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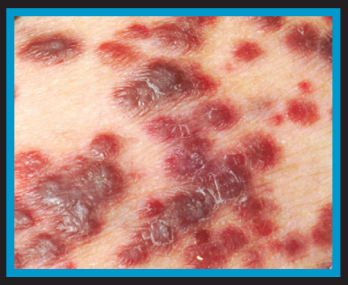
CE Continuing Education

CME/CE Article #1

Initiating Antiretroviral Therapy, Beyond the *Guidelines*.....2

Patricia Kloser, MD, MPH, FACP, Professor Medicine and Public Health, UMDNJ; with Virginia Allread, MPH, Global Program Director and AIDSLine Editor, UMDNJ



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New Jersey's Impression on AIDS 2012

Virginia Allread, AIDSLine Editor, FXB Center, UMDNJ

Based on the number of poster exhibitions and presentations at AIDS 2012 authored by individuals employed by agencies based here in New Jersey, one can confidently state that HIV-related research, care, treatment, prevention and support activities conducted across the state of New Jersey have contributed greatly to the global body of HIV-related knowledge. The following is a sampling of some of the activities conducted in New Jersey and reported at the AIDS 2012 conference that took place in Washington D.C. July 22-27.

HIV testing and epidemiology

Nearly a third of the 20 papers authored by individuals employed by governmental and not-for-profit organizations based in New Jersey were on testing, HIV surveillance, or HIV-related epidemiology. The first five papers focus on HIV testing: nucleic acid amplification testing (NAAT) to detect acute HIV infection, unlinked anonymous testing, routine testing in an emergency department or dental setting. The sixth paper is on the epidemiology of cancer risk among infants perinatally exposed to antiretroviral (ARV) medications.

"Detecting acute HIV (AHI) infection in a Newark, New Jersey hospital setting" was authored by staff from University of Medicine and Dentistry of New Jersey (UMDNJ) (Eugene Martin, Debbie Mohammed, Gratian Salaru, Joanne Corbo, Michael Jaker, Sandra Scott, Evan Cadoff) and from New Jersey Department of Heath (NJDOH), Sindy Paul, as well as researchers at the University of Washington. Between February 2010 and February 2012, pooled NAAT and rapid HIV testing were offered to emergency department patients and outpatients seen at University Hospital in Newark. NAAT testing permits identification of acute or recent HIV infections. In the study, rapid testing identified 116 antibody positive individuals (0.94%); 55% of those testing negative consented to NAAT. NAAT identified an additional 8 HIV-positive samples amongst those that had originally tested negative, increasing HIV case detection by 6.9%. Authors calculated that an additional 8 individuals would likely have been identified as HIV-positive had they also agreed to NAAT. Interestingly, all NAAT positive screens were male. The paper concluded that NAAT of HIV antibody negative blood substantially increased HIV case detection.

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CE CONTINUING EDUCATION

Initiating Antiretroviral Therapy, Beyond the *Guidelines*

Release date: December 1, 2012 • Expiration date: November 30, 2013 • Course code: 14HC05 • Nursing credit for this activity will be provided through November 30, 2014.

SPONSOR:

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STATEMENT OF NEED:

HIV Prevention Trials Network (HPTN) 052 demonstrated that earlier use of ARVs by HIV-infected heterosexuals partnered with uninfected individuals (serodiscordant couples) reduced HIV transmission by 96%. The study also demonstrated that participants who delayed ARV therapy until their CD4 cell counts were an average of 230 experienced a shorter time to primary clinical event, including AIDS-defining disease than participants who began ARV therapy sooner (an average CD4 cell count of 440). The current version (dated March 27, 2012) of the *United States' Guidelines for the Use of Antiretroviral Agents in HIV-1-Infected Adults and Adolescents* (the *Guidelines*) supports the findings of HPTN 052 as well as findings from other recent studies in recommending that all HIV-infected individuals initiate ARV therapy, regardless of CD4 cell count.

Evidence from *AIDS 2012* and reports from clinicians suggest that there are two knowledge gaps related to the current Guidelines: many physicians who are not HIV specialists are unaware that the *Guidelines* were updated in March 2012 and are defaulting to guidance in earlier publications. Secondly, prescribers would benefit from guidance on how to tailor the recommendations in the *Guidelines* to individual client need.

TARGET AUDIENCE:

This activity is designed for physicians, nurses, social workers, health educators, and other health care professionals in New Jersey who are involved in the care of people with HIV.

METHOD OF PARTICIPATION:

Participants should read the learning objectives, review the activity in its entirety, and then complete the self-assessment test, which consists of a series of multiple-choice questions. Upon completing this activity as designed and achieving a passing score of 70% or more on the self-assessment test; participants will receive a letter of credit and the test answer key four (4) weeks after receipt of the self-assessment test, registration, and evaluation materials. This activity may also be completed online at ***http://ccoe.umdnj.edu/catalog/***. Estimated time to complete this activity as designed is 1.17 hours for nurses, and 1.25 hours for physicians.

LEARNING OBJECTIVES:

Following completion of this activity, participants should be able to:

1. Discuss treatment as prevention.
2. Summarize recommendations from the *Guidelines* on initiating antiretroviral therapy.
3. Implement a tailored ARV therapy regimen for patients with HIV, as recommended by the *Guidelines*.

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This activity is awarded 1.17 contact hours (60 minute CH).

Nurses should claim only those contact hours actually spent participating in the activity.

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PEER REVIEW:

In order to help ensure content objectivity, independence, and fair balance, and to ensure that the content is aligned with the interest of the public, UMDNJ-CCOE has resolved all potential and real conflicts of interest through content review by non-conflicted, qualified reviewers. This activity was peer-reviewed for relevance, accuracy of content and balance of presentation by Joanne Phillips, RN, MS; and Renee Powell, BS, RN.

Field test: This activity was pilot-tested for time required for participation by David John Cennimo, MD; Jojy Cheriyan, MD, MPH, MPhil; Anna M. Haywood, RN, MSN; Mary C. Krug, RN, MSN, APN; Debbie Mohammed, MS, MPH, APRN-BC, AACRN; and Kara Winslow, BSN, RN.

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NEW JERSEY AIDSLine December 2012

Initiating Antiretroviral Therapy, Beyond the *Guidelines*

Patricia Kloser, MD, MPH, FACP, Professor Medicine and Public Health, UMDNJ; with Virginia Allread, MPH, Global Program Director and AIDSLine Editor, UMDNJ

LEARNING OBJECTIVES:

By the end of this activity participants will be able to:

1. **Discuss** treatment as prevention.
2. **Summarize** recommendations from the *Guidelines* on initiating antiretroviral therapy.
3. **Implement** a tailored ARV therapy regimen for patients with HIV, as recommended by the *Guidelines.*

Introduction

One of themes that resonated for so many of the 23,000 attendees of *AIDS 2012*, the XIX International AIDS Conference that took place in July in Washington D.C., was a renewed sense of hope and optimism. Not only a renewed confidence in the discovery of an effective vaccine, but—believe it or not—a sense of optimism in the search for a ***cure***. The search for a cure is not new, but recent developments have reinvigorated the discussion about how to bring focus to cure-related research questions. As importantly, there was enthusiasm for the prospect of reducing, possibly even eliminating human immunodeficiency virus (HIV) transmission. Secretary of State Hillary Rodham Clinton stated "the idea of an AIDS-free era is ambitious, though it is possible. …An AIDS-free era would be one of the biggest gifts a United States could give to a common future." Underpinning the idea of an AIDS-free era is the use of antiretroviral (ARV) therapy as prevention, that is, to prevent further infection, particularly in sexual partners. Treatment as prevention may be one of the key factors explaining why new HIV infections are currently at their lowest levels since 1997.[1,2]

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HIV Prevention Trials Network (HPTN) 052 treatment as prevention study

Initial results from the landmark National Institutes of Health (NIH)-funded treatment as prevention study (HPTN 052)—with sites in Botswana, Brazil, India, Kenya, Malawi, South Africa, Thailand, United States and Zimbabwe—demonstrated that earlier use of ARVs by HIV-infected heterosexuals partnered with uninfected individuals (serodiscordant couples) reduced HIV transmission by 96%[3]. Of the 39 HIV-1 transmission events, 28 were genetically linked to the partner enrolled in the study. Of the 28 linked transmissions, only 1 occurred in the early-therapy group, whereas 27 occurred in the delayed-therapy group. Of these 27 transmissions, 9 were man-to-woman, 18 were woman-to-man, and all occurred when the infected partner was not receiving ARV therapy.[4] The one transmission in the early-therapy group seems to have occurred before the infected partner achieved viral suppression.

HPTN 052 demonstrated that earlier use of ARVs by HIV-infected heterosexuals partnered with uninfected individuals (serodiscordant couples) reduced HIV transmission by 96%.

In two years of follow-up analysis of the 1,761 HIV-infected HPTN 052 study participants, researchers compared those who delayed ARV therapy until their CD4 cell counts were an average of 230 with those who began ARV therapy sooner (an average CD4 cell count of 440). The delayed group experienced a shorter time to a primary clinical event, including AIDS-defining disease and all types of tuberculosis (TB). In total, there were 91 primary clinical events in the delayed treatment group versus 71 in the immediate group. This included 71 cases of AIDS-defining disease in the delayed treatment group versus 49 in the immediate group, and 34 cases of TB in the delayed group versus 17 in the immediate group. The trial provides evidence that earlier ARV therapy delays AIDS-related health events as well as death.[3]

In a separate modeling analysis designed to predict the clinical impact, costs and cost-effectiveness of the earlier ARV therapy strategy, HPTN 052 researchers compared the delayed treatment (CD4 cell counts of less than 250) versus earlier treatment (350–550) data in South Africa and India. They found that in both countries early ARV therapy increases patient survival, prevents costly opportunistic infections—partially offsetting the costs of treatment—averts HIV transmission, and is cost-effective within a five-year span and very cost-effective over a lifetime.[3]

Individual versus community rights

Treatment as prevention is a term increasingly used to describe the use of long-term ARV therapy in a person who is HIV-infected to decrease the risk of further HIV transmission.

The dovetailing of individual and public health benefits that are suggested by the findings of the HPTN 052 study provides impetus for treatment as prevention initiatives to move forward. On a population level, if the number of people taking ARV therapy rises, community viral load decreases, resulting in a reduction of new HIV infections. San Francisco was the first health department in the world to offer treatment to all people diagnosed with HIV, regardless of cell count. The increased access meant that the average viral load among people living with HIV fell by 40% between 2004 and 2008, and this coincided with new infections dropping by a third.[5]

On a population level, the use of treatment as prevention is still widely debated. Any public health initiative must also consider the rights of the individual. ARV therapy can cause serious side effects and can lead to drug resistance if not taken exactly as prescribed. Therefore an HIV-infected person has the right to decide whether or not to take ARV therapy (see case studies that follow this article). Individuals may refuse to take ARV therapy if they do not need it for their own health; forcing them to take ARV therapy against their will could be seen as an abuse of human rights.

Another potential issue is the concern that those on ARV therapy might become overly confident in the preventive effects of treatment, and more likely to engage in high-risk behavior. A study of men who have sex with men (MSM) in Boston who were taking ARV therapy found that 18% had HIV in their blood, and 50% had HIV in their semen. The presence of the virus was strongly associated with the presence of genital infections and inflammation, and a recent history of unprotected sex. The study suggests that risk of transmission for the individual on ARV therapy is influenced by a number of factors.[5]

United States *Guidelines*

According to the current version (dated March 27, 2012) of the United States' *Guidelines for the Use of Antiretroviral Agents in HIV-1-Infected Adults and Adolescents* (hereafter referred to as the *Guidelines*) the primary goals for initiating ARV therapy are to:

- Reduce HIV-associated morbidity and prolong the duration and quality of survival
- Restore and preserve immunologic function
- Maximally and durably suppress plasma HIV viral load
- Prevent HIV transmission

According to the *Guidelines*, ARV therapy has reduced HIV-related morbidity and mortality and has reduced perinatal and behavior-associated transmission of HIV. HIV suppression with ARV therapy may decrease inflammation and immune activation thought to contribute to higher rates of cardiovascular and other end-organ damage. Viral suppression delays or prevents drug-resistance mutations, preserves CD4 cell count, and confers substantial clinical benefits.

Achieving viral suppression requires the use of ARV regimes that combine drugs from two or more drug classes. Suppression of viral load to undetectable levels in an ARV therapy-naive patient usually occurs within the first 12–24 weeks of ARV therapy initiation, with significant reduction in the first 3–5 weeks. Predictors of virologic success include:[6]

- High potency of ARV regimen
- Excellent adherence to treatment regimen
- Low baseline viremia
- Higher baseline CD4 cell count (>200 cells/mm^3) and
- Rapid reduction of viremia in response to treatment

Strategies to achieve treatment goals

Providers and patients must work together to define individualized strategies to achieve treatment goals, which requires a balance of sometimes competing considerations:

- Pretreatment drug-resistance testing: Studies suggest that the presence of transmitted drug-resistant viruses (which may be prevalent in 6–16%[7] of ARV therapy-naïve patients) may lead to suboptimal virologic responses. Therefore, resistance testing is recommended and a genotypic assay is preferred to guide selection of initial ARV therapy regimen.
- Selection of initial combination regimen: Selection is usually based on the *Guidelines* and tailored for the individual patient to enhance adherence. Individual regimen choice is based on pretreatment drug-resistance testing, side effect profile, comorbidities, interactions with concomitant medications, and convenience.
- Improving adherence: Conditions that promote adherence should be maximized before and after initiation of ARV therapy.[6] See Box 2 for more on adherence.

Timing of ARV therapy initiation

The general principles when considering ARV therapy initiation include the following (see Box 1):

- Untreated HIV infection may have detrimental effects at all stages of infection.
- Earlier treatment may prevent the damage associated with HIV replication during early stages of infection.
- ARV therapy is beneficial even when initiated later in infection; however, later therapy may not repair damage associated with viral replication during early stages of infection.
- Sustaining viral suppression and maintaining higher CD4 count, mostly as a result of effective combination ARV therapy, may delay, prevent, or reverse some non-AIDS-defining complications.[6]

Box 1: Guidelines Panel recommendations on initiation of ARV therapy[6]

ARV therapy is recommended for all HIV-infected individuals. The strength of this recommendation varies on the basis of pretreatment CD4 cell count:

- CD4 cell count <350 cells/ mm^3 (AI)
- CD4 cell count 350 to 500 cells/ mm^3 (AII)
- CD4 cell count >500 cells/ mm^3 (BIII)

Patients starting ARV therapy should be willing and able to commit to treatment and should understand the benefits and risks of therapy and the importance of adherence (AIII). Patients may choose to postpone therapy, and providers, on a case-by case basis, may elect to defer therapy on the basis of clinical and/or psychosocial factors.

Rating of Recommendations: A = Strong; B = Moderate; C = Optional

Rating of Evidence: I = data from randomized controlled trials; II = data from well-designed nonrandomized trials or observational cohort studies with long-term clinical outcomes; III = expert opinion

Conditions favoring more rapid initiation of therapy

Regardless of CD4 cell count, initiation of ARV therapy is strongly recommended for individuals with the following conditions:

- Pregnancy (AI): Clinicians should refer to the perinatal guidelines for more detailed recommendations on the management of HIV-infected pregnant women.
- History of an AIDS-defining illness (AI).
- HIV-associated nephropathy (HIVAN) (AII) at the earliest sign of renal dysfunction.
- HIV/hepatitis B virus (HBV) coinfection (AII): ARV therapy should include drugs with activity against both HIV and HBV.
- Hepatitis C virus (HCV) (BII): ARV therapy may slow the progression of liver disease by preserving or restoring immune function and reducing HIV-related immune activation and inflammation. Although ARV therapy should be initiated for most HIV/HCV-coinfected patients regardless of CD4 cell count, in ARV therapy-naïve patients with CD4 cell counts >500 cells/mm^3 some clinicians may choose to defer ARV therapy until completion of HCV treatment. In patients with lower CD4 cell counts (e.g., <200 cells/mm^3), it may be preferable to initiate ARV therapy and delay HCV therapy until CD4 cell counts increase.
- Significant risk of cardiovascular disease (CVD) (BII), as assessed by medical history and established estimated risk calculations.
- HIV-associated dementia and other severe central nervous system (CNS) opportunistic infections (OIs).
- Some other OIs (see also "Acute opportunistic infections" below).
- Lower CD4 cell counts (e.g., <200 cells/ mm^3).
- Rapidly declining CD4 cell counts (e.g., >100 cells/ mm^3 decrease per year).
- Higher viral loads (e.g., >100,000 copies/mL).[6]

ARV therapy should also be offered to patients who are at risk of transmitting HIV to sexual partners (AI [heterosexuals] or AIII [other transmission risk groups]).

Acute opportunistic infections

- In patients with opportunistic conditions for which no effective therapy exists (e.g., cryptosporidiosis, microsporidiosis, progressive multifocal leukoencephalopathy) but in whom ARV therapy may improve outcomes by improving immune responses, the benefits of ARV therapy outweigh any increased risk; therefore, treatment should be started as soon as possible (AIII).
- In the setting of other OIs, such as *Pneumocystis jiroveci* pneumonia (PCP), early initiation of ARV therapy is associated with increased survival; therefore, ARV therapy should not be delayed (AI).
- In the setting of some OIs, such as cryptococcal meningitis or nontuberculous mycobacterial infections, for which immediate therapy may increase the risk of immune reconstitution inflammatory syndrome (IRIS), a short delay before initiating ARV therapy may be warranted (CIII).[6]
- In patients with active TB, the *Guidelines* recommend initiating TB treatment first, followed by ARV therapy within the following timeframes:
  - Patients with CD4 cell counts <50 cells/ mm^3 — initiate ARV therapy within 2 weeks of starting TB treatment.
  - Patients with CD4 cell counts ≥50 cells/ mm^3 with clinical disease of major severity (as defined in the Guidelines) — initiate ARV therapy within 2 to 4 weeks of starting TB treatment.

- Patients with CD4 cell counts ≥50 cells/mm^3 — ARV therapy can be delayed beyond 2 to 4 weeks but should be initiated by 8 to 12 weeks of TB treatment (the World Health Organization recommends ARV therapy initiation within 8 weeks[8]).

As noted in Case study 3, which follows this article, where there is treatment available the presenting OI is typically treated first followed by ARV therapy initiation. Even when initiating ARV therapy, it is more important to get the patient on the right regimen rather than to start immediately.

See the *Guidelines and the Guidelines for Prevention and Treatment of Opportunistic Infections in HIV-Infected Adults and Adolescents* for a more detailed discussion on when to initiate ARV therapy in the setting of a specific OI.

Box 2: Adherence

Adherence

The importance of excellent adherence to ARV therapy cannot be underestimated. Excellent adherence is necessary to ensure suppression of viral load to undetectable levels. Adherence studies conducted in the early era of combination ARV therapy regimens found that virologic failure is much less likely to occur in patients who adhere to more than 95% of their prescribed doses. More recent studies (using boosted PIs and non-nucleoside reverse transcriptase inhibitors) have suggested that the longer half-lives of boosted PIs and efavirenz may make the drugs more forgiving of lapses in adherence.[9]

Factors associated with nonadherence

A number of factors have been associated with poor adherence, including the following:

- Low levels of health literacy or numeracy (ability to understand numerical-related health information)
- Certain age-related challenges (e.g., polypharmacy, vision loss, cognitive impairment)
- Younger age
- Psychosocial issues (e.g., depression, homelessness, low social support, stressful life events, or psychosis)
- Nondisclosure of HIV serostatus
- Neurocognitive issues (e.g., cognitive impairment, dementia)
- Active (but not history of) substance abuse, particularly for patients who have experienced recent relapse
- Stigma
- Difficulty with taking medication (e.g., trouble swallowing pills, daily schedule issues)
- Complex regimens (e.g., high pill burden, high-frequency dosing, food requirements)
- Adverse drug effects and patient concerns about side effects
- Nonadherence to clinic appointments
- Cost and insurance coverage issues
- Treatment fatigue[6]

Interventions to improve adherence

Before writing the first prescriptions, the clinician should assess the patient's readiness to take medication; ask about potential barriers such as those listed above; assess the patient's understanding of the disease and the regimen; and assess the patient's social support, housing, work and home situation, and daily schedules.

During the past several years, a number of advances have simplified many regimens, particularly those for treatment-naive patients. Prescribing regimens that are simple to take, have a low pill burden and low-frequency dosing, have no food requirements, and have low incidence and severity of adverse effects will facilitate adherence.

