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ABOUT THE COVER – “THE RED RIBBON”
In the right corner of this abstract image of a virus is “The Red Ribbon.” In 1991, a decade after the emergence of HIV, a group of 12 artists gathered to discuss a new project for Visual Aids: a New York arts organization that raises awareness of HIV. They were photographers, painters, filmmakers and costume designers, and they sat around in the shared gallery space in New York’s East Village. After a short brainstorm they had come up with a simple idea that later became one of the most recognized symbols of the decade: the red ribbon, worn to signify awareness and support for people living with HIV.

Within weeks of the red ribbon idea being born, world-famous actors starting wearing the red ribbon to high-profile award ceremonies such as the Oscars and talking about why it was important. The media also caught on, and within a short time, the red ribbon symbol became universally recognized. The Red Ribbon continues to be a powerful force in the efforts to increase public awareness of HIV.
HIV Still Needs our Focus

Originating in non-human primates in west-central Africa and jumping to humans in the early twentieth century, HIV (Human Immunodeficiency Virus) was a disease without a name when first clinically observed in the United States in 1981. Its first published notice occurred in the June 5, 1981 issue of the CDC’s Morbidity and Mortality Weekly Report which cited five cases of Pneumocystis pneumonia in gay male patients at UCLA Medical Center. That report marked the official start of the AIDS pandemic. By August 1982, the CDC had coined an official name: Acquired Immune Deficiency Syndrome (AIDS), and by 1983, two separate research groups declared that a new retrovirus was its cause. By May 1986, this novel retrovirus would be renamed HIV.

Many of Mississippi’s practicing physicians came of age with the emergence of HIV. As we trained as medical students and residents, we watched the treatment of HIV/AIDS evolve in front of us. We shared the phobias of the community around us as we cautiously provided front-line care for those infected, ever fearful of a needle-stick. The first documented AIDS case in Mississippi occurred in 1981 as a “strange” case of Pneumocystis pneumonia (identified in 1983 by the Department of Health on review of records). In JMSMA’s January 1988 AIDS special issue, Dr. Ed Thompson, then state epidemiologist, presciently commented that HIV “is becoming a heterosexual disease. It simply started out as a homosexual disease.” I’ve seen that in my own practice. All of my early HIV/AIDS patients were homosexual men. My most recent diagnosis of HIV, which occurred less than a year ago, was in a heterosexual male.

Much has changed in HIV treatment since that first case was recognized 34 years ago. This month, your JMSMA presents a special edition on current HIV treatment. Our brilliant state epidemiologist Dr. Thomas Dobbs has assisted your editors as this edition’s editor, and I thank Dr. Dobbs and all the contributors for their exemplary efforts to provide our readers significant and up-to-date information on this dangerous retrovirus still very much among us.

Contact me at lukelampton@cableone.net.
– Lucius M. Lampton, MD, Editor

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HIV from a Personal and Public Health Perspective: Early Diagnosis is the Key

THOMAS E. DOBBS, III, MD, MPH
State Epidemiologist, Mississippi State Department of Health

There are over 1.2 million Americans living with HIV; approximately one in six are unaware of his or her status. Early detection and treatment of HIV has numerous complimentary benefits, including prolonged life of the individual and diminished transmission to others. Successful treatment of HIV, particularly early in the course of the disease, can lead to a relatively normal life expectancy. From a public health perspective, diagnosis and treatment are clearly linked to reduced transmission. Awareness of one’s HIV status is associated with a decrease in risky behaviors, and successful treatment, with a fully suppressed viral load, makes an individual practically non-contagious. The diagnosis of HIV is often delayed, with one-third of Americans infected for greater than seven years before detection, leading to detrimental health effects and unnecessary transmissions. By improving detection and successfully engaging patients in care, the annual infection rate in the U.S. could be cut in half.

