Human Immunodeficiency Virus (HIV)

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Case Presentation

Jane is a 23-year-old-female with perinatal human immunodeficiency virus (HIV) infection who presents to her primary care physician (PCP) to discuss preconception care. She has been relatively healthy since her diagnosis of HIV at age 2, when she was found to be HIV-positive after a hospitalization for *Pneumocystis* pneumonia. She was placed on trimethoprim-sulfamethoxazole prophylaxis at age 2 after her hospitalization and followed with a pediatric HIV specialist until recently. She reports taking various medications as a child and teenager for her HIV disease and noted variable adherence to therapy during her childhood years. She knows that she had problems with drug resistance that required changes in medications during her childhood but is not sure to which agents her virus has developed resistance. Jane reports that her mother managed her medications until about age 16, when she began taking them on her own. She became aware of her diagnosis at age 12, when her family disclosed her HIV status to her, and she admits to refusing medications around that time due to difficulty adjusting to the diagnosis. She attended counseling from age 14–16 to help her cope with the stigma associated with her disease and the challenges she felt as she became interested in dating and sexual activity. She became active in a youth-with-HIV support group and learned to become more responsible for her own health care. Jane has managed her own medications since age 16, and has been on her current antiretroviral (ARV) regimen since age 19. She has maintained viral suppression (viral load <200 on HIV RNA testing) for the past 4 years with her current regimen of tenofovir, emtricitabine, darunavir, and ritonavir.

Her current medical problems include obesity with a body mass index (BMI) of 32, history of major depression in remission on fluoxetine, and asthma, which is currently well controlled on a moderate-dose inhaled corticosteroid and as-needed inhaled short-acting bronchodilator. She has a history of sexually transmitted infection (STI) with *Chlamydia trachomatis* at age 18, but has had no further STI since that time and her most recent testing 6 months ago was negative. She has kept up to date with all health screenings that she has been informed she needed, including cervical cancer screening, which she started at age 19 and has annually. Jane reports that her routine vaccinations are "up to date" and mentioned that she completed the entire human papillomavirus (HPV) vaccination series "several years ago." She is a lifelong nonsmoker, but was exposed to passive smoke as a child due to her

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mother's cigarette usage. Jane drinks about 2–4 alcoholic beverages per month and denies all illicit drug use, including marijuana.

Jane has had four lifetime sexual partners and had her first sexual activity at age 17, with an older male she met through friends. She admits to intermittent condom usage as a teenager, but has used condoms with every sexual encounter with her current partner. She has never been pregnant, and is not currently on birth control. One year ago, she began dating her current sexual partner, whom she met while in college. They became sexually active 10 months ago, after she disclosed her HIV status to him, and they have used barrier contraceptives (male condom) faithfully without evidence of malfunction. The couple were recently married and have started to discuss having children. Her husband has been tested serially during their relationship and has remained HIV-negative. Jane is here to establish primary care with an adult care provider, as she has only followed up with her pediatric HIV team until now. She wants to discuss strategies to prevent HIV transmission during sexual activity and possible pregnancy, as well as chronic disease management and health maintenance now that she has made it to adulthood with her perinatal HIV infection. She is very concerned about life expectancy, as her mother died at age 40 from HIV-related end-stage renal disease (ESRD), despite being on combination antiretroviral therapy (cART). She wants to discuss how to remain healthy in adulthood with HIV.

Case Discussion

Preconception Counseling in HIV-Infected Women

Although it would have been unthinkable only a few decades ago, children born with HIV are living well into adulthood—life expectancy improving every year [1, 2]. With the advances in prevention of maternal-to-child transmission decreasing the risk of HIV transmission to less than 2 %, primary care providers should expect to offer counseling in patients with HIV infection interested in conception.

Consideration for preconception counseling to couples where at least one partner has HIV include:

1. Prevention of maternal-to-child transmission (MTCT) of HIV by HIV-infected women
2. Prevention of HIV transmission in serodiscordant couples
3. Medical concerns in HIV-infected pregnant women, including perinatally infected women.

Prevention of Maternal-to-Child Transmission of HIV

Women who are well controlled on combination antiretroviral therapy (cART) and continue to be adherent to care during conception and pregnancy are unlikely to vertically transmit HIV to their offspring. Untreated women with HIV have approximately a 12–40 % chance of transmission, but this risk can be decreased to 2 % or less with antepartum treatment with ARVs, postexposure prophylaxis of the infant, and avoidance of breastfeeding [3]. These three strategies are responsible for the dramatic decrease in MTCT in developed countries such as the United States. Nevertheless, annually, between 150 and 200 infants born to HIV-infected women in the United States are perinatally infected with HIV. Most are born to women who are either unaware of their HIV status or not engaged in HIV care [4]. For Jane, the major predictor of the ability to prevent transmission of HIV to her offspring is her adherence to cART during her pregnancy and maintenance of an undetectable viral load. Preconception counseling should include discussion of continued adherence to her current therapy. Her current regimen is one of several preferred regimens for prevention of MTCT (PMTCT), and, per current guidelines for PMTCT she should remain on her current regimen as her HIV disease is stable and she has maintained viral suppression for the preceding 12 months [5].