The first principle of successful treatment is negotiation of an understandable plan to which the patient can commit. Establishing a trusting relationship over time and maintaining good communication will help to improve adherence and long-term outcomes. Effective interventions identified in recent studies include:

- Multiple home visits by nurses
- Five-session group intervention
- Pager messaging
- Couples-based interventions
- Strengthening social support ("treatment buddy")
- Substance abuse therapy
- Directly observed therapy (DOT): one of the disadvantages of DOT is that the benefits are rarely sustained after transitioning the patient out of DOT[6]

Assessing adherence

There are a number of methods to assess adherence:

- Self-report using one of the available reliable and valid instruments at each and every clinic visit[10,11]
- Routine monitoring of HIV viral load
- Pharmacy refill data
- Pill count

It is the responsibility of the entire health care team—nurses, nurse practitioners, pharmacists, medication managers, and social workers—to assess adherence at every clinical encounter and determine if additional adherence intervention is warranted.

Continuous assessment and counseling make it possible for the clinician to intervene early to address barriers to adherence occurring at any point during treatment.

Conditions where deferral of therapy may be considered

Some patients and their clinicians may decide to defer therapy on the basis of clinical or personal circumstances. According to the *Guidelines*, deferring therapy for the reasons discussed below may be reasonable in patients with high CD4 cell counts (e.g., >500 cells/ mm^3) but deferring therapy in patients with much lower CD4 cell counts (e.g., <200 cells/ mm^3) should be considered only in rare situations and should be undertaken with close clinical follow-up.

- **When there are significant barriers to adherence:** At any CD4 cell count, adherence to therapy is essential to achieve viral suppression and prevent emergence of drug-resistance mutations. The currently preferred ARV therapy regimens are better tolerated than previous regimens, leading to improved adherence as well as greater effectiveness and lower frequency of emerging drug resistance. Nonetheless, in patients with higher CD4 cell counts who are at risk of poor adherence, it may be prudent to defer treatment while addressing the barriers to adherence. However, in patients with conditions that require urgent initiation of ARV therapy (see "Conditions favoring more rapid initiation of therapy", on page 5), therapy should be started while simultaneously addressing barriers to adherence. See Box 2 for further discussion of adherence.

Adherence studies conducted in the early era of combination ARV therapy regimens found that virologic failure is much less likely to occur in patients who adhere to more than 95% of their prescribed doses.

- **Presence of comorbidities that complicate or prohibit ARV therapy:** Deferral of ARV therapy may be considered when either the treatment or manifestations of other medical conditions could complicate the treatment of HIV infection or vice versa. Examples include:
  - Surgery that may result in an extended interruption of ARV therapy.
  - Treatment with medications that have clinically significant drug interactions with ARV therapy and for which alternative medications are not available.

The assumption is that ARV therapy will be initiated after the conflicting condition has resolved.

- **Long-term non-progressors and elite HIV controllers:** A small subset of ARV-untreated HIV-infected individuals (~3–5%) can maintain normal CD4 cell counts for many years (long-term non-progressors), and an even smaller subset (~1%) can maintain suppressed viral loads for years (elite controllers). Although therapy theoretically may be beneficial for patients in either group, clinical data supporting therapy for non-progressors and elite controllers are lacking.
- **Development of resistance:** Evidence thus far indicates that resistance occurs more frequently in individuals who initiate therapy later in the course of infection than in those who initiate ARV therapy earlier. But this may be due, at least in part, to the fact that late initiators are more likely to suffer from mental illness, substance abuse, and/ or poverty, all of which can contribute to viral resistance directly or indirectly.[12]
- **ARV drug toxicities and quality of life:** Earlier initiation of ARV therapy at higher CD4 cell counts (e.g., >500 cells/mm^3) results in greater cumulative time on therapy. The Data Collection on Adverse Events of Anti-HIV Drugs Study (also referred to as the D:A:D study) found an increased incidence of CVD associated with cumulative exposure to some drugs in the nucleoside reverse transcriptase inhibitor (NRTI) and PI drug classes. In the Strategies for Management of Antiretroviral Therapy (SMART) study, continuous exposure to ARV therapy was associated with significantly greater loss of bone density. There may be unknown complications related to cumulative use of ARV drugs for many decades (see the *Guidelines* for a list of known ARV-associated toxicities). Nevertheless, assuming treatment will continue for several decades regardless of when therapy is initiated, the incremental increase in drug exposure associated with starting therapy at higher CD4 cell counts represents a small percentage of the total time on ARV therapy for most patients.
- **ARVs and side effects:** ARV therapy is expected to improve the quality of life for patients with HIV. However, some side effects of ARV therapy may impair the quality of life, especially those who are asymptomatic at initiation of therapy. For example, efavirenz (EFV) can cause neurocognitive or psychiatric side effects and all the PIs have been associated with gastrointestinal (GI) side effects. Furthermore, some patients may find that the inconvenience of taking medication every day outweighs the overall benefit of early ARV therapy and may choose to delay therapy.

Helping patients with drug costs

In New Jersey, the AIDS Drug Distribution Program (ADDP) pays the cost of HIV-related drugs for New Jersey residents with HIV who earn less than 500% of federal poverty level (see *http://www.state.nj.us/health/aids/freemeds.shtml*).

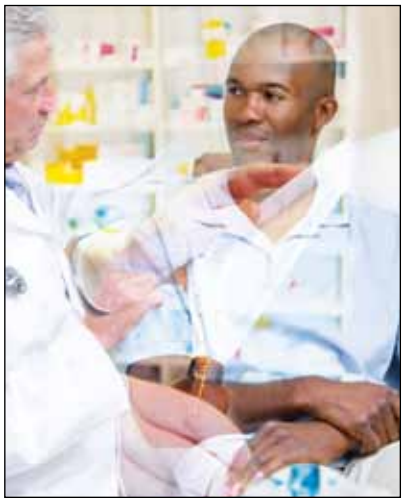
Those who do not qualify for ADDP may find the cost of HIV drugs unaffordable. Enquire with drug manufacturers, many of them offer assistance to purchase their drugs. For example, the makers of Atripla, Bristol-Myers Squibb & Gilead Sciences, have created a program to provide temporary assistance to eligible patients applying for, or enrolling in, prescription coverage plans.

Those who have insurance may find the cost of their co-pay barely affordable. Clinicians should work with privately insured patients to identify ways to make their co-pay more affordable. For example, find out if the co-pay for a 90-day supply is less per month than a 30-day supply. Enquire about mail order prescriptions as they occasionally offer lower co-pays than pharmacies. Some patients prefer separate prescriptions for each of the three drugs as the co-pay for all three drugs may be less than a single prescription for the co-formulated drug.

- **Cost**: In resource-rich countries, the cost of ARV therapy exceeds $10,000 per year. However, several modeling studies support the cost effectiveness of ARV therapy initiated soon after diagnosis. One study reported that the annual cost of care is 2.5 times higher for patients with CD4 cell counts <50 cells than for patients with CD4 cell counts >350 cells.[13] See also discussion of HPTN 052 at the beginning of this article.

The need for early diagnosis of HIV

Fundamental to the earlier initiation of ARV therapy (as recommended in the *Guidelines*) is the assumption that patients will be diagnosed early in the course of HIV infection, making earlier initiation of ARV therapy an option. Unfortunately, most HIV-infected patients are not diagnosed until they are at much later stages of disease. Despite the 2006 Centers for Disease Control and Prevention (CDC) recommendations[14] for routine, opt-out HIV screening, regardless of perceptions about a patient's risk of infection, the median CD4 cell count of newly diagnosed patients remains in the ~200 cells/ mm^3 range. The exception is pregnant women diagnosed during prenatal care, who have a much higher median initial CD4 cell count. Compared with other groups, nonwhites, injecting drug users, and older patients more often receive a delayed diagnosis of HIV infection and a substantial proportion of these individuals develop AIDS-defining illnesses within 1 year of diagnosis.



Therefore, for the current treatment guidelines to have maximum impact, routine HIV screening per current CDC recommendations is essential. As has been done in prenatal care settings in New Jersey, routine testing models can be adapted to any healthcare setting, including emergency departments, sexually transmitted infection clinics, and primary care. (See cover article "New Jersey's Impression on AIDS 2012", which includes a summary of two studies on routine testing in the Emergency Department at University Hospital in Newark as well as research into dentists willingness to conduct HIV screening in general practice settings.) Routine testing should be coupled with marketing of these testing activities through healthcare provider recommendation as well as materials such as flyers and posters. Those who are newly diagnosed must be provided with post-test counseling, including education about HIV disease and linked to care for full evaluation, follow-up, and management. Once patients are in care, focused effort is required to retain them in care if the full benefit of early diagnosis and treatment are to be achieved for the infected individuals and their sexual partners.

Putting the *Guidelines* into clinical practice—author's commentary

The decision on when to initiate ARV therapy is typically based on provider-patient consultations that include education and counseling on the patient's health, lifestyle, sexual practices, perspectives on taking medicine, motivation to adhere to a care plan, and the ability of the healthcare setting to support the patient's decision. The following scenarios serve to explain further.

Patients with CD4 cell count above 500: This is the client scenario that until recently the *Guidelines* recommended deferring treatment. Individual client education would include a discussion of the pros and cons of taking ARV therapy as discussed in this article. Counseling of these clients, assuming they are otherwise healthy and neither pregnant nor planning to get pregnant, is likely to focus on a cost-benefit analysis for that particular client. Factors in that analysis might include:

- The patient's willingness to take medications and likelihood of excellent adherence (see Case Study 2, the story of Giovana, who had a history of negative experiences taking medications).
- Patient's willingness to tolerate side effects.
- Patient's sexual practices, including number of partners, willingness to use condoms, and HIV status of partner(s).
- Patient's health, particularly if the patient has any of the conditions described in "Conditions favoring more rapid initiation of therapy", on page 5.
- Any other life activities that may affect HIV transmission (history of injecting drug use, pregnancy intentions, etc).

When counseling these patients, provide them with both the pros and cons of starting ARV therapy, and let them know that you, as the clinician, will support their decision whether it is to initiate or defer.

Patients with CD4 cell count between 350–500: Counsel these patients similarly to those with a CD4 cell count above 500, except that they should be informed that the literature clearly supports initiating ARV therapy for their immediate and long-term health as well and to reduce risk of transmission to sexual partners.

If the patient opts to delay treatment, consider setting up a "contract" with him or her. The discussion could proceed as follows: "I understand why you prefer to delay treatment. I think that is a reasonable and appropriate decision for you. What I'd like to see you do, to ensure you preserve your health, is to get enough sleep and attend mental health counseling sessions as we discussed previously. We'll continue to measure your CD4 cell count every three months. At what CD4 cell count do you think you should start ARV therapy?" Assuming the patient provides a reasonable response such as 325, then continue: "So if your CD4 cell count ever falls below 325, then you'll be willing to start ARV therapy?" The counseling session would continue based on the client's response and his/her situation. It would include additional health education advice and support—such as safer sex—based on the patient's educational and support needs. Record in the patient's notes the CD4 cell count when he/she agreed to initiate ARV therapy; this threshold is the core of the provider-patient contract. It is important to note that these patients should not be put into a situation where they are feeling pressured to initiate ARV therapy, as this may result in their dropping out of care.

It is important to note that the above cost-benefit scenarios are applicable to patients who are neither pregnant nor planning to get pregnant. The *Guidelines* clearly state that women who are pregnant should be started on ARV therapy as soon as possible if they are in need of treatment for their own health but may be delayed until after the first trimester if they do not require immediate initiation of therapy for their own health. The counseling of pregnant women reluctant to initiate therapy needs to include discussion of the infant's as well as the mother's health. See *Reducing the Risk of Perinatal HIV Transmission in New Jersey and the U.S.: Legal and Clinical Strategies* in the June 2012 edition of AIDSLine and *Recommendations for Use of Antiretroviral Drugs in Pregnant HIV-1-Infected Women for Maternal Health and Interventions to Reduce Perinatal HIV Transmission in the United States* (available at http://aidsinfo.nih.gov/contentfiles/PerinatalGL.pdf).

Patients with CD4 cell count below 350: These patients need to know that the *Guidelines* strongly recommend ARV therapy. If patients are not convinced of the benefits of ARV therapy based on a summary of the evidence, then they will need opportunity to ask questions and provided with counseling to overcome any barriers. For those with reservations about starting ARV therapy:

- Explore the reasons the patient wants to defer treatment and counsel him/her on each of the barriers and fears.
- Build up trust and confidence; provide education to encourage without being perceived as bullying.
- Try negotiating or making a deal: for example recommend starting cotrimoxazole (trimethoprim-sulfamethoxazole), if indicated, but delaying ARV therapy until the next visit. In the meanwhile, educate the patient about the pros and cons of initiating ARV therapy. As suggested for patients with CD4 cell counts between 350–500, negotiate a new cut off point, perhaps 300.
- Most patients with HIV have other health conditions. If the patient has, for example CVD, discuss the benefits of ARV therapy on CVD.
- Ask "If you have to take a pill, what's the worst side-effect you can think of?" Based on drug-resistance testing, laboratory findings (anemia, liver function, etc), lifestyle (chaotic versus regimented, consumption of alcohol or drugs, etc), suggest a regimen. Explain the "good, bad and ugly" of each of the drug candidates. So for tenofovir: "it's an amazing drug, easy to swallow, few side effects, once daily dosing; but it has been known to decrease the ability of the kidneys to work properly. If you go on tenofovir, we'll monitor your kidneys function closely." Ask the patient how he/she feels about this. If the client is not willing to accept the risks associated with tenofovir, then maybe this drug should not be considered as a potential candidate.

Encourage the patient to make a decision with physician guidance. During the first 4–6 weeks of treatment, schedule weekly appointments if possible (if the patient is well, appointments can be cancelled or conducted by phone). Four weeks after initiation of therapy, check viral load—which should be declining—and conduct other lab tests as indicated by underlying conditions and drugs. After the 4 week visit, appointments should be guided by CD4 cell count and patient need. Three case studies are outlined on the following pages to illustrate how the *Guidelines* can be tailored to individual patient need.

Case studies

Case study 1: JT

- JT is a Caucasian man who has sex with men. He is a well-educated professional who was found to be HIV-positive during routine screening when he was in his 50s. He is now in his 70s and is still employed. His long-term partner died a number of years ago, he has recently started seeing a new partner to whom he has disclosed his HIV status and with whom he has a monogamous relationship. They always use condoms.

Clinical presentation and physical exam

- Although he is borderline hypertensive, his hypertension is well-controlled. Except for arthritis, he's never been ill. He had a total hip replacement a few years ago.
- Physical exam: normal except for scars from the orthopedic surgery.

Initial management

- JT has never been on ARVs or OI prophylaxis. Although he drinks moderately—sometimes a bit more than "moderately" and possibly even "heavy" at times—he lives an otherwise healthy lifestyle, has never smoked or used drugs.
- JT returns to the clinic six-monthly to yearly. He is long-term nonprogressor.

Pertinent laboratory results

- CD4 cell count: almost always (with rare exception) above 500, often near 800.
- Viral load: 100s-low 1000s, not undetectable.

Pros and cons of ARVs for this patient

- Despite the occasional heavy drinking, he is monogamous and practices safer sex. As such, JT's risk to public health is negligible.
- If he went on ARV therapy his viral load might become undetectable. JT is in his 70s with what appears to be an age-appropriate healthy immune system. The addition of ARV therapy may not provide substantial benefit but could cause medical harm: mitochondrial toxicity, hematologic (if prescribed zidovudine) or renal insufficiency, lipid abnormalities, diabetes, lipoatrophy, or lipodystrophy and exacerbate his hypertension. ARV therapy might put unnecessary stress on his liver (risk of hepatotoxicity given his drinking) and kidneys, which might increase risk of coronary heart disease given his hypertension.
- JT takes his blood pressure medications regularly, he doesn't miss appointments, and he always ensures his blood work is completed before scheduled appointments. Nonetheless, he does not particularly want to go on ARV therapy.
- The *Guidelines* suggest that JT should initiate ARV therapy, although this would be a moderate (not a strong) recommendation as his CD4 cell count is typically above 500. From a public health perspective, a clinician might opt to encourage treatment under the assumption that he is sexually active. But the author decided not to treat JT because he stated that he currently has only one partner and wasn't seeking to be involved with anyone else. In the event that he unexpectedly found himself in another relationship, he is a committed condom user. So, given his current good health, and the fact that the risks of ARV therapy might be greater than the benefits, he participated in the decision to delay ARV therapy. JT knows that he can change his mind and request treatment at any time.

Comments

- Even where there are underlying health issues, a patient with HIV and his provider may still decide to delay ARV therapy given the patient's overall good health, age, and social situation.

Case studies

Case study 2: Giovana

- Giovana is 43 year old woman who used illicit drugs until about 10 years ago when she "hit bottom", went for methadone treatment, and started mental health counseling. Today her physical presence belies her history of drug misuse as she is athletic in appearance, and in September was tanned after a summer in the sun. In between her fitness routine she makes time for a boyfriend, with whom she states she has a monogamous relationship and uses condoms.
- Giovana has one child, who is now an adult.
- Giovana has taken medication in the past but it tends to make her sick, even at low dosages.
- Like JT, she always attends medical appointments and ensures that her blood work is completed on time.
- This patient regularly attends her gynecological appointments and is to-date with her Pap smears.

Clinical presentation and physical exam

- When Giovana initially presented 9 or 10 years ago, it was for symptoms that were diagnosed as Hepatitis B. At that time she was screened for HIV and found to be positive.

Initial management

- Giovana has never been on ARVs or OI prophylaxis.

Pertinent laboratory results

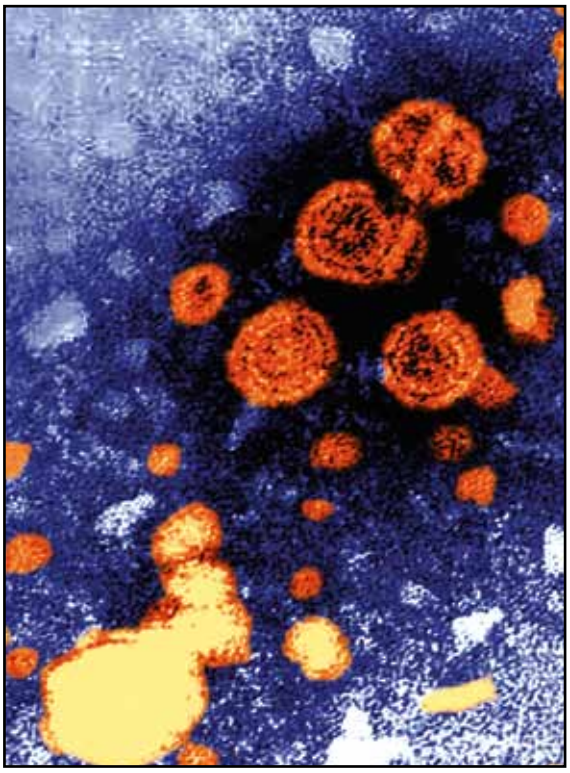
- Hepatitis B antibody negative, core positive, surface antigen negative
- HIV viral load: low, less than 10,000
- CD4 cell count: 350–750
- Liver function: normal

Pros and cons of ARVs for this patient

- Given that she is in a stable relationship with one partner to whom she has disclosed and with whom she practices safer sex, is not planning to get pregnant, and no longer injects drugs, she does not pose a threat to public health. She is asked at each visit about her sexual partners to monitor risk of further transmission.
- Giovana is fairly young. Because of her age, this patient's life expectancy is longer than JT's, suggesting that she can benefit more from earlier ARV therapy initiation. Nonetheless, Giovana has elected to defer treatment primarily because of the extensive problems she has had taking medications in the past. She fears that given her history of hepatitis, ARV therapy may attenuate liver disease progression.
- In an effort to avoid alienating Giovana, the author continues to provide her with education about ARV therapy and support her confidence in her ability to handle any unforeseen side effects should she start ARV therapy. She and the author have a contract to start ARV therapy should her CD4 cell count fall below 350.

Comments

- Giovana's and JT's cases both highlight the fact that every patient is an individual. And the individual patient's needs, issues, history, situation and personality must be considered in the decision to initiate or delay ARV therapy.



Description:Transmission electron micrograph of hepatitis B virions, also known as Dane particles. Virus. Provider: CDC/Dr. Erskine Palmer
www.newswise.com/articles/toward-explaining-why-hepatitis-b-hits-men-harder-than-women

Case studies

Case study 3: Ms. R

- Ms. R is a 47 year old Latina woman who started using drugs at the age of 12. She now uses cocaine, heroin and crack cocaine. At admission to the Emergency Department, she reported using 2 "bundles" and 3 "bags" of heroin every day, i.e., 23 bags/day (a bundle weighs, give or take, about a gram and sells for about $100).
- Ms. R has no reportable income, nor does she have anyone who is supporting her financially, despite her $100–$230/day habit. She is homeless, lives on the street, and does whatever it takes to support her habit.

