Diagnosing HIV Infection in Adult Patients in the Intensive Care Unit

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HIV-infected adults admitted to hospitals for critical care services have unique needs the provider must recognize to deliver optimal care. Unfortunately, many of these patients are unaware of their HIV serostatus on admission to the intensive care unit (ICU), resulting in the need for more specific and tailored screening and diagnostic procedures in the ICU environment.

Intensive care nurse practitioners, physicians, and physician assistants who are responsible for diagnosing and directing care in the ICU should have a solid understanding of the procedures involved in screening patients for HIV, diagnosing HIV-related diseases, and recognizing the diagnostic parameters associated with classifying HIV infection and AIDS. However, the literature on this topic is scant.

We explore the procedures associated with HIV screening and diagnosis in the ICU and describe clinical procedures associated with informed consent, disclosure of serostatus to patients and families, and the classification of HIV infection and AIDS using Centers for Disease Control and Prevention (CDC) guidelines.

HIV Infection in the United States

HIV infection continues to be a prevalent national health problem. Most recent estimates have indicated that 1.2 million persons ages 13 years or older were living with HIV in the United States (CDC, 2012). In addition, 156,300 (12.8%) of these persons were undiagnosed (CDC, 2012). Adult HIV incidence data have shown that new infections remained higher in African Americans (49.4%), Hispanics (18.4%), and for persons of multiple races (10.6%; CDC, 2015a). Males continued to constitute the majority of diagnoses (81%; CDC, 2015a). Men who have sex with men (MSM) had a rising incidence of infection (up to 70% when including injecting drug-using MSM), while heterosexual contact was attributed to 24% of new infections (CDC, 2015a). The southern region of the United States had the highest incidence rate of infections (18.5%), with rates in the Northeast (14.2%), West (11/2%), and Midwest (8.2%) being lower. Persons ages 20 to 29 years had the highest incidence of infection (70.1%; CDC, 2015a).

While specific numeric data regarding diagnoses of AIDS (Stage 3) are not reported here, they trended downward overall but were comparable in regard to race/ethnicity, sex, mode of transmission, region, and age. Similar to new diagnoses of AIDS, deaths in those with HIV also decreased in the last reporting period. However, these data included individuals whose deaths may not have been attributable to HIV. Deaths in individuals with a prior diagnosis of AIDS also decreased, with death rates in MSM, Whites, and Asians remaining stable (CDC, 2015a).

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HIV Infection in the Intensive Care Unit

It is difficult to determine the precise number of HIV-infected adults being treated in ICUs. This is because these individuals often either (a) present with needs for intensive care services that may not be related to HIV infection (Akgun & Miller, 2016) or (b) are not screened for HIV in the ICU. Patients who are infected with HIV but present with problems such as myocardial infarction, cerebrovascular accident, diabetic ketoacidosis, or other conditions managed within the ICU but determined to be unrelated to a patient's immune status, may not prompt the ICU clinician to screen for HIV. In fact, in regions where antiretroviral treatment (ART) is accessible, non-AIDS conditions account for the majority of ICU admissions in people living with HIV infection (PLWH; Akgun & Miller, 2016). In patients presenting with HIV-related complications, *Pneumocystis jirovecii* (formerly *Pneumocystis carinii*) pneumonia accounted for a significant proportion of ICU admissions (Akgun & Miller, 2016; University of California, San Francisco, 2006).

PLWH admitted to the ICU increased in age from the mid-30s to the mid-40s after the availability of ART (Akgun & Miller, 2016), yet this cohort of ICU patients has remained significantly younger than noninfected counterparts (Akgun & Miller, 2016; Akgun, Pisani, & Crothers, 2011; Akgun et al., 2013). Since the availability of ART, 5% to 18% of hospitalizations for PLWH included admission to the ICU, and HIV-associated non-AIDS diseases of the cardiovascular, pulmonary, renal, gastrointestinal, and hepatic organs accounted for the majority of ICU admission diagnoses (Barbier et al., 2014). This does not, however, negate the need for ICU clinicians to know the HIV serostatus of their patients. This is because opportunistic infections and HIV-related diseases continue to affect risk for ICU admission and outcomes. Medical ICU admissions in HIV-infected adults have been found to be more frequent than adults not infected with HIV (Akgun et al., 2013). These patients also have higher 30-day mortality and higher rates of need for mechanical ventilation (Akgun et al., 2013). In addition, this impact has been disproportionate in patients with newly diagnosed HIV infection (Akgun et al., 2013; Barbier et al., 2014).

