Chapter 13
Human Immunodeficiency Virus and Acquired Immunodeficiency Syndrome

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Etiology and Pathogenesis

Acquired immunodeficiency syndrome (AIDS) is the term initially used by the Centers for Disease Control and Prevention (CDC) in 1981 to describe the phenomenon of young homosexual men in New York and San Francisco dying from infections that individuals with healthy immune systems could fight off easily. Although many suspected a viral cause, this was not confirmed until 1983. The viral cause of AIDS was given the name "human immunodeficiency virus" (HIV), and researchers later identified that AIDS is a late manifestation of this infection [1].

HIV is an RNA retrovirus that is able to attach to and enter CD4+ immune cells in humans (including T cells, T helper cells, dendritic cells, and macrophages) and integrate itself into the host genome. The virus has a complex life cycle that then leads to viral propagation and constant generalized immune system activation. Over time, these immune cells decrease in number and in function, leaving individuals vulnerable to opportunistic infections and tumor growth due to impaired immune system protection, still referred to as AIDS [1, 2].

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Clinical Presentation and Natural History of HIV

The presentation and course of HIV infection may vary widely between individuals. The CDC divides HIV infection into three different stages of disease.

Stage 1: Acute HIV Infection

In early HIV infection, the virus is actively replicating within immune cells in the bloodstream and lymph nodes [3]. Some people may be asymptomatic during this time, while others show signs and symptoms of mild illness, often mimicking the common cold or other minor infections. Common signs and symptoms during this stage of infection are shown in Table 13.1 and are sometimes collectively referred to as acute retroviral syndrome. As these findings can be very nonspecific, practitioners must maintain a high level of suspicion for acute HIV infection [4]. Individuals can be highly infectious during this stage of illness as the viral load can be very high, making transmission to others more efficient.

Stage 2: Clinical Latency

During the second stage of HIV infection, individuals are largely asymptomatic and may not have any clinical signs or symptoms of HIV. During this time, the viral load initially drops as the immune system works to suppress the infection. Over time, HIV weakens the immune system by infecting and killing CD4+ immune cells, which progressively decrease in number. The viral load starts to increase again as the immune system is unable to suppress the infection. When the CD4+ T cell count

Table 13.1 Clinical signs and symptoms of acute HIV infection

Sign/symptom	Frequency in presentation of acute HIV (%)
Fever	75
Fatigue	68
Myalgia	49
Skin rash	48
Headache	45
Pharyngitis	40
Cervical adenopathy	39
Arthralgia	30
Night sweats	28
Diarrhea	27

Adapted from Daar et al. [4]

drops below 500 cells/μL, some individuals may start to develop symptoms such as fatigue, fever, weight loss, and chronic diarrhea. They may also start to develop some mild opportunistic infections such as oral thrush and may manifest oral hairy leukoplakia associated with Epstein-Barr virus infection [5].

Stage 3: AIDS

Once the CD4+ T cell count drops below 200 cells/μL or a person is diagnosed with a characteristic opportunistic infection (see Table 13.2), they are classified as stage 3 disease, or AIDS. In untreated HIV, the incubation period before the onset of AIDS ranges from 1 to 14 years with an average of 6 years. Of those infected, 50–70% are referred to as *typical progressors* and may progress to AIDS over 8–10 years. Five to ten percent are referred to as *rapid progressors* and can develop AIDS within 2–3 years. *Long-term nonprogressors* are individuals who have not yet developed any symptoms of AIDS after 10 or more years since the initial infection (about 5% of those infected) [5].

Epidemiology

Prevalence

According to the CDC, an estimated 1.12 million persons aged 13 years or older were living with HIV in the United States at the end of 2015. Of these individuals, 162,500 (14.5%) were undiagnosed and unaware of their infection [6].

Table 13.2 Examples of opportunistic illnesses and infections in stage-3 HIV

Opportunistic illnesses and infections in stage-3 HIV	
Bacterial sinusitis/pneumonia	Herpes zoster
Candidiasis	Histoplasmosis (disseminated)
Cerebral toxoplasmosis	Kaposi sarcoma
Cervical carcinoma, invasive	*Mycobacterium avium* complex
Coccidioidomycosis	*Mycobacterium tuberculosis*
Cryptococcosis	Non-Hodgkin lymphoma
Cryptosporidiosis	*Pneumocystis jiroveci* pneumonia
Cytomegalovirus disease	Progressive multifocal leukoencephalopathy
Central nervous system lymphoma	*Salmonella* septicemia, recurrent
Herpes simplex virus	Wasting syndrome attributed to HIV

Adapted from Selik et al. [61]

Incidence

Overall incidence of new HIV infection in the United States has been relatively stable from 2011 to 2016 with around 40,000 new infections per year. However, the incidence for those aged 25–34 years has been slowly *increasing* over this same time period, accounting for 34.3% of all new HIV infections in 2016 [7].

Age

As of 2015, there were an estimated 60,300 persons between the ages of 13 and 24 years of age living with HIV in the United States (making up 5.4% of the total prevalence of HIV). Of these youth, 51.4% were undiagnosed and unaware of their infection, making this the largest percentage of undiagnosed HIV infection compared to any other age group [6]. Given the higher incidence of new HIV infection in adolescents and young adults (AYAs), many strategies to address HIV in the United States have focused on this age group.

Gender

According to CDC data from 2016, males account for the majority of HIV diagnoses in all age groups, making up 84% of those 13–19 years old and 89% of those 20–24 years old who are diagnosed with HIV [8]. In the National Transgender Discrimination Survey in 2011, 2.64% of transgender adults reported a diagnosis of HIV, over four times the rate of HIV in the general US population [9].