Clinical presentation and physical exam

- During the late summer of 2012, Ms. R presented to the Emergency Department complaining of pain all over her body. She had a 103° temperature and weighed 80 pounds.
- Upon examination it was obvious that she was in physical distress, she had multiple skin lesions — probably insect bites and dermatitis. She could not swallow because of the pain in her throat. She was short of breath, hypotensive, had a rapid heartbeat and an abnormal chest exam.
- Ms. R was also dehydrated. At 80 pounds she was emaciated with temporal wasting, poor dentition, and hair loss. She was later found to be anemic. She was unkempt.
- Based on laboratory testing, she was diagnosed with PCP, oral esophageal candidiasis, and likely Mycobacterium avium complex (MAC).

Initial management

- Given Ms. R's physical distress and social situation (homeless with no visible signs of financial support), the author admitted her to the in-patient ward.
- The author suspected that as soon as her "high" wore off, she would be in considerable pain and susceptible to leaving the Emergency Department against advice to search for drugs. As such she was given a narcotic analgesic to prevent sudden drug withdrawal. This step created the time necessary to start treating the most urgent conditions.
- Ms. R was put on oxygen and IV fluids; she was administered steroids for the PCP, which coincidently helped with appetite.
- The plan was to treat her acute infections and then, within about 6 weeks, initiate ARV therapy. The delay in ARV therapy would lower risk of reactivation of the recently treated infections (identified while she was an in-patient).

Pertinent laboratory results

- CD4 cell count: 5
- Hemoglobin: 7.8
- WBC: 2.1
- Liver function: abnormal
- Viral load: 453,000

Pros and cons of ARVs for this patient

- Ms. R cannot start ARV therapy until her acute infections have been treated, which is expected to take 4–6 weeks from diagnosis.
- Even before counseling Ms. R, the author felt that given this patient's poor prognosis in the absence of ARVs and her risk of transmitting HIV to others, that she had a responsibility to the public and to this patient to ensure that Ms. R initiated ARV therapy. Treatment for a patient such as Ms. R is analogous to treating a patient with active TB: not only do they need to take treatment for their own health, but also to reduce risk of further transmission (Ms. R is assumed to exchange sex for drugs and needle sharing to inject drugs cannot be ruled out).
- The factor that would limit Ms. R's ability to stay drug-free and start healing was poverty. Until some of this woman's practical needs were met, her ability to adhere to an ARV therapy regimen would be very difficult. Ms. R was eventually accepted to a residential special care facility for people living with HIV, where her medical, emotional, social and drug treatment needs would be met 24/7.

Subsequent visits

- Had Ms. R not been accepted to the local residential special care facility, she would have required weekly consultations for emotional, social and medical support.

Comments

- Healthcare providers have to address mental health, substance abuse, and poverty before ARV therapy can have its intended effect.
- Had this patient been discharged from the Emergency Department and referred for out-patient care, Ms. R would have certainly been dead within a matter of weeks. Given the miraculous success stories seen in patients with advanced AIDS started on ARV therapy, Ms. R too, has much hope. But the key to this hope is controlling her drug habit and finding relief from the poverty that surrounds her so that she can focus on her own health and take the simple steps needed to recover: eat a sufficient amount of nutritious food and adhere to a medical regimen.
- Homeless patients and those who are drug users are often viewed by the healthcare system as too much work. But even for patients unwilling or unable to give up drugs, clinicians can effect harm reduction behavioral changes that reduce risk of further HIV transmission (methadone maintenance for heroin users, oral administration rather than injecting, use of clean needles rather than sharing, etc). Without intervention, drug-using clients can do much harm to themselves and to those in their community (particularly if they exchange sex for drugs or share needles to inject drugs). Healthcare providers have an obligation to provide compassionate care for these very sick patients, if not for the patient herself, then for those with whom the patient has sex or injects drugs.
- Despite the availability of early ARV therapy, there are still patients with HIV in our own communities who enter care at death's doorstep.

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   - HIV screening is recommended for patients in all health-care settings after the patient is notified that testing will be performed unless the patient declines (opt-out screening).
   - Persons at high risk for HIV infection should be screened for HIV at least annually.
   - Separate written consent for HIV testing should not be required; general consent for medical care should be considered sufficient to encompass consent for HIV testing.
   - Prevention counseling should not be required with HIV diagnostic testing or as part of HIV screening programs in health-care settings."

   The recommendations were "intended for all health-care providers in the public and private sectors, including those working in hospital emergency departments, urgent care clinics, inpatient services, substance abuse treatment clinics, public health clinics, community clinics, correctional health-care facilities, and primary care settings."

Initiating Antiretroviral Therapy, Going Beyond the *Guidelines*

POST TEST — Page 1 of 1

CE CONTINUING EDUCATION

Questions refer to the content of the article. To receive CME/CE/CEU credit: complete exam, registration, and evaluation forms on-line at *http://ccoe.umdnj.edu/catalog* or fill in the forms on the following pages, and mail or fax to UMDNJ-CCOE (see Registration Form).

1. Which of the following is **CORRECT** about the results from the HPTN 052 study:
   - A. Earlier HIV treatment is cost-effective.
   - B. Providing ARV therapy to HIV-infected individuals earlier delays AIDS-related health events as well as death.
   - C. Earlier use of ARV therapy reduced HIV transmission by 96%.
   - D. B and C only.
   - E. All of the above.

2. Which of the following statements about "treatment as prevention" is **FALSE**?
   - A. "Treatment as prevention" includes prevention of mother-to-child transmission of HIV initiatives.
   - B. Suppression of viral load to undetectable levels in an ARV therapy-naive patient usually occurs within the first 2–5 weeks of ARV therapy initiation, so treatment can be considered prevention approximately 10 days after ARV therapy initiation.
   - C. "Treatment as prevention" describes the use of long-term ARV therapy in a person who is HIV-infected to decrease the risk of further HIV transmission.
   - D. On a population level, "treatment as prevention" results in a reduction of HIV transmission when the percentage of people with HIV taking ARV therapy increases and community viral load decreases.

3. All of the following are predictors of virologic success **EXCEPT**:
   - A. High potency of ARV regimen.
   - B. Excellent adherence to treatment regimen.
   - C. Low baseline CD4 cell count.
   - D. Rapid reduction of viremia in response to treatment.
   - E. All of the above are predictors of virologic success.

4. Initiation of ARV therapy is strongly recommended, regardless of CD4 cell count, with any of the following conditions **EXCEPT**:
   - A. Pregnancy.
   - B. Long-term non-progression.
   - C. History of an AIDS-defining illness.
   - D. HIV-associated nephropathy.
   - E. Hepatitis B virus coinfection.

5. San Francisco was the first health authority in the world to offer treatment to all people diagnosed with HIV, regardless of cell count. The increased access meant that new infections dropped by approximately:

   A. 15% B. 27% C. 33%
   D. 42% E. 51%

6. In patients with HIV who have active TB:
   - A. Initiate TB treatment first, followed by ARV therapy within 2 weeks of starting TB treatment in patients with CD4 cell counts <50 cells/mm^3.
   - B. Initiate TB treatment and ARV therapy together.
   - C. Initiate TB treatment first, followed by ARV therapy initiation 14 weeks after starting TB treatment in patients with CD4 cell counts ≥50 cells/mm^3.
   - D. If pregnant, delay TB treatment until after delivery.

7. The *Guidelines* state that a clinician may decide to defer treatment in all of the following scenarios **EXCEPT**:
   - A. When there are significant barriers to adherence.
   - B. In the presence of comorbidities that complicate or prohibit ARV therapy.
   - C. In patients at risk of cardiovascular disease (CVD).
   - D. In long-term non-progressors and elite HIV controllers.

8. The median CD4 cell count of newly diagnosed patients in the United States is:
   - A. ~200 CD4 cell count.
   - B. ~300 CD4 cell count.
   - C. ~400 CD4 cell count.
   - D. ~500 CD4 cell count.

9. TIMING of ARV therapy initiation for an individual patient in clinical practice will depend on all of the following **EXCEPT**:
   - A. Patient's likelihood of excellent adherence to their treatment regimen.
   - B. Patient's sexual practices.
   - C. Patient's health.
   - D. Results of pretreatment drug-resistance testing.

Initiating Antiretroviral Therapy, Beyond the *Guidelines*

REGISTRATION FORM

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SELF-ASSESSMENT TEST *Circle the best answer for each question.*				
1. A B C D E	**3.** A B C D E	**5.** A B C D E	**7.** A B C D	**9.** A B C D
2. A B C D	**4.** A B C D E	**6.** A B C D	**8.** A B C D	

– PLEASE PRINT –

First Name M.I. Last Name Degree

Daytime Phone # Evening Phone #

Fax # E-mail

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Affiliation/Specialty

Indicate the type of continuing education credit you wish to obtain as a result of your participation in this activity.

☐ **Nurses:** 1.17 CNE Contact Hour(s). Contact Hours Claimed: _____

☐ **Physicians:** 1.25 *AMA PRA Category 1 Credit(s)™*: Credits Claimed: _____

☐ **General:** Continuing Education Units (CEUs) (up to 0.125) Claimed: _____

One credit/contact hour for each hour of participation. Continuing Education Units: one unit per ten hours of participation.
I attest that I have completed this activity as designed. I will report the number of credits/contact hours claimed during my filing of continuing education credit with professional organizations, licensing boards, or other agencies.

Signature Date

Release date: December 1, 2012 • Expiration date: Credit for this activity will be provided through November 30, 2014.
A CE credit letter will be mailed to you in approximately 4 weeks.

UMDNJ-Center for Continuing & Outreach Education
PO Box 1709 • Newark, New Jersey 07101-1709 • Phone: 973-972-4267 or 1-800-227-4852 • Fax: 973-972-7128

CE Activity Code: 14HC05 — This form may be photocopied.

Initiating Antiretroviral Therapy, Beyond the *Guidelines*

REGISTRATION FORM

CE CONTINUING EDUCATION

The planning and execution of useful and educationally sound continuing education activities are guided in large part by input from participants. To assist us in evaluating the effectiveness of this activity and to make recommendations for future educational offerings, please take a few moments to complete this evaluation form. Your response will help ensure that future programs are informative and meet the educational needs of all participants.

CCOE
Center for Continuing & Outreach Education

Please note: CE credit letters and long-term credit retention information will only be issued upon receipt of completed evaluation form.

PROGRAM OBJECTIVES: Having completed this activity, are you better able to:

		Strongly Agree				Strongly Disagree
Objective 1:	Discuss treatment as prevention.	5	4	3	2	1
Objective 2:	Summarize recommendations from the *Guidelines* on initiating antiretroviral therapy.	5	4	3	2	1
Objective 3:	Implement a tailored ARV therapy regimen for patients with HIV, as recommended by the *Guidelines*.	5	4	3	2	1

OVERALL EVALUATION:	Strongly Agree				Strongly Disagree
The information presented increased my awareness/understanding of the subject.	5	4	3	2	1
The information presented will influence how I practice.	5	4	3	2	1
The information presented will help me improve patient care.	5	4	3	2	1
The authors demonstrated current knowledge of the subject.	5	4	3	2	1
The program was educationally sound and scientifically balanced.	5	4	3	2	1
The program avoided commercial bias or influence.	5	4	3	2	1
The self-assessment was appropriate and helpful.	5	4	3	2	1
Overall, the program met my expectations.	5	4	3	2	1
I would recommend this program to my colleagues.	5	4	3	2	1

Based on the content of the activity, what will you do differently in the care of your patients? (check one)

- ☐ Implement a change in my practice.
- ☐ Seek additional information on this topic.
- ☐ Do nothing differently. Current practice reflects activity recommendations.
- ☐ Do nothing differently as the content was not convincing.
- ☐ Do nothing differently. System barriers prevent change.
- ☐ Not applicable. I do not see patients in my current position.

If you anticipate changing one or more aspects of your practice as a result of your participation in this activity, please provide us with a brief description of how you plan to do so.

_____

May we contact you in two months to see how you are progressing on the changes indicated above?

☐ Yes. Please provide your email address. _____

☐ No. I do not wish to participate participate in the follow-up assessment.

If you are not able to effectively implement what you learned at this activity, please tell us what the system barriers are (e.g., reimbursement issues, managed care rules, formulary decisions, countervailing practice guidelines, etc).

_____

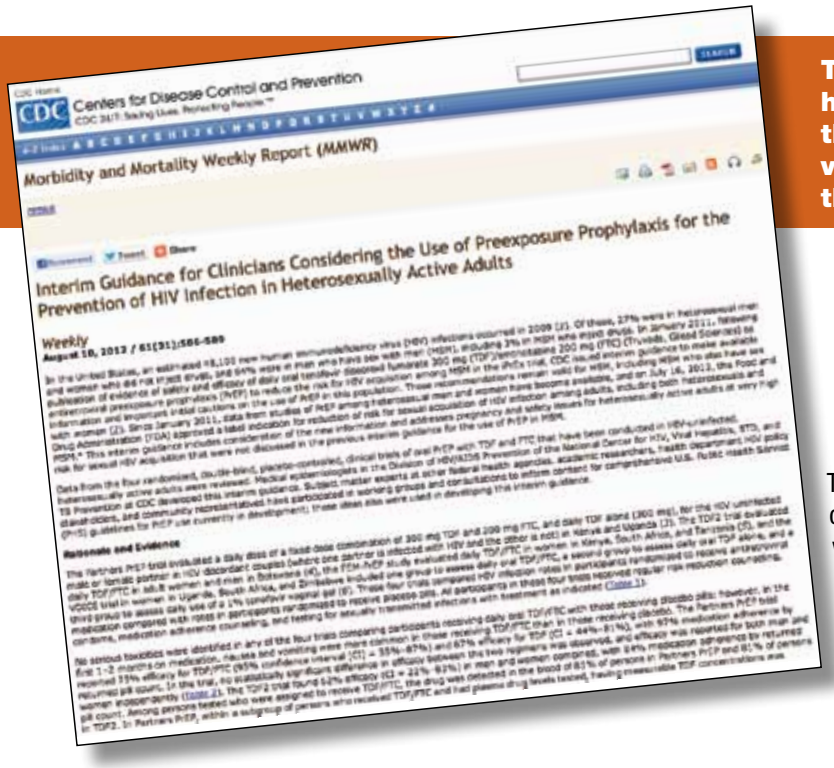
Please list any topics that you would like addressed in future educational activities.

_____

CE Activity Code: 14HC05 — This form may be photocopied.

CDC Issues Interim PrEP Guidelines for Heterosexual Adults

In August 2012, the Centers for Disease Control and Prevention (CDC) released interim guidelines for clinicians prescribing antiretroviral medicine to prevent acquisition of HIV in heterosexual men and women, stating that pre-exposure prophylaxis (PrEP) with daily doses of oral tenofovir disoproxil fumarate 300 mg (TDF)/emtricitabine 200 mg (FTC) (Truvada, Gilead Sciences) can be safe and effective in reducing risk of infection. The new guidelines complement those issued in January 2011 for PrEP use of antiretrovirals for men who have sex with men.


Centers for Disease Control and Prevention

Morbidity and Mortality Weekly Report (MMWR)

Interim Guidance for Clinicians Considering the Use of Preexposure Prophylaxis for the Prevention of HIV Infection in Heterosexually Active Adults

Weekly
August 10, 2012 / 61(31);586-589

The guidelines for heterosexual adults are based on results from four trials supporting the efficacy of oral TDF/FTC. (See the August 10, 2012 *Morbidity and Mortality Weekly Report* for further information.) Two other studies were also reviewed: one using oral TDF/FTC and one using TDF alone, both of which were discontinued early because of lack of efficacy. Suboptimal adherence played a role in the inability of these two interventions to demonstrate efficacy, but there may have been other factors as well.

Interim guidance for clinicians considering PrEP

The following is a summary of CDC's interim guidance for clinicians considering the use of PrEP for men who have sex with men (MSM) and heterosexually active adults at very high risk for HIV acquisition through sex (e.g., those with partners known to have HIV infection):

1. PrEP should only be used among individuals who have been confirmed to be HIV-negative.
2. PrEP use may be one of several options to help protect the HIV-negative partner in discordant couples during attempts to conceive.
3. PrEP should never be seen as the first line of defense against HIV. Clients on PrEP should still:
   - Use condoms correctly and consistently.
   - Get tested to know their status and that of their partner(s).

Taking PrEP daily is critical. PrEP provides a high level of protection only to those who take the pills regularly. In the trials, protection was very low among those who did not adhere well to the daily regimen.

   - Get screened — and treated if needed — for other sexually transmitted infections (STIs).
   - Get information and support to reduce drug use and sexual risk behavior.
   - Reduce their number of sexual partners.

Taking PrEP daily is critical. PrEP provides a high level of protection only to those who take the pills regularly. In the trials, protection was very low among those who did not adhere well to the daily regimen.

Before initiating PrEP, determine eligibility:

- Document negative HIV antibody test(s) immediately before starting PrEP medication.
- Test for acute HIV infection if patient has symptoms consistent with acute HIV infection.
- Confirm that patient is at substantial, ongoing, high risk for acquiring HIV infection.
- Confirm that calculated creatinine clearance is ≥60 mL per minute (via Cockcroft-Gault formula).

Other recommended actions:

- Screen for hepatitis B infection; vaccinate against hepatitis B if susceptible, or treat if active infection exists, regardless of decision about prescribing PrEP.
- Screen and treat as needed for STIs.
- Begin PrEP medication regimen: prescribe 1 tablet of TDF/FTC daily.
- In general, prescribe no more than a 90-day supply, renewable only after HIV testing confirms that patient remains HIV-uninfected.

- If active hepatitis B infection is diagnosed, consider using TDF/FTC for both treatment of active hepatitis B infection and HIV prevention.
- Provide risk-reduction and PrEP medication adherence counseling and condoms.

Follow-up while PrEP medication is being taken

- Every 2–3 months, conduct HIV antibody testing; document negative result.
- Evaluate and support PrEP medication adherence at each follow-up visit, more often if inconsistent adherence is identified.
- Every 2–3 months, assess risk behaviors and provide risk-reduction counseling and condoms. Assess STI symptoms and, if present, test and treat for STIs as needed.
- Every 6 months, test for STIs even if patient is asymptomatic, and treat as needed.
- Three months after initiation, then yearly while on PrEP medication: check blood urea nitrogen and serum creatinine.

On discontinuing PrEP (at patient request, for safety concerns, or if HIV infection is acquired):

- Conduct HIV testing to confirm if HIV infection has occurred.
- If HIV positive, order and document results of resistance testing and establish linkage to HIV care.
- If HIV negative, establish linkage to risk-reduction support services as indicated.
- If active hepatitis B was diagnosed at initiation of PrEP, consider appropriate medication for continued treatment of hepatitis B.

CDC and other United States Public Health Service agencies are currently developing guidelines on the use of PrEP as part of a comprehensive set of HIV prevention services that will include specific recommendations for use with MSM and heterosexually active adults at very high risk for HIV acquisition. ❖

Criticism of approval of TDF/FTC for PrEP

Although CDC has released interim guidance for healthcare providers electing to provide PrEP, this decision has not met with unanimous support. AIDS Healthcare Foundation (AHF), the nation's largest HIV nonprofit medical provider, opposes the Food and Drug Administration's (FDA) approval of Gilead Sciences' Truvada (TDF/FTC) for use as PrEP to prevent transmission of HIV. AHF's concern has been echoed by other public health experts, including The Lancet, American Public Health Association, British HIV Association and British Association for Sexual Health.

AHA believes that PrEP is an unacceptable health and safety risk, on both personal and public health fronts. According to an article in JAMA, common adverse reactions in people who take PrEP include headache, abdominal pain, and weight loss. Safety concerns include impairment of kidney and liver function and decreases in bone mineral density. The long-term safety of the drug in healthy people is unknown because the available studies have only lasted several years. According to the Lancet, public health concerns include the risk of resistance: "Expanding the use of antiretrovirals to include pre-exposure prophylaxis will increase the risk of resistance, which is already a serious problem. HIV is a rapidly evolving virus and development of resistance creates the need for ever changing regimens of drugs in various classes."

Because protection with PrEP is unlikely to be 100%, some critics have also articulated concerns over the potential decrease in safer sex. The Lancet noted that "making drugs available as prophylaxis could encourage high-risk sexual behavior among those who believe themselves to be protected."

Dr. Alain Lafeuillade, Chief of the Department of Infectious Diseases at Toulon General Hospital (France) and Chairman of the International Symposium on HIV & Emerging Infectious Diseases, went so far as to comment that, "The vote [the panel's decision to recommend PrEP] can only be explained by the lack of independence of the agency from financial and other powers because this is an absurd way to face the HIV pandemic."

