The Human Immunodeficiency Virus and the Colon and Rectal Surgeon

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ABSTRACT

A knowledge of the human immunodeficiency virus (HIV) is important in colon and rectal surgery. This article reviews our increasing knowledge of the virology of HIV and the occupational exposure risks of surgeons and their assistants. The current pharmacologic treatment of HIV is also reviewed.

KEYWORDS: Human immunodeficiency virus (HIV), acquired immunodeficiency syndrome (AIDS), infection control, antiviral drugs

Objectives: Upon completion of this article, the reader should be able to describe the impact of HIV/AIDS in colon and rectal surgery and be familiar with universal precautions and the medical treatment of HIV.

Since the initial case report of five homosexual men in 1981, the number of individuals with human immunodeficiency virus (HIV)/AIDS has grown exponentially.¹ Through 2002 the estimated number of patients with the diagnosis of AIDS in the United States was 886,575. Adult and adolescent AIDS cases totaled 877,275, with 718,002 cases in males and 159,271 cases in females. Through the end of 2002, 9300 AIDS cases were estimated in children under age 13. The estimated number of deaths of persons with AIDS was 501,669, including 496,354 adults and adolescents, and 5315 children under age 15.² Of note is that in 2002 over 55% of new cases of HIV/AIDS were in African Americans and that from 1998 to 2002, while the incidence of AIDS decreased among Caucasian and Hispanic patients, it increased substantially among African Americans and American Indians.³ Despite widespread dissemination of information about the transmission of HIV/AIDS, there has been no change in the three most common exposure risks. Men who have sex with men account for 55% of HIV/AIDS,

intravenous drug use 25%, and high-risk heterosexual behavior 10%. This article will discuss the virology of HIV and the risks of occupational exposure and briefly introduce the latest in the ever-changing pharmacologic treatment of HIV. Other conditions associated with HIV infection will be covered elsewhere in this issue of *Clinics in Colon and Rectal Surgery*.

HIV or the human immunodeficiency virus is a retrovirus that has an RNA genome contained within a capsid and a lipid envelope. HIV enters lymphocytes and monocytes by binding of the viral glycoprotein cell surface receptors with the host cell surface CD4 molecule and a cellular chemokine receptor.⁴ This results in a fusion of the viral envelope to the cell membrane and a release of the viral capsid into the host cytoplasm. HIV is not just one virus. There are a variety of viral subtypes that have differences in transmission and progression.⁵

HIV can be broadly classified into two groups based on the virus's affinity for specific immunologic cell types. Macrophage tropic species primarily infect macrophages and primary T cells and poorly infect CD4+ T

Sexually Transmitted Diseases of the Colon, Rectum, and Anus; Editor in Chief, David E. Beck, M.D.; Guest Editor, Mark L. Welton, M.D. *Clinics in Colon and Rectal Surgery*, volume 17, number 4, 2004. Address for correspondence and reprint requests: David A. Margolin, M.D., Department of Colon and Rectal Surgery, Ochsner Clinic Foundation, 1514 Jefferson Hwy., New Orleans, LA 70121. E-mail: damargolin@ochsner.org. ¹Department of Colon and Rectal Surgery, Ochsner Clinic Foundation, New Orleans, Louisiana. Copyright © 2004 by Thieme Medical Publishers, Inc., 333 Seventh Avenue, New York, NY 10001, USA. Tel: +1(212) 584-4662. 1531-0043,p;2004,17,04,215,220,ftx,en;ccrs00189x.

cells. This subtype tends to be more easily transmitted through sexual contact. T cell tropic species infects primarily CD4⁺ T-lymphocytes and is primarily transmitted via direct inoculation.⁶

After binding to the host cell membrane, the viral capsid releases viral particles and viral RNA into the host cell cytoplasm. There the viral RNA is converted by cellular reverse transcriptase to a DNA copy. The reverse transcriptase incorporates an incorrect nucleotide every 1500 to 4000 bases. This accounts for the rapid progression of DNA mutations. The new double-stranded DNA is incorporated into the host chromosomes where it is then transcribed into messenger RNA (mRNA). The mRNA is then translated to make proteins that are further modified to destroy the host cell and form mature infectious viral particles.

As can be expected, HIV has a profound impact on all facets of the immune system. In the cellular immune system HIV causes a decrease in CD4 cells and their ability to interact with natural killer cells as well as decreasing NK cell-mediated cytotoxicity. The virus also decreases monocyte-mediated phagocytosis, chemotaxis, intracellular killing, and cytokine expression. HIV impairs neutrophil-mediated intracellular killing and phagocytosis. In the humoral immune system, HIV decreases B cell numbers, causes polyclonal activation of B cells, and increases the production of nonspecific immunoglobulins G, A, and M.