Prevention of Horizontal Transmission of HIV in Serodiscordant Couples

When counseling serodiscordant couples on conception, providers should stress the low (but not zero) risk of HIV transmission when the HIV-infected partner maintains an undetectable viral load. In this case, Jane's viral load is below the level of detection on the HIV RNA assay used, and has been that way for several years. An additional strategy to minimize risk to her new husband would be to engage in unprotected sexual intercourse only during ovulation, to maximize her chances of conception during the unprotected encounter [5]. Using methods such as home ovulation prediction kits can help the couple decide on an optimal time for unprotected intercourse. Artificial insemination (either in a medical setting or at home using a syringe method) is the safest option for Jane and other HIV-positive women in serodiscordant couples to ensure zero risk of HIV transmission to sexual partners during fertility attempts. Studies are currently underway to look at the use of pre-exposure prophylaxis (PrEP) in HIV-positive females in heterosexual, serodiscordant couples who are actively trying to conceive. Currently, the only U.S. Food and Drug Administration (FDA)-approved medication for use in PrEP is tenofovir-emtricitabine single-dose combination pill.

PrEP is taken 1 tablet daily by the HIV-negative partner to decrease risk of HIV transmission. PrEP has been shown in numerous studies to be safe and effective in decreasing HIV transmission. The PartnersPrEP study enrolled HIV-negative women in heterosexual, serodiscordant couples to use PrEP daily compared to placebo and showed significant reduction in HIV transmission risk to HIV-negative women with persistently detectable levels of PrEP drug in the bloodstream during the study period [6]. Incidence of pregnancies in the PartnersPrEP study was 10 %. Women who became pregnant had high medication adherence (97 % of prescribed doses overall), had similar adherence in the periconception period, and did not vary from total adherence overall, suggesting PrEP use was sustainable in women wishing to conceive [7]. Mothers who had received PrEP in the study were no more likely to experience preterm birth, congenital anomalies, or growth suppression in their infants than those who received placebo [8]. In addition, the Antiretroviral (use in) Pregnancy Registry has not shown any evidence of increases in birth defects in infants exposed to tenofovir-emtricitabine during gestation [9].

There are no studies looking at the efficacy of PrEP in HIV-infected patients on cART with viral suppression, but PrEP appears to be a useful tool to decrease HIV transmission among serodiscordant couples attempting to conceive. A recent study looking at intermittent use of PrEP immediately before and after sexual activity to prevent HIV transmission also adds to the body of evidence of PrEP efficacy, with an 82 % relative risk reduction in HIV acquisition [10]. In this study of PrEP in men who have sex with men (MSM) without HIV infection, detection of serum blood levels of tenofovir and emtricitabine were over 80 %, and the median use of medication was 15 pills per month [10]. It is unclear if the same level of protection would be possible with less frequent dosing.

Chronic Medical Conditions in Women with HIV Infection

Both prolonged HIV infection and medications used to treat the disease can lead to medical issues. This will need to be discussed with Jane and her husband prior to conception. Primary care physicians are well equipped to assist Jane's HIV care team in screening and management of comorbidities. With her current cART regimen, there are several medical risks to be considered. Protease inhibitors, while among the preferred agents for use during pregnancy, increase the risk of metabolic disorders, such as hyperlipidemia and hyperglycemia. Pregnant women on protease inhibitor therapy should be considered for early screening with oral glucose tolerance testing and should receive dietary counseling to prevent gestational diabetes [5]. Tenofovir has been associated with decreased bone density in women and men on therapy [11]. Instructions on

strategies to improve bone health during pregnancy and beyond should be included in her preconception counseling.

In addition, Jane has a higher risk of HIV-related chronic disease due to prolonged HIV infection. Adults with perinatal infection of HIV are at risk for end-organ damage related to prolonged periods of HIV viremia throughout their lifetimes. Presumably, in Jane's case, she has been in care for at least the previous 7 years, and she should have received screening for chronic medical conditions related to HIV such as renal insufficiency, diabetes, hyperlipidemia, and mental health disorders. If such screening has not been done, it may be helpful to screen prior to conception. With the consideration of pregnancy, it will also be important for her to establish an adult care team, including an adult HIV provider (infectious disease trained subspecialist or generalist with HIV expertise) and obstetrical provider with experience in the care of HIV-infected women. Given her perinatal HIV infection and young age, her care may still be under her pediatric HIV care team, and she should ideally transition to an adult care team prior to her pregnancy.