CDC. "Interim Guidance for Clinicians Considering the Use of Preexposure Prophylaxis for the Prevention of HIV Infection in Heterosexually Active Adults". *Morbidity and Mortality Weekly Report.* August 10, 2012. Accessed August 30, 2012 at: http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6131a3.htm?s_cid=mm6131a3_w

CDC. "Interim Guidance: Pre-exposure prophylaxis for the prevention of HIV infection in men who have sex with men". *Morbidity and Mortality Weekly Report.* January 28, 2011. Accessed September 5, 2012 at: http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6003a1.htm

The Center for Global Health Policy. *Science Speaks, HIV & TB News.* August 9, 2012. Accessed on August 31, 2012 at: http://sciencespeaksblog.org/2012/08/09/cdc-issues-interim-guidelines-on-preexposure-antiretroviral-use-for-heterosexual-adults/#axzz258ZtXrZ6

Steinbrook, R. "Preexposure Prophylaxis for HIV Infection". *JAMA.* September 5, 2012—Vol 308, No. 9

CE CONTINUING EDUCATION

Epidemiology, Screening, Diagnosis, and Prognosis for Cancer in HIV/AIDS

Release date: December 1, 2012 • Expiration date: November 30, 2014 • Course code: 14HC06 • Nursing credit for this activity will be provided through November 30, 2014.

SPONSOR:

Sponsored by François-Xavier Bagnoud Center, School of Nursing, University of Medicine and Dentistry of New Jersey and UMDNJ-Center for Continuing and Outreach Education.

GRANTOR ACKNOWLEDGEMENT:

This activity is supported by an educational grant from the New Jersey Department of Health (NJDOH)—Division of HIV, STD and TB Services, through an MOA titled "Education and Training for Physicians and other Healthcare Professionals in the Diagnosis and Treatment of HIV/AIDS."

STATEMENT OF NEED:

With the advent of antiretroviral therapy (ART), the number of individuals living with HIV and AIDS has increased compared to the pre-ART era. In the era of ART, the population with HIV is aging; they are less likely to die of AIDS-related conditions and more likely to experience the chronic conditions experienced by the general population, including cancers.

While the incidence of AIDS-defining cancers has decreased, non-AIDS defining cancers has climbed. Not only do people with HIV tend to develop these cancers earlier (e.g., in one study those with HIV developed lung cancer at a median age of 50, whereas the median age in the general population was 54), but they tend to be diagnosed in later stages, typically stage III or IV. For example, in one study of non-small cell squamous cell carcinoma of the lung, 74% of individuals with HIV were diagnosed with stage IIIB and IV disease. Survival rates for stage IIIB/IV were 25% at 1 year and 0% at 3 years. Both examples illustrate the lack of awareness around the prevalence of non-AIDS defining cancers in people with HIV, leading to a paucity of education and support to prevent these cancers, late screening and untimely diagnosis.

TARGET AUDIENCE:

This activity is designed for physicians, nurses, social workers, health educators, and other health care professionals in New Jersey who are involved in the care of people with HIV.

METHOD OF PARTICIPATION:

Participants should read the learning objectives, review the activity in its entirety, and then complete the self-assessment test, which consists of a series of multiple-choice questions. Upon completing this activity as designed and achieving a passing score of 70% or more on the self-assessment test; participants will receive a letter of credit and the test answer key four (4) weeks after receipt of the self-assessment test, registration, and evaluation materials. This activity may also be completed online at *http://ccoe.umdnj.edu/catalog/*. Estimated time to complete this activity as designed is 1.03 hours for nurses, and 1.0 hour for physicians.

LEARNING OBJECTIVES:

Following completion of this activity, participants should be able to:

1. Recognize the changing epidemiology of cancer in people with HIV, including the decline in AIDS-defining cancers as well as the rise in non-AIDS defining cancers.
2. Seek opportunities to screen for and diagnose cancer in people with HIV/AIDS.
3. Ensure that all patients with HIV/AIDS are provided with cancer prevention education.

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Activity author

Cindy Hou, DO, MBA, Garden State Infectious Diseases Associates

ACCREDITATION STATEMENTS:

CME

UMDNJ-Center for Continuing and Outreach Education is accredited by the Accreditation Council for Continuing Medical Education to provide continuing medical education for physicians.

UMDNJ-Center for Continuing and Outreach Education designates this enduring material for a maximum of 1.0 *AMA PRA Category 1 Credit*™. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

CNE

UMDNJ-Center for Continuing and Outreach Education is an approved provider of continuing nursing education by NJSNA, an accredited approver by the American Nurses Credentialing Center's Commission on Accreditation. Provider Number TP173-12/12-15. Provider Approval is valid through December 31, 2015.

This activity is awarded 1.03 contact hours (60 minute CH).

Nurses should claim only those contact hours actually spent participating in the activity.

Approved provider status refers only to continuing education activities and does not imply ANCC COA or NJSNA endorsement of any commercial products.

CEU

UMDNJ-CCOE certifies that this continuing education offering meets the criteria for up to 0.1 Continuing Education Units (CEUs), provided the activity is completed as designed. One CEU equals 10 contact hours of participation in an organized continuing education experience under responsible sponsorship, capable direction and qualified instruction. Participants should only claim those contact hours actually spent participating in the activity.

PEER REVIEW:

In order to help ensure content objectivity, independence, and fair balance, and to ensure that the content is aligned with the interest of the public, UMDNJ-CCOE has resolved all potential and real conflicts of interest through content review by non-conflicted, qualified reviewers. This activity was peer-reviewed for relevance, accuracy of content and balance of presentation by Joanne Phillips, RN, MS; and Renee Powell, BS, RN.

Field test: This activity was pilot-tested for time required for participation by David John Cennimo, MD; Jojy Cheriyan, MD, MPH, MPhil; Anna M. Haywood, RN, MSN; Mary C. Krug, RN, MSN, APN; Debbie Mohammed, MS, MPH, APRN-BC, AACRN; Kinshasa Morton, MD; and Kara Winslow, BSN, RN.

DISCLOSURE DISCLAIMER:

In accordance with the disclosure policies of UMDNJ and to conform with ACCME and FDA guidelines, individuals in a position to control the content of this educational activity are required to disclose to the activity participants: 1) the existence of any relevant financial relationship with any entity producing, marketing, re-selling, or distributing health care goods or services consumed by, or used on, patients, with the exemption of non-profit or government organizations and non-health care related companies, within the past 12 months; and 2) the identification of a commercial product/device that is unlabeled for use or an investigational use of a product/device not yet approved.

Disclosure Declarations: There were no relevant financial relationships to disclose reported by the activity directors, author, planning committee members, peer reviewers or field testers.

OFF-LABEL/INVESTIGATIONAL USE DISCLOSURE:

This activity does not contain information of commercial products/devices that are unlabeled for use or investigational uses of products not yet approved.

CONTENT DISCLAIMER: The views expressed in this activity are those of the faculty. It should not be inferred or assumed that they are expressing the views of NJDOH – Division of HIV, STD and TB Services, any manufacturer of pharmaceuticals or devices, or UMDNJ. It should be noted that the recommendations made herein with regard to the use of therapeutic agents, varying disease states, and assessments of risk, are based upon a combination of clinical trials, current guidelines, and the clinical practice experience of the participating presenters. The drug selection and dosage information presented in this activity are believed to be accurate. However, participants are urged to consult all available data on products and procedures before using them in clinical practice.

PRIVACY POLICY: To review UMDNJ's privacy policy, please see: http://ccoe.umdnj.edu/general/privacypolicy.html. Please direct CE related or technical questions to UMDNJ at 973-972-4267 or email ccoe@umdnj.edu.

NEW JERSEY AIDSLine December 2012

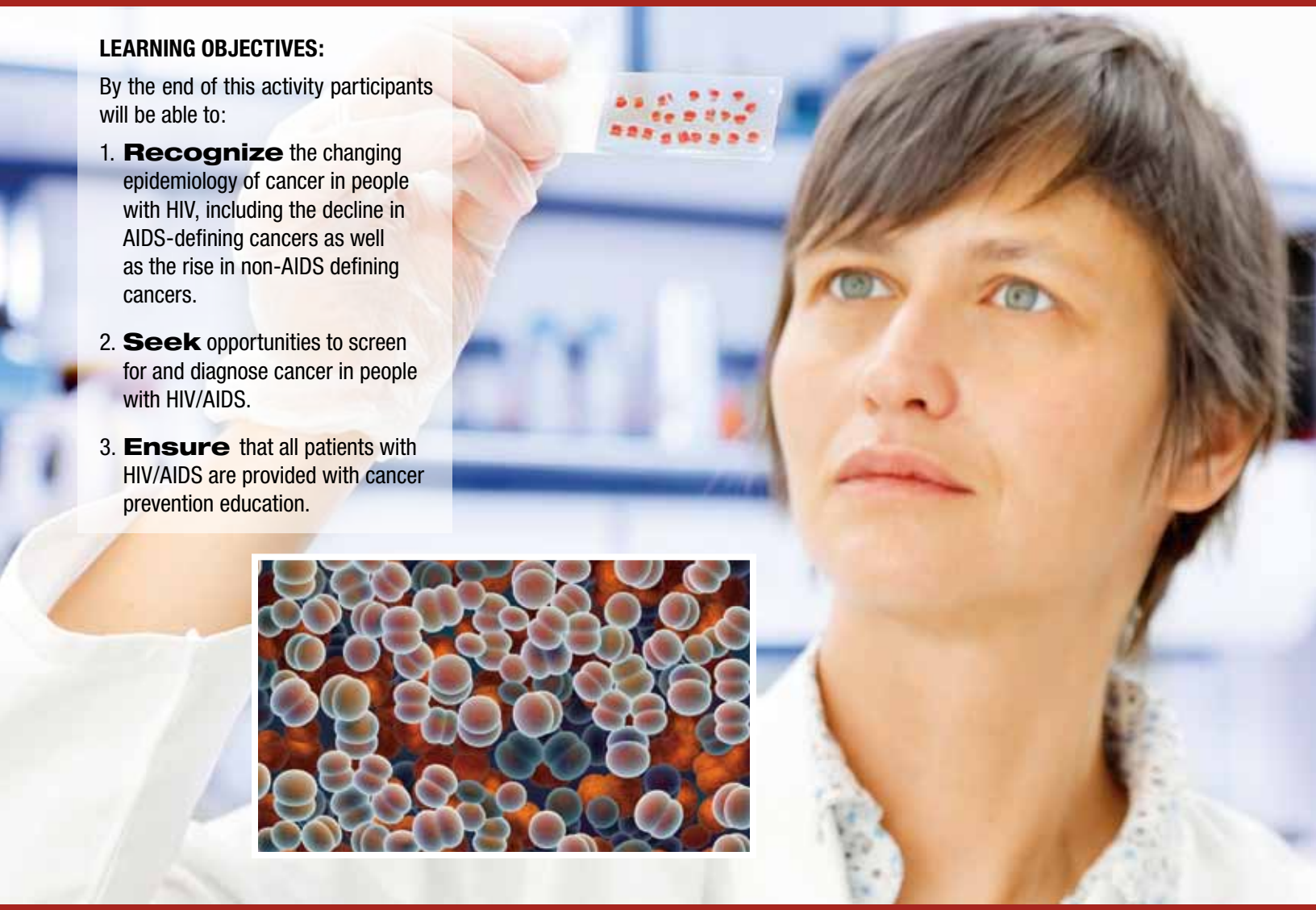
Epidemiology, Screening, Diagnosis, and Prognosis for Cancer in HIV/AIDS

Cindy Hou, DO, MBA, Garden State Infectious Diseases Associates

LEARNING OBJECTIVES:

By the end of this activity participants will be able to:

1. **Recognize** the changing epidemiology of cancer in people with HIV, including the decline in AIDS-defining cancers as well as the rise in non-AIDS defining cancers.
2. **Seek** opportunities to screen for and diagnose cancer in people with HIV/AIDS.
3. **Ensure** that all patients with HIV/AIDS are provided with cancer prevention education.



Release date: December 1, 2012 • Expiration date: November 30, 2014 • Course code: 14HC06 • Nursing credit for this activity will be provided through November 30, 2014.

To receive continuing education (CE) credit, complete the exam, registration, and evaluation forms on-line at *http://ccoe.umdnj.edu/catalog/* or that follow this article.

NJ Health New Jersey Department of Health

François-Xavier Bagnoud Center
School of Nursing, University of Medicine & Dentistry of New Jersey

Introduction

With the advent of antiretroviral therapy (ART), the number of individuals living with human immunodeficiency virus (HIV) and acquired immunodeficiency syndrome (AIDS) has increased compared to the pre-ART era. The US AIDS population increased four-fold from 1991–2005. At the end of 2009, the estimated number of people age 13 and older living with HIV infection in the United States was 1,148,200. This figure included an estimated 476,186 people with an AIDS diagnosis.[1] In the era of ART, the population with HIV is aging; they are less likely to die of AIDS-related conditions and more likely to experience the chronic conditions experienced by the general population, including cancers. While HIV survival rates have improved, the morbidity and mortality associated with cancers in these patients is an area that deserves heightened attention.

When reviewing cancers in people with HIV/AIDS, it is helpful to distinguish between those that are AIDS-defining and those that are non-AIDS defining cancers. According to the Center for Disease Control and Prevention (CDC), the AIDS-defining cancers include Kaposi sarcoma, Burkitt's lymphoma, immunoblastic lymphoma, primary central nervous system lymphoma, and invasive cervical cancer.[2] All the other cancers are designated as non-AIDS defining (see Table 1).

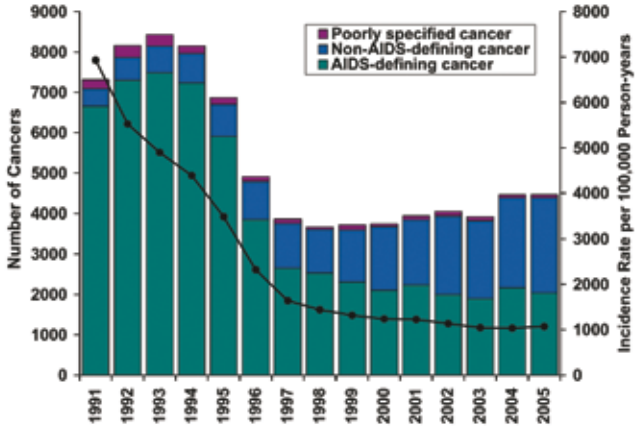
Epidemiology

Researchers have examined age at the time of cancer diagnosis, and certain trends have been noted. While the general population was diagnosed with lung cancer at a median age of 54 years, AIDS patients were diagnosed with lung cancer at an earlier age of 50. For anal cancer, AIDS patients were diagnosed at a median age of 42 compared to 45 in the non-HIV infected population. Conversely, people with AIDS were diagnosed with Hodgkin disease at a slightly later age: 42 compared with 40. For most cancers, diagnoses were established at similar ages for those with AIDS when compared with the general population.[3]

Of the many non-AIDS defining cancers, this article will describe cancers of the liver, hepatobiliary tract, colon, anus and Hodgkin disease along with a discussion of the AIDS-defining cancers.

Figures 1 illustrates the estimated counts and standardized rates of AIDS-defining cancers among people living with AIDS in the United States by calendar year and age group. Figure 2 shows the estimated counts and standardized rates of non-AIDS defining cancers among people living with AIDS in the United States by calendar year and age group. The bars for 0–12 year olds in panels in both figures are difficult to see because of small numbers of cancers in this age group (122 AIDS-defining cancers and 25 non-AIDS-defining cancers, total for the 15 year time period). Bars depict the estimated number of cancers in people with AIDS, and points connected by lines depict incidence rates standardized to the 2000 US AIDS population by age group, race, and sex.[4]

Figure 1: Number of AIDS-defining cancers



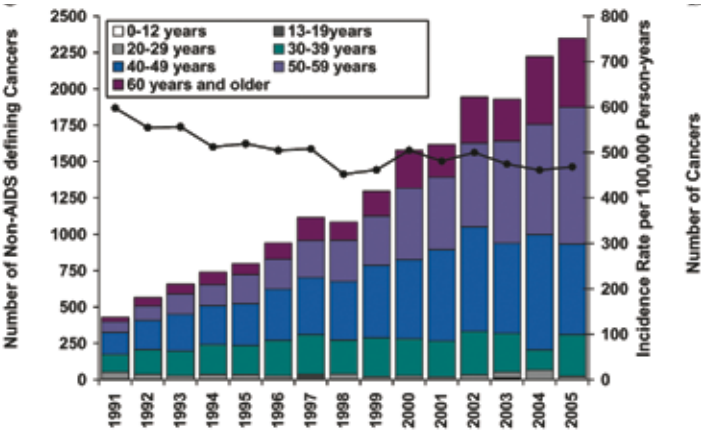
Over the past two decades, the AIDS-defining cancers have decreased by more than three-fold and the non-AIDS defining cancers increased three-fold.

Over the past two decades, the AIDS-defining cancers have decreased by more than three-fold and the non-AIDS defining cancers increased three-fold.[4] Although ART has lowered the rates of Kaposi sarcoma and non-Hodgkin lymphoma, there has been no significant improvement in the incidence of those impacted by invasive cervical cancer.[5]

Table 1: AIDS-defining and non-AIDS defining cancers

AIDS-defining cancers	Non-AIDS defining cancers with increased incidence in people with HIV[6]	
■ Kaposi sarcoma	■ Anal	■ Lip
■ Burkitt's lymphoma	■ Angiosarcoma	■ Liver
■ Immunoblastic lymphoma	■ Brain and CNS	■ Lung
■ Primary central nervous system lymphoma	■ Colorectal	■ Multiple myeloma
■ Invasive cervical cancer	■ Esophagus	■ Pancreas
	■ Heart	■ Penile
	■ Hodgkin disease	■ Pharynx
	■ Kidney	■ Skin cancer
	■ Larynx	■ Stomach
	■ Leukemia	■ Testicular
	■ Leiomyosarcoma	■ Tongue
		■ Vulva/vagina

Figure 2: Number of non-AIDS defining cancers



HIV and cancer risk

Cancer is a significant cause of mortality and morbidity in people infected with HIV; 30–40% will develop a malignancy during their lifetime. Not only do the AIDS-defining cancers occur with greater frequency in people with HIV than in unaffected individuals, people with HIV also experience an increased risk for numerous non-AIDS defining cancers (see Table 1).[5, 6] The increased risk of cancer in HIV is likely multifactorial. Infected individuals have weakened immune systems. In comparison with the general population, they tend to have a higher prevalence of co-infection with cancer-related viruses such as human herpes virus-8 (HHV-8), Epstein-Barr virus (EBV), human papillomavirus (HPV), as well as hepatitis B and C (see Table 2). People with HIV have a higher prevalence of smoking and excessive alcohol intake, which are known risk factors for cancer.[5] Tobacco use has been linked with cancers of the bladder, cervix, esophagus, kidney, mouth, nasal cavity, lung, pancreas, stomach, and throat.[7] Alcohol abuse has been implicated in cancers of the breast, esophagus, larynx, liver, and pharynx.[8] It is important that clinicians inquire about tobacco and alcohol intake, as both are potentially modifiable risk factors.

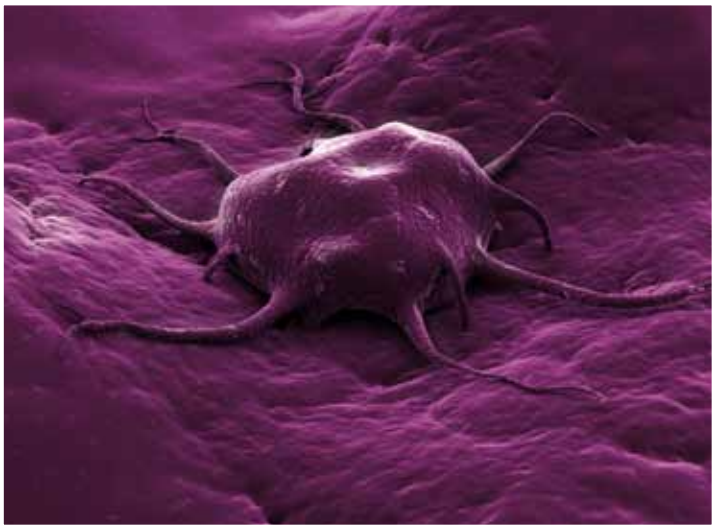


Table 2: Cancer-related viruses and their associated cancers[5]

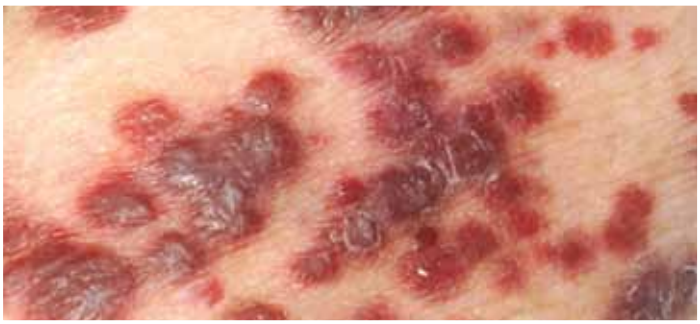
Virus	Associated cancers
HHV-8	Kaposi sarcoma
EBV	Non-Hodgkin lymphoma, Hodgkin lymphoma
HPV	Cervical, anal, penile, vaginal, vulvar, head, oropharynx (back of the throat, including the base of the tongue and tonsils), and neck cancers
Hepatitis B and C	Liver cancer

AIDS-defining cancers

Kaposi sarcoma (KS)

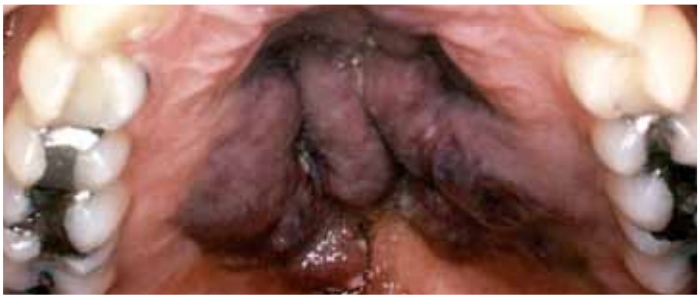
This AIDS-defining cancer has been referred to as epidemic KS. Widespread use of ART led to a decrease in incidence from 15.2 per 1000 patient-years to 4.9 per 1000 patient-years. The standardized incidence ratio in people with HIV is 3,640 times that of the general population (i.e., people with HIV are 3,640 times more likely to develop KS than the general population).[9]

The etiologic agent is HHV-8, a type of human herpes virus, which may be transmitted by saliva.[9] HHV-8 has also been implicated in lymphoproliferative diseases like Castleman's disease and primary effusion or body cavity lymphoma, all of which can be seen in HIV.