To better define symptomatic HIV infection as well as the associated medical, neoplastic, and infectious conditions, the US Centers for Disease Control and Prevention (CDC) published specific criteria defining

Table 1 The 1993 AIDS Surveillance Case Definition of the US Centers for Disease Control and Prevention

A diagnosis of AIDS is made whenever a person is HIV positive and:

- he or she has a CD4⁺ cell count < 200 cells/ μ L, or
- his or her CD4⁺ cells account for < 14% of all lymphocytes, or
- that person has been diagnosed with one or more of the AIDS-defining illnesses listed below.

AIDS-defining illnesses:

- Candidiasis of bronchi, trachea, or lungs
- Candidiasis, esophageal
- Cervical cancer, invasive*
- Coccidioidomycosis, disseminated
- Cryptococcosis, extrapulmonary
- Cryptosporidiosis, chronic intestinal (> 1-month duration)
- Cytomegalovirus disease (other than liver, spleen, or lymph nodes)
- Cytomegalovirus retinitis (with loss of vision)
- Encephalopathy, HIV-related[#] (see Dementia)
- Herpes simplex: chronic ulcer(s) (> 1-month duration) or bronchitis, pneumonitis, or esophagitis
- Histoplasmosis, disseminated
- Isosporiasis, chronic intestinal (> 1-month duration)
- Kaposi's sarcoma
- Lymphoma, Burkitt's
- Lymphoma, immunoblastic
- Lymphoma, primary, of brain (primary central nervous system lymphoma)
- *Mycobacterium avium* complex or disease caused by *M. kansasii*, disseminated
- Disease caused by *Mycobacterium tuberculosis*, any site (pulmonary* or extrapulmonary[#])
- Disease caused by *Mycobacterium*, other species, or unidentified species, disseminated
- *Pneumocystis jiroveci* (formerly *carinii*) pneumonia
- Pneumonia, recurrent*
- Progressive multifocal leukoencephalopathy
- *Salmonella* septicemia, recurrent
- Toxoplasmosis of brain (encephalitis)
- Wasting syndrome caused by HIV infection[#]

Additional illnesses that are AIDS defining in children, but not adults

- Multiple, recurrent bacterial infections[#]
- Lymphoid interstitial pneumonia/pulmonary lymphoid hyperplasia

Centers for Disease Control. 1993 Revised classification system for HIV infection and expanded surveillance case definition for AIDS among adolescents and adults. MMWR Morb Mortal Wkly Rep 1992; 41(RR-17):1-19.

*Added in the 1993 expansion.

[#]Added in the 1987 expansion.

Table 2A CDC Categorization of HIV/AIDS

The 3 CD4 Count Categories*	
Category 1	> = 500 cells/ μ L or more
Category 2	200–499 cells/ μ L
Category 3	< 200 cells/ μ L

*Categorization should be based on the lowest accurate CD4 count, not necessarily the most recent one. That is, a patient whose CD4 count declined steadily over a period of months until it reached 180 cells/ μ L, but then rose above 200 cells/ μ L again and remained at that level (perhaps as the result of antiretroviral treatment), would be placed in Category 3, not Category 2.

AIDS. These criteria were initially published in 1986 and revised in 1993 (Tables 1 and 2).⁷ Additionally, AIDS may be defined by a CD4 count of < 200 cells/ μ L or < 14% of all lymphocytes, even in the absence of the listed conditions.

OCCUPATIONAL EXPOSURE

While the risk of contracting HIV from high-risk behaviors is well known, there is a significant amount of misinformation disseminated concerning the occupational risks of HIV contraction. The risk and correct information concerning occupation exposures of HIV/AIDS is particularly germane to colon and rectal surgeons due to the incidence of anorectal manifestations of HIV. As of January 2003, 24,800 individuals with AIDS had a history of working in the health-care industry. This accounts for 5% of patients with HIV/AIDS (Table 3). Despite this large number of individuals, there have only been 57 health-care personnel in the United States who have been documented as having seroconverted to HIV following an occupational exposure⁸ (Table 4). Twenty-six of these individuals have developed AIDS. The predominant source of exposure was a percutaneous exposure (84%), by either an inadvertent puncture or a cut. Currently there have been no documented cases following a needlestick with a solid surgical needle. Of the 57 patients with documented occupational exposure, there were no surgeons and only 2 surgical technologists in this group. As of December 2001 there have been no new documented cases of occupationally acquired HIV/AIDS.