Informed Consent in the ICU

While screening for HIV is a primary public health directive aimed at early detection of HIV, many persons with risk factors fail to obtain annual screening (U.S. Preventative Task Force [USPTF], 2013). This suggests that many adults who have HIV infection are unaware of being infected with HIV when they present for critical care services. Because CDC guidelines recommend universal opt-out HIV screening for all patients ages 13 to 64 years in any health care setting (CDC, 2010; CDC, 2015b; Morris, 2009; USPTF, 2013), the ICU can be an ideal environment for screening.

The CDC (2010) no longer recommends separate written consent for HIV screening. Instead, general consent for care is considered inclusive for HIV screening. Patients who are conscious and capable of comprehending the risks and benefits of HIV screening need to be notified that HIV screening is going to be performed. These patients can then opt out of screening by declining verbally (CDC, 2010). However, this isn't always possible in patients requiring intensive care services because a large number of ICU patients aren't able to verbally decline an HIV test secondary to a compromised neurologic or mental status, artificial airway, or need for sedation. A patient's health care surrogates should be informed regarding the need for HIV screening and be given the opportunity to opt out on the patient's behalf. When this isn't possible, clinicians might consider obtaining surrogate markers of HIV infection (such as CD4+ T cell counts, see below, or HIV viral load measures); however, this has been identified in the literature as an unethical attempt to circumvent restrictions (Irwin, Lilly, & Rippe, 2013). In a study by Thornhill, Mandersloot, Bath, and Orkin (2014) in the United Kingdom, nonconsenting ICU patients were screened under a "best interests principle on the basis of high local HIV prevalence" (p. 1460), emphasizing that clinicians can make a decision to test for HIV in clinical situations where it is needed and where the patient is unable to give consent based on the need to provide the best possible care. In the United States, state regulations identify procedures involved with HIV screening in nonconsented patients (Halpern, 2005).

Providing prevention education and/or posttest counseling with HIV screening is not required (CDC, 2010).

Nevertheless, because some jurisdictions might preclude opt-out screening for HIV, it is important for the clinician to be familiar with his or her state-specific HIV-screening regulations regarding informed consent and pre-/posttest counseling. Consideration of policies and procedures related to HIV screening in the facility at which the clinician practices is also paramount; similar to variation in state regulations, not all facilities specify opt-out procedures for HIV screening.

Methods of Screening for HIV in the ICU

Clinical methods for screening patients for HIV in the ICU are the same as those employed in outpatient settings. HIV-1 and HIV-2 can be detected by serologic tests that detect antibodies or virologic tests that can detect HIV antigens or ribonucleic acid (RNA; CDC, 2010). Antibody tests are traditionally conducted using conventional enzyme immunoassays, but rapid serologic testing can provide an accurate presumptive diagnosis within 30 minutes (Blackwell, 2009; CDC, 2010).

A positive serologic or rapid immunoassay screen is confirmed by supplemental antibody testing; the Western Blot is most frequently used for confirmation (Blackwell, 2009; CDC, 2010), but newer methods are available and clinicians should consult with their laboratories for the best available testing methods. A screening method gaining traction is point-of-service (POS) HIV screening (Blackwell, 2009). These screening tools, U.S. Food and Drug Administration-approved in 2002 (Blackwell, 2009), employ four tests that use either blood from a finger stick or oral fluid (i.e., a swab from the patient's buccal mucosa; Blackwell, 2009). While POS screening is traditionally associated with outpatient care, research has shown it to be feasible in hospital settings as well (Becker et al., 2013; Blackwell, 2009; Broeckaert & Challacombe, 2015).

Research conducted on the use of POS screening tests in hospitals has largely concentrated on their use in emergency settings (Freeman, Sattin, Miller, Dias, & Wilde, 2009; Sattin, Wilde, Freeman, Miller, & Dias, 2011), where they have been associated with a significant amount of acceptance by patients and clinicians. However, data also support POS HIV screening of admitted patients in acute care environments to be acceptable, feasible, effective, and cost effective (Burns et al., 2012). A recent study by Montoy, Dow, and Kaplan (2016) showed that using POS HIV testing in an urban teaching hospital and regional trauma center greatly increased HIV screening, particularly when an opt-out rather than opt-in approach was used. White and colleagues (2011) found similar results in addition to a completion rate of 99.8%. POS tests have a greater than 99% accuracy rate (Broeckaert & Challacombe, 2015).