Pathophysiology of HIV and Its Effects on Immunity

HIV is a non-oncogenic virus of the Retroviridae family, and belongs to the *Lentivirus* genus. There are two types of HIV (HIV-1 and HIV-2), with the vast majority of disease caused by HIV-1. HIV-2 exists primarily in West Africa, and HIV-1 is the predominant virus type in the Western world. HIV invades helper T (CD4) lymphocytes, integrates its viral DNA into the host DNA as part of the replication process, and destroys the host cell. CD4 cells help CD8 cells activate into cytotoxic T cells and help B cells produce antibodies (humoral immunity). Specialized CD4 cells, called Th17 cells, assist in the recruitment of neutrophils to the site of bacterial infections and are a key component of mucosal immunity as well. The loss of CD4 T cells (through both direct HIV infection and cytotoxic T cell-mediated destruction), monocytes and macrophages, as well as suppressed mucosal immunity predispose HIV-infected patients to opportunistic infections, fungal infections, severe infections with enteric organisms, and malignancies.

HIV is transmitted through transmission of infected blood and/or bodily fluids. Infection with HIV may predate clinical symptoms by 5–10 years, and progression from infection to disease tends to be slow, with the exception of children who are infected with HIV, who tend to progress more rapidly. In the first few weeks of early infection, HIV viremia is high and CD4 cells dramatically decline as infected cells are cleared by cytotoxic T cells. Over the following months to years, CD4 cells rebound and HIV viremia stabilizes until immunodeficiency is present, and viremia is able to proceed unchecked. During the period of clinical latency after acute HIV infection, reservoirs of HIV-infected cells develop, and these reservoirs are resistant to treatment with antiviral agents. Latent HIV infection in resting T cells and other reservoirs is responsible for the chronic nature of the disease and the requirement for lifelong antiretroviral therapy for control of the HIV disease.

Epidemiology of HIV Infection in U.S. Young Adults

HIV surveillance data from the Centers for Disease Control (CDC) show youth ages 13–24 living with HIV infection in the U.S. totaled over 64,000 by the end of 2012. In 2010, youth accounted for 26 % of new HIV infections (estimated at 12,200), despite constituting only 17 % of the U.S. population. Underrepresented minority groups are overrepresented in the HIV epidemic among youth. African-American youth made up 57 % of newly infected youth, and young men who have sex with men (YMSM) constituted 72 % of new HIV infections among adolescents and young adults. Eighty percent (80 %) of these new diagnoses are in the 20- to 24-year-old age group [12].

Year-end 2013 estimates of HIV prevalence in the 20- to 24-year-old age group report 33,000 young adults with HIV living in the U.S., with only 50 % being aware of their diagnosis. The highest rates of HIV prevalence are in the southern United States, District of Columbia, and urban areas in the northeastern U.S., with rates higher than the U.S. average (0.8 % prevalence among 20- to 24-year-olds in D.C. vs 0.3 % U.S average) [12]. Expanded HIV testing among high-risk groups such as youth ages 20–24 and African-American YMSM have helped to increase the number of young people who are newly aware of their HIV status. As these persons become linked to care and begin to access the healthcare system, primary care physicians will likely participate in their care as they transfer into the adult healthcare system.

Nearly 11,000 youth and young adults in the U.S. and U.S. territories as of 2010 were living with perinatal HIV infection, constituting approximately 18 % of the HIV-infected population. More than 40 % of perinatally infected youth have been diagnosed with acquired immunodeficiency syndrome (AIDS) at some point during their lifetimes, representing a population with high potential for early comorbidity [13]. As these patients continue to age and transition to adult care, adult providers will need to be attentive to the medical challenges of this group, particularly as data on long-term prognosis and long-term health concerns are just becoming available.

Characteristics of Perinatally Versus Behaviorally Infected Youth and Young Adults

Most youth and young adults living with HIV were infected through horizontal/behavioral transmission [12]. Sexually active youth are at risk of HIV infection due to behaviors such as decreased condom usage compared to older adults, substance abuse, and multiple sexual partners—particularly older partners [14, 15]. Centers for Disease Control and Prevention data from 2014 report that youth and young adults aged 13–24 had the second highest incidence of new HIV infection in the U.S., and youths representing ethnic and sexual minorities are overrepresented. As young adults with horizontally transmitted HIV transition to adult health care, it is important to recognize that they may still engage in high-risk behaviors and may be unaware of their risks, therein increasing their exposure to other sexually transmitted infections (STIs). Data from a sample of 143 sexually active HIV-positive youth showed that there was no difference in sexual risk behaviors between perinatally infected and heterosexually infected youth, suggesting that secondary STI prevention is an essential component of primary care for all HIV-infected youth, not just those with horizontal transmission [16].