As can be seen from the above data, the risk of seroconversion from occupational exposure is rare. Nonetheless, due to the devastating consequences, developing effective prevention strategies is mandatory. The major categories of intervention are education, workplace infection control, and engineering controls.

The first two categories are best addressed by instating universal precautions. Under universal precautions, blood and certain body fluids of all patients are considered potentially infectious for HIV, HBV, and other blood-borne pathogens. The CDC recommends the following⁹:

1. All health-care workers should routinely use appropriate barrier precautions to prevent skin and mucous-membrane exposure when contact with blood or other body fluids of any patient is anticipated. Gloves should be worn for touching blood and body fluids, mucous membranes, or nonintact skin of all patients; for handling items or surfaces soiled with blood or body fluids; and for performing venipuncture and other vascular access procedures. Gloves should be changed after contact with each patient. Masks and protective eyewear or face shields should be worn during procedures that are likely to generate droplets of blood or other body fluids to prevent exposure of mucous membranes of the mouth, nose, and eyes. Gowns or aprons should be worn during procedures that are likely to generate splashes of blood or other body fluids.
2. Hands and other skin surfaces should be washed immediately and thoroughly if contaminated with blood or other body fluids. Hands should be washed immediately after gloves are removed.
3. All health-care workers should take precautions to prevent injuries caused by needles, scalpels, and other sharp instruments or devices during procedures; when cleaning used instruments; during disposal of used needles; and when handling sharp instruments after procedures. To prevent needlestick injuries, needles should not be recapped, purposely bent or broken by hand, removed from disposable syringes, or otherwise manipulated by hand. After they are used, disposable syringes and needles, scalpel blades, and other sharp items should be placed in puncture-resistant containers for disposal; the puncture-resistant containers should be located as close as practical to the use area. Large-bore reusable needles should be placed in a puncture-resistant container for transport to the reprocessing area.
4. Although saliva has not been implicated in HIV transmission, to minimize the need for emergency mouth-to-mouth resuscitation, mouth-pieces, resuscitation bags, or other ventilation devices should be available for use in areas in which the need for resuscitation is predictable.
5. Health-care workers who have exudative lesions or weeping dermatitis should refrain from all direct patient care and from handling patient-care equipment until the condition resolves.

While several authors have shown that use of universal precautions has decreased the incidence of occupational exposure to HIV, compliance with these procedures has been problematic. In their 2004 study, Ferguson and coauthors showed that almost 45% of health-care workers did not wear gloves 100% of the time they were subject to blood or body fluids, and less than 61% washed their hands less than 100% of the time.

Table 2B CDC Categorization of HIV/AIDS

The 3 Clinical Categories

Category A	One or more of the conditions listed below in an adolescent or adult (aged 13 years or older) with documented HIV infection. Conditions listed in Categories B and C must not have occurred. <ul style="list-style-type: none"> • Asymptomatic HIV infection • Persistent generalized lymphadenopathy (PGL) • Acute (primary) HIV infection with accompanying illness (sometimes known as seroconversion illness) or history of acute HIV infection
Category B*	Consists of symptomatic conditions in an HIV-infected adolescent or adult that are not included among conditions listed in Category C and that meet one of the following criteria: <ul style="list-style-type: none"> • The conditions are attributed to HIV infection or are indicative of a defect in cell-mediated immunity, or • The conditions are considered by physicians to have a clinical course or to require management that is complicated by HIV infection <p>This category includes all such symptomatic conditions, with the exception of those placed in Category C. Examples of conditions in this category include, but are not limited to: bacillary angiomatosis; candidiasis (thrush) in the mouth and/or upper throat; candidiasis of the vagina and/or vulva which is persistent, frequent, or responds poorly to treatment; cervical abnormalities of moderate or severe extent or cervical cancer; constitutional symptoms such as fever (38.5°C) or diarrhea lasting longer than 1 month; herpes zoster (shingles) involving at least two distinct episodes or more than one dermatome (skin area); idiopathic thrombocytopenia purpura; listeriosis; oral hairy leukoplakia; pelvic inflammatory disease; particularly if complicated by tubo-ovarian abscess; peripheral neuropathy.</p>
Category C [#]	Includes the following conditions listed in the AIDS surveillance case definition: <ul style="list-style-type: none"> • <i>Candida</i> in the esophagus, trachea, bronchi, or lungs • Invasive cervical cancer • Coccidioidomycosis • <i>Cryptococcus</i> outside the lungs • Cryptosporidiosis with diarrhea lasting for > 1 month • Cytomegalovirus disease outside the liver, spleen, or lymph nodes • Cytomegalovirus retinitis • Herpes simplex virus causing prolonged skin problems or involving the lungs or esophagus • HIV-related encephalopathy • Chronic intestinal isosporiasis lasting > 1 month • Kaposi's sarcoma • Burkitt's, immunoblastic, or primary (i.e., not involving other parts of the body) brain lymphoma • Widespread <i>Mycobacterium avium intracellulare</i>, <i>M. kansasii</i>, or other species • <i>Pneumocystis jiroveci</i> (formerly <i>carinii</i>) pneumonia • Recurrent bacterial pneumonia • Progressive multifocal leukoencephalopathy • Recurrent <i>Salmonella</i> septicemia • Toxoplasmosis of the brain • HIV wasting syndrome