Race/Ethnicity

New HIV infections continue to disproportionately affect individuals within communities of color. Of the estimated 8536 youth aged 13–24 years who were diagnosed with new HIV infections in 2016, 4629 (54.2%) identified as Black/African American and 2040 (23.9%) identified as Hispanic/Latinx [7].

Transmission Category

As seen in Table 13.3, the most common route of transmission in AYA males is male-to-male sexual contact, while the most common route in AYA females is heterosexual contact [8].

Table 13.3 Diagnoses of HIV infection among male and female adolescents and young adults, by age group and transmission category, 2016 – United States and six dependent areas

	Males				Females			
	13–19 years		20–24 years		13–19 years		20–24 years	
Transmission category	No.	%	No.	%	No.	%	No.	%
Male-to-male sexual contact	1321	92.7	5595	91.6	–	–	–	–
Injection drug use (IDU)	15	1.0	88	1.4	17	6.5	76	10.4
Male-to-male sexual contact and IDU	40	2.8	188	3.1	–	–	–	–
Heterosexual contact[a]	42	3.0	234	3.8	222	84.2	650	88.2
Other[b]	6	0.4	6	0.1	25	9.4	10	1.4
Total[c]	**1424**	**100**	**6111**	**100**	**264**	**100**	**737**	**100**

Adapted from the Centers for Disease Control and Prevention [8]

[a]Heterosexual contact with a person known to have, or to be at high risk for, HIV infection

[b]Includes hemophilia, blood transfusion, perinatal exposure, and risk factor not reported or not identified

[c]Because column totals for numbers were calculated independently of the values for the subpopulations, the values in each column may not sum to the column total

Homelessness

AYAs experiencing homelessness are at increased risk for HIV as well as other sexually transmitted infections (STIs). Some studies estimate that 2–11% of youth experiencing homelessness in the United States are living with HIV. This means that they are at 2–10 times the risk of acquiring an HIV infection when compared to the general youth population [10]. Much of this increased risk has been attributed to increased risk behaviors such as risky sexual practices, exchanging sexual acts for survival, injection drug use, and needle sharing. Those experiencing homelessness also often have other psychosocial stressors such as poverty, mental illness, and alcohol and drug use [11]. One study looking into social networks has shown that youth who are centrally associated with other youth experiencing homelessness have more sexual risk-taking behaviors than youth who have more peripheral social positions. This may indicate that exposure to and normalization of risk-taking behaviors of other youth experiencing homelessness may increase participation in these behaviors, placing individuals at higher risk for HIV [12].

Transmission

Modes of Transmission

The transmission of HIV infection occurs by the transfer of the virus in body fluids from an infected individual to an uninfected individual, specifically through blood, semen, pre-seminal fluid, vaginal secretions, rectal secretions, and breast milk. The virus in these fluids must come into contact with the uninfected person through a

mucous membrane (found in the mouth, penis, vagina, and rectum), damaged tissue (i.e., cuts), or directly into the bloodstream (needle stick or placental transmission from mother to child) [13].

Rates of Transmission

Different modes of transmission have different rates of transferring the infection from the infected person to the uninfected person (see Table 13.4). These differences in transmission rates are often accounted for by the type of epithelium or protective lining of different anatomic sites and the potential for breakdown of this protection [14]. It is worth noting that although HIV has been found in saliva, tears, urine, and sweat, there have been no cases of HIV transmission occurring via these fluids.

HIV Testing

Consent and Confidentiality

HIV screening or testing should always be voluntary and only performed with the individual's knowledge and consent. Many settings have incorporated consent for HIV screening into the general informed consent for medical care, and a separate

Table 13.4 Estimated per-exposure risk for acquiring HIV from an infected source

Type of exposure	Rate of HIV acquisition per 10,000 exposures[a]
Blood transfusion	9250
Receptive anal intercourse	138
Needle sharing during injection drug use	63
Percutaneous needle stick	23
Insertive anal intercourse	11
Receptive penile-vaginal intercourse	8
Insertive penile-vaginal intercourse	4
Receptive oral intercourse	Low risk
Insertive oral intercourse	Low risk
Biting	Negligible risk
Spitting	Negligible risk
Throwing body fluids (including semen or saliva)	Negligible risk
Sharing sex toys	Negligible risk

Adapted from Centers for Disease Control and Prevention [14]

[a]Factors that may increase the risk of HIV transmission include sexually transmitted infections, acute- and late-stage HIV infection, and high viral load. Factors that may decrease the risk of HIV transmission include condom use, male circumcision, antiretroviral treatment with viral suppression, and preexposure prophylaxis. None of these factors are accounted for in the transmission rates shown

consent specific to HIV testing is not recommended. Patients should not only be advised of the confidential nature of testing results but also be informed of the requirement of HIV case reporting to the state or local health department. In many states, adolescents under the age of 18 can consent to HIV testing, but this may vary based upon the state in which the test is performed. Professionals should become familiar with the public health statutes in their specific state and strive to protect the privacy and confidentiality of the patient [15].

Pretest Counseling

Prior to HIV testing, patients should be given written or oral information including an explanation of HIV infection, the routine screening recommendations for all individuals, and the meanings of positive and negative results. The individual should also be given the opportunity to ask questions and the ability to decline testing. Any declined test should be documented in the medical record [15].

HIV Testing Recommendations

The CDC recommends that HIV screening be performed routinely in all healthcare settings for patients aged 13–64 years on an opt-out basis. This means that all patients are offered HIV screening as part of their regular medical care but have the option to decline the test [15]. The US Preventive Services Task Force (USPSTF) recommendations for screening are very similar to the CDC but recommend routine screening for those aged 15–65 years. Screening in youth less than 13–15 years of age should occur for those determined to be at increased risk [16].