The South is the new epicenter of HIV transmission in the U.S., and Mississippi has an underappreciated prominence even within this high burden region. Mississippi ranks 6th in the nation in AIDS cases and the Jackson metropolitan area is a frequent leader in HIV transmission among U.S. cities, particularly among young African-Americans. Though certain groups are at higher risk of HIV, the disease affects all strata of society regardless of age, gender or ethnicity. Young adults account for the highest number of infections annually in MS, but a significant minority are diagnosed even at advanced age. Fourteen percent of new diagnoses in Mississippi in 2014 occurred in those greater than 50 years of age, with the oldest diagnosed at age 69. Approximately 1 in 100 African American males, 1 in 200 African American Females and 2 in 1,000 white males in Mississippi are living with HIV infection. Information on risk-factors for HIV infection are frequently not volunteered in the context of a routine medical encounter; or exposure may have occurred many years past. In a high HIV burden state like Mississippi, questions about risk factors for HIV should be a component of all medical assessments. Given the long latency between HIV infection and AIDS (approximately 10 years), diagnosis should be pursued prior to the development of symptoms when treatments are most effective at restoring health. This is analogous to our approach to breast cancer, where early detection leads to markedly improved outcomes.

The United State Preventive Task Force (USPTF) currently recommends universal HIV testing for all persons aged 15 – 65. A single test is appropriate for individuals at low risk, but annual testing should be performed on those at higher risk, including: injection-drug users, persons exchanging sex for money, and sex partners of those with HIV or at higher risk of HIV infection. Sexually active men who have sex with men should be tested every six months. All pregnant women, even those at apparent low risk, should be tested for HIV in the first trimester, and women at higher risk or in areas of high HIV prevalence should be retested in the third trimester. Women presenting in labor without known HIV status should be tested immediately and treated as HIV infected if the initial test is positive, without waiting for a confirmatory test. Written consent for HIV testing in Mississippi is not required and the practice is strongly discouraged. All testing should be performed in an opt-out format, providing the patients with the knowledge that the test is going to occur as a component of routine care. Written consent processes discourage testing and can stigmatize those that assent in writing.

HIV testing is a covered service by most major insurance carriers. For those without insurance or in geographically isolated areas, free and confidential HIV testing is available at all county health departments. All individuals testing positive for HIV are contacted by representatives of the Mississippi State Department of Health (MSDH) in order to identify others in need of testing, and to ensure linkage to care and needed support services. Throughout Mississippi, care and treatment for HIV is available regardless of insurance status and can be coordinated through MSDH or the Mississippi network of Ryan White providers. A lack of resources should not be considered a barrier to testing or engagement in HIV care.

In alignment with CDC and USPTF guidelines, the Mississippi State Department of Health supports the routine testing of Mississippians for HIV. It is appropriate to test those without identifiable risk factors a single time on the initial engagement in care using an opt-out testing strategy. Those at higher risk should be tested at least annually and all pregnant women should be tested at least once within the first trimester. The availability of HIV testing as a covered service by insurance carriers, and the option of free and confidential testing at all county health departments, ensure that financial impediments to testing are minimal. The simple act of testing for and diagnosing HIV infections in MS holds the promise of drastically reducing unnecessary infections and prolonging life.

THOMAS E. DOBBS, III, MD, MPH
State Epidemiologist, Mississippi State Department of Health

JOURNAL MSMA HIV SPECIAL EDITION GUEST EDITORIAL

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Pre- and Post-Exposure Prophylaxis and the Changing Paradigm of HIV Prevention

JAMES BENJAMIN BROCK, MD AND LEANDRO ANTONIO MENA, MD
Division of Infectious Diseases, University of Mississippi Medical Center
Introduction
Prevention of HIV transmission is a major public health priority, and it is the first topic addressed in the National HIV/AIDS Strategy for the United States. Many interventions have demonstrated efficacy in reducing HIV transmission, including condom use, male circumcision, needle exchange, universal precautions, screening and treatment of sexually transmitted infections, and individual interventions that reduce risk behaviors, among others. Antiretrovirals (ARVs) to treat HIV-infected patients have been demonstrated to significantly reduce mother-to-child transmission of HIV, as well as sexual transmission of HIV to uninfected partners. The effectiveness of these strategies has substantial impact when implemented in conjunction rather than individually, especially in the setting of dedicated sexual health education and patient centered risk reduction counseling.