Centers for Disease Control. 1993 Revised classification system for HIV infection and expanded surveillance case definition for AIDS among adolescents and adults. MMWR Morb Mortal Wkly Rep 1992; 41(RR-17):1-19.

*For classification purposes, Category B conditions take precedence over those in Category A. For example, a patient previously treated for oral or persistent vaginal candidiasis (and who has not developed a category C disease) but who is now asymptomatic should be classified in clinical Category B.

[#]For classification purposes, once a Category C condition has occurred, the person will remain in Category C.

The reasons given for not using precautions were: using precautions would have interfered with patient care; the precautions were not warranted; workers did not anticipate the potential for exposure; and high job demands had caused respondents to be in a hurry.¹⁰ As expected, these reasons were not acceptable and it is imperative that all health-care professionals utilize universal precautions. In addition to universal precautions, presum-

ably safer devices have been implemented to minimize exposure. These include improved glove technology, needleless intravenous administration systems, modified (e.g., self-capping) intravenous catheters, and improved phlebotomy equipment.

Unfortunately, even with the most stringent control, occupational exposure occurs. Therefore it is imperative that a postexposure protocol be in place to

Table 3 Adults Reported with AIDS and a History of Employment in Healthcare, Where Job Is Known, by Occupation, as of December 2002*

Occupation	Number
Nurses	5378
Health aides	5638
Technicians	3182
Physicians	1792
Therapists	1082
Dental workers	492
Paramedics	476
Surgeons	122
Other	5050
Total	23,212

*<http://www.cdc.gov/ncidod/hip/BLOOD/hivpersonnel.htm>.

Table 4 Healthcare Personnel with Documented and Possible Occupationally Acquired AIDS/HIV Infection, by Occupation, as of December 2001*

Occupation	Documented
Nurse	24
Laboratory worker, clinical	16
Physician, nonsurgical	6
Laboratory technician, nonclinical	3
Housekeeper/maintenance worker	2
Technician, surgical	2
Embalmer/morgue technician	1
Health aide/attendant	1
Respiratory therapist	1
Technician, dialysis	1
Dental worker, including dentist	—
Emergency medical technician/paramedic	—
Physician, surgical	—
Other technician/therapist	—
Other health-care occupation	—
Total	57

*<http://www.cdc.gov/ncidod/hip/BLOOD/hivpersonnel.htm>.

minimize the consequences. In 2001, the US Public Health Service published guidelines that recommended the use of postexposure antiretroviral chemoprophylaxis (Table 5).¹¹

MEDICAL TREATMENT

The medical treatment of HIV/AIDS is in a constant state of evolution. Current therapies involve combinations of drugs with different mechanisms of action, termed highly active antiretroviral therapy, HAART. The goal is to decrease the viral load and simultaneously improve immune function. While infectious disease specialists coordinate medical therapy, surgeons who treat these patients need a general knowledge of these drugs and their limitations and side effects.

There are currently four major classifications of antiretroviral drugs available. This list includes nucleoside analogue reverse transcriptase inhibitors, nonnucleoside reverse transcriptase inhibitors, protease inhibitors, and fusion inhibitors. These antiretroviral medications work by inhibiting 1 of 3 steps in the life cycle of HIV. All reverse transcriptase inhibitors inhibit viral conversion of RNA to DNA after the virus enters the cell but before it enters the nucleus. This category includes six nucleoside reverse transcriptase inhibitors (zidovudine, didanosine, zalcitabine, stavudine, lamivudine, and abacavir), one nucleotide reverse transcriptase inhibitor (tenofovir disoproxil fumarate), and three non-nucleotide reverse transcriptase inhibitors (nevirapine, delavirdine, and efavirenz).