Some notable differences have been observed in young adults vertically (vHIV+) and horizontally (hHIV+) infected with HIV. When compared to uninfected and hHIV+ cohorts, young adult vHIV+ have a higher incidence of mental health conditions as well as lower academic achievement and are less likely to have sustained viral suppression [14]. The reasons for these differences are not completely clear but are likely in part due to the stress and challenges of chronic disease management in vHIV+ youth. In those vHIV+ youth who were on cART therapy early (by age 5), prevention of HIV encephalopathy appears to provide protection against cognitive delays. However, for those perinatally infected who were not on early therapy or for those with a history of HIV encephalopathy, neurological comorbidities are not uncommon [17]. These young adults may present with cognitive delays, history of stroke with resultant disability, learning disabilities, and other neurological disorders [18]. Such neurocognitive effects present additional challenges for disease self-management and engagement in care and may require a different approach from the adult provider, including inclusion of immediate family, extended family, and friends to help with medical decision-making and medication adherence.

Although data on young adults with perinatal HIV infection is minimal, existing data point to

other potential concerns due to long-term HIV infection and prolonged exposure to antiretroviral medications. Issues such as hyperlipidemia and insulin resistance that develop during early childhood may predispose vHIV+ young adults to early cardiac disease [19]. Typically vHIV+ youth have higher drug resistance than behaviorally infected counterparts due to lapses in treatment during adolescence and varied ART options in early childhood, including single ART therapy. Thus, they may have more complicated medical regimens and experience higher side effects. This may also negatively affect adherence to therapy [20]. Finally, for many young adults with perinatal HIV infection, issues such as sexual and reproductive health may not have been adequately addressed during adolescence due to caregiver fear of HIV transmission. Timing of disclosure of their disease by providers or family varies but often occurs during early adolescence for most with perinatal HIV infection [21, 22]. For many HIV-positive youth, abstinence-based counseling may have been their only reproductive health education, and awareness of contraceptive options may be minimal. Primary care providers should not assume that even by early adulthood, vHIV+ patients are aware of and practicing "safe" sexual practices and have discussed contraceptive options that are available for prevention of pregnancy. Similar to age-matched cohorts, pregnancies in perinatally infected women are most commonly unplanned [23].

Special Populations

Young MSM of Color

Minority populations in the U.S. are overrepresented in the HIV epidemic and none more so than young men who have sex with men (YMSM). African-American YMSM account for more than 50 % of YMSM infected with HIV, and YMSM account for more than 80 % of HIV infections in males between 13 and 24 years of age [24]. Young males tend to have older sexual partners, putting themselves at increased risk for coercive sexual practices [24]. In addition, studies have shown MSM of color tend to have relatively small, homogenous sexual networks and that HIV and other STIs can rapidly spread throughout these networks [25, 26]. Providers should frequently screen HIV-positive YMSM for intimate partner violence and coercive sexual activity, since YMSM of color tend to engage older partners and may be at a power disadvantage in the relationship. Discussion of current sexual practices as well as risk assessment and screening for STIs should be a part of primary care for YMSM with HIV. PrEP for HIV-negative partners of HIV-infected YMSM may also be a powerful tool to prevent continued spread of HIV in the sexual networks of YMSM of color. Generalists caring for HIV-positive YMSM (as well as at risk HIV-negative men) should be aware of PrEP and consider prescribing PrEP to decrease transmission among this group of patients.

African-American Women

Young African-American women have high rates of HIV infection in the U.S., primarily through heterosexual activity with older men [27]. A small case-control study conducted in 2003–2004 of HIV-infected black women and matched controls (black women at risk for HIV infection) in North Carolina showed HIV-infected women were more likely to exchange basic needs or drugs for sex (p value = 0.01) and were more likely to have sexual partners with a prior history of incarceration (p value = 0.04) [28]. This suggests that economic disadvantage and reliance on a partner for substantive needs increase the risk for HIV infection among African-American women. A component of patient-centered care for young African-American women with HIV should include evaluation of their current living situation to screen for transactional sex that may increase the risk for other STIs as well as intimate partner violence and loss of power arising from such relationships.

Socioeconomically Disadvantaged Youth

Despite improved access to health care through both the Ryan White Care Act, which provides HIV primary care services for HIV-infected men, women, and children, as well as the Affordable Care Act (ACA), young adults with HIV continue to face difficulty engaging in HIV care and being retained in treatment. Poverty remains an independent risk factor for HIV infection and failure to be retained in HIV care [29]. Socioeconomically disadvantaged youth and young adults have unique challenges remaining in HIV care, including lack of transportation, unemployment, and lack of health insurance. As a result, they may require additional strategies to maintain viral suppression. In order to better engage young adults with HIV, it is vital for providers to address social issues such as high unemployment rates, HIV stigma and disclosure, and lack of social supports. Young adults living in poverty also have less opportunity to learn key self-management skills that may help them cope with chronic disease. Special attention should be placed on educating young adults about their disease and the importance of self-care in preventing additional HIV-related comorbidities.