In regards to antiretroviral therapy, it has long been postulated and recently demonstrated in a large, randomized clinical trial that effective combination antiretroviral therapy (cART) administered to HIV-infected partners in serodiscordant (one partner HIV-positive and the other HIV-negative) heterosexual couples can decrease HIV transmission to the HIV-negative partner by 96%. There is good evidence from models that this strategy, now known as “Treatment as Prevention” may also be effective in reducing the HIV infection rate among men who have sex with men (MSM). High ARV coverage may reduce the infectivity of the HIV-diagnosed population, but the effectiveness of treatment as prevention will be limited unless the undiagnosed population is reduced by frequent HIV testing and immediate linkage to HIV care and treatment. Likewise, antiretroviral therapy has been administered to uninfected individuals with substantial exposure to HIV, such as neonates of HIV-infected mothers, victims of sexual abuse, recent sexual exposures to HIV infected sexual partners, recent injection drug use where needles were shared with individuals of unknown HIV status or known to be HIV-infected, and in occupational settings such as healthcare or law enforcement where workers become exposed to potentially infectious bodily fluids, all forms of post-exposure prophylaxis or PEP. The premise of these strategies lies on the understanding that the systemic administration of HIV drugs, resulting in adequate concentrations at the site of exposure, should reduce the risk of infection. In recent years, an increasing body of evidence from research studies and implementation projects suggest that there may be better protection if drugs are available before the exposure and that pre-exposure prophylaxis or PrEP is feasible and cost-effective.

Evolution of ARV for prevention
Animal studies using simian immunodeficiency virus (SIV) and HIV-2 have demonstrated both the natural history of early HIV infection and the feasibility of pharmacologic HIV prevention strategies. Vaginal inoculation of SIV in macaques revealed presence of virus in dendritic cells within an hour, invasion of lymph nodes within 2 days, and dissemination to the bloodstream within 5 days. This information supports a small window of opportunity to initiate therapy after an exposure. Likewise, administration of tenofovir was shown to be protective in macaques after exposure to SIV, but effectiveness decreased significantly over a short period of time, especially after 72 hours had elapsed. Shorter courses (3-10 days) also had limited effectiveness, although longer courses (28 days) demonstrated good results. Regimens not containing tenofovir (zidovudine/lamivudine/indinavir) were not shown to be effective in these animal studies. Macaque and humanized mouse models of oral and topical pre-exposure prophylaxis (PrEP) with tenofovir and emtricitabine provided efficacy measurements of daily and episodic regimens against mucosal transmission of HIV.

Prevention of mother-to-child (vertical) transmissions has been one of the greatest success stories in the fight against HIV, particularly in the developed world where these transmissions are now uncommon events thanks to the routine HIV screening of all pregnant women. Several strategies, including elective cesarean for viremic mothers and abstinence from breastfeeding, must be acknowledged in the prevention of vertical transmission, but pharmacologic interventions are the cornerstone of vertical transmission prevention. Mother-to-child transmission has been studied extensively, and multiple combinations are now acceptable cART regimens for infected mothers. Equally important to the development of PEP/PrEP, ARV administration to neonates of HIV-infected mothers has been demonstrated to decrease vertical transmission and is now standard practice.

Occupational post-exposure prophylaxis
For ethical and technical reasons, a randomized controlled trial of post-exposure prophylaxis is unlikely to be performed. However, animal models and data from studies of vertical transmission support its plausibility, and its widespread use is further supported by observational data. In a case-control study of needlestick injury in healthcare workers, prompt initiation of zidovudine was associated with an 81% decrease in risk of acquisition of HIV.

According to the Public Health Service Guidelines for Occupational Exposure to HIV, exposures considered high risk for HIV infection include percutaneous injury (needlestick, especially with a hollow needle) or exposure of mucous membranes or non-intact skin to infectious bodily fluids or tissue, which include blood and cerebrospinal, peritoneal, pleural, pericardial, synovial, and amniotic fluids. Serum and vaginal secretions are potentially infectious but are not implicated in occupational HIV infection. Other fluids, including saliva, feces, and vomitus, are not considered infectious unless visibly bloody.

The average risk of HIV infection after percutaneous exposure to HIV-infected blood is estimated to be 0.3% and that of mucous membrane exposure by HIV-infected blood is 0.09%. Risk of infection after exposure
to bodily fluids other than blood is uncertain but felt to be substantially lower. Also, degree of viremia in the peripheral blood affects the infectious inoculum and thus the risk of infection. In other words, patients with virologic suppression on cART are less likely to transmit HIV to healthcare workers than those with high viral loads. Inoculum size also affects the risk of transmission, and larger volumes of blood are transmitted with devices visibly contaminated with the patient’s blood, hollow-bore needles or needles inserted directly into blood vessels, and deep injuries.