All pregnant individuals should be screened for HIV early in each pregnancy, and any declined test should be documented in the medical record. All patients starting treatment for tuberculosis should also be screening for HIV. In addition, patients seeking testing or treatment for sexually transmitted infections (STIs) should be screened routinely for HIV during each visit [15].

Repeat screening (at least annually) is recommended for those who are likely to be at high risk for HIV. This includes those whose sexual partners are living with HIV and are not virally suppressed, those who use injection drugs and their partners, those who exchange sex for survival (money, food, shelter, drugs, etc.), men who have sex with men, and persons who themselves or whose sex partners have had more than one sexual partner since their most recent HIV test [15]. Youth who are on preexposure prophylaxis (PrEP) for HIV prevention must have an HIV screen every 3 months to safely administer the medication. A recent systemic review looking into the benefits and harms of more frequent than annual HIV screening in men who have sex with men revealed that there is insufficient evidence to change the recommendation to more frequent screening. However, several modeling studies in

the review did predict that more frequent screening in this population (every 3–6 months) may be cost-effective compared with annual screening [17]. Repeat screening in those who are not likely to be at high risk for HIV should be performed based on the clinical judgment of the provider [15].

Diagnostic HIV testing should be conducted in all individuals with signs or symptoms of HIV infection or with an AIDS-defining opportunistic infection. If acute retroviral syndrome is possible, it is recommended to use a plasma RNA test in addition to an HIV antibody test [15].

HIV Testing Methods

Many tests have been developed for the detection of HIV infection. Over time, the tests have become easier to administer with quicker results and earlier detection from the time of infection. The currently available testing methods are shown in Table 13.5. Enzyme-linked immunoassay (EIA) methods are often available as rapid tests, giving results within 1–20 minutes of performing the test. These rapid tests (oral swabs or blood samples) are often used for HIV screening due to lower cost, easy administration in any setting, and the ability to provide the result during the same encounter. Western blot and viral load testing require analysis in a laboratory and are more expensive; thus, they are not recommended for HIV screening. Western blot may be used for confirmatory testing after a positive EIA test, but this has largely been replaced by HIV RNA PCR (viral load). Viral load testing can be used for initial HIV testing if there is a clinical suspicion for acute HIV infection that may be missed by other testing methods. Viral load testing is also used to monitor the course of treatment of HIV with the goal of suppressing the viral load to undetectable [18–20].

Table 13.5 HIV diagnostic testing windows

Testing method	Target of detection	Estimated window from infection to positive result, days
First-generation EIA	IgG antibody	35–45
Second-generation EIA	IgG antibody	25–35
Third-generation EIA	IgG and IgM antibody	20–30
Fourth-generation EIA	IgG and IgM antibody + p24 antigen	15–20
Western blot	IgG and IgM antibody	Indeterminate: 35–50
		Positive: 45–60
Viral load (cutoff 50 copies/mL)	HIV RNA	10–15
Viral load, ultrasensitive (cutoff 1–5 copies/mL)	HIV RNA	5

Adapted from: Branson and Stekler [18], Cohen et al. [19], Owen [20]
EIA enzyme-linked immunoassay, *IgG* immunoglobulin G, *IgM* immunoglobulin M, *RNA* ribonucleic acid

Posttest Counseling

HIV test results should be communicated to patients as soon as possible in order to maximize the number of individuals who are aware of their HIV status.

Negative Result

Testing results that are negative for HIV can be communicated to patients without direct personal contact between the patient and provider. Patients who are at increased risk for HIV should be given recommendations for repeat screening. Those who want assistance with modifying risk behaviors should also be provided with referrals to risk-reduction services. These may include prevention services (such as PrEP or PEP) or risk-reduction counseling (discussed in the section on prevention), treatment for STIs, substance use treatment, mental health treatment, or other supportive services [15].

Positive Result

Testing results that are positive for HIV should be communicated through personal contact by the provider with an emphasis on preserving confidentiality. Any positive rapid HIV test result is preliminary and must be confirmed by further testing before the diagnosis of HIV is established. Any individuals who have a confirmed diagnosis of HIV infection should be linked to clinical care as soon as possible and referred to supportive services. Rapid initiation of treatment improves retention in care and can reduce transmission of HIV. Practitioners should strongly encourage patients with HIV infection to disclose their diagnosis to their spouses as well as any current or previous sex partners and recommend that they also be tested for HIV. Health departments are able to assist patients in this process while preserving confidentiality. In addition, any positive HIV testing results must be reported to the state or local health department, and patients should be made aware that this report will be made [15].

HIV Testing Rates

Rates of testing for HIV among youth experiencing homelessness tend to be higher than the rates among youth in the general population. Many studies indicate that more than half of homeless youth have ever been tested for either HIV or STIs compared to 22.6% of sexually active youth in the general population. Some factors associated with increased rates of testing in youth experiencing homelessness include youth who self-identified as gay, identified as Hispanic, used injection drugs, and used drop-in centers. Many studies in this area use convenience samples

of homeless youth and are not able to be generalized to youth outside of these samples. It is also difficult to determine the structural factors such as service utilization that likely impacts the rates of HIV testing [21].

HIV Prevention

Since the beginning of the HIV epidemic, many medical, scientific, and public health advances have decreased the number of new infections from an estimated 130,000 in 1985 down to an estimated 37,600 in 2014 [22].