Common Comorbidities in HIV-Infected Adolescents

Sexually Transmitted Infections

Youth with HIV infection (through either horizontal or vertical transmission) commonly acquire other STIs, noted either at the time of initial diagnosis or during routine follow-up visits. Analyses of perinatally infected patients in the Pediatric HIV/AIDS Cohort Study (PHACS) registry showed that 62 % of sexually active HIV-positive youth reported unprotected sexual activity [30]. A single-center, retrospective analysis of urban HIV-infected youth (primarily via horizontal transmission) also documented evidence of unprotected sexual activity as measured by STI acquisition. In this cohort, 76 % of youth reported using barrier contraceptive methods "intermittently," yet during the 3-year period studied, 67 % contracted an STI. Risk factors for STI acquisition in this cohort included lack of HIV virological control and number of sexual partners. Notably, sexual preference was not seen to be an indicator of risk for STI in this cohort [31]. Some studies have shown that HIV-positive youth use barrier contraception less often than HIV-negative youth, particularly those with higher numbers of sexual partners [32]. Further review of longitudinal data from the most recent National Youth Risk Behavioral Survey in 2013 shows that the percentage of youth who used a condom during their last sexual intercourse has not topped 65 % since 1991 and has actually declined over the last decade (2003–2013) [33]. For the adult provider, it is important to recognize that STI risk reduction has not been as effective as it should be for the current generation of adolescents. HIV-infected young adults are no more likely to utilize STI risk reduction strategies, such as condom usage, and should therefore be counseled on secondary risk reduction for HIV transmission and STIs at every visit. Providers should screen for *Neisseria gonorrhoeae* (rectal, pharyngeal, and urethral), *C. trachomatis* (urethral) and syphilis in young men and women with risk factors, and Hepatitis C in young MSM and people who inject drugs (PWID). All those not immunized against Hepatitis B should be vaccinated. Risk factors for new STI acquisition include high-risk sexual behaviors, such as lack of condom usage, sexual intercourse while intoxicated, anal intercourse, MSM, and multiple or new sexual partners.

Mental Illness and Substance Abuse

Mental health disorders are not uncommon for healthy adolescents and young adults, and those with HIV are at even higher risk for development of mental health conditions and substance abuse. The Substance Abuse and Mental Health Services Administration (SAMHSA) National Survey on Drug Use and Health report from 2014

recorded that one in five young adults aged 18–25 reported a mental illness in the previous year and that 4 % were diagnosed with a serious illness [34]. More than 40 % of youth have experienced a behavioral health problem by the time they reach seventh grade. Despite the fact that an estimated 2.8 million adolescents had at least one major depressive episode in the year prior to being surveyed, only 41 % actually received treatment for their condition [34]. Disparities exist in the general population of youth and young adults with mental health disorders, and these disparities are even more profound for those with HIV infection.

A study of predominantly African-American youth living with HIV in New York City showed that 24 % reported clinically significant levels of depressive symptoms using a validated tool for screening for depression [35]. A meta-analysis of youth with perinatal HIV infection noted parental or caregiver health was associated with depression and anxiety in the youth, with those patients in homes with caregivers with functional limitations due to mental health conditions having higher risks of developing mental health disorders themselves. This same study also noted various other issues that impacted mental health of youth living with perinatal HIV infection, including death of parents and peers, stigma, concerns over disclosure, and development of healthy identity [36]. Perinatally infected youth are, by definition, the offspring of an HIV-infected parent (or 2) and represent failure of preventive strategies for maternal-to-child transmission of HIV. Risks for lack of adherence to MTCT prevention, such as substance abuse, lack of HIV care, psychiatric conditions in the mother, poverty, and insecurity of food and housing, represent the conditions in which many of these youth lived. These young adults have often experienced significant trauma related to chronic illness, disability, and potential loss of a parent, and they may have been subject to instability in their home environment from these or other issues such as parental substance abuse, involvement in the foster care system, and lack of social supports. HIV-infected youth also have a higher incidence of experiencing or witnessing violence. A cohort study of inner city HIV-positive youth from 2009 described high percentages of youth with a history of sexual or physical abuse as well as intimate partner violence. These experiences were also associated with psychological disorders such as major depression, posttraumatic stress disorder, and generalized anxiety [37].

When compared to other adults, transitional age persons (ages 21–25) have some of the highest rates of high-risk drinking behavior, with 43 % of young adults in this age range reporting binge drinking [34]. Youth living with HIV are similarly likely to report high-risk substance abuse behaviors, such as binge drinking, use of marijuana and other drugs, as well as use of drugs during sexual activity. In addition, among youth living with HIV, substance abuse is associated with decreased adherence to cART and risky sexual behaviors. Screening for substance abuse in persons living with HIV is recommended at least yearly and more often if issues of adherence to therapy arise.

