support services continue to be crucial elements of HIV care and treatment for older adults. The risk for mild to serious cognitive impairment among people with HIV increases with age, especially in people with a history of alcohol dependence. Cognitive

impairment also may be caused by thyroid dysfunction; cerebrovascular and neurodegenerative diseases; and vitamin deficiency as well as by HIV itself, HCV, and other opportunistic infections. HIV-associated inflammation may cause central nervous system (CNS) changes, and the immune response to HIV may cause CNS damage.⁵⁵ ART continues to be the therapy of choice for these conditions, and new treatments are being studied.

Antiretroviral Toxicity

HIV medication may be hard for older adults to tolerate because they are more likely to have comorbid conditions. Polypharmacy (multiple medications or pill burden) increases the risk of drug interactions. Moderate to serious laboratory abnormalities in levels of creatinine, cholesterol, glucose, hemoglobin, and neutrophils (white blood cells that fight bacterial infections) are

more common in older adults than in their younger counterparts.^{9,56} Antiretroviral agents for older patients should be selected to reduce toxicity risk. Although information on optimal drug levels in older persons is limited, therapeutic drug monitoring may be useful for those who experience drug side effects.

Looking Forward

People who are HIV positive are living longer as a result of continuing advances in treatment, but they face increased risk of developing conditions that are traditionally associated with aging. As clinicians strive to address the complex medical and psychosocial issues of the growing population of older adults living with HIV, researchers seek an understanding of the interactions among HIV disease, aging, and drug toxicity.

REFERENCES

- Centers for Disease Control and Prevention (CDC). HIV and AIDS among persons aged 50 and over. 2008. www.cdc.gov/hiv/topics/over50/resources/factsheets/pdf/over50.pdf
- CDC. Cases of HIV infection and AIDS in the United States and dependent areas, 2006. *HIV/AIDS Surveillance Report*, 2008. Available at: www.cdc.gov/hiv/topics/surveillance/resources/reports/2006report/pdf/2006SurveillanceReport.pdf
- Linley L, Hall HI, An Q, et al. HIV/AIDS diagnosis among persons fifty years and older in 33 states, 2001-2005. National HIV Prevention Conference (abstract B08-1); December 2007. Atlanta, GA.
- Carré N, Deveau C, Belanger F, et al. Effect of age and exposure group on the onset of AIDS in heterosexual and homosexual HIV-infected patients. SEROCO Study Group. *AIDS*. 1994;8:797-802.
- Pezzotti P, Phillips AN, Dorrucci M, et al. Category of exposure to HIV and age in the progression to AIDS: longitudinal study of 1199 people with known dates of seroconversion. HIV Italian Seroconversion Study Group. *BMJ*. 1996;313(7057):583-6.
- Porter K, Babiker A, Bhaskaran K, et al; CASCADE Collaboration. Determinants of survival following HIV-1 seroconversion after the introduction of HAART. *Lancet*. 2003;362(9392):1267-74.
- Grabar S, Weiss L, Costagliola D. HIV infection in older patients in the HAART era. *J Antimicrob Chemother*. 2006;57:4-7.
- Sabin C; Collaboration of Observational HIV Epidemiological Research Europe (COHERE) Study. Response to Combination ART: Variation by Age. 14th Conference on Retroviruses and Opportunistic Infections (abstract 528); February 25-28, 2007. Los Angeles.
- Silverberg MJ, Leyden W, Horberg MA, et al. Older age and the response to and tolerability of antiretroviral therapy. *Arch Intern Med*. 2007;167:684-91.
- Armstrong GL. Injection drug users in the United States, 1979-2002: an aging population. *Arch Intern Med*. 2007;167:166-73.
- Egger M, May M, Chêne G, et al; ART Cohort Collaboration. Prognosis of HIV-1-infected patients starting highly active antiretroviral therapy: a collaborative analysis of prospective studies. *Lancet*. 2002;360(9327):119-29.
- May M, Sterne JA, Sabin C, et al; Antiretroviral Therapy (ART) Cohort Collaboration. Prognosis of HIV-1-infected patients up to 5 years after initiation of HAART: collaborative analysis of prospective studies. *AIDS*. 2007;21:1185-97.
- Ackers A, Bernstein L, Henderson S, et al. Factors associated with lack of interest in HIV testing in older at-risk women. *J Women's Health*. 2007;16:842-58.
- Henderson SJ, Bernstein LB, George DM, et al. Older women and HIV: how much do they know and where are they getting their information? *J Am Geriatr Soc*. 2004;52:1549-53.
- Inungu J, Schilling K, Mumford V. HIV testing among women in the United States. CDC Prevention Conference; December 2-5, 2007. Atlanta, GA. Available at: www.cdcnpin.org/2007_National_HIV_Prev_Conf/Public/ViewDocument.aspx?DocumentID=1f010370-ce94-440b-b7b8-5e21cdb1af20.
- De Wit S, Sabin CA, Weber R, et al. Incidence and risk factors for new onset diabetes mellitus in HIV infected patients: the D:A:D study. *Diabetes Care*. 2008;31:1224-9.
- Wohl DA, McComsey G, Tebas P, et al. Current concepts in the diagnosis and management of metabolic complications of HIV infection and its therapy. *Clin Infect Dis*. 2006;43:645-53.
- DAD Study Group; Friis-Møller N, Reiss P, Sabin CA, et al. Class of antiretroviral drugs and the risk of myocardial infarction. *N Engl J Med*. 2007;356:1723-35.
- Calmy A, Nguyen A, Montecucco F, et al; STACCATO study team. HIV activates markers of cardiovascular risk in a randomized treatment interruption trial: STACCATO. 15th Conference on Retroviruses and Opportunistic Infections (abstract 140); February 3-6, 2008. Boston.
- Phillips AN, Carr A, Neuhaus J, et al. Interruption of antiretroviral therapy and risk of cardiovascular disease in persons with HIV-1 infection: exploratory analyses from the SMART trial. *Antivir Ther*. 2008;13:177-87.