Treatment as Prevention (TasP)

One major advance in preventing new HIV infections has been termed treatment as prevention (TasP). In 2016, in the landmark HIV Prevention Trials Network 052 study, it was shown that early initiation of antiretroviral therapy (ART) was associated with a 93% relative reduction in the risk of transmission when compared to delayed ART. This study also established that in participants who were stably virally suppressed throughout the study, there were zero linked infections observed [23]. In the same year, the PARTNERS study showed that in heterosexual couples who did not use condoms, there were no transmissions of HIV from partners living with HIV who were virally suppressed [24]. After the release of this information in 2016, the Prevention Access Campaign launched the slogan *Undetectable = Untransmittable* (*U = U*) [25]. In 2017, the CDC officially recognized that individuals who take ART and achieve an undetectable viral load do not sexually transmit the infection to their partners [26].

Preexposure Prophylaxis (PrEP)

Preexposure prophylaxis (PrEP) is a relatively new HIV prevention method. In order to work, an individual who is HIV-negative takes one daily pill in order to prevent HIV infection. The medication approved by the US Food and Drug Administration (FDA) in 2012 for use in adults for this purpose is called Truvada (a combination of two antiretroviral medications, tenofovir disoproxil fumarate and emtricitabine). This medication has been shown to be safe and is effective at reducing the risk of HIV from sexual transmission by more than 90% when taken daily [27]. Recently, in 2018, based on studies of medication safety and efficacy in AYAs, the FDA expanded the indication for Truvada for PrEP in any individuals, including minors, who weigh at least 35 kg [28]. In 2019, a second medication (Descovy) was approved by the FDA for use as PrEP in any individuals weighing at least 35 kg, excluding vaginal HIV exposures [29].

Table 13.6 Preexposure prophylaxis (PrEP) visit recommendations

Laboratory test or counseling	Initial visit	1 mo	3 mo	6 mo	9 mo	12 mo, etc.
HIV antibody, blood (every 3 mo)[a]	+	+/−[f]	+	+	+	+
Creatinine (every 6 mo)[b]	+		+/−[f]	+	+/−[f]	+
Weight (every 6 mo)[b]	+		+/−[f]	+	+/−[f]	+
Hepatitis B surface antibody[c]	+					
Hepatitis B surface antigen[c]	+					
Hepatitis C virus antibody[c]	+					
Urine pregnancy (if applicable)	+/−[f]	+/−[f]	+/−[f]	+/−[f]	+/−[f]	+/−[f]
RPR (every 3–6 mo)[d]	+	+/−[f]	+/−[f]	+	+/−[f]	+
GC/CT (every 3–6 mo)[d]	+	+/−[f]	+/−[f]	+	+/−[f]	+
Medication counseling[e]	+	+	+	+	+	+
Adherence counseling	+	+	+	+	+	+
Risk reduction counseling	+	+	+	+	+	+

RPR rapid plasma reagin test for syphilis, *GC* gonorrhea, *CT* chlamydia

[a]Rapid blood HIV testing is valid, but oral swabs are not adequate. A viral load may be sent if there have been possible symptoms of acute HIV in the prior 1–2 months

[b]Creatinine and weight are used to calculate creatinine clearance (CrCl must be ≥60 to be on Truvada without renal dosing)

[c]Hepatitis is not a contraindication to Truvada, but individuals must be counseled that their hepatitis may reactivate when discontinuing Truvada; consider referral to a specialist. Those who are nonimmune to hepatitis B should be vaccinated

[d]Frequency of STI screening should be based upon risk factors and patient preference. GC/CT screening should be performed at any sites of sexual contact (urine, vaginal, rectal, pharyngeal)

[e]Medication counseling should include discussions about time to efficacy (reaches maximum levels in rectal tissue in 7 days, maximum levels in other sites in 20 days), efficacy (reduces the risk of HIV from sex by >90% and from injection drugs by >70%), and side effects (i.e., headache, abdominal pain, and decreased appetite that usually resolve over time)

[f]More frequent screening should take place based upon clinical suspicion for the disease or condition

PrEP can be initiated by any prescribing practitioner and should be discussed with any patients who are at risk for HIV or who are requesting PrEP. The CDC has created guidelines and supplemental reports to assist providers in delivering this important service to prevent HIV infection [27, 30]. Please see Table 13.6 for an example of recommended tasks during PrEP visits.

Recent data from the IPERGAY study in 2017 showed that "on-demand" PrEP may be highly efficacious at preventing HIV among men who have sex with men at risk for the infection with a relative reduction of 97% in new HIV infections compared to placebo. This regimen consists of taking two tablets of Truvada 2–24 hours before sex and one tablet at both 24 and 48 hours after sex [31]. Since many individuals in the study were using on-demand PrEP frequently, many were taking an average of 15 doses per month. Thus, this efficacy may be confounded by the finding in previous PrEP studies that those who took 4 doses of PrEP per week were able to achieve 96% relative risk reduction [32]. However, the efficacy of on-demand PrEP is further supported by the pharmacology of Truvada dosing for men who have sex with men and transgender women in the Cell PrEP study. This study found that

after 4 initial doses of Truvada, medication levels corresponded to a 98% relative risk reduction in 84% of participants [33]. The convenience of on-demand PrEP for those with infrequent sexual exposures must be balanced with the fact that the regimen must be started prior to sexual activity and would require future-oriented thinking. This may be difficult for younger patients or those who have psychosocial stressors that may impact adherence. Current evidence supports on-demand PrEP as an alternative dosing strategy in those with infrequent sexual exposures and offers much more protection than no PrEP at all.

With the emergence of new prevention methods and efforts to increase patient access and retention, many sites have incorporated PrEP and PEP "navigators" to assist with patient care for these prevention methods. These peer navigators can assist with engaging patients in care, providing information and counseling regarding HIV and PrEP/PEP, as well as helping patients to navigate the healthcare system (insurance, payment assistance, pharmacies, etc.). These services are essential, especially for youth seeking HIV prevention services.