Kaposi sarcoma on the skin of an AIDS patient. National Cancer Institute (AV-8500-3620), http://visualsonline.cancer.gov/details.cfm?imageid=2168

KS can involve the skin, oral mucosa, lymph nodes, gastrointestinal tract, liver, lung, and spleen. In most initial presentations, the skin alone is involved.[10] The cutaneous lesions can be firm, papular, or even nodular, but they generally do not cause pain. A classic appearance in fair-skinned individuals is violaceous, but in dark-skinned individuals, the lesions can be brown or even black. Common sites affected include the face, oral cavity, legs and feet.[9] Aside from the skin, gastrointestinal involvement is also common. Pulmonary involvement usually represents progression or advanced disease and can even cause death.[10] Pulmonary KS tends to occur in persons with AIDS who have CD4 cell counts less than 100; the patient typically has more than 50 skin lesions although the number may be far fewer or even absent.[9]



An oral Kaposi sarcoma lesion. Silverman, S. University of California, San Francisco. Public Health Image Library, Centers for Disease Control and Prevention (Image ID# 6072) 1987. http://phil.cdc.gov/phil/home.asp

While cutaneous KS has a classic appearance, the diagnosis of KS should not be based solely on appearance but rather by a punch biopsy of the dermatologic lesion. When pulmonary involvement is suspected, bronchoscopy may reveal violaceous lesions, but biopsy is relatively contraindicated as there is a risk for bleeding.[9]

Non-Hodgkin lymphoma

Like KS, ART has led to decreases in the incidence of systemic non-Hodgkin lymphoma (the AIDS-defining non-Hodgkin lymphomas include Burkitt's lymphoma and Immunoblastic lymphoma). Compared to the general population, the risk of non-Hodgkin lymphoma is 77 times greater in persons with HIV.[4] Prognosis is influenced by a number of factors. ART is associated with improved prognosis, whereas other factors such as age older than 35, extent of tumor burden, CD4 cell count less than 100, and a history of intravenous drug use are poor prognostic predictors.[9]

Systemic non-Hodgkin lymphoma is categorized histologically: diffuse large B-cell lymphoma, B-cell immunoblastic lymphoma, and small non-cleaved cell lymphoma.[11] Cases can also be grouped by severity: indolent or low grade, intermediate-grade, and high-grade. The intermediate and high-grade lymphomas are more closely associated with persons who have progressed to AIDS.[9]

EBV has been identified in up to 40% of cases in patients coinfected with HIV and non-Hodgkin lymphoma. Both EBV and HHV-8 have been seen in primary effusion or body cavity lymphoma, a variant of a non-Hodgkin lymphoma.[9]

Classic symptoms associated with non-Hodgkin lymphoma include fevers, weight loss, and night sweats while on physical exam, painless lymphadenopathy might be detected. Extranodal disease is very common: central nervous system disease is seen in 42% of patients and bone-marrow disease in 33% of patients. Non-Hodgkin lymphoma of the gastrointestinal tract is also common. Less common sites include the gingiva, paranasal sinuses, and the heart.[11]

In the course of workup for non-Hodgkin lymphoma, testing may include a complete blood count (CBC), lymph node biopsy, bone marrow aspiration, and biopsy of the lesion.[11]

Primary central nervous system lymphoma (PCNSL)

Whereas the previous lymphomas were systemic diseases, PCNSL—another AIDS-defining cancer—is restricted to the central nervous system. As in systemic non-Hodgkin disease, the Epstein-Barr virus has also been implicated in PCNSL, which occurs 1,000 times more often in persons with HIV than in unaffected individuals. It is commonly seen in advanced AIDS; mean CD4 cell count at time of diagnosis is approximately 50. In the era of ART, the incidence of PCNSL has declined significantly.[9]

Clinical manifestations include changes in mental status, personality, and memory. Individuals can develop headaches, cranial nerve palsies, and even seizures. CT scans and MRIs performed with contrast may show lesions of the brain. Imaging studies show solitary or multiple lesions, the latter occurring in up to 50% of PCNSL cases. Toxoplasmosis is the most important differential diagnosis for brain lesions when PCNSL related to AIDS is suspected. Serology for toxoplasma antibody should be obtained before considering more invasive tests, such as a brain biopsy. An alternative procedure would be a lumbar puncture, as cytology can be obtained to evaluate for the presence of malignancy.[9]

Prognosis without therapy is extremely poor, with a mean survival of one to three months. Additional poor prognostic factors include age of 50 years or more, elevated serum lactate dehydrogenase, elevated cerebrospinal fluid protein concentration, and disease involving the periventricular region, basal ganglia, brainstem, and cerebellum.[12]

Invasive cervical cancer (ICC)

Squamous intraepithelial lesions (SIL), precursors to ICC, occur five times more often in people with HIV than in the general population.[13] Fortunately, early detection of cervical dysplasia is possible through Pap smears and targeted human papillomavirus (HPV) testing. HPV can lead to SIL or even ICC.[14] Table 3 reviews additional recommendations for prevention of cervical cancer.

Because there is a higher prevalence of SIL in HIV, the recommendations for screening are different than in the general population. Within the first year of an HIV diagnosis, experts recommend two Pap smear tests and cervical cytology screenings. The tests can be performed six months apart. If both of these are normal, then testing can be modified to just once a year. If testing shows ASC-H (atypical squamous cells—cannot rule out high-grade squamous intraepithelial lesion), LSIL (low-grade squamous intraepithelial lesion), or HSIL (high-grade squamous intraepithelial lesion), then some experts suggest that a colposcopy should be performed.[15]

Within the first year of an HIV diagnosis, experts recommend two Pap smear tests and cervical cytology screenings. The tests can be performed six months apart. If both of these are normal, then testing can be modified to just once a year.

Table 3: Prevention of cervical cancer in people with HIV[16, 14]

HPV vaccine: in non-vaccinated* men and women with HIV through the age of 26, give 3 doses (at 0, 1 and 6 months). In patients uninfected with HPV, the vaccine prevents cervical cancer. In patients already infected with an HPV type (e.g., HPV type 16), the vaccine does not protect against the development of cervical cancer caused by that HPV type, but can protect against cervical cancer caused by other HPV types (e.g., HPV type 18). *CDC recommends routine HPV vaccination for all girls and boys at 11–12 years of age.
Routine gynecology evaluations: including Pap smears to detect for HPV as well as cervical dysplasia.
Primary prevention: consistent use of barrier protection during sexual intercourse and reduction in the number of sexual partners.

Even after ICC is diagnosed, ART should be considered in the treatment of patients with HIV or AIDS. Although ART has not made an enormous impact in the incidence of cervical cancer—unlike non-Hodgkin lymphoma and Kaposi sarcoma—it may have a role in preventing the development of cervical dysplasia and decreasing recurrence of disease when combined with standard therapy, and possibly even converting lesions from high to low grade.[9]

Non-AIDS defining cancers

The cancers that are not considered AIDS-defining cancers are referred to as non-AIDS defining cancers. In the United States, the aging and growth of the population with HIV afforded by ART has resulted in an increase in non-AIDS defining cancers. In 1991–1995, less than 10% of cancers in people with HIV were non-AIDS defining, and in 2001–2005, this increased to 48.3%. About half of the cases were attributed to cancers of the anus, liver, lung, and Hodgkin lymphoma.[4]

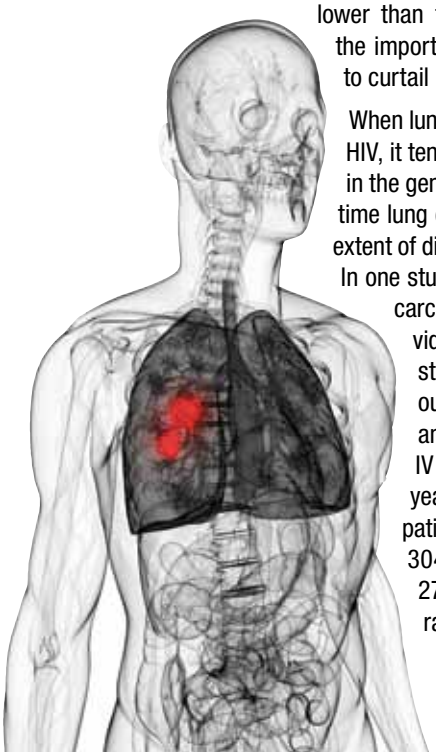
Lung cancer

Of all of the non-AIDS defining cancers, the one that causes the highest mortality is lung cancer. Compared to the general population, people with HIV have a 2–4 fold greater risk of developing lung cancer.[17] A meta-analysis comparing the incidence rates of lung cancer in the pre-ART and post-ART eras found a dramatic increase in disease. Before ART was introduced, the incidence of lung cancer in people living with HIV was 0.8 per 10,000 patient-years. The incidence increased to 6.7 per 10,000 patient-years following the introduction of ART—8.93 times higher.[18]

Smoking cessation website resources

- American Cancer Society: http://www.cancer.org/healthy/stayawayfromtobacco/guidetoquittingsmoking/index.htm
- American Heart Association, HIV and Smoking Cessation: http://www.heart.org/HEARTORG/Conditions/More/HIVandYourHeart/HIV-and-Smoking-Cessation_UCM_315431_Article.jsp
- CDC Quit Smoking: http://www.cdc.gov/tobacco/quit_smoking/
- NJ QuitLine: http://www.njquitline.org/treatment.html
- Smokefree.gov: http://www.smokefree.gov/

A Swiss cohort study found a high prevalence of tobacco abuse in patients with HIV (73%), as compared with matched controls. Amongst heavy smokers, there was a higher risk for lung cancer. Patients with HIV who quit were still at risk for lung cancer, but the likelihood was far lower than for active smokers—emphasizing the importance of smoking cessation efforts to curtail lung cancer in HIV.[19]



When lung cancer is diagnosed in those with HIV, it tends to present at an earlier age than in the general population. Additionally, by the time lung cancer is diagnosed, the stage and extent of disease is likely to be very advanced. In one study of non-small cell squamous cell carcinoma of the lung, 74% of individuals with HIV were diagnosed with stage IIIB and even stage IV disease out of a scale of severity between IA and IV. Survival rates for stage IIIB/IV were 25% at 1 year and 0% at 3 years. At the time of cancer diagnosis, patients had a mean CD4 cell count of 304 cells (range = 3–1,361) and only 27% of patients had undetectable viral loads.[17]

Case study 1

History

- A 56 year old Hispanic man diagnosed with HIV two years ago.
- His current antiretroviral regimen includes raltegravir (Isentress) and emtricitabine/tenofovir (Truvada). Approximately one month ago, he had a CD4 count of 500 and a viral load of < 20.
- The patient was referred to general surgery for further evaluation of a bothersome hernia. In preparation for the hernia surgery the following were ordered: electrocardiogram (EKG), chest radiograph (CXR) and coagulation studies (PT/INR).
- All of these studies were sent to the ordering physician, with copies (on the request of the patient) to his HIV provider.

Pertinent laboratory results

- EKG: normal sinus rhythm without any acute ST or T wave changes
- PT/INR: unremarkable
- CXR: showed a very large left-sided effusion

Initial management

- When the patient was notified of the CXR finding, he incidentally remarked that he had felt more dyspnea on exertion. He had smoked a pack of cigarettes/day for about 30 years, and was still smoking, albeit at a 1/2 pack per day.
- The patient was set up for an interventional radiology-guided aspiration of the left pleural effusion. Fluid was sent for cell count, culture, and review by pathology. Ultimately, the fluid culture did not reveal any bacteria; unfortunately, cytology showed presence of metastatic adenocarcinoma with lung cancer as the primary site.
- He underwent staging CT scans, which were notable for hepatic lesions felt to be malignant in nature and innumerable brain lesions.

Comments

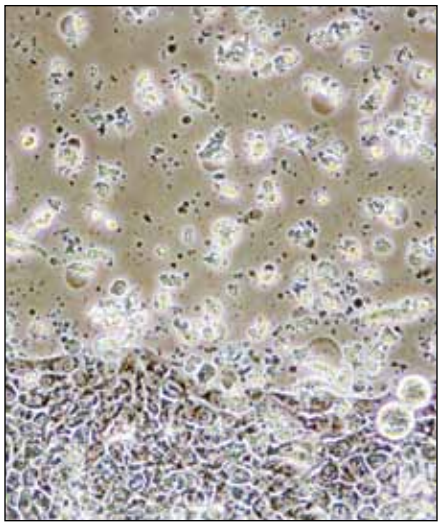
- This case illustrates that by the time lung cancer is diagnosed in patients with HIV, it can be at an advanced stage. There are no specific recommendations to screen for lung cancer, but HIV providers should continue to emphasize the importance of smoking cessation as a potential modifiable risk factor.

Hepatobiliary cancer

Hepatobiliary tract (liver, bile duct, and gallbladder) cancers tend to be aggressive and to recur even after treatment. In one analysis, researchers examined registry linkage data from the United States HIV/AIDS Cancer Match Study. They specifically calculated the standardized incidence ratios (SIRs) on risk of hepatobiliary cancer in HIV and AIDS in comparison with the general population. The study found a higher risk of hepatocellular carcinoma in AIDS as compared with HIV and non-HIV patients as well as an elevated SIR for other types of liver cancers along with tumors of the bile duct.[20]

Colon cancer

In the general population, a screening colonoscopy for colon malignancy is recommended at the age of 50, although it may be performed earlier, for example, due to family history. Currently, screening recommendations for patients with HIV are the same as for those who are HIV-negative. There has been little research on the extent to which screening for colorectal cancer occurs in patients with HIV. In one study at a Veterans Administration outpatient clinic, researchers examined colorectal screening measures, including fecal occult blood testing, flexible sigmoidoscopy, air contrast barium enema, and colonoscopy, in HIV-infected versus HIV-uninfected control patients. Compared to their HIV-uninfected cohorts, those with HIV were statistically less likely to have undergone at least one of these tests. In addition, control patients were more up-to-date with the colorectal cancer screening tests than those with HIV.[21]



Microscope view of colon cancer cells in tissue culture showing walls, nucleus and organelles.

In a different study, researchers examined the results of screening colonoscopies in asymptomatic patients with HIV older than 50 and found that colon cancer and pre-cancerous lesions were uncovered to a greater degree in HIV-infected individuals. Furthermore, adenomas of 6–9 millimeters were found more often in HIV patients, whereas hyperplastic polyps were found more often in controls. In the HIV cohort, diagnosis of colorectal adenocarcinoma occurred at a younger age, and the extent of the cancer tended to be more advanced—stage III or IV.[22]

Case study 2

History

- A 50 year old Korean-American woman has been living with HIV for the past ten years.
- She has been adherent to her antiretroviral regimen of emtricitabine/tenofovir/efavirenz. A year ago, her CD4 cell count was 650 and viral load was undetectable (<24 copies/ml). Because of her stellar numbers, she had become accustomed to seeing her HIV provider about two times a year, but cancelled her last visit because of a major snowstorm.
- Although she has a family doctor, she did not feel the need to see him on a routine basis. She instead presented to her HIV provider and incidentally was noted to have bloody stools as well as dyspnea on exertion.
- On history, the patient's mother had a rectal cancer, diagnosed at the age of 35.
- On physical examination, the patient looked more fatigued and less upbeat than normal. A rectal examination revealed no gross abnormalities.

Pertinent laboratory results

- Fecal occult blood: positive
- Historical data: hemoglobin—9.8 g/dl last year
- New laboratory data: hemoglobin—7 g/dl and microcytic anemia

Initial management

- As the patient had bloody stools and dyspnea on exertion, she was admitted to the hospital for further evaluation.
- For symptomatic anemia, she received packed red blood cell transfusions.
- The gastroenterology service evaluated the patient and felt that a diagnostic colonoscopy was necessary. Gross findings on the colonoscopy included polyps, which were biopsied.
- The patient received another transfusion, and was discharged with a hemoglobin of 10 g/dl as well as instructions to follow up with the gastroenterologist for results of the biopsies.
- Unfortunately, the pathology for the polyp came back as adenocarcinoma. As a result, the patient was referred to hematology/oncology for further management.

Comments

- This case demonstrates the utility of a colonoscopy to detect the etiology of bloody stools and to uncover tumors. Even if patients are not symptomatic, it is important to perform screening colonoscopies in all patients starting at the age of 50, as would be considered in the general population. In this particular patient, family history of a tumor at the age of 35 in a first-degree relative should have led to a screening colonoscopy earlier, and potentially, detection and removal of polyps before they became cancerous.

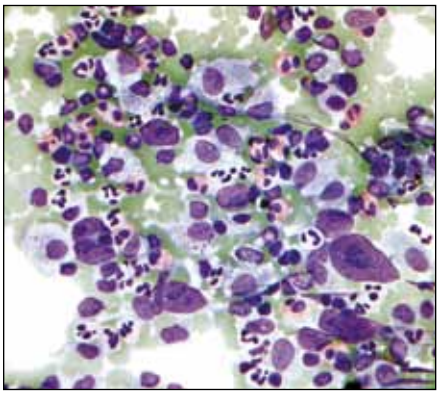
Anal cancer

Anal cancer is not commonly seen but it should be considered in men who have sex with men (MSM), especially those who engage in anal receptive intercourse.[9] Researchers studied rates of anal cancer in HIV infected versus uninfected individuals by using data from 10 cohorts in the United States and 3 cohorts in Canada. The highest incidence of anal cancer occurred in HIV-infected men who have sex with men: 131 per 100,000 person-years (the number of years that study participants have been under observation). In comparison, the incidence rate in HIV-infected men (who were not MSM) was 46 per 100,000 person-years and 30 per 100,000 person-years in HIV-infected women. While this study observed rates, there were limitations including lack of analysis on the extent of anal cancer screening, detection of HPV, quantification of tobacco abuse, and analysis of all sexual behaviors.[23]

Anal cancer screening is one way to screen for anal cancers and precancerous lesions, but it is not widely accepted. Advocates for screening believe that cytology is as effective for detecting anal disease as it is for cervical disease, but opponents point out that treatments for anal intraepithelial neoplasia often fail and there are no data suggesting that such treatment prevents cancer. Currently, national expert groups, including CDC and the Infectious Diseases Society of America, do NOT recommend routine anal cytology screening.[24] However, some local entities, such as the New York State Department of Health, recommend anal cytology for certain populations.[25]

Hodgkin disease

While not an AIDS-defining cancer, Hodgkin disease has been found in individuals with HIV to a greater extent than in the general population. On a histologic basis, Hodgkin disease can be further categorized into subgroups such as nodular sclerosis, mixed cellularity, and lymphocyte depletion. Patients with HIV are more likely to be diagnosed with mixed cellularity and lymphocyte depletion than nodular sclerosis, which is the most frequently seen type in those who are HIV-uninfected. Patients with HIV are more likely to be diagnosed with stage III and IV Hodgkin disease, which are the more advanced forms.