HIV-Associated Neurocognitive Conditions

Perinatally infected young adults with increased HIV severity (at any point during their childhood) are at risk for neurocognitive effects of HIV infection. Risk factors for neurocognitive disease include history of HIV encephalopathy, higher peak viral load, and earlier nadir CD4 count [17]. Behaviorally infected youth have also been found to exhibit impairments in neurocognitive function, although it is unclear if these are premorbid impairments or are due directly to HIV infection. Abnormalities include psychomotor and cognitive slowing, deficits in learning and memory and executive function, as well as fine motor impairments [17]. A meta-analysis of studies looking at cognitive deficits in children with HIV (most via perinatal transmission) have shown lower performance on standardized tests of cognition and IQ when compared to healthy controls, as well as poorer academic performance of varying types (learning

disabilities, failing, or repeating grade levels) among HIV-infected youth [18]. There is little data on prevention of neurocognitive impairment in this patient population, and risk factors for development are not consistent among studies. However, most studies of pediatric HIV patients suggest that although disease severity is associated with worse performance on measures of cognition, cART alone does not slow or prevent cognitive impairment and psychosocial wellbeing of the youth, and caregivers may be vitally important to diminishing any negative impact of HIV infection and treatment on cognitive development in youth and adolescents [18]. Some adult providers may not consider issues such as home environment and prior parental or caregiver mental health as predictors of neurocognitive development in their patient population, but they should address these issues with their young adult patients who are living with HIV. In addition, providers should have a strong index of suspicion regarding potential neurocognitive deficits in these patients and how these deficits may affect the ability of patients to engage in adult activities such as employment and post-secondary education as well as their engagement with the health care system.

Metabolic Disease in HIV Infection

Several metabolic complications associated with cART have been documented in youth and young adults living with HIV, including lipodystrophy, hyperlipidemia, poor bone health, micronutrient deficiencies, and insulin resistance [19]. Protease inhibitors increase the risk of metabolic disorders, such as hyperlipidemia and hyperglycemia. Patients on protease inhibitor therapy should be screened early and often for the development of diabetes, particularly in those who are also obese. However, there are no long-term studies of outcomes of metabolic complications of therapy in this age group, and no recommendations on screening for metabolic disease exist for adolescents and young adults. Care for these patients are extrapolated from care of adults with HIV infection [38]. As a result of cART-associated lipodystrophy and HIV effects on pancreatic function, some youth and young adults with HIV develop elevated serum triglyceride and low-density lipoprotein (LDL) cholesterol levels as well as insulin resistance. Because these conditions have been associated with an increased risk of cardiovascular disease among adults with HIV, concern for similar outcomes among youth and young adults with HIV is raised. The effects of ART on bone development and bone mineral density in HIV-infected youth are unknown, but among HIV-infected adults, decreases in bone mineral density are associated with increased risk of fractures in Caucasian and African-American patients [39]. However, decreases in bone density with specific ARVs, such as tenofovir, appear to be reversible and bone density has been shown to return to normal after cessation. More importantly, uncontrolled HIV viremia has also been shown to adversely affect bone health in adults with HIV. HIV has been associated with increased fracture risk in men. There are no evidence-based recommendations on use of dual-energy X-ray absorptiometry (DEXA) scanning for osteopenia and osteoporosis screening in young adults with HIV.

Special Topics in Youth and Young Adults Living with HIV Infections

Reproductive Health in Young Women Living with HIV

HIV does not appear to affect fertility for young women with HIV, and pregnancies are common in this group. As in all women of reproductive age, the primary care physician should counsel young women with HIV on their options for pregnancy prevention. Because ARVs have multiple drug–drug interactions, previously there were concerns regarding both the effectiveness of hormonal contraception as well as a possible association with injectable hormonal contraception and HIV transmission among women receiving ARVs. However, the U.S. Guidelines for the Medical Eligibility for Contraception

reaffirmed that women with HIV can use any form of hormonal contraception (both progesterone only and combination estrogen-progesterone regimens) without restriction [40]. Women who are interested in pregnancy prevention should be started on hormonal contraception (oral, injectable, or preferably long-acting reversible contraception [LARC]) immediately to prevent unwanted pregnancy. Additionally, they do not require dosing adjustment of ARV medication or drug-level monitoring after the initiation of hormonal contraception.

Retention in Care for Youth with HIV

The National HIV/AIDS Strategy has listed five major components of the HIV Care Continuum: (1) diagnosis, (2) linkage to care, (3) retention and engagement in care, (4) prescription of antiretroviral therapy, and (5) viral suppression. In every aspect of the care continuum, youth and young adults lag behind the general population of those with HIV. Approximately 50 % of youth with HIV are undiagnosed [24]. Of those ages 13–24 living with HIV in 2011, only 73 % were linked to care, compared to 80 % overall [41]. Of the approximately 13,000 youth linked to HIV care, only 56 % of them have achieved viral suppression [42]. Primary care providers caring for this group of patients should expect that retention in care and viral suppression will continue to be challenging and should screen for barriers to adherence to therapy at each visit, even if they are not providing HIV care themselves. Identifying and addressing potential threats to adherence may decrease likelihood of development of drug-resistant virus and HIV-related comorbidities.