Postexposure Prophylaxis (PEP)

While PrEP is a preventive medication that is taken all of the time to preemptively cover possible exposures to HIV, postexposure prophylaxis (PEP) is an emergency medical regimen given after a substantial possible exposure to HIV to decrease the risk of contracting HIV. In order to differentiate the two, some describe PrEP as the "birth control" for HIV and PEP as the "emergency contraception" for HIV infection. PEP must be started within 72 hours of the possible HIV exposure and consists of three antiretroviral medications (as opposed to two medications in PrEP). In occupational HIV exposure data, PEP demonstrated an 81% reduction in the odds of contracting HIV with 28 days of treatment [14].

PEP can also be initiated by any prescribing practitioner. The preferred medication regimen for adults and adolescents aged ≥13 years with normal kidney function is Truvada (tenofovir disoproxil fumarate and emtricitabine) once daily *with either* dolutegravir 50 mg once daily *or* raltegravir 400 mg twice daily. This combination is taken for 28 days to complete the course of PEP. At that time, those who are at continued risk for HIV should be transitioned to PrEP for continued protection against future possible exposures. The CDC has also created guidelines to assist providers in delivering PEP [14].

Risk-Reduction Counseling

In order to achieve primary prevention of HIV infection, providers must also effectively promote behavioral change through risk-reduction counseling. This method creates a dialogue between the patient and the provider to increase knowledge,

skills, and self-efficacy while acknowledging the individual's feelings, beliefs, attitudes, and values [34].

In this patient-centered counseling session, the discussion is built around previously obtained information including sexual history (number of partners, gender of partners, sexual practices, patterns of condom use, and pregnancy prevention), drug and/or alcohol use prior to or during sexual activity, use of injection drugs, and history of STI/HIV testing and infection. The practitioner can ask them to identify any of these behaviors they would like to change. After assessing their willingness to change, the practitioner can assist the patient in identifying a safer goal behavior that can reduce or prevent the risk of HIV. This is followed by praising planned or accomplished efforts and helps them to identify any barriers to change. The final step for the session is for the patient to identify a specific step they can take to help create this change [34]. Many of the fundamentals of this counseling strategy are based in motivational interviewing (MI), and training in MI is advisable for those administering risk-reduction counseling. Risk-reduction counseling can take place in a 15- to 20-minute session and can be carried out by a variety of providers [35].

Other Barriers to Prevention

Despite having effective ways to prevent HIV, the literature shows that there are barriers to accessing these services and ideal outcomes. For example, TasP could have the potential to stop any new HIV infections if it were able to be fully implemented. One study, however, notes that this strategy alone has limitations in real-world populations where even slight delays in testing, treatment, and adherence would keep the transmission rate from reaching zero. This method must likely be combined with other existing HIV prevention methods in order to have the maximal effect on transmission. This required multifaceted approach may make financial allocation difficult in where to place priority [36].

There are also many barriers that exist for youth to access HIV prevention services. Compounded onto other baseline social determinants of health are the issues of consent and confidentiality, financial barriers, and even the stigma associated with sexual activity and HIV, even in seeking prevention services. One study examining barriers to HIV prevention for the young black MSM population identified that these youth have inadequate access to culturally competent prevention services including limited services in areas where they live and a deficiency of these services within correctional institutions. The authors recommend structural interventions to eliminate barriers to HIV testing and prevention and to provide these youth with skills to navigate the complex healthcare system [37].

Once programs are in place that youth can access, services must also be tailored to ensure completion of the interventions. One study examined if motivational barriers would predict youth retention in an HIV prevention counseling program. Those younger participants who felt pressured to attend the program as well as those who

perceived the program as ineffective had lower rates of retention. The authors recommend that programs should ensure that younger clients do not feel coerced into participation and that practitioners make every effort to communicate the efficacy of the intervention. Programs should also help participants foster a sense of self-relevance with the intervention in order to improve retention [38].

HIV Prevention Research in Homeless Youth

A systematic review in 2011 looked at different interventions to modify HIV sexual risk behaviors in youth experiencing homelessness. The review only found three eligible studies and was unable to estimate the effectiveness of the interventions due to high variability in the studies and lack of rigorous methodology. This lack of evidence for prevention work is a large area for improvement within research on homeless youth [39].

Few studies have looked into identifying specific correlates or predictors of HIV risk behaviors in youth experiencing homelessness. One such study found that female sex, belonging to a sexual minority group, depression, alcohol use to intoxication, and frequent traveling between cities were associated with unprotected sex [40]. For homeless youth, Internet use and social networking that maintains connections to family or home-based peers has been associated with decreased unprotected sex and lower sexual risk behavior [41, 42]. In looking at factors associated with homeless youths' motivation to change HIV risk behaviors, shorter period of current homelessness was the only factor that predicted higher levels of motivation to change HIV risk behaviors [43]. Future studies should focus on ways to improve HIV prevention strategies for youth experiencing homelessness.

HIV Management

Since the first antiretroviral medication (zidovudine, "AZT") was developed and approved by the FDA in 1987, there have been many breakthroughs in the area of HIV management. One such advancement was the development of protease inhibitor medications that allowed for the first highly active antiretroviral treatment (HAART) in 1995 and led to the first decline in new HIV cases since the epidemic began. In 1990, the Ryan White Act was passed by the Congress allowing for the creation of a federal funding program to support community-based care and treatment services for HIV, which still allows for increased access to care for patients to this day [44].