REFERENCES (continued)

- 21 Law MG, Friis-Møller N, El-Sadr WM, et al; D:A:D Study Group. The use of the Framingham equation to predict myocardial infarctions in HIV-infected patients: comparison with observed events in the D:A:D Study. *HIV Med.* 2006;7:218-30.
- 22 Sabin C, Worm S, Weber R, et al; D:A:D Study Group. Do thymidine analogues, abacavir, didanosine and lamivudine contribute to the risk of myocardial infarction? The D:A:D Study. 15th Conference on Retroviruses and Opportunistic Infections (abstract 957c); February 3-6, 2008. Boston.
- 23 Cinti SK, Gandhi T, Riddell J 4th. Non-AIDS-defining cancers: should antiretroviral therapy be initiated earlier? *AIDS Read.* 2008;18:18-20, 26-32.
- 24 Grulich AE, van Leeuwen MT, Falster MO, et al. Incidence of cancers in people with HIV/AIDS compared with immunosuppressed transplant recipients: a meta-analysis. *Lancet.* 2007;370(9581):59-67.
- 25 Monforte A D, Abrams D, Pradier C et al; D:A:D Study Group. HIV-induced immunodeficiency and risk of fatal AIDS-defining and non-AIDS-defining malignancies: results from the D:A:D Study. 14th Conference on Retroviruses and Opportunistic Infections (abstract 84); February 25-28, 2007. Los Angeles.
- 26 American Cancer Society. Guidelines for the early detection of cancer. 2008. Available at: www.cancer.org/docroot/PED/content/PED_2_3X_ACS_Cancer_Detection_Guidelines_36.asp?sitearea=PED. Accessed October 20, 2008.
- 27 Barbaro G, Barbarini G. HIV infection and cancer in the era of highly active antiretroviral therapy. *Oncol Rep.* 2007;17:1121-6.
- 28 Spano JP, Carcelain G, Katlama C, et al. Non-AIDS-defining malignancies in HIV patients: clinical features and perspectives. *Bull Cancer.* 2006;93:37-42.
- 29 Hallan SI, Dahl K, Oien CM, et al. Screening strategies for chronic kidney disease in the general population: follow-up of cross sectional health survey. *BMJ.* 2006;333(7577):1047.
- 30 Röling J, Schmid H, Fischereder M, et al. HIV-associated renal diseases and highly active antiretroviral therapy-induced nephropathy. *Clin Infect Dis.* 2006;42:1488-95.
- 31 Lucas GM, Mehta SH, Atta MG, et al. End-stage renal disease and chronic kidney disease in a cohort of African-American HIV-infected and at-risk HIV-seronegative participants followed between 1988 and 2004. *AIDS.* 2007;21:2435-43.
- 32 Lucas GM, Lau B, Atta MG, et al. Chronic kidney disease incidence and progression to end-stage renal disease in HIV-infected individuals: a tale of two races. *J Infect Dis.* 2008. 197(11): 1490-2.
- 33 Gupta SK, Eustace JA, Winston JA, et al. Guidelines for the management of chronic kidney disease in HIV-infected patients: recommendations of the HIV Medicine Association of the Infectious Diseases Society of America. *Clin Infect Dis.* 2005;40:1559-85.
- 34 Valle R, Haragsim L. Nephrotoxicity as a complication of antiretroviral therapy. *Adv Chronic Kidney Dis.* 2006;13:314-9.
- 35 Sulkowski MS, Thomas DL. Hepatitis C in the HIV-infected person. *Ann Intern Med.* 2003;138:197-207.
- 36 Graham CS, Baden LR, Yu E, et al. Influence of human immunodeficiency virus infection on the course of hepatitis C virus infection: a meta-analysis. *Clin Infect Dis.* 2001;33:562-9.
- 37 Bica I, McGovern B, Dhar R, et al. Increasing mortality due to end-stage liver disease in patients with human immunodeficiency virus infection. *Clin Infect Dis.* 2001;32:492-7.
- 38 Weber R, Sabin CA, Friis-Møller N, et al. Liver-related deaths in persons infected with the human immunodeficiency virus: the D:A:D study. *Arch Intern Med.* 2006;166:1632-41.