After a high risk exposure as described above occurs, if the patient’s HIV status is positive or unknown, prompt cleaning of the wound by soap and water (Needlesticks should not be squeezed.) and initiation of post-exposure prophylaxis should occur. Effectiveness of PEP is time-dependent, most effective if initiated within several hours of exposure, and far less effective if started after 72 hours. If the patient’s HIV status is unknown, HIV screening should be performed on the patient, preferably by rapid test to expedite evaluation and treatment. If rapid test cannot be performed, treatment should not be delayed while awaiting serologic test results. HIV resistance testing can also be considered in HIV-positive source patients as that may augment the PEP regimen chosen.

THE PREVENTION OF HIV INFECTION IS COMPLEX AND FOUNDED ON ALTERED RISK BEHAVIOR...

The preferred PEP regimen according to the PHS guidelines is tenofovir/emtricitabine 300 mg/200 mg (Truvada) daily with raltegravir 400 mg (Isentress) twice a day for 28 days. Older prospective studies reported a majority of PEP prescriptions not completing a full 28-day course, the major reason being medication side effects. The current regimen is generally well-tolerated and chosen mainly for that reason. Of note, the PHS guidelines were published before the commercial availability of dolutegravir (Tivicay), a once-daily antiretroviral in the same ARV class as raltegravir, which is likely equally effective, well-tolerated, more conveniently-dosed, and recommended first-line with tenofovir/emtricitabine in the New York State Department of Health Guidelines on HIV Prophylaxis Following Occupational Exposure.

Follow-up by a healthcare provider should be done during therapy to assess tolerability and adherence, and complete blood counts, renal, and hepatic function tests should be obtained at baseline and 2 weeks after exposure. HIV serology (preferably by 4th generation antibody-antigen assay) should be performed at baseline, 2 weeks, 6 weeks, and 4 or 6 months after exposure (4 months if 4th generation test used, 6 months if older generation test used). Patients with positive HIV serologic screens should be referred for cART.

Non-occupational post-exposure prophylaxis (nPEP)
With animal models, perinatal, and occupational data supporting pharmacologic HIV prevention methods, observational studies investigated the association of HIV transmission with receipt of post-exposure prophylaxis after exposure to HIV through sex or injection drug use. While limited by study design, multiple prospective cohorts and registries have supported the feasibility and efficacy of nPEP. Similar to PEP effectiveness decreases substantially over a short period of time and is unlikely to be of benefit more than 72 hours after exposure. Greatest benefit is achieved when initiated within a few hours of exposure. Initiation of nPEP should not await consultation by an HIV specialist. Limitations of nPEP include lack of awareness among healthcare providers and the community, as well as lack of belief in its efficacy.

Non-occupational exposures are stratified as high- and low-risk, and the decision to start nPEP is individualized based on this stratification and the timing of the exposure greater than or less than 72 hours. High-risk exposures include anal intercourse, vaginal intercourse, and needle-sharing by an individual known to be HIV-infected. Lower risk exposures include oral sex. Exposure of mucous membranes or non-intact skin to urine, saliva, tears, or nasal secretions are considered of negligible risk, unless the secretions are visibly contaminated with blood. Bite wounds have rarely been reported as causes of HIV transmission and are generally considered of low to negligible risk.

If an individual presents less than 72 hours after a high-risk exposure and the source contact is HIV-positive or of unknown HIV serostatus, a rapid HIV screen is recommended for the exposed individual followed by prompt initiation of nPEP if the screen is negative. If a rapid HIV screen is unavailable, nPEP should be initiated promptly while awaiting the screening test. The decision to initiate nPEP in the setting of high-risk exposure after more than 72 hours have elapsed must be individualized, and nPEP is not recommended in the setting of low-risk or negligible exposures. Recommended regimens are currently extrapolated from the PEP guidelines as the most recent nPEP guidelines were published by CDC in 2005 prior to the availability of integrase inhibitors. Tenofovir/emtricitabine 300 mg/200 mg (Truvada) daily and raltegravir 400 mg (Isentress) twice a day for 28 days is thus the recommended first-line regimen for nPEP, and Truvada daily with dolutegravir 50 mg (Tivicay) once a day can be considered. The initial dose should not be delayed and should be administered in the clinical site of the evaluation. The patient should be discharged from the site with at least 3 days’ supply of drug in hand to prevent lapse in therapy.