Protease inhibitors inhibit the action of the HIV protease, namely, cleaving protein products of the viral structural genes into the functional subunits needed to create new infectious virions. Viral particles are still produced when the protease is inhibited, but these particles are ineffective at infecting new cells. There are six protease inhibitors currently in use: saquinavir, zalcitabine, indinavir, nelfinavir, amprenavir, and lopinavir.

The third mechanism inhibits the fusion of the viral and host membranes. By attaching itself to the HIV envelope glycoprotein gp41, fusion inhibitors prevent

Table 5 Current US Public Health Service Recommendations for Chemoprophylaxis of Occupational Exposures to HIV

HIV exposures with a recognized transmission risk	"Basic regimen"	Zidovudine (ZDV) plus lamivudine (3TC)
	Alternative	Stavudine (D4T) plus lamivudine
HIV exposures for which the nature of the exposure suggests an elevated transmission risk*	"Basic regimen"	Stavudine plus didanosine (ddI) [†]
	"Basic regimen" plus	Indinavir [†]
	one of the following agents	Nelfinavir
		Abacavir
		Efavirenz [†]

[†]Agents not advisable for use in pregnancy and increasingly not recommended in practice.

*Elevated risk is associated with "larger" volume of blood and/or blood containing a high titer of HIV.

formation of the "hairpin" structure required for fusion of the HIV and host cell membranes, and thus prevent viral entry into the host cell. There is currently one fusion inhibitor available: enfuvirtide.

In July of 2004, the International AIDS Society panel published their current recommendations for the treatment of HIV infection.¹² This document recommends antiviral treatment for all patients with symptomatic HIV. They also recommend that treatment of asymptomatic individuals be based on CD4 counts. Treatment should be instituted for individuals with CD4 counts below 200 cells/ μ L. For counts above 350 cells/ μ L, treatment should be individualized and disease progression closely monitored. For those patients with counts between 250 and 350 cells/ μ L, the data regarding the efficacy of treatment are less sound, but treatment with HAART should be considered. As mentioned above, drug therapy is in a constant state of evolution and is best managed by an infectious disease specialist.

REFERENCES

1. Gottlieb MS, Schroff R, Schanker HM, et al. Pneumocystis carinii pneumonia and mucosal candidiasis in previously healthy homosexual men: evidence of a newly acquired cellular immunodeficiency. *N Engl J Med* 1981;305:1425-1431
2. Centers for Disease Control and Prevention. Division of HIV/AIDS statistics. <http://www.cdc.gov/hiv/stats.htm#cumaims>. Accessed July 4, 2004
3. Cases of HIV infection and AIDS in the United States by race/ethnicity, 1998-2002. HIV/AIDS Surveillance Supplement Report. Center for Disease Control and Prevention 2003;10:1-38. Accessed June 30, 2004
4. Wyatt R, Sodroski J. The HIV-1 envelope glycoproteins: fusogens, antigens and immunogens. *Science* 1998;280:1884-1888
5. Hu DJ, Buve A, Bagg J, van der Groen G, Dondero TJ. What role does HIV-1 subtype play in the transmission and pathogenesis? An epidemiological perspective. *AIDS* 1999;13:873-881
6. Moore JP, Trkola A, Dragic T. Co-receptors for HIV-1 entry. *Curr Opin Immunol* 1997;9:551-562
7. Centers for Disease Control. 1993 Revised classification system for HIV infection and expanded surveillance case definition for AIDS among adolescents and adults. *MMWR Morb Mortal Wkly Rep* 1992;41(RR-17):1-19
8. Centers for Disease Control and Prevention. Issues in a healthcare setting. <http://www.cdc.gov/ncidod/hip/BLOOD/hivpersonnel.htm>. Accessed July 4, 2004
9. Aug MMWR.21, 1987. <http://www.cdc.gov/mmwr/preview/mmwrhtml/00023587.htm>. Accessed July 4, 2004
10. Ferguson KJ, Waitzkin H, Beekmann SE, Doebbeling BN. Critical incidents of nonadherence with standard precautions guidelines among community hospital-based health care workers. *J Gen Intern Med* 2004;19:726-731
11. Centers for Disease Control and Prevention. Updated US Public Health Service guidelines for the management of occupational exposures to HBV, HCV, and HIV and recommendations for post exposure prophylaxis. *MMWR Morb Mortal Wkly Rep* 2001;50(RR-11):1-52
12. Yeni PG, Hammer SM, Hirsch MS, et al. Treatment for adult HIV infection: 2004 recommendations of the International AIDS Society-USA Panel. *JAMA* 2004;292:251-265