- 39 Carrat F, Bani-Sadr F, Pol S, et al; ANRS HCO2 RIBAVIC Study Team. Pegylated interferon alfa-2b vs standard interferon alfa-2b, plus ribavirin, for chronic hepatitis C in HIV-infected patients: a randomized controlled trial. *JAMA.* 2004;292:2839-48.
- 40 Chung RT, Andersen J, Volberding P, et al; AIDS Clinical Trials Group A5071 Study Team. Peginterferon Alfa-2a plus ribavirin versus interferon alfa-2a plus ribavirin for chronic hepatitis C in HIV-coinfected persons. *N Engl J Med.* 2004;351:451-9.
- 41 Torriani FJ, Rodriguez-Torres M, Rockstroh JK, et al; APRICOT Study Group. Peginterferon Alfa-2a plus ribavirin for chronic hepatitis C virus infection in HIV-infected patients. *N Engl J Med.* 2004;351:438-50.
- 42 Thio CL, Seaberg EC, Skolasky R Jr, et al; Multicenter AIDS Cohort Study. HIV-1, hepatitis B virus, and risk of liver-related mortality in the Multicenter Cohort Study (MACS). *Lancet.* 2002;360(9349):1921-6.
- 43 Thio CL, Locarnini S. Treatment of HIV/HBV coinfection: clinical and virologic issues. *AIDS Rev.* 2007;9:40-53
- 44 Sulkowski MS, Benhamou Y. Therapeutic issues in HIV/HCV-coinfected patients. *J Viral Hepat.* 2007;14:371-86.
- 45 Brown TT, Qaqish RB. Antiretroviral therapy and the prevalence of osteopenia and osteoporosis: a meta-analytic review. *AIDS.* 2006;20:2165-74
- 46 Cazanave C, Dupon M, Lavignolle-Aurillac V, et al; Groupe d'Epidémiologie Clinique du SIDA en Aquitaine. Reduced bone mineral density in HIV-infected patients: prevalence and associated factors. *AIDS.* 2008;22:395-402.
- 47 Anastos K, Lu D, Shi O, et al. The association of bone mineral density with HIV infection and antiretroviral treatment in women. *Antivir Ther.* 2007;12:1049-58.
- 48 Fernández-Rivera J, García R, Lozano F, et al. Relationship between low bone mineral density and highly active antiretroviral therapy including protease inhibitors in HIV-infected patients. *HIV Clin Trials.* 2003;4:337-46.
- 49 Clay PG, Voss LE, Williams C, et al. Valid treatment options for osteoporosis and osteopenia in HIV-infected persons. *Ann Pharmacother.* 2008;42:670-9.
- 50 Hornberg MA, Silverberg MJ, Hurley LB, et al. Effects of depression and selective serotonin reuptake inhibitor use on adherence to highly active antiretroviral therapy and on clinical outcomes in HIV-infected patients. *J Acquir Immune Defic Syndr.* 2008;47:384-90.
- 51 Tegger MK, Crane HM, Tapia KA, et al. The effect of mental illness, substance use, and treatment for depression on the initiation of highly active antiretroviral therapy among HIV-infected individuals. *AIDS Patient Care STDS.* 2008;22:233-43.
- 52 Treisman G, Angelino A. Interrelation between psychiatric disorders and the prevention and treatment of HIV infection. *Clin Infect Dis.* 2007;45 Suppl 4:S313-7.
- 53 Justice AC, McGinnis KA, Atkinson JH, et al; Veterans Aging Cohort 5-Site Study Project Team. Psychiatric and neurocognitive disorders among HIV-positive and negative veterans in care: Veterans Aging Cohort Five-Site Study. *AIDS.* 2004;18 Suppl 1:S49-59.
- 54 Rabkin JG, McElhiney MC, Ferrando SJ. Mood and substance use disorders in older adults with HIV/AIDS: methodological issues and preliminary evidence. *AIDS.* 2004;18 Suppl 1:S43-8.
- 55 Becker JT, Lopez OL, Dew MA, et al. Prevalence of cognitive disorders differs as a function of age in HIV virus infection. *AIDS.* 2004;18 Suppl 1:S11-8.
- 56 Knobel H, Guelar A, Valldecillo G, et al. Response to highly active antiretroviral therapy in HIV-infected patients aged 60 years or older after 24 months follow-up. *AIDS.* 2001;15:1591-3.