Medication regimens continue to improve with fewer pills required per day, less side effects, and better suppression of the virus in individuals living with HIV. While the science of HIV treatment has advanced rapidly, many barriers remain in all areas of management that require continued investigation and development of improved treatment models.

HIV Care Continuum

Dr. Edward Gardner and his team first described the different levels of engagement in HIV care in 2011. They recognized that in order to fully benefit from antiretroviral medications, patients must not only be tested and treated but must also be regularly engaged in their medical care, receive medications, and adhere to the recommended treatment [45]. This "care continuum" (see Fig. 13.1) became more widely disseminated through the formation of the HIV Care Continuum Initiative, created via Execute Order by President Barack Obama in 2013. This framework has been adopted internationally and has been used to establish measurable indicators for HIV care. Using this continuum, the current National HIV/AIDS Strategy (NHAS) for the United States outlines measurable outcome indicators in order to assess the progress of improving HIV care [46].

Diagnosis and Testing

In order to first identify those who should receive HIV treatment, individuals must be tested for HIV and diagnosed with the infection. The recognition of this important step in treatment has prompted the previously discussed HIV screening recommendations from the CDC and USPSTF. However, despite these recommendations, many individuals living with HIV remain unaware of their infection with youth and young adults aged 13–34 years having the highest proportion of undiagnosed

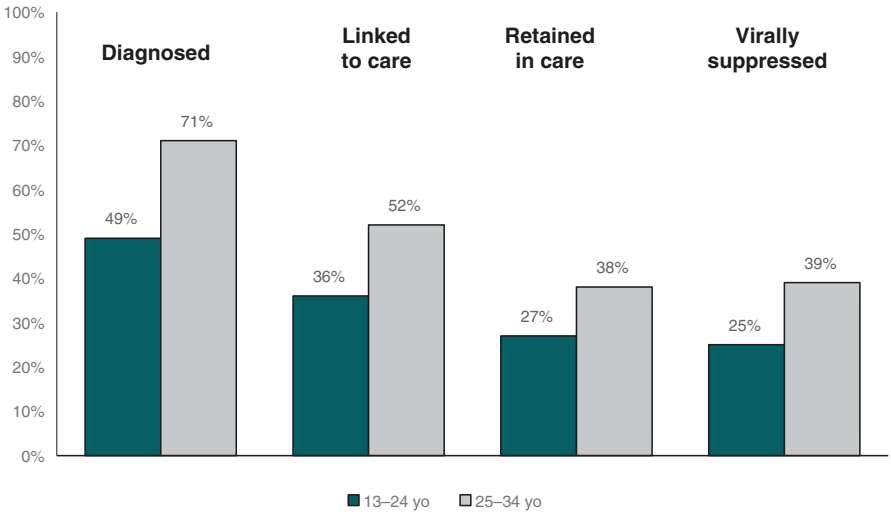

Fig. 13.1 HIV care continuum data in adolescents and young adults, 2015. (Adapted from Centers for Disease Control and Prevention [48])

HIV. These individuals are unable to proceed with any treatment until they are aware of the infection [47, 48]. To address this barrier, the NHAS has set the goal of increasing awareness of HIV status to 90% among those living with HIV by 2020 [46].

In order to continue to improve in this area, providers, clinics, and agencies serving youth experiencing homelessness should strive to offer HIV screening to all youth as recommended by the CDC. By using tests that allow for rapid results with a shorter time-to-positivity window, more youth will be able to find out their HIV status during the same visit, earlier in the course of infection. This is particularly important for youth who may be transiently housed or who move frequently between service providers.

Linkage to Care

This step of the continuum refers to connecting individuals who are diagnosed with HIV to a care provider. The NHAS goal for 2020 is to link 85% of people living with HIV to a care provider within 1 month of diagnosis. Care models that have had higher success with linkage to care in vulnerable populations involve the collaboration of interdisciplinary providers with multiple sites of service access [47].

Retention in Care

According to the CDC, individuals are considered "retained in care" if they have had at least two visits for HIV medical care, at least 3 months apart, within the past year [47]. It is often difficult to estimate the rates of retention in care in any population that may have more transient housing and changes sites of service utilization. Some areas of the country have established inter-agency partnerships (such as the Hollywood Homeless Youth Partnership) in order to help find and track youth who may move frequently between local service sites [49].

Viral Suppression

The primary goal of public health interventions in HIV management is achieving viral suppression (most recent viral load of <200 copies/mL, performed within the last year) using antiretroviral therapy [49]. The NHAS goal for 2020 is to achieve viral suppression in 80% of those diagnosed with HIV infection [46]. This final step of the continuum has the potential to improve the health of individuals living with HIV and prevent transmissions of the infection to others. Although this is the ultimate goal of management, individuals should be encouraged at every level of the continuum. Providers need to be aware of and to address the societal determinants of health for individuals living with HIV as these can have complex impacts on engagement in the HIV care continuum.

Components of HIV Treatment

As there is no current cure for HIV infection, the primary goal of treatment is to reduce associated morbidities and to improve the quality and length of life through suppression of the viral load and improvement in immune function. This section briefly reviews some principles of HIV treatment. Please note that patient care should involve the assistance of an HIV specialist when possible given the complexity of testing and medication selection.

Initial Testing

After the confirmed diagnosis of HIV infection, individuals should receive a CD4 cell count and percentage, HIV RNA level, HIV genotype (test for resistance), complete blood count with differential, complete metabolic panel including hepatic and renal function, fasting blood glucose and lipid panel, vitamin D level, urinalysis, tuberculosis screening, STI screening (syphilis, gonorrhea, chlamydia), viral hepatitis screening, and cervical and/or anal Pap testing if indicated. Additional laboratory tests may be sent for specific patients or if certain medications may be used for HIV treatment [50].