Thus, patients being screened for HIV in the ICU might benefit from the use of POS screening methods rather than traditional laboratory serum screening methods because the turn-around time for results is much faster (Broeckaert & Challacombe, 2015). For example, a serum-based enzyme-linked immunosorbent assay could take a considerable amount of time for analysis by the facility's laboratory, or even longer if the sample has to be sent elsewhere. It must be emphasized that nurses and other health care professionals who administer POS screening tests must be properly trained (Broeckaert & Challacombe, 2015) and that a diagnosis of HIV is made only after the full range of testing, including RNA levels, has been completed (Becker et al., 2013; Blackwell, 2009; Broeckaert & Challacombe, 2015; CDC 2015b).

Disclosure of Serostatus to Patients and Families

State regulations stipulate when a patient's HIV serostatus can be disclosed to others. For example, the State of Michigan requires health care providers to disclose a patient's HIV serostatus to at-risk third parties under certain circumstances (Vernillo, Wolpe, & Halpern, 2007). Generally, "Clinicians cannot discuss a patient's HIV diagnosis with the patient's family or friends unless the individual is the legal surrogate" (Morris, 2009, p. 98). Vernillo and colleagues (2007) provided additional direction on disclosure of HIV diagnoses to health care surrogates by ICU clinicians. These researchers recommend disclosure in situations in which HIV infection represented a "primary cause" (p. 125) of the patient's

critical illness or if the surrogate would be harmed by a failure to disclose the patient's HIV serostatus.

CDC HIV Staging and Clinical Implications

After an adult patient is diagnosed with HIV infection, the ICU clinician needs to determine if that infection is contributing to his or her clinical presentation. Coupled with physical examination and other diagnostic procedures appropriate to the patient's conditions, the HIV-infected patient's immune status and extent of HIV infection can be determined by CD4+ T cell counts and HIV RNA levels.

The CDC (revised in 1993) classification system for HIV-Infected Adults and Adolescents (U.S. Department of Health and Human Services [USDHHS], 2014) grouped HIV infection into one of three overarching categories based on a patient's CD4+ T cell count. This is considered in conjunction with a history of HIV-related conditions that qualify the patient for a subcategory within each overarching category (Table 1). Patients in Category A are those who are asymptomatic, with acute HIV infection, or who have persistent generalized lymphadenopathy. Those in Category A with CD4+ T cell counts greater than or equal to 500 cells/μL are considered to be category A1, those with CD4+ T cell counts of 200-499 cells/μL are considered to be category A2, and those with less than 200 cells/μL are A3. The same CD4+ T cell count divisions are used for Category B1, B2, and B3, and C1, C2, and C3. However, those in Category B are considered to have or have had symptomatic conditions (those attributed to HIV infection, those that indicate a defect in cell-mediated immunity, or those with a clinical course complicated by HIV infection; Table 2). In addition, those in Category C are considered to have or have had an AIDS-indicator condition (specific opportunistic infections, listed by the CDC; Table 3).

It is important to note that, "The CDC categorization of HIV/AIDS is based on the lowest documented CD4 cell count and on previously diagnosed HIV-related conditions" (USDHHS 2014, p. 95). For example, if a patient had a condition that once met category C criteria but is now asymptomatic, s/he remains classified as Category C. Any patient with a CD4+ T cell count less than 200 cells/μL is considered to have a diagnosis of AIDS (USDHHS, 2014). This would include all patients in Categories A3, B3, or C3. It is important for the ICU clinician to understand the significant clinical distinction between a diagnosis of HIV infection and a diagnosis of AIDS. While the CDC classification system for HIV-Infected Adults and Adolescents (USDHHS, 2014) does not use assessment of HIV RNA levels to determine classification, most HIV specialists do not make clinical decisions without both CD4+ T cell counts and HIV RNA levels. Appropriate interdisciplinary consultation between intensive care clinicians and infectious disease/HIV-specialists is a vital clinical consideration.

Table 1. CDC Classification System for HIV-Infected Adults and Adolescents

CD4+ T Cell Count	A[a]	B[b]	C[c]
≥500 cells/μL	A1	B1	C1
200-499 cells/μL	A2	B2	C2
<200 cells/μL	A3	B3	C3

Note. CDC = Centers for Disease Control and Prevention.
a. Asymptomatic HIV, acute HIV, or persistent generalized lymphadenopathy.
b. Symptomatic conditions (see Table 2).
c. AIDS-indicator conditions (see Table 3); adapted from U.S. Department of Health and Human Services, 2014.