Micrograph showing Hodgkin's lymphoma (field stain). Copyright © 2011 Nephron. http://commons.wikimedia.org/wiki/File:Hodgkin_lymphoma_cytology_large.jpg

The disease can spread to extranodal sites, such as the bone marrow and liver. Such extranodal involvement, along with poor histologic subtype and advanced stage, are poor prognostic factors. These patients may not respond as well to treatment, or the therapeutic effects may not be as long-lasting.[9]

Prevention and screening

As cancer is too often detected at an advanced stage in people living with HIV, it is critical to ensure that prevention and screening tools are employed by clinicians. All patients with HIV or AIDS should be educated on preventive measures to reduce their risks for cancer. Key steps to prevent cancer or to detect it early include:[5, 8]

1. Every patient should be placed on ART, as this has been shown to decrease the risks of Kaposi sarcoma and non-Hodgkin lymphoma. Guidelines for treatment with ART are comprehensively reviewed in: *http://aidsinfo.nih.gov/guidelines/html/1/adult-and-adolescent-treatment-guidelines/0/.*
2. Every patient should be counseled on the risks of tobacco abuse and provided with advice and support for smoking cessation. Smoking is linked to cancers of the bladder, cervix, esophagus, kidney, mouth, nasal cavity, lung, pancreas, stomach, and throat.
3. Every patient should be counseled on the risks of alcohol abuse and provided with support to reduce alcohol consumption. Excessive alcohol intake has been implicated in cancers of the breast, esophagus, larynx, liver, and pharynx.
4. Every patient should be screened for hepatitis B and C, as these viruses are risk factors for hepatocellular carcinoma. If the patient is positive for hepatitis B and/or C, then staging laboratory studies should be performed. Treatment for hepatitis B and C should be considered. If there is non-immunity to hepatitis B, vaccinate the patient.
   - **Guidelines for treatment of HIV and hepatitis B:** *http://aidsinfo.nih.gov/guidelines/html/1/adult-and-adolescent-arv-guidelines/25/hiv-hbv*
   - **Guidelines for treatment of HIV and hepatitis C:** *http://aidsinfo.nih.gov/guidelines/html/1/adult-and-adolescent-arv-guidelines/26/hiv-hcv*
5. All HIV-infected men and women up to the age of 26 should receive the 3-shot vaccine series against HPV, as this virus is a risk factor for cancer. Women should receive screening Pap smears and mammograms, as well as annual gynecology evaluations.
6. All patients should be referred for screening colonoscopies by the age of 50, or as indicated by symptoms and family history. All family histories should be reviewed for cancer and age at cancer diagnosis.
7. In addition, every patient should be counseled on safer sex. Counseling should be based on a sexual history and guidance framed around the "Five P" approach—partners, prevention of pregnancy, protection from STDs, practices, and past history of STDs. For more information on STD and HIV prevention counseling see CDC's Sexually Transmitted Diseases Treatment Guidelines, page 3. Available at: *http://www.cdc.gov/mmwr/pdf/rr/rr5912.pdf*.

Anal cytology screening (anal pap) in HIV infected women and men who have sex with men is not considered standard of care but is performed in some centers. Clinical trials are ongoing.[26]

Garden State Infectious Diseases Associates, P.A., and Health Maintenance

Nurses and physicians at Garden State Infectious Disease Associates routinely implement the following measures to decrease the risks of cancer in our patients:

1. Nurses ask about tobacco use at every clinic visit. If smoking is ongoing, the physician counsels on smoking cessation.
2. Annual Pap smears and mammograms are requested and tracked.
3. Hepatitis B and C are checked, and vaccines are provided if the patient is hepatitis B (and/or hepatitis A) antibody-negative.
4. Patients are referred for screening colonoscopies at the age of 50, as clinically indicated, or based on family history.

Prognosis and mortality

Researchers conducted a retrospective study of HIV patients in care at an urban center who were diagnosed with cancer over a ten-year period from 2000–2010. In total, there were 447 patients in whom 470 cancers were diagnosed. The median age at the first cancer diagnosis was 50. The majority of patients were male (79%) and African-American (85%). Most patients (81%) were smokers, while a history of either alcohol or intravenous drug use was common at 49% and 46%, respectively. Forty-three percent of patients were co-infected with hepatitis C. There was a higher prevalence of non-AIDS defining cancers.[27]

The cancers diagnosed in this cohort were aggressive in nature. For example, the median cancer stage at diagnosis was already advanced at stage III. The type of treatment included chemotherapy (50%), radiation (37%), and surgery (25%). Mortality rates were higher than expected: 42% at 2 years, 33% at 1 year and 7% at 1 month. Mortality tended to be from complications due to the tumors themselves, not from HIV.[27]

Conclusions

Clients with HIV are living longer, and like the general population are at risk for age-related problems, including tumors. While AIDS-defining cancers are on the decline, non-AIDS defining malignancies are rising. In certain cancers, the age at diagnosis may be younger than in the non-HIV population, and the disease may be at an aggressive or more advanced stage by the time the tumor is detected. This is why there is such an urgency to educate patients about prevention and early screening. Important cancer prevention measures include complete tobacco cessation, screening colonoscopies, Pap smears, hepatitis B/C screening and treatment, and ART. Lastly, there is a need for better screening methods so that tumors are detected at an earlier stage when prognosis is more optimistic.

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    - Inquire about anal symptoms, such as itching, bleeding, diarrhea, or pain
    - Perform a visual inspection of the perianal region
    - Perform a digital rectal examination

    They also recommend that clinicians refer women with cervical HSIL and any patient with abnormal anal physical findings for high-resolution anoscopy and/or examination with biopsy of abnormal tissue. Obtain anal cytology at baseline and annually in the following HIV-infected populations:
    - Men who have sex with men
    - Any patient with a history of anogenital condylomas
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CE CONTINUING EDUCATION

Epidemiology, Screening, Diagnosis, and Prognosis for Cancer in HIV/AIDS

POST TEST — Page 1 of 1

Questions refer to the content of the article and the notes that follow. To receive CME/CE/CEU credit: complete exam, registration, and evaluation forms on-line at *http://ccoe.umdnj.edu/catalog/* or fill in the forms on the following pages, and mail or fax to UMDNJ-CCOE (see Registration Form).

1. The AIDS-defining malignancies include all of the following **EXCEPT**:

   A. Non-Hodgkin lymphoma

   B. Kaposi sarcoma

   C. Lung cancer

   D. Invasive cervical cancer

2. Which of the following is a **FALSE** statement?

   A. Tobacco abuse is a risk factor for esophageal cancer.

   B. Within the first year of an HIV diagnosis, experts recommend two Pap smear tests and cervical cytology screening.

   C. The HPV vaccine is contraindicated in HIV as it is a live vaccine.

   D. EBV has been implicated in the pathogenesis of primary central nervous system lymphoma.

3. Which of the following does **NOT** explain why people with HIV may have an increased risk of cancer?

   A. They have weakened immune systems.

   B. They have had long term use of antiretroviral medications.

   C. They are more likely than the general population to be co-infected with cancer-related viruses, such as HHV-8, EBV, HPV or hepatitis B/C.

   D. They are more likely than the general population to have used excessive tobacco or alcohol.

4. Studies on people with HIV diagnosed with colon cancer indicate that diagnosis more commonly occurs at:

   A. Stage 0

   B. Stage I

   C. Stage II

   D. Stage III

5. There is an increased risk of cancer in people with HIV. Many reasons can account for this risk, including all of the following **EXCEPT**:

   A. Co-infection with hepatitis B

   B. Co-infection with human papillomavirus

   C. Heavy tobacco abuse

   D. Co-infection with herpes simplex virus (HSV-I)

6. In patients with AIDS, the median age at diagnosis of lung cancer is:

   A. 30 years old

   B. 40 years old

   C. 50 years old

   D. 60 years old

7. In Kaposi sarcoma, the following is a **FALSE** statement:

   A. The incidence of Kaposi sarcoma in people with HIV has fallen.

   B. Human herpes virus-6 is the etiologic agent.

   C. Pulmonary Kaposi sarcoma may represent late disease.

   D. The gastrointestinal tract, oral mucosa, lymph nodes, liver, and spleen may be involved in Kaposi sarcoma.

8. Which of the following is **UNLIKELY** to reduce risk of cancer in people with HIV:

   A. Delaying initiation of antiretroviral therapy.

   B. Supporting a patient to stop smoking.

   C. Treating hepatitis B.

   D. Ensuring patients undergo annual cervical Pap smear tests and cervical cytology screening.

9. People with HIV who have cancer are **more likely** to die from cancer progression than from HIV infection.

   A. True

   B. False

10. Antiretroviral therapy has lowered rates of certain types of cancers, **EXCEPT** for:

    A. Invasive cervical cancer

    B. Kaposi sarcoma

    C. Non-Hodgkin lymphoma

Epidemiology, Screening, Diagnosis, and Prognosis for Cancer in HIV/AIDS

REGISTRATION FORM

CCOE Center for Continuing & Outreach Education

In order to obtain continuing education credit, participants are required to:

(1) Read the learning objectives, review the activity, and complete the post-test.

(2) Complete this registration form and the activity evaluation form on the next page. Record your test answers below.

(3) Send the registration and evaluation forms to: UMDNJ-Center for Continuing and Outreach Education
• VIA MAIL: PO Box 1709, Newark, NJ 07101-1709 • VIA FAX: (973) 972-7128

(4) Retain a copy of your test answers. Your answer sheet will be graded and if you achieve a passing score of 70% or more, a credit letter and the test answer key will be mailed to you within four (4) weeks. Individuals who fail to attain a passing score will be notified and offered the opportunity to complete the activity again.

Online option: This activity will be posted at *http://ccoe.umdnj.edu/catalog* where you may obtain a credit letter upon successful completion of the online post-test and evaluation. ***Please note: CE credit letters and long-term credit retention information will only be issued upon receipt of completed evaluation form.***

SELF-ASSESSMENT TEST *Circle the best answer for each question.*					
1. A B C D	**3.** A B C D	**5.** A B C D	**7.** A B C D	**9.** A B	
2. A B C D	**4.** A B C D	**6.** A B C D	**8.** A B C D	**10.** A B C	

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Indicate the type of continuing education credit you wish to obtain as a result of your participation in this activity.

☐ **Nurses:** 1.03 CNE Contact Hours. Contact Hours Claimed: _____

☐ **Physicians:** *1.0 AMA PRA Category 1 Credit™* : Credits Claimed: _____

☐ **General:** Continuing Education Units (CEUs) (up to 0.1) Claimed: _____

One credit/contact hour for each hour of participation. Continuing Education Units: one unit per ten hours of participation.
I attest that I have completed this activity as designed. I will report the number of credits/contact hours claimed during my filing of continuing education credit with professional organizations, licensing boards, or other agencies.

Signature Date

Release date: December 1, 2012 • Expiration date: November 30, 2014 • Credit for this activity will be provided through November 30, 2014.
A CE credit letter will be mailed to you in approximately 4 weeks.

UMDNJ-Center for Continuing & Outreach Education
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CE Activity Code: 14HC06 — This form may be photocopied.

Epidemiology, Screening, Diagnosis, and Prognosis for Cancer in HIV/AIDS

EVALUATION FORM

CE CONTINUING EDUCATION

The planning and execution of useful and educationally sound continuing education activities are guided in large part by input from participants. To assist us in evaluating the effectiveness of this activity and to make recommendations for future educational offerings, please take a few moments to complete this evaluation form. Your response will help ensure that future programs are informative and meet the educational needs of all participants.

UMDNJ CCOE Center for Continuing & Outreach Education

Please note: CE credit letters and long-term credit retention information will only be issued upon receipt of completed evaluation form.

PROGRAM OBJECTIVES: Having completed this activity, are you better able to:

		Strongly Agree				Strongly Disagree
Objective 1:	Recognize the changing epidemiology of cancer in people with HIV, including the decline in AIDS-defining cancers as well as the rise in non-AIDS defining cancers.	5	4	3	2	1
Objective 2:	Seek opportunities to screen for and diagnose cancer in people with HIV/AIDS.	5	4	3	2	1
Objective 3:	Ensure that all patients with HIV/AIDS are provided with cancer prevention education.	5	4	3	2	1

OVERALL EVALUATION:	Strongly Agree				Strongly Disagree
The information presented increased my awareness/understanding of the subject.	5	4	3	2	1
The information presented will influence how I practice.	5	4	3	2	1
The information presented will help me improve patient care.	5	4	3	2	1
The authors demonstrated current knowledge of the subject.	5	4	3	2	1
The program was educationally sound and scientifically balanced.	5	4	3	2	1
The program avoided commercial bias or influence.	5	4	3	2	1
The self-assessment was appropriate and helpful.	5	4	3	2	1
Overall, the program met my expectations.	5	4	3	2	1
I would recommend this program to my colleagues.	5	4	3	2	1

Based on the content of the activity, what will you do differently in the care of your patients? (check one)

- ☐ Implement a change in my practice.
- ☐ Seek additional information on this topic.
- ☐ Do nothing differently. Current practice reflects activity recommendations.
- ☐ Do nothing differently as the content was not convincing.
- ☐ Do nothing differently. System barriers prevent change.
- ☐ Not applicable. I do not see patients in my current position.

If you anticipate changing one or more aspects of your practice as a result of your participation in this activity, please provide us with a brief description of how you plan to do so.

_____

May we contact you in two months to see how you are progressing on the changes indicated above?

☐ Yes. Please provide your email address. _____

☐ No. I do not wish to participate participate in the follow-up assessment.

If you are not able to effectively implement what you learned at this activity, please tell us what the system barriers are (e.g., reimbursement issues, managed care rules, formulary decisions, countervailing practice guidelines, etc).

_____

Please list any topics that you would like addressed in future educational activities.

_____

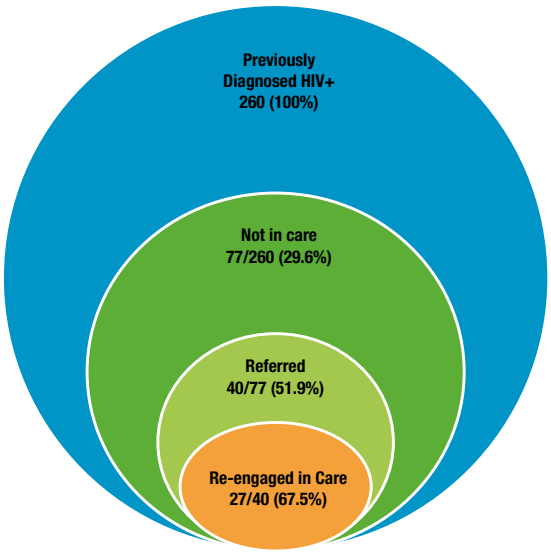
CE Activity Code: 14HC06 — This form may be photocopied.

New Jersey's Impression on AIDS 2012 (continued from page 1)

continued from page 1

"Reengagement into medical care from an urban emergency department" was authored by Debbie Mohammed, as well as Mumah Tawe, Jared Khan, Sandra Scott, and Michael Jaker from UMDNJ working in collaboration with Sindy Paul from NJDOH. From July to December 2011, patients aged 18–64 years seeking services in the Emergency Department at University Hospital in Newark were routinely offered rapid HIV testing. Of the 9,099 people offered HIV testing, more than half (52.6%) declined; 5.4% (n=260) of those who declined testing, did so because they already knew that they were HIV-infected.

Figure 1: Percentage of patients reengaged in care



Mohammed, Debbie. Percentage of patients re-engaged.
http://pag.aids2012.org/abstracts.aspx?aid=12445

According to focus group participants, barriers to HIV testing included:

- **Fear.** That is, fear of the unknown, fear of needles, of their results, of death, of being stigmatized because of HIV infection, of pain and suffering, of having to disclose names of sexual partners, of having to change sexual behavior
- Not caring
- Not having time to test
- Lack of transportation
- Confidentiality concerns
- Limited availability of local health departments to offer testing

Facilitators of HIV testing included:

- Needing to know HIV status
- Testing locations that offered privacy or were outside of the community
- Having oral and rapid test options
- Concerns about past sexual behavior
- Wanting to maintain health and safety

In Ms. Mohammed's third poster, "***Anonymous unlinked seroprevalence surveys: an evaluation tool for prevention efforts"*** (authored with Mumah Tawe, Jared Khan, Michael Jaker, Sandra Scott from UMDNJ as well as Charlotte Sadashige and Sindy Paul from the NJDOH), she concluded that HIV seroprevalence among patients at the University Hospital Emergency Department (Newark) decreased by 37.5% from 2002 to 2008. This finding is based on Anonymous Unlinked HIV Surveys using discarded blood specimens, which found an overall 10.4% seropositivity in 2002 and 6.5% in 2008. Interestingly the seroprevalence fell for all racial/ethnic groups, gender, and ages with the exception of persons aged 55-64 which increased slightly from 6.3% to 7.6%.

HIV seroprevalence among patients at the University Hospital Emergency Department (Newark) decreased by 37.5% from 2002 to 2008.

HIV-infected patients who self-reported that they were not in medical care (77 of the 260 who reported that they were HIV-infected) were provided appointments for the hospital's Infectious Disease Clinic. Reengagement into medical care is important to prevent disease transmission and decrease morbidity, mortality, and healthcare expenditures. Figure 1 is a pictorial representation of the percentage of patients reengaged in care.

On the topic of HIV testing and barriers to testing, S. Chen from UMDNJ collaborated with researchers in Florida and Kentucky (***"HIV testing barriers, facilitators and behavioral change for rural African American men"***) to examine barriers, facilitators and possible behavior change associated with HIV testing and disclosure of HIV test results among rural African American men who self-identify as heterosexual. Although the study took place in two rural counties and one urban county in North Florida, its findings may still be applicable to settings in New Jersey.

Barbara Greenberg from UMDNJ's Dental School in Newark was one of seven authors on an oral abstract (***"Dentist's willingness to offer oral HIV rapid testing: results from a nationally representative survey"***) presenting the results of a nationally representative survey of general dentists that examined barriers and facilitators to offering oral HIV rapid testing at chair side (n=1802, 70% response rate). Their study concluded that dentists appear potentially willing to perform HIV screening within general practice settings. Patients' and colleagues' perceptions appear important in shaping dentists' attitudes and likely behavior concerning this service.

The last poster in the epidemiology category (***"Cancer among children with perinatal exposure to HIV and antiretroviral medications, New Jersey, 1995-2010"***) is a study by researchers at CDC

working in collaboration with Sindy Paul, Abdel Ibrahim, John Ryan, Miranda Chan, and Xiaoling Niu at the NJDOH. They found that children born to HIV-infected women in New Jersey between 1995 and 2008 were no more likely to develop cancer than the general New Jersey and United States population less than 15 years old. This study—which cross-referenced names of children who were HIV-exposed listed in the Enhanced HIV/AIDS Reporting System (eHARS) with data from the New Jersey State Cancer Registry—identified four cases of cancer among 3,087 HIV-exposed children. The study, which did not include children with HIV, alleviates concerns about cancer risk among infants perinatally exposed to ARVs.

Clinical science

At least five of New Jersey's papers came out of the HIV Prevention Trials Network (HPTN) 064 study, providing much-needed insight into the incidence of HIV in this group of young at-risk women as well as HIV-related risk factors. Other papers in this category include one on measuring adherence and two on mental health of people with HIV.

In their study (***"Self-reported adherence measures: utility and assessment"***) Dean Wantland, William Holzemer, Sue Willard, Teri Lindgren, and Lucille Sanzero Eller, all from Rutgers College of Nursing in Newark used three self-report measurement scales to determine patient adherence to antiretroviral treatment (ART) adherence: 30-day-adherence recall scale (30Arec), 30-day-adherence self-rating (30ASR), and number of missed medications (MM). Given that only 19% of 1,414 patients on ART showed 100% adherence for the combined three-scale total, the authors noted the lack of consistency in the measurement scales. In their conclusion they stated that "being so variable, but convenient to obtain, self-reported adherence levels should be confirmed with the patient both in clinical and research venues." In reference to findings specific to adherence, interestingly, the authors reported that there was no significant difference in adherence by regimen type or number of years taking medications.

Given that depressive symptoms in people living with HIV (PLHIV) are associated with poor treatment adherence, risky behaviors and poorer outcomes, a second paper by the Rutgers College of Nursing group—this one presented by Lucille Sanzero Eller and included Dean Wantland and William Holzemer as authors (**"Depressive symptoms, self-esteem, self-efficacy and self-compassion in people living with HIV"**)—concluded that self-care constructs, including evaluation of self-worth (self-esteem), self-efficacy in managing HIV (chronic disease self-efficacy), and being kind/non-judgmental to oneself (self-compassion) may be related to depressive symptoms in PLHIV. The authors reviewed a convenience sample of 2,182 PLHIV enrolled from HIV clinics and service organizations in the United States, Canada, Puerto Rico, Namibia, China, and Thailand from February 2010 to July 2011. Their study found that those with depressive symptoms were significantly younger (45.4 vs. 47.4 years); female or transgender (32.3% vs. 26.8%), had less education (28.5% vs. 19.0% less than high school) and inadequate income (16.9% vs. 28.8% adequate).