Immunization Needs of Young Adults with HIV

All patients with HIV should receive vaccination against influenza yearly as well as one-time vaccination with 13-valent conjugate pneumococcal vaccine and 23-valent polysaccharide pneumococcal vaccine. In addition, patients with HIV infection are at high risk of human papillomavirus (HPV)-related cancers, and so both men and women under the age of 26 should receive vaccination against HPV (2-valent HPV for women or 4-valent or 9-valent for either women or men). HIV is also an indication for vaccination against Hepatitis B virus for all individuals and for Hepatitis A virus for men who have sex with men. HIV is not an independent risk factor for meningococcal disease but young adults should receive age-appropriate vaccination against meningococcal A, C, W, and Y disease during late adolescence if not addressed previously [42].

HPV-Related Cancer Screening

HPV-related cancers include cervical, many anogenital cancers, and some oropharyngeal cancers. Patients with HIV are at higher risk of HPV-related cancers, and this risk is present for both men and women, regardless of type of sexual activity. HIV-infected individuals have a higher prevalence of cancer risk factors, including smoking and oncogenic HPV infection of the oral and genital track, compared to the general U.S. population, which may have an additive effect when combined with immunosuppression from HIV [43–45]. Due to the elevated risk of HPV-related cancers, there are specific recommendations regarding screening for HPV-related disease in women (see Table 11.1) [46, 47].

People with HIV infection have a 30-fold increase in lifetime risk for anal cancer and a fourfold increase in 5-year mortality from invasive anal cancer compared to HIV-unaffected individuals. This disparity continues to exist even when controlling for history of receptive anal intercourse [48]. Although there are no current guidelines for HPV-related anal cancer screening, several studies reviewed the use of anal cytology and high-resolution anoscopy (HRA) as a tool for screening for anal dysplasia and invasive anal cancer in HIV-infected persons. A retrospective cohort analysis of the development of incident invasive anal cancer in HIV-positive

Table 11.1 Recommendations for cervical cancer screening in HIV-infected women compared to general population

	Age < 30		Age 30 or greater	
	HIV (+)	HIV (−)	HIV (+)	HIV (−)
Initiation of Screening	Within 1 year of first sexual activity but no later than age 21[a,b]	Age 21	At time of HIV diagnosis	At initial evaluation if not previously screened
Type of Screening	Pap Test (Cytology) Only	Pap Test (Cytology) Only	Pap (Cytology) + HPV co-testing	Pap (Cytology) + HPV co-testing (age 35 and older)
Screening Interval	Initial: Every 12 months[c]	Initial: Every 3 years	Negative cytology with negative HPV: 3 years Negative cytology with positive HPV (non-16/18): Pap and HPV co-testing in 12 months Negative cytology with positive HPV (16/18): referral for colposcopy	Negative cytology with negative HPV: 5 years Negative cytology with positive HPV (non-16/18): pap and HPV co-testing in 12 months Negative cytology with positive HPV (16/18): referral for colposcopy
	Every 3 years after 3 consecutive negative tests[d,e]	Every 3 years[d,e]	Every 3 years[e,f]	Every 5 years[e,f] until age 65

Adapted from [46, 47]
[a]Women 21–29 years newly infected with HIV should be tested at time of initial HIV diagnosis
[b]Regardless of mechanism of HIV transmission (perinatal or acquired)
[c]Some centers recommend repeat Pap in 6 months after initial Pap in HIV-positive women
[d]Until age 30. After age 30, women should receive co-testing if available
[e]Assuming previous testing negative for abnormal cytology and/or high-risk HPV
[f]Acceptable to have Pap test alone every 3 years after 3 annual consecutive negative tests if co-testing not available

persons after baseline anal cytology demonstrated an association between initial high-grade squamous epithelial lesion (HSIL) and the development of invasive anal cancer (IAC). After a median of 4 years of follow-up, 1.65 % of persons with initial HSIL on baseline cytology developed IAC, with a hazard ratio of 2.92 for development of IAC compared to those without HSIL on baseline cytology [49]. A 2013 study of HIV-positive men with and without a history of receptive anal intercourse (RAI) demonstrated a link between HPV infection and abnormal anal cytology and histology irrespective of RAI history, suggesting that sexual behaviors are not predictive of risk for anal cancer [50]. Reviews of current practices worldwide for anal cancer screening show a mixture of the use of anal cytology and/or high-resolution anoscopy for screening in HIV-positive men and women, and HIV-positive MSM are more likely to be screened than other populations [51]. In the same review, more than 50 % of respondents recommended screening every 2 years with HRA in immunosuppressed patients. While waiting for full recommendations to be developed, the primary care physician should at a minimum discuss anal cancer screening with HIV-infected patients and identify a high-quality referral center performing high volumes of HRA screening to refer to should the patient be interested in screening.