Principles of ART

The basic principle of ART is to use multiple mediations that are directed against different stages of the HIV life cycle in order to make treatment more effective and avoid the development of resistance to medications. There are currently six drug classes used to treat HIV. Usual medication regimens consist of using three different medications from at least two different drug classes. Medications are selected based upon the patient's HIV genotype, coexisting conditions, and potential medication interactions. Practitioners also try to choose a regimen that has the lowest number of pills per day and are more tolerable with less side effects [50].

Until relatively recently, providers often delayed treatment with ART until a patient's immune system began to weaken and approach the diagnosis of AIDS (CD4+ count of $\leq$350 cells/mL). The landmark START (Strategic Timing of Antiretroviral Treatment) study in 2015 showed that early initiation of ART provided net benefit over delayed treatment by decreasing rates of opportunistic infections, AIDS-related cancers, liver and renal disease, cardiovascular disease, and death [51]. Patients are now started on ART as early as possible after diagnosis with HIV in order to improve their health and prevent new HIV infections through TasP. Effective viral suppression and continued engagement in HIV care have the ability to extend the mortality of those living with HIV to that of the general population.

Although everyone with HIV should be on ART as much as possible, there are times when individuals are unable to adhere to their medical regimen. This may be due to difficulties with housing, money, insurance, healthcare access, stigma, mental health, substance use, or a multitude of other psychosocial stressors. At times, it may be advisable to take a break from ART and concentrate on addressing these other stressors. Individuals who are less adherent to their medications may be at higher risk of inducing resistance to the medications and may make continued HIV treatment much more difficult in the future.

Monitoring

Those who are asymptomatic and on ART should be monitored with bloodwork every 3–6 months with CD4+ cell count and percentage, HIV viral load, urinalysis, hepatic and renal function, as well as fasting lipids and glucose level [50]. Patients should also be monitored for side effects, adherence, opportunistic infections, and psychosocial stressors.

Risk Reduction

All individuals living with HIV should be counseled on the modes of transmission of HIV and ways to reduce the risk of transmitting the infection to others. It is safe for those living with HIV to be in close contact with others (HIV is only spread through sexual contact, exposure to infected blood or breast milk, and perinatal transmission). While bathroom facilities can be shared, it is important to note that those living with HIV should not share hygiene items such as toothbrushes or razors.

To decrease transmission, individuals should notify sexual partners and health providers of their HIV status, use condoms with sexual activity, encourage HIV-negative partners to use PrEP (or PEP if needed), avoid sharing any syringes or needles, perform screening for STIs regularly, and adhere to their ART medications. Those who are living with HIV are also not able to donate blood, semen, or body organs. Those who are or may become pregnant should be counseled on ways to decrease transmission to their partners during conception and methods for decreasing transmission to their future children. They should also be offered options for family planning and pregnancy prevention as indicated [50, 52].

Opportunistic Infections (OIs)

OIs (Table 13.2) are those infections that healthy individuals are usually able to fight off or prevent with an intact immune system but can cause severe or prolonged disease in those living with HIV and a compromised immune system.

Prophylaxis

Prophylaxis and treatment for opportunistic infections are guided by the CD4+ cell count and percentage as well as any signs or symptoms of infection. Patients often become vulnerable to some of these infections (such as *Pneumocystis* pneumonia) when their CD4+ cell count approaches or drops beneath 200 cells/mL. The risk of infections associated with end-stage AIDS (such as *Mycobacterium avium* complex) increases when the CD4+ cell count goes below 75 cells/mL. Prophylaxis for these conditions may be discontinued once the CD4+ cell count has been above 200 cells/mL for at least 3 months [50].

Evaluation

Professionals who do not routinely work with patients living with HIV may become overly concerned by any sign of potential infection. It is important to remember that all people occasionally experience fever, sore throat, cough, diarrhea, or other common indications of mild infection. Patients living with HIV who have signs or symptoms of acute infection should first have a standard evaluation by a medical provider as is recommended for any individual living with or without HIV infection. If there is suspicion for a possible OI, the patient's CD4+ cell count should be measured. Those with a normal cell count and mild symptoms should be treated as any other individual. If symptoms are severe and prolonged or if the CD4+ cell count is less than 200 cells/mL, the patient should be further evaluated for an OI and may require consultation with an HIV or infectious disease specialist.

Vaccination

In an effort to decrease opportunistic and other infections in those living with HIV, certain immunizations are recommended. Some must be given when the CD4+ cell count is above 200 cells/mL, particularly live viral vaccines. These vaccines include *Streptococcus pneumoniae*, influenza (inactivated), hepatitis A and B series, human papillomavirus (HPV) series, varicella series, tetanus/diphtheria/pertussis (TdaP), and meningococcus [50].

Addressing Barriers to Care

As previously described, engagement in all levels of the HIV care continuum is required for successful viral suppression in HIV treatment. There are many barriers to optimal HIV care for youth and young adults that are further amplified in those experiencing homelessness. As with many areas of medicine, the societal determinants of health must be addressed in order to increase access to and engagement in care [53].

Adherence

Many barriers to care can have a direct or indirect effect on the ability of a patient to adhere to their medical treatment plan. Table 13.7 outlines examples of barriers that can affect adherence to HIV treatment in adolescents and young adults. AYAs experiencing homelessness often have many of the barriers listed that overlap based on their psychosocial development, support system, and comorbid conditions.