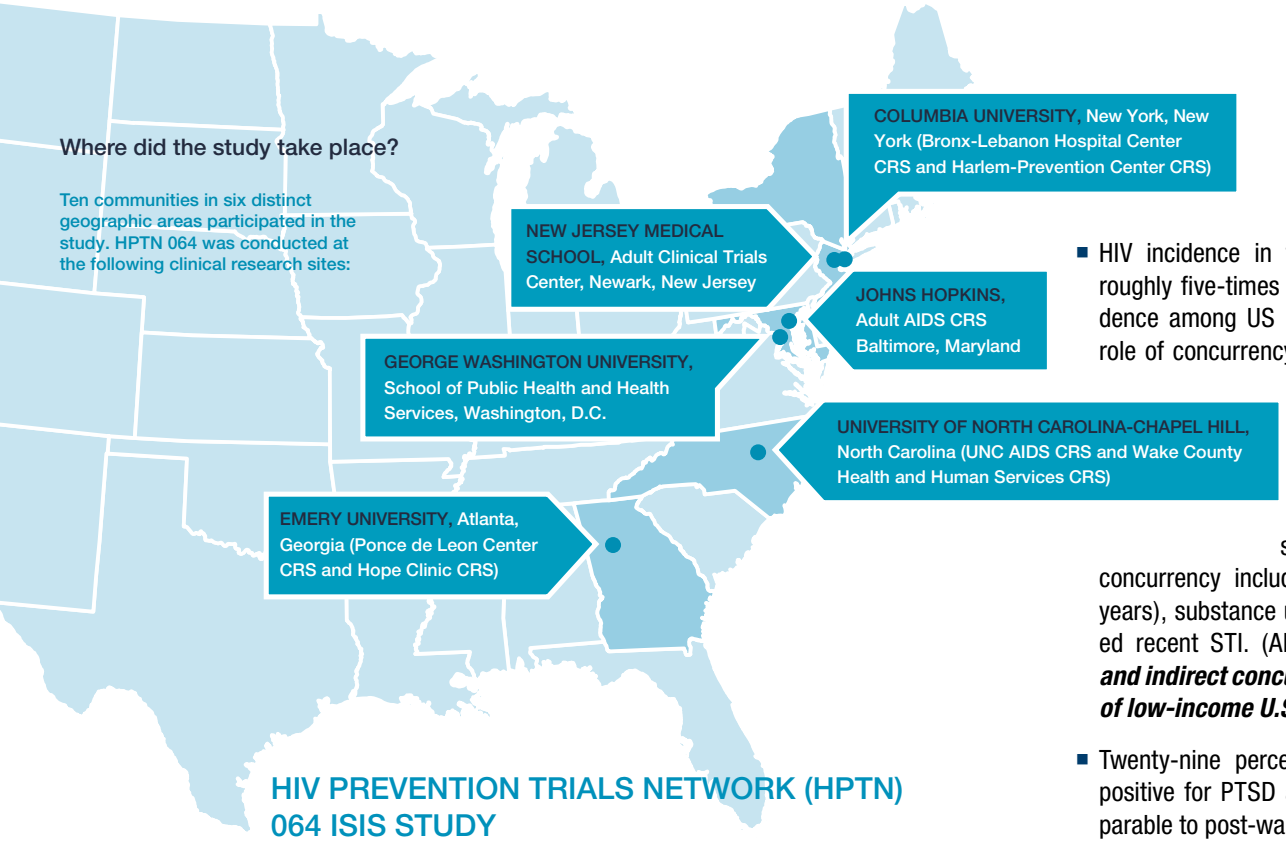
Another finding from the same study (**"Impact of HIV stigma on disclosure of HIV status"**) reported that participants with poorer physical or mental health or with depressive symptoms reported higher levels of HIV stigma. There were significantly higher levels of HIV stigma reported for those who reported they had disclosed their HIV status to their partner, children, relatives, neighbors, friends, or community. Providers are reminded that requesting people with HIV to disclose has the potential to increase the amount of perceived HIV stigma they receive and may have a negative impact on their perceived physical and mental health.

Sally Hodder from the University of Medicine and Dentistry New Jersey (UMDNJ) collaborated with researchers in eight other sites across the United States in the ***HPTN 064, Women's HIV Seroincidence Study (ISIS)***. The study recruited women ages 18-44 years in ten US communities (two of which were in Newark) characterized by high rates of HIV and poverty. Of the 2,099 women, none was diagnosed with HIV at the beginning of the study, 88% were Black, mean age was 29 years, and 44% had annual household income <$10,000). Findings from ISIS include the following:

- In the six months prior to study enrollment, ISIS participants had high rates of individual and partner risk (a median of 2 partners, 88% reported having at least one high risk male partner, and 31% were in concurrent partnerships—when the woman or her partner has more than one partner at a time), including high rates of unprotected anal sex (38% reported anal sex, 80% of which was unprotected at last episode). Women who reported high risk behaviors were more likely to: not know their last partner's HIV status, exhibit symptoms of depression or post-traumatic stress disorder (PTSD) and binge drink—suggesting the need to combine HIV risk reduction with mental health services for women at risk for HIV. (Abstract entitled: ***"Correlates of individual and partner sexual risk behaviors in US women participants in HPTN 064."***)

Children born to HIV-infected women in New Jersey between 1995 and 2008 were no more likely to develop cancer than the general New Jersey and United States population less than 15 years old.

New Jersey's Impression on AIDS 2012 (continued from page 31)



HIV PREVENTION TRIALS NETWORK (HPTN) 064 ISIS STUDY

STUDY PARTICIPANTS

2,099
WOMEN

18–44
YEARS OLD

88%
BLACK

12%
HISPANIC/ LATINA

- HIV incidence in this group was 0.24%, roughly five-times CDC estimated HIV incidence among US black women. Given the role of concurrency in driving high rates of sexually transmitted infections (STIs) including HIV among black US women, the study found that factors associated with partner concurrency include: younger age (18-26 years), substance use, and > 1 self-reported recent STI. (Abstract entitled: ***"Direct and indirect concurrency among a cohort of low-income U.S. women."***)

- Twenty-nine percent of women screened positive for PTSD at baseline, this is comparable to post-war veterans and four times higher than lifetime prevalence in the general population. Factors independently associated with having PTSD included childhood abuse, ongoing abuse, food insecurity, forgone healthcare, and being in poor to fair health. Having social support (≥ 3 friends) was protective. Those with PTSD were more likely to use drugs at least weekly and had an increased risk of reporting an STI at 6 months, known correlates of HIV risk. (Abstract entitled: ***"High rates of post-traumatic stress disorder among a cohort of low-income U.S. women in high HIV prevalence communities."***)

Providers are reminded that requesting people with HIV to disclose has the potential to increase the amount of perceived HIV stigma they receive and may have a negative impact on their perceived physical and mental health.

- Women enrolled in the ISIS study decreased their substance use frequency during the 6 to 12 months of the study. Women with lower baseline incomes were more likely to decrease their substance use frequency (≤$10,000 versus >$20,000). (Abstract entitled: ***"Substance use patterns and changes over time in a cohort of high-risk heterosexual women in the United States."***)

- In self-administered, semi-quantitative anonymous exit interviews at their last study visit, 92% of ISIS study participants reported interest in participating in a future HIV prevention studies, 79% reported their experience in this study made them change their behavior in some way, 73% reported increased condom use, 70% decreased drug use, and 66% decreased alcohol use. Authors (Shobha Swaminathan, Rondalya DeShields, Eileen Rios, C. Torres, K. Abbas and Sally Hodder) suggested that frequent study contact with HIV testing and counseling may have resulted in a decrease in risk behaviors. (Abstract entitled: ***"Reported behavior change and attitudes on prevention studies in Newark"***.)

Program design

Anushua Sinha presented a paper (**"Cost-effectiveness of test and treat prevention in a high HIV prevalence U.S. city"**) on behalf of her colleagues—Francesca Escaleira and Sally Hodder who are also from UMDNJ, Ruthie Birger and Bryan Grenfell from Princeton University, and Timothy Hallet from Imperial College London. The paper used mathematical modeling to assess cost-effectiveness of three test-and-treat strategies:

- **Intervention 1:** increased HIV testing coverage
- **Intervention 2:** increased HIV testing coverage + case management
- **Intervention 3:** increased HIV testing coverage + case management + universal ART

The authors found that for Newark—which has one of the most severe HIV epidemics in the United States—Interventions 1, 2, and 3 averted a median of 142, 581, and 658 (respectively) incident cases per year. These interventions also averted 162, 826, and 901 (respectively) HIV-related deaths per year. They concluded that test-and-treat strategies, particularly testing combined with case management with or without universal ART, may substantially decrease HIV transmission in Newark, prevent HIV-related deaths, and do so in a cost-effective fashion.

Bob Baxter, North Jersey Community Research Initiative (NJCRI) in Newark, is the only New Jersey AIDS 2012 author (**"First federal support for community-based syringe exchange programs: a panel presentation by SAMHSA grantees"**) employed by a non-governmental organization. The paper—co-authored with colleagues from Delaware, Illinois, Connecticut, New York and from SAMHSA—reported on 2010 SAMHSA-funded programs (including one at NJCRI) that used Federal funds to support initiatives that make direct referrals from existing syringe exchange programs (SEPs) to treatment. Each of the SAMHSA sites expanded and enhanced their existing services by collaborating with local or on-site SEPs. Preliminary data suggest these 10 programs are more likely to engage injection drug users, increase access, reduce barriers and improve overall health outcomes than programs that remain unaffiliated with SEPs. Comparison data showed increases in abstinence, social connectedness and stable housing and decreases in arrests. Participants were 3% less likely to inject drugs, 2.5% less likely to have unprotected sex, and 96% less likely to have sex with an HIV positive individual.

Global HIV

At least two individuals working for universities in New Jersey presented posters describing work conducted overseas.

Donald R. Hoover, who is based Rutgers University in New Brunswick published two papers (**"Trends in AIDS defining cancers during scale-up of ART in Rwanda: 2007-2011"** and **"Epidemiology of AIDS defining and non-AIDS defining malignancies before and during HAART era in southern Rwanda"**) with researchers in New York, London, as well as Kigali and Huye-Butare in Rwanda. Authors concluded that during the scale-up of ART in Rwanda from 2007–2011, the proportion of all cancers that were Kaposi's Sarcoma (KS) and non-Hodgkin Lymphoma (NHL) declined significantly. However, cervical cancer showed a statistically non-significant increase. The authors found significant reductions in AIDS-defining cancers (ADCs)—which include KS and NHL—relative to non-ADCs. These findings are similar to those described in non-African settings, and suggest that the burden of KS and NHL, but not cervical cancer, will decrease with continued scale up of ART. For more on this topic, refer to the article entitled *"Epidemiology, Screening, Diagnosis, and Prognosis for Cancer in HIV/AIDS"* (starting on page 18) in this edition of AIDSLine.

WE-ACTx is a community-based initiative to increase Rwandan women's and children's access to HIV testing, care, treatment and support, in particular to help survivors of the 1994 genocidal rape and sexual violence.

By March 2011, the transition plan was successfully executed with no disruption in services or facility closures, making Guyana the first PEPFAR-supported country to assume all functions of its HIV program previously supported by technical assistance partners.

Virginia Allread and her colleagues Nicole Jordan-Martin, Deborah Storm and Andrea Norberg at the FXB Center, School of Nursing at UMDNJ (**"Exit planning and transition of HIV care and treatment services: a case study from Guyana"**) provided an overview of the FXB Center's work with the Ministry of Health and CDC in Guyana between 2005 and 2011 to establish and scale-up comprehensive HIV care and treatment in that country's public sector. The last three years focused on transitioning services to Ministry of Health leadership and included initiatives to assess, strengthen and expand human resource capacity through training and mentoring and post-transition monitoring. By March 2011, the transition plan was successfully executed with no disruption in service delivery or facility closures, making Guyana the first President's Emergency Plan for AIDS Relief (PEPFAR) supported country to assume all functions of its HIV program previously supported by technical assistance partners. ❖

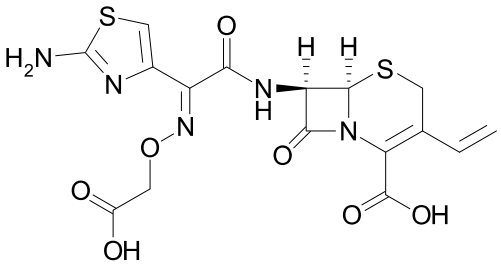
CDC Updates Gonorrhea Treatment Guidelines

In an effort to avert a public health crisis

Antibiotic resistance is a problem clinicians have battled in the treatment of gonorrheal infection. The bacteria has grown resistant to every drug ever used to treat it, including sulfonamides, penicillin, tetracycline, and most recently fluoroquinolones. Only the cephalosporins—cefixime and ceftriaxone—are left to effectively treat the disease.

Now, evidence from CDC's Gonococcal Isolate Surveillance Project suggests that cefixime is becoming less effective in treating gonorrhea. These findings led CDC to stop recommending cefixime as a first-line treatment option for gonorrhea in the United States. The updated guidelines were published in CDC's *Morbidity and Mortality Weekly Report* dated August 10, 2012.

Chemical structure of cefixime



"As cefixime is losing its effectiveness as a treatment for gonorrhea infections, this change is a critical preemptive strike to preserve ceftriaxone, our last proven treatment option," said Kevin Fenton, MD, director of the CDC's National Center for HIV/AIDS, Viral Hepatitis, STD and TB Prevention. "Changing how we treat infections now may buy the time needed to develop new treatment options."

The change marks an end to CDC recommending oral antibiotic treatment as the first line of defense for gonorrhea, and now instead recommends that infections be treated with the injectable antibiotic ceftriaxone in combination with one of two other oral antibiotics (see box).

Gonorrhea is a sexually transmitted infection that is a major cause of pelvic inflammatory disease, ectopic pregnancy, and infertility and can facilitate HIV transmission. CDC estimates there are more than 700,000 gonorrhea infections each year in the United States; it is the United States' second most commonly reported notifiable infection.

Updated recommended treatment regimens for gonococcal infections

Uncomplicated gonococcal infections of the cervix, urethra, and rectum

Recommended regimen

- Ceftriaxone 250 mg in a single intramuscular dose PLUS
- Azithromycin 1 g orally in a single dose OR
- Doxycycline 100 mg orally twice daily for 7 days*

Alternative regimens if ceftriaxone is not available:

- Cefixime 400 mg in a single oral dose PLUS
- Azithromycin 1 g orally in a single dose OR
- Doxycycline 100 mg orally twice daily for 7 days* PLUS
- Test-of-cure in 1 week

Alternative regimen if patient has severe cephalosporin allergy:

- Azithromycin 2 g in a single oral dose PLUS
- Test-of-cure in 1 week

Uncomplicated gonococcal infections of the pharynx

Recommended regimen

- Ceftriaxone 250 mg in a single intramuscular dose PLUS
- Azithromycin 1 g orally in a single dose OR
- Doxycycline 100 mg orally twice daily for 7 days*

** Because of the high prevalence of tetracycline resistance among Gonococcal Isolate Surveillance Project isolates, particularly those with elevated minimum inhibitory concentrations to cefixime, the use of azithromycin as the second antimicrobial is preferred.*

CDC Updates Gonorrhea Treatment Guidelines

Healthcare providers are on the front lines in the fight against gonorrhea and play a critical role in the response. To further guard against the threat of drug resistance, providers should closely monitor for ceftriaxone treatment failure. According to the new guidelines, providers should:

- Take a sexual history (see the June 2012 issue of New Jersey *AIDSLine*, available at http://fxbcenter.org/education/index.html or CDC's 2010 *Sexually Transmitted Diseases Treatment Guidelines*, available at http://www.cdc.gov/std/treatment/2010/). This will help the provider know which STDs to test the patient for and at which anatomic sites.
- Make every effort to evaluate and treat all patients' sex partners from the previous 60 days.
- Treat all patients diagnosed with gonorrhea promptly according to CDC's updated treatment guidelines.
- Closely monitor for ceftriaxone treatment failure. Patients who have persistent symptoms should return one week after treatment for a test-of-cure using a culture-based gonorrhea test. Ensure that the patient's sex partners from the preceding 60 days are evaluated promptly with culture* and treated as indicated.
- Ensure that patients treated with either of the alternative treatment options (see box on page 34) return one week after treatment for a test-of-cure using a culture-based test* or a NAAT for *N. gonorrhoeae* if culture is not readily available.
- Report any suspected treatment failure to local or state public health officials within 24 hours.

"As cefixime is losing its effectiveness as a treatment for gonorrhea infections, this change is a critical pre-emptive strike to preserve ceftriaxone, our last proven treatment option," said Kevin Fenton, MD, director of the CDC's National Center for HIV/AIDS, Viral Hepatitis, STD and TB Prevention. "Changing how we treat infections now may buy the time needed to develop new treatment options."

* All positive cultures for test-of-cure should undergo phenotypic antimicrobial susceptibility testing.

CDC. *Morbidity and Mortality Weekly Report*. "Update to CDC's Sexually Transmitted Diseases Treatment Guidelines, 2010: Oral Cephalosporins No Longer a Recommended Treatment for Gonococcal Infections". Accessed August 30, 2012 at: http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6131a3.htm?s_cid=mm6131a3_w

CDC. *CDC Fact Sheet: Gonorrhea Treatment Guidelines, Revised Guidelines to Preserve Last Effective Treatment Option.* Accessed August 30, 2012 at: http://www.cdc.gov/nchhstp/Newsroom/docs/2012/GonorrheaTreatmentGuidelinesFactSheet8-9-2012.pdf

Tuberculosis in New Jersey: Jigna's Story

Adapted from New Jersey Medical School Global Tuberculosis Institute, "Finding my Voice" TB and Cultural Competency, Notes from the Field, Issue #14, Spring 2012

I asked Jigna Rao, given her experience, what would be her primary message to AIDSLine readers. She responded, without hesitation, by stating that she would like to ask clinicians to consider a tuberculosis (TB) or extra-pulmonary TB diagnosis in any patient from a TB endemic country, regardless of class. We'll get back to the issue of class later in this article, as class is intimately tied to how Jigna, a woman in her 30s, experienced TB and the response she received from family and friends. Also, she said, of course TB treatment is important, but that's a given. The component of care that is often overlooked is the need for support from others going through the same experience, peer support. It was a lack of support that exacerbated the stigma she felt as a result of her TB diagnosis.

Let me tell you a bit more about Jigna and why her experience with TB continues to be a valuable lesson for those of us in the healthcare field. Jigna and her new husband, Prakash, moved to the United States from India in 2000. Shortly thereafter the couple decided that it was time to start a family. After months of trying on their own, without a favorable outcome, they decided to consult with an infertility specialist, who put her on an infertility treatment plan. After 9 months of painful and invasive treatments that resulted in failure, Jigna and her husband decided to consult another specialist. The 2nd specialist agreed with Jigna that instead of a treatment plan, there was an immediate need to investigate the reason for Jigna's infertility and then develop a plan around it. During the next 9 months, Jigna underwent laparoscopic surgery and was eventually given a diagnosis of pelvic TB.

Pelvic TB

Pelvic TB often produces no symptoms even as it advances and affects internal organs, including the reproductive system. Asymptomatic pelvic TB may go undetected for 10 to 20 years until is discovered, typically in the course of assessing complaints of infertility, pelvic pain or menstrual irregularities.

Although pelvic TB is considered rare in the west, in India one physician estimates that 30-40% of infertile women may have had pelvic TB at some stage of their life.[1] The fallopian tube is the organ most commonly affected. Drug treatment is similar to that of pulmonary tuberculosis, although criteria for assessing the effectiveness of therapy are lacking. In-vitro fertilization with embryo transfer remains the most effective method of treating associated infertility; nonetheless, return to fertility after treatment is not encouraging.[2]

After successfully completing treatment for TB, and making a full recovery, Jigna then spent two years trying to conceive through in-vitro fertilization (IVF), but as warned by her physicians, the procedures were unsuccessful. The 3½ years spent "fighting for a chance for motherhood" changed her life.

Jigna's case does reinforce the message to consider TB and extra-pulmonary TB when providing care to someone from a TB endemic country or who has spent time in a TB endemic area. I'd like to let Jigna tell you, in her own words, what I think is the second lesson learned from her case.

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"My husband and I were completely unprepared to learn that TB was at the root of our struggle with infertility. I had hardly been sick for more than a few days in the six years since we arrived in the US! Being asymptomatic made it harder for me to fully accept the diagnosis. Educating me on extra-pulmonary TB was a challenge for my doctors, since they had very little experience with it themselves. Growing up in Mumbai I never saw an anti-TB public health campaign featuring people who looked like my middle class family. I never knew of anyone in our high-rise apartment building being sick with TB. Like my family and friends, I strongly associated TB with impoverished communities and environments where people lacked sanitation, adequate shelter, and food. Somehow we believed TB was confined to those environments and had no power to infect people in neighborhoods like ours. As I began to emerge from denial about my diagnosis, I realized we associated TB with more than physical weakness and uncleanliness. Even though we had a basic understanding of how TB is spread, we shared an unspoken sense that people who developed TB disease must also have some moral failure, vices, or a wicked lifestyle. TB happened to other people, who we would have described as alien and somehow "less" than us. Awareness of TB-related stigma hit me hard and I was trying to come to terms with the reality that TB would leave me infertile."

Jigna and her husband, Prakash.