Non-HPV-Related Cancer Screening

Kaposi sarcoma and non-Hodgkin's Lymphoma, the two AIDS-defining malignancies, have decreased in the cART era, due to improvements in immunodeficiency status in patients on cART. However, adults who were diagnosed with AIDS during childhood continue to be at risk for development of AIDS-defining malignancies, although at a much lower incidence than prior to

Table 11.2 Health maintenance screening guidelines for primary care of patients with HIV. Adapted from [38]

Screening	Interval	Reason for recommendation
Digital rectal exam	Consider annually	Examination for anal lesions, anal warts and other HPV-related changes
Depression screening	Annually	Depression is the most common mental health co-morbidity in PLWH
Fasting glucose or HgA1c	Annually	Screening for diabetes due to metabolic dysfunction in HIV infection
Fasting lipid profile	Annually	Screening for hyperlipidemia due to metabolic dysfunction in HIV infection
Trichomoniasis	Annually in women	Increased risk of STI acquisition in women with untreated trichomoniasis
Tobacco use screening and cessation counseling	Annually, and at each visit for active tobacco users	Association with smoking and disease progression in HIV and HIV-associated co-morbidities
STI testing-syphilis, gonorrhea and chlamydia	Annually for those at risk for STIs	Increased incidence of non-HIV STI infection in youth and young adults with HIV due to continued high-risk sexual practices
Alcohol and drug screening	Annually, and at each visit for active users	Increased incidence of alcohol and drug use as part of high-risk sexual behaviors in young adults with HIV
Secondary HIV prevention	At each visit if possible	Prevention of HIV transmission
Medication adherence	At each visit if possible	Maintenance of viral suppression
Intimate Partner Violence screening	At least annually and more often if needed	Patients with HIV are at higher risk of intimate partner violence than general population

HPV human papilloma virus, *PLWH* people living with HIV, *STI* sexually transmitted infection

the cART era [52]. A systematic review also showed an increase in non-AIDS-defining cancers after the introduction of cART, particularly HPV-related anal cancer [53]. A review of cancer registries shows a lower than average risk for prostate and breast cancers but a statistically significant increase in HPV-related cancers as well as Hodgkin's lymphoma, lung, liver, leukemia, and poorly specified cancers [54].

HIV Primary Care Screening

Health maintenance screening is also necessary in young adults transitioning to adult medical care. Young adults with HIV should have yearly preventative medicine visits to address chronic disease management and screening for common comorbidities. The Infectious Diseases Society of America (IDSA) and HIV Medicine Association (HIVMA) released updated guidelines in 2013 for primary care for adults with HIV. Health maintenance activities that are specific to young adults with HIV infection which could be delivered in a primary care practice have been summarized below (see Table 11.2) [38].

Conclusion

Youth and young adults are living with HIV, and life expectancy continues to approach that of non-HIV infected individuals. The majority of HIV-infected adults, regardless of route of transmission, will live with HIV as a chronic medical condition and will need providers skilled in chronic disease management to help them lead healthy lives. Primary care physicians are essential in the care of all patients with chronic disease, but perhaps more so in a population for which their survival is

so dependent on strict medication adherence and chronic disease self-management. As more data on the natural history of adolescents and young adults with HIV develop, physicians will need to remain up to date on recommendations for disease screening and chronic disease management for those living with HIV (Appendix). As these patients transition to adult services, special attention should be given to the challenges unique to HIV-infected patients, including mental health concerns, secondary HIV prevention, increased risk for secondary cancers, and lifelong medication adherence.

Appendix

Human immunodeficiency virus (HIV) condition fact sheet		
Definition	Human immunodeficiency virus (HIV) is a retrovirus that infects helper T lymphocytes and causes CD4 cell depletion resulting in a chronic immunodeficiency • HIV causes AIDS (acquired immunodeficiency syndrome) • Due to advances in treatment, HIV infection is now a chronic disease which is manageable with combination antiretroviral therapy (cART)	
Epidemiology	• Advances in cART have resulted in extended life expectancy for those living with HIV disease • Youth and young adults with perinatal HIV infection make up 18 % of cases of persons with HIV • More than 40 % of perinatally infected persons have been diagnosed with AIDS during their lifetime • Approximately 1 in 4 new HIV infections are in persons age 13–24, and sexual and ethnic minorities are significantly over-represented	
Special considerations	Adolescents and young adults with HIV are at risk for the following conditions related to HIV disease and treatment	
	• Neurocognitive effects of prolonged HIV disease in perinatally infected persons • Metabolic disease, such as diabetes and hyperlipidemia • HPV-related malignancies • Stigma and concerns with HIV disclosure • Disease progression related to non-adherence to therapy	• Body image concerns from lipodystrophy • Secondary HIV prevention • Higher incidence of STI infection and substance abuse in certain populations, such as young men who have sex with men
	Individuals are at heightened risk for chronic conditions, including • Non-AIDS-defining malignancies such as HPV-related cancers (particularly anal cancers), lung cancers, and Hodgkin's lymphoma • Diabetes and hyperlipidemia • Depression and anxiety	
Recommended screening	Annual screening for • Diabetes • Sexually transmitted infections (STI) • Mental health disorders and substance abuse • Hyperlipidemia • Cervical cancer in women (every 3 years after three consecutive normal screenings)	

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