Conclusion

PLWH admitted to hospitals for intensive care services have unique needs that the provider must

Table 2. Examples of Category B Symptomatic Condition

- Bacillary angiomatosis
- Oropharyngeal candidiasis (oral thrush)
- Vulvovaginal candidiasis, persistent or resistant
- Pelvic inflammatory disease (PID)
- Cervical dysplasia (moderate to severe)/cervical carcinoma in situ
- Hairy leukoplakia, oral
- Herpes zoster (shingles), involving two or more episodes or at least one dermatome
- Idiopathic thrombocytopenia purpura
- Constitutional symptoms, such as fever (>38.5°C) or diarrhea (lasting > 1 month)
- Peripheral neuropathy

Note. Adapted from U.S. Department of Health and Human Services, 2014.

Table 3. Category C AIDS-Indicator Conditions

- Bacterial pneumonia (2 or more episodes in 12 months)
- Candidiasis of the bronchi, trachea, or lungs
- Candidiasis, esophageal
- Cervical carcinoma, invasive (confirmed by biopsy)
- Coccidioidomycosis, disseminated or extrapulmonary
- Cryptococcus, extrapulmonary
- Cryptosporidiosis, chronic intestinal (>1-month duration)
- Encephalopathy, HIV-related
- Herpes simplex, chronic ulcers (>1 month in duration), or bronchitis, pneumonitis, or esophagitis
- Histoplasmosis, disseminated or extrapulmonary
- Isosporiasis, chronic intestinal (>1-month duration)
- Kaposi sarcoma
- Lymphoma, Burkitt, immunoblastic, or primary central nervous system
- *Mycobacterium avium* complex (MAC) or *Mycobacterium kansasii*, disseminated or extrapulmonary
- *Mycobacterium tuberculosis*, pulmonary or extrapulmonary
- *Mycobacterium*, other or unidentified species, disseminated or extrapulmonary
- Progressive multifocal leukoencephalopathy (PML)
- *Salmonella* septicemia, recurrent (nontyphoid)
- Toxoplasmosis of the brain
- Wasting syndrome caused by HIV (involuntary weight loss > 10% of baseline body weight) associated with either chronic diarrhea (2 or more loose stools per day ≥ 1 month) or chronic weakness and documented fever for ≥ 1 month

Note. Adapted from U.S. Department of Health and Human Services, 2014.

recognize to deliver optimal care. Because many of these patients are unaware of their HIV serostatus on initial presentation to the ICU, intensive care nurse practitioners, physicians, and physician assistants who are responsible for diagnosing and directing care in the ICU should have a solid understanding of the procedures involved in screening patients for HIV, diagnosing HIV disease in adults, and recognizing the diagnostic parameters associated with progression to AIDS.

We have provided a brief overview of the current epidemiologic data regarding HIV incidence and prevalence in the United States and within U.S. ICUs. In addition, information was provided regarding some of the ethical and technical issues involved with informed consent and disclosure of HIV serostatus to ICU patients and their families. Methods employed to screen and diagnose HIV in ICU patients were also discussed. Finally, the CDC HIV classification system based on CD4+ T cell count and patient clinical history/presentation was reviewed, with specifics for each category outlined.

The literature on this topic is significantly lacking. There are substantial gaps in both research pertaining to screening and diagnosing of HIV in the ICU and the implementation of screening and diagnosis of HIV in ICU settings (Thornhill et al., 2014). Future studies on the topic should be rigorous, with inclusion of large, representative, and diverse samples. These studies need to focus on the best mechanisms to encourage ICU clinicians to screen patients for HIV infection, and they should examine how a new diagnosis of HIV impacts ICU care.

The ICU can be an ideal environment to screen patients for HIV (Thornhill et al., 2014). Rapid diagnosis of HIV and prompt staging can help guide ICU clinicians in determining the impact that HIV infection and depleted immune conditions might have on a patient's clinical presentation. Perhaps more importantly, data suggest hospital-based HIV screening can lead to improved linkages to care (Broeckaert & Challacombe, 2015). In fact, patients screened in hospital settings using rapid POS tests have been found to have service linkage rates between 80% and 100% (Becker et al., 2013; Christopoulos et al., 2011; Freeman et al., 2009; Kendrick, Krox, Couture, & Weinstein, 2004; Sattin et al., 2011; Sherman, Elrod, Allen, & Eckardt, 2014). Thus, screening for HIV in the ICU could be considered not only a standard of individual patient care, but a public health mandate as well.

Disclosures

The authors report no real or perceived vested interests that relate to this article that could be construed as a conflict of interest.

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