"As I began to tell family and friends of my diagnosis, I saw that many of them shared my unspoken belief that only people with moral failures succumb to TB."

"As I began to tell family and friends of my diagnosis, I saw that many of them shared my unspoken belief that only people with moral failures succumb to TB. Their facial expressions and body language changed, sometimes very subtly and sometimes in ways that were impossible to ignore. Some people abruptly ended a conversation with me when I spoke of the diagnosis. With others, just the look in their eye let me know that as a person with TB, I had become less valued in their eyes. Worried about how people we knew here in the US and back in India would react, some well-meaning family members counseled me not to speak about my diagnosis. I knew that my talking about TB affected their social standing — in our culture as well as others, the stigma of TB affects not only the patient but the entire family. The feeling that I had something to hide, that TB was not something I could talk openly about, was hurtful and left me feeling emotionally isolated. I understood why people go to great lengths to hide the disease, even to the point of avoiding clinics or public health officials associated with TB. Fortunately, those nearest to me reacted differently. My husband and several family members threw themselves into supporting me throughout treatment."

"When I completed treatment and my doctors declared me completely recovered from TB, I began to reconstruct my life. I restarted my career along new lines, developed new hobbies, and made new friendships. My husband and I had to rethink how we would create the family we so wanted. This process helped me to accept the permanent consequences of pelvic TB and think about a new future, one different than I had always imagined, but full of its own promise. But my experience with TB never completely left me. I was left newly sensitized to the emotional dimensions of illness and how lonely and isolating the experience of disease can be, especially when one's disease is unfamiliar to healthcare providers in a particular setting, as was my experience being treated for pelvic TB in the US."

"Even more important to me were conversations with TB patients. When I had TB, I knew no one who was like me. Not having anyone around who shared my experience contributed to my sense of isolation. Every time I sat down with a patient to talk about what to expect from TB treatment, answer questions, sympathize, and provide living proof that there is life after TB, I felt a little stronger. I could see that talking with me was positive for patients, and knowing that my ordeal with TB had been useful for someone else meant the experience had constructive outcomes, not solely negative consequences for my life."

Advocacy in the Global Fight against TB

Fear that TB-associated stigma will outlast the course of the disease and permanently damage one's social identity adds layers of emotional distress, grief, even depression, to the experience of TB. Healthcare providers can address the impact of TB-related stigma with education to highlight that TB is transmitted through the air and is fully curable. Education can calm patients' fears that TB disease results from physical or moral failings. Advocacy can address public misperceptions that underpin the stigma.

Jigna's story illustrates the importance of advocacy at a local level. But advocacy at a national and global level are also important. TB advocacy involves the dissemination of information to influence policy development and implementation, public opinion, service provisions, and communities and individuals affected by TB. The World Health Organization houses the global Stop TB Partnership, which recognizes advocacy as essential to its overall mission of TB elimination through high-quality care and treatment and effective control strategies.

Stop TB USA is a member of the global Stop TB Partnership and chaired by New Jersey Medical School Global Tuberculosis Institute's Eileen Napolitano. Stop TB USA is comprised of public and private organizational and individual partners with a mission to strengthen TB prevention, care and control in the US, in collaboration with the Division of TB Elimination, US Centers for Disease Control and Prevention.

The World Health Organization declared TB a global emergency in 1993 in recognition of its growing importance as a public health problem worldwide and a major cause of morbidity and mortality in many countries.

- About one-third of the world's population has latent TB, that is, they have been infected with *Mycobacterium tuberculosis* but are not (yet) ill and cannot transmit the disease.
- Globally in 2011, 8.7 million people fell ill with TB and 1.4 million died from TB.[3]
- While much of this disease is occurring in low- and middle-income countries, the US is not immune to TB. Over 10,000 TB cases occurred in 2011 in this country. More than 11 million people living in the United States have latent TB infection. Although those with latent TB do not have symptoms, 5–10% will eventually develop TB disease if not treated.[4] The good news is that both TB and latent TB are treatable.

The Partnership's objectives are to create a social movement for public awareness, community empowerment and policy action to:

- Mobilize and actively support resources for TB elimination in the US at the national, state, and local levels
- Serve as a channel of scientific and public health knowledge for the public and policy makers on the status of TB elimination globally, nationally, and at state and local levels
- Educate the public and policy makers about the need for sustaining community public health activities for the elimination of TB
- Provide a framework to bring partners together and increase community participation in the global and national tuberculosis elimination effort

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Resources for Advocacy

Website-based resources for advocacy include the following:

- ACTION (http://www.action.org/), a global partnership of advocacy organizations working to influence policy and mobilize resources to fight diseases of poverty and improve equitable access to health services, was founded in 2004 with the shared mission of mobilizing new resources against TB.
- Stop TB Partnership (http://www.stoptb.org/), includes nearly 1000 partners in 100 countries as a force transforming the fight against TB. Partners include international and technical organizations, government programs, research and funding agencies, foundations, NGOs, community groups and the private sector. The Stop TB Partnership Secretariat is housed by the World Health Organization.

Empowered patients are healthcare providers' most powerful ally in treating TB. Patients can become empowered by learning their rights and speaking with other TB patients.

- The World Health Organization has endorsed the Patient's Charter for Tuberculosis Care: Patient's Rights and Responsibilities, which defines patients' essential role in high quality care, mobilizing community support for TB services, and building political and health systems capacity to meet the challenge of TB control and elimination. http://www.who.int/tb/publications/2006/istc_charter.pdf
- Although online patient communities are not as common in TB as other conditions, individuals are increasingly sharing their experiences and responding to others' stories through blogs related to TB treatment. Doctors without Borders hosts an interactive blog, see the TB & Me blog at http://msf.ca/blogs/tb/tag/support/?gclid=CI-8k4C-Q7q0CFcnc4AodbD-m6Q
- Outside the field of TB, there are many resources related to patient advocacy. As an example, see the Side-Out Foundation's advocacy website, developed for people affected by breast cancer: http://www.side-out.org/cancer-resources/how-to-be-an-advocate/medical-advocacy/

Finally, there are many resources related to general healthcare advocacy.

- The Agency for Healthcare Research and Advocacy, an agency of the US Department of Health and Human Services, houses a wealth of information for patients, providers, researchers, and policymakers at http://www.ahrq.gov/
- Christopher and Dana Reeve Foundation's Advocacy toolkit is available at http://www.christopherreeve.org/atf/cf/%7B3d83418f-b967-4c18-8ada-adc2e5355071%7D/ADVOCACYTOOLKITRF311B.PDF
- The guide "Being a Healthy Adult: How to Advocate for Your Health and Health Care" from University of Medicine and Dentistry of New Jersey is available at: http://rwjms.umdnj.edu/boggscenter/products/documents/TransitiontoAdultHealthcare-EN-complete.pdf

The New Jersey Medical School Global Tuberculosis Institute's *TB & Cultural Competency, Notes from the Field* is available at: http://www.umdnj.edu/globaltb/products/newsletter.htm. ❖

1. Dr Parul Sehgal. *Pelvic tuberculosis and Infertility.* Accessed on October 29, 2012 at http://drparulsehgal.com/News/Pelvic%20tuberculosis%20and%20Infertility.shtml
2. Aliyu MH, Aliyu SH, Salihu HM. Department of Epidemiology, University of Alabama at Birmingham, 35294. "Female genital tuberculosis: a global review". *Int J Fertil Womens Med.* 2004 May-Jun;49(3):123-36
3. World Health Organization. October 2012. *Tuberculosis, Fact sheet N°104.* Accessed on November 9, 2012 at http://www.who.int/mediacentre/factsheets/fs104/en/
4. CDC. December 12, 2011. *New, Simpler Way to Treat Latent TB Infection.* Accessed November 9. 2011 at http://www.cdc.gov/Features/TuberculosisTreatment/index.html

New Jersey's success in the In+Care Campaign

Jane Caruso, M.S., Ryan White Part D Project Director, New Jersey Department of Health

The Health Resources and Services Administration together with the National Quality Center have teamed up on a national retention campaign referred to as the In+Care Campaign. The In+Care Campaign aims to keep patients in care — if patients stay in care, they get the services that they need to stay healthy. The In+Care Campaign includes 484 providers nationally who currently manage the care of 421,697 patients.

Forty Ryan White Cross Part Collaborative providers in the state of New Jersey have incorporated the In+Care Campaign into clinical and data collection procedures. Merging the efforts of the Cross Part Collaborative with the In+Care Campaign goals streamlines data collection and provides a statewide picture of our collective ability to respond to patient retention challenges.

New Jersey's In+Care Team, from left to right: Roseanne Marone, Michael Hager, Jean Haspel, and Jane Caruso. The Team is available to provide guidance and support to strengthen local retention activities.

The In+Care Campaign aims to keep patients in care — if patients stay in care, they get the services they need to stay healthy.

Agencies in the In+Care Campaign are engaged in the following activities:

- Reporting on four uniform campaign-related measures via an already existing Ryan White online database
- Implementing improvement activities to support patient retention
- Routinely sharing updates to highlight improvement strategies and challenges
- Joining when possible, regional/local face-to-face meetings of peer In+Campaign participants

After five rounds of statewide data collection (10 months of data), New Jersey is performing better than the national average in the following measures (see Figure 1).

- Percentage of patients with a medical visit in the first half of the year who did NOT have a medical visit in the second half of that year ("Gap", note that for this variable, the lower the percentage, the better; hence New Jersey's 11% reflects better performance than the national average of 14%).
- The percentage of patients with a medical visit in the first quarter of a given two-year period who also had a medical visit in each of the subsequent three quarters of that two-year period ("Frequency").
- Percentage of patients that were newly enrolled in the first trimester of a given year who had a medical visit in the subsequent two trimesters of that year (new patients "New Pts").

The remaining measure is: The percentage of HIV positive patients with an undetectable viral load, or a viral load less than 200 copies ("VLS").

New Jersey's In+Care Campaign stars

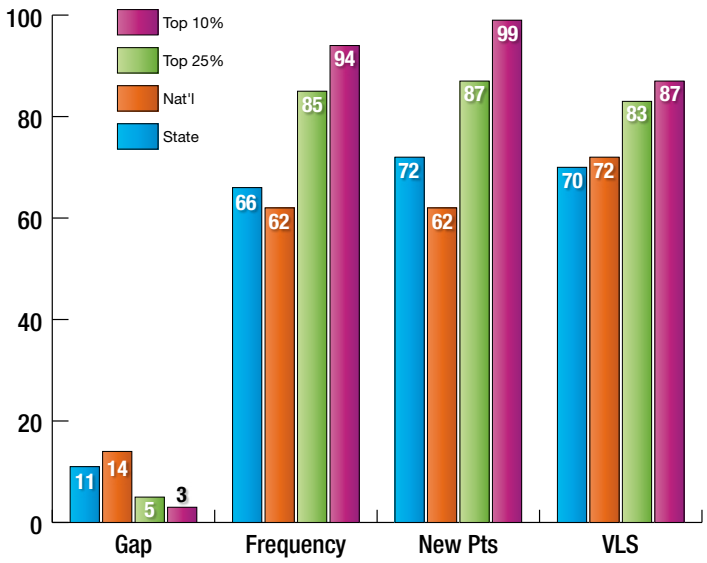
Three agencies have made outstanding progress in their rates of viral load suppression (80% or greater):

- Garden State ID at Kennedy Hospital
- Hackensack University
- St. Mary's Hospital-Passaic

Seven agencies achieved a "Gap" measure under 5%:

- Jersey Shore University Medical Center Pediatrics
- Plainfield Neighborhood Health Center
- Hackensack University Medical Center
- St. Mary's Hospital-Passaic
- Eric B. Chandler
- St. Joseph's Hospital and Medical Center
- Henry J. Austin

Figure 1: New Jersey In+Care Cycle 5 Data



3 agencies have made outstanding progress in their rates!

Garden State ID at Kennedy Hospital | Hackensack University | St. Mary's Hospital-Passaic

Efforts in New Jersey are championed by Jane Caruso from the State Department of Health, who is New Jersey's designated coach, and

- **Jean Haspel** from Atlanticare in Atlantic City in the south (*Jean.Haspel@atlanticare.org*)
- **Roseanne Marone** from RWJ in New Brunswick in the north (*Maronero@umdnj.edu*)

Michael Hager (*mth02@health.state.ny.us*) from the National Quality Center is overseeing the entire national project and is a mentor and support person.

Any agency that wants guidance, support or technical assistance in developing a strategy to improve retention, should contact: **Jane Caruso** (*jane.caruso@doh.state.nj.us*) or 609-777-7748.

Health Insurance Continuation Program Update

Sindy M. Paul, MD, MPH, FACPM, Medical Director, New Jersey Department of Health
Lisa H. Cummings, RN, MS, Research Scientist, New Jersey Department of Health

The New Jersey Department of Health (NJDOH), Division of HIV, STD and TB Services (DHSTS), Health Insurance Continuation Program (HICP) provides financial assistance for eligible HIV-infected New Jersey residents to maintain continuity of health insurance or to receive medical benefits under a health insurance premium. The financial eligibility criteria are the same as for the New Jersey AIDS Drug Distribution Program, recipients must:

- Earn no more than 500% of the Federal Poverty Level
- Live in the state of New Jersey
- Be HIV-infected

Letters describing the recent HICP changes will be sent to enrollees, case managers, and DHSTS grantees. HICP staff are available Monday to Friday 8:00 am to 4:00 pm at 1-800-353-3232 to answer questions.

DHSTS recently reviewed HICP. This review was conducted to assure that HICP complies with all the current Health Resources and Services Administration (HRSA) requirements and is providing the best quality service possible to applicants and enrollees. Program revisions resulting from the review include the following:

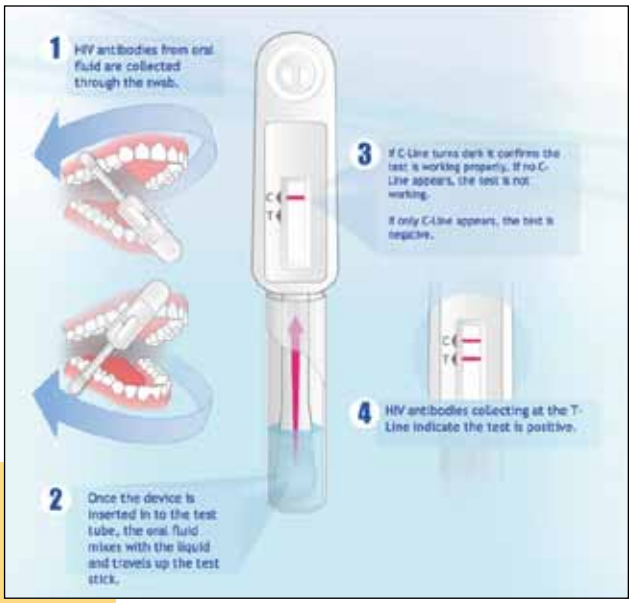
- **Recertification application:** As mandated by HRSA, HICP now requires applicants to complete a recertification application six (6) months after the initial enrollment date. Applicants are not required to submit any additional documentation when returning their recertification application, UNLESS the client needs to change or update information in the original application.
- **Annual recertification application:** The annual recertification application will continue to be required. The annual recertification process requires the client to provide full documentation, including the Physician Certification, income tax return, recent pay stubs, insurance cards, etc.

Recertification applications have been simplified. Clients are mailed a print out of the information that HICP already has on file. They are then asked to carefully review this information and make any necessary changes. If there are no changes, clients must certify that all current information is correct by signing the application, and returning it to HICP. If recertification applications are not returned to HICP in a timely fashion, clients will lose their health insurance benefits. ❖

In-home HIV Testing

Alicia Gambino, MA, MCHES, Director of Public Education, New Jersey HIV/AIDS/STD/Hepatitis Hotline

Further to Food and Drug Administration (FDA) approval in October of this year, the in-home oral HIV test became available, making it easier for Americans to know their HIV status. The $40.00 test kit, marketed as OraQuick®, uses a mouth swab and yields test results in approximately 20 minutes; it is approved for those 17 years and older. Since test kits are administered by the consumer, results should be considered preliminary and confirmed by a healthcare provider.



Home testing will be a huge step in the fight against HIV. According to CDC, about 20% of the 1.2 million HIV-infected Americans do not know they have the disease. In addition, about 50,000 more get infected each year. Home testing removes some of the barriers to HIV testing, hopefully encouraging more people to know their HIV status and to enter care if infected. This is particularly important as we move towards "test and treat" whereby anyone testing HIV-positive, regardless of CD4 cell count, is provided with antiretroviral therapy.

> The availability of an HIV test as easy to use as a home-pregnancy kit is yet another step in the normalization of a disease that was once seen as a mark of shame and a death sentence.
>
> —*New York Times* (July 3, 2012)

There are a number of resources for anyone who would like further information about HIV testing, HIV care and treatment, or anything else HIV-related. The State of New Jersey funds the New Jersey AIDS/HIV/STD Hotline (phone: 800-624-2377; e-mail: 8006242377@njpies.org). New Jersey AIDS/HIV/STD Hotline professionals are available 24 hours a day, 7 days a week, every day of the year. Hotline staff provide telephone consultation for the public and healthcare professionals seeking information about HIV and other sexually transmitted diseases including hepatitis. Callers receive information tailored to their needs: discussion about prevention, referrals for counseling and testing sites and other related services, and information on treatment and adverse reactions to medications. Callers can also e-mail or text questions to the hotline at 8006242377@njpies.org. Other resources for further information include the U.S. Centers for Disease Control and Prevention (CDC) National Prevention Information Network, located at: http://www.cdcnpin.org/scripts/search/OrgSearch.aspx. In addition, OraSure Technologies—which develops, manufactures and markets OraQuick—operates a 24/7 toll-free support center. ❖

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www.fxbcenter.org
www.umdnj.edu/ccoe
http://www.state.nj.us/health/aids/index.shtml

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save the dates

23rd Annual HIV Medical Update
December 5, 2012 • Crowne Plaza Hotel, Cherry Hill, NJ

HIV Clinical Update
Wednesday, June 12, 2013 • New Brunswick Hyatt

For more information:
Contact Michelle Thompson at *ccthomps@umdnj.edu* or (973) 972-1293.

NY/NJ AETC Cervical Pap Test Training Program for Clinical Providers in New Jersey
A CME/CE program developed to provide HIV clinicians with the knowledge, skills, and support to perform cervical Pap tests and pelvic exams for HIV-positive women as recommended by national guidelines, to reduce the barriers for clinicians and patients associated with lower cervical Pap test rates, and ultimately, to improve Pap test clinical rates.
For more information: 212-304-5530 or *http://www.nynjaetc.org/on-demand/cervicalpapprogram.html*

HIV/AIDS Training & Information Resources

New Jersey Department of Health – Division of HIV, STD and TB Services (NJDOH-DHSTS)
(609) 984-5874 • Hotline: (800) 624-2377
www.state.nj.us/health/aids
- NJ HIV/AIDS statistical reports, regulations, forms, and links to HIV care, prevention programs, and training New Jersey rapid testing site: www.state.nj.us/health/aids/rapidtesting
- New Jersey AIDS/STD Hotline: (800) 624-2377

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(973) 972-5644 • Fax: (973) 972-0397 • http://www.fxbcenter.org/
- HIV/AIDS conferences, training
- Free online continuing education (CE) credits for healthcare professionals
- HIV/AIDS MEDICAL UPDATE SERIES: with funding from NJDOH
- Free on-site HIV medical education for healthcare sites: contact Michelle Thompson at (973) 972-1293 or ccthomps@umdnj.edu

US Dept. of Health & Human Services
- HIV/AIDS treatment guidelines: www.aidsinfo.nih.gov
- National Institutes of Health clinical trials database: http://clinicaltrials.gov

Centers for Disease Control (CDC) – Division of HIV/AIDS Prevention
- Key resources: www.cdc.gov/hiv/hivinfo.htm#WWW

HRSA: Health Resources and Services Administration of the US Department of Health and Human Services: http://www.hrsa.gov
- HAB: HIV/AIDS Bureau of HRSA: http://hab.hrsa.gov
- TARGET Center: Ryan White Program Resources: www.careacttarget.org
  National Quality Center: (HRSA-HAB): www.nationalqualitycenter.org

FDA MedWatch: (800) FDA-1088; Subscribe to e-bulletin: www.fda.gov/medwatch/elist.htm

- AIDS Education and Training Centers (AETC)
- Resources for clinicians and educators:
- AETC National Resource Center: www.aidsetc.org
- National HIV/AIDS Clinicians' Consultation Center: http://www.nccc.ucsf.edu/
- National Center for HIV Care in Minority Communities: http://nchcmc.org/
- Warmline: (800) 933-3413
- Post-Exposure Prophylaxis Hotline/PEPline: (888) 448-4911
- Perinatal HIV Hotline: (888) 448-8765
- The NY/NJ AETC: www.nynjaetc.org
- AIDS InfoNet: HIV treatment fact sheets in English and 10 other languages: www.aidsinfonet.org

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