In order to address these barriers to adherence, many intervention models have been trialed for efficacy in improving patient adherence. A recent systematic review and meta-analysis on adherence found that interventions focusing on behavioral strategies, particularly habit-based interventions, were more effective than cognitive strategies to change participants' knowledge and/or beliefs [54]. A pilot study examined the use of a cell phone support intervention to improve adherence and psychosocial outcomes for youth living with HIV. This study found preliminary data that supports this intervention for decreasing perceived stress, substance use, depression, and increasing self-efficacy in comparison to those who received standard care [55].

A recent randomized control trial looked into using mindfulness-based stress reduction (MBSR) in youth living with HIV. Results suggest that those who participated in the intervention reported improved problem-solving coping and life satisfaction with lower levels of aggression. Individuals in the MBSR group also had significantly lower viral load measurements which may indicate improved medication adherence as well [56]. As of particular concern for youth experiencing homelessness, a recent meta-analysis looked into the effect of housing stability on medication adherence in HIV treatment. The study found that patients with more

Table 13.7 Barriers to adherence in AYAs living with HIV

Medical barriers	*Developmental barriers*
Lack of understanding about condition or medications	Underdeveloped problem-solving skills
Complexity of the medical regimen (i.e., number of pills, frequency)	Preoccupation with self-image
Adverse effects of treatment	Need for peer acceptance
If asymptomatic, difficulty accepting implications of the disease	Difficulty with future-directed thinking (present oriented)
Psychosocial barriers	Desire to establish independence and self-sufficiency
Lack of adult and peer social support	*HIV stigma barriers*
Busy or unstructured life or schedule	Fear of disclosure of HIV status to others
Lack of stable housing	Difficulty coming to terms with a life-threatening illness
Co-occurring mental health or substance use condition	Distrust of healthcare providers and systems

Adapted from Simons and Belzer [62]

stable housing had better adherence to their medications, but this difference was small. Some treatment guidelines and practitioners advocate for deferring HIV treatment until after housing and other psychosocial needs are met, which may need to be reconsidered based upon these new findings [57].

Psychosocial Support and Trauma-Informed Care

Youth experiencing homelessness who have acquired HIV through risk behaviors often experience rejection, stigma, violence, and discrimination after disclosure of their HIV status. Many are at increased risk for substance use, mental health conditions, and sexual victimization. Specific actions can be taken in order to provide high-quality care for these youth and young adults and to establish comprehensive multifaceted services [58].

Services should be structured to be youth-friendly and focus on confidentiality, stigma, and HIV disclosure. Improved outcomes are reported when confidentiality and privacy policies are discussed during each visit and implemented for all youth. Services should address ways that youth can cope with their diagnosis of HIV in a developmentally appropriate fashion that works to destigmatize their illness. Case management and interdisciplinary care teams (physicians, nurses, mental health providers, dieticians, social workers, etc.) should be available to provide a medical home to address all societal determinants of health and strive to provide continuity of care. Secure messaging that is Health Information Portability and Accountability Act (HIPAA)-compliant through mobile phones, the Internet, and social media can also be used to improve engagement in care and adherence to medications [58].

The Ryan White HIV/AIDS Program (RWHAP) currently provides support for direct healthcare services and support for more than 50% of all people living with diagnosed HIV in the United States. These services are patient-centered and coordinated with city, state, and local community-based organizations to provide efficient linkage to care, healthcare services, and supportive services for low-income individuals living with HIV. This program is essential to ensuring that people living with HIV are able to fully participate in the HIV care continuum by striving to address the psychosocial determinants of health [59].

Current Status of HIV Care and Homelessness

Data on the current status of HIV care in the United States is constantly updating and changing. Specific HIV data on youth experiencing homelessness can be difficult to assess, but the RWHAP's most recent report included data on housing status for all individuals living with HIV served by the program. In 2016, among those who reported stable housing, 86.1% were virally suppressed, compared to 78.9% of those reporting temporary housing, and 72.0% of those reporting unsta-

ble housing. This percentage of viral suppression in those reporting unstable housing has, however, increased since 2010 from 54.8%. Viral suppression among youth aged 13–24 years has also improved from 46.6% in 2010 to 71.1% in 2016 [59].

The impact of housing status on engagement in the HIV care continuum has been demonstrated in several studies, and those who are experiencing homelessness have also been shown to be less likely to adhere to HIV treatment. Participants in studies of supportive housing programs have reported the greatest benefit from positive relationships with case managers and assistance with changing health behaviors, improving adherence, maintaining stable housing, and improving overall well-being. Through continuous improvement in patient-centered supportive housing program development and interventional research, more adolescents and young adults will have the resources and support for engagement in the full HIV care continuum [60].

Take-Home Points

1. Despite improvements in HIV care and prevention, new infections continue to disproportionately affect marginalized populations at the highest rates, including adolescents and young adults, those experiencing homelessness, LGBTQ populations, and people of color.
2. Over time, HIV infection can cause a decrease in immune system function and resultant vulnerability to opportunistic infections.
3. All youth experiencing homelessness should be offered screening for HIV and other sexually transmitted infections at least annually.
4. All youth should receive information about recent advances in HIV prevention strategies such as TasP, PrEP, and PEP and linked to appropriate services.
5. Risk reduction strategies including condom use should be encouraged in order to minimize the risk for HIV and other STIs.
6. Providers should be aware of the signs and symptoms of HIV infection and have a high index of suspicion for acute HIV in at-risk populations.
7. Those with a new diagnosis of HIV should be linked to care as soon as possible to optimize continued engagement in care, adherence to ART, and viral suppression.
8. Programs should strive to provide comprehensive case management and interdisciplinary care to support youth living with or at risk for HIV.
9. HIV care and prevention has advanced rapidly in the past 35 years and HIV surveillance data has reflected improvements in the epidemic.
10. Continued improvement in housing resources is essential for ending homelessness and HIV in the United States.

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