Evaluation after a high risk exposure is also an opportunity to address exposure to other bacterial STDs, including syphilis, gonorrhea, and Chlamydia, as well as sexual health in general. Education on sexual risk reduction strategies includes adherence to condom use and avoidance of higher risk sexual practices and is vitally important to the success of a pharmacologic prevention effort. With the exception of high risk exposure due to sexual assault, there is generally a high likelihood of future high risk exposure, and referral for pre-exposure prophylaxis (PrEP) should strongly be considered in patients receiving a course of nPEP if the exposure is not an isolated one or if more than one course of nPEP is sought. More information on local clinics offering PrEP in Mississippi can be found by calling 1-844-YES-PREP.
HIV serologic testing of the source contact in the setting of unknown serostatus is generally not feasible but is recommended. If the source contact is available for serologic testing, HIV resistance testing can be sent as it may impact the choice of nPEP regimen, and if the source’s HIV screen returns negative, then nPEP can be discontinued. Similar to follow-up with PEP, patients prescribed a course of nPEP should be evaluated for tolerability, adherence, and sexual practices. Follow-up HIV serologic testing should be performed at 4 weeks, 3 months, and 6 months. Again, patients with positive HIV serologic screens should be referred for cART.

The Era of PrEP emerges
One of the major concerns with nPEP is the prescription of multiple courses for those with more than one high risk exposure. Continuous therapy was considered as a feasible approach to prevent HIV infection in high risk individuals, and multiple randomized, placebo-controlled clinical trials have demonstrated the efficacy of tenofovir once daily and tenofovir/emtricitabine once daily in preventing HIV infection. Modified intention-to-treat analyses in these trials demonstrated efficacy of 44-75%, but efficacy increased to 85-90% in the subset of subjects with detectable drug levels, a surrogate marker of at least moderate adherence. Mathematical modeling using drug levels predicts 99% efficacy in those taking PrEP 7 days per week, 96% in those taking it 4 days per week, and 76% in those taking it 2 days per week. Also, pharmacokinetic studies suggest that maximal rectal tissue concentration of tenofovir is not achieved until day 7, and maximal blood and vaginal tissue concentrations are not achieved until day 20, further supporting the need for adherence for this intervention to work effectively.

Common concerns regarding nPEP and PrEP include selection of drug resistance if infection develops and an increase in high risk sexual behaviors due to perceived reduced risk of HIV acquisition. Resistant virus was detected in many of the PrEP clinical trials and was slightly higher in the treatment than the placebo arms. Those with drug resistant virus in the treatment arms were mostly infected at baseline prior to starting PrEP, which supports the need to confirm HIV-negative status prior to starting PrEP. In addition, high risk sexual behaviors have been observed to decrease after initiating PrEP, which is felt to be due to engagement in one’s health after starting an HIV prevention strategy.

Evaluation of the patient being considered for PrEP begins with a sexual and substance use history. High risk behaviors include an ongoing sexual relationship with an HIV-infected partner, any anal sex without condoms in the last six months, vaginal sex with a man who has sex with men and women (behaviorally bisexual), condomless sex in the last six months with anyone of unknown HIV status, injection drug use with either needle-sharing or participating in opioid treatment program in the last six months, or in MSM with an STD reported or diagnosed in the last six months. If individuals meet any of the above criteria and are HIV-negative, they may be candidates for PrEP.

Following the patient history, HIV screening should be performed, which either can be done by rapid testing or a formal serum test. Newer, 4th generation screening tests have the benefit of detection up to 2 weeks after exposure, decreasing the likelihood of false negative screening results, usually due to recent, acute HIV infection. Patients complaining of symptoms of a viral infection in the last 4 weeks, such as fever, malaise, rash, or pharyngitis, which may suggest acute HIV infection, should have a
follow-up screening test either one month later by another rapid test, now by a 4th generation test, or now by a PCR-based test before initiating PrEP.

If patients are confirmed to be HIV-negative, non-pharmacologic strategies for HIV prevention should first be discussed, which include consistent and proper condom use, abstinence from higher risk sexual activities such as condomless anal intercourse, abstinence from needle sharing, and substance use counseling if appropriate. Patients should also be screened for concomitant STIs, including syphilis, gonorrhea, and Chlamydia.

Exclusion criteria for prescription of Truvada for PrEP include chronic kidney disease with eGFR less than 60 mL/min. Also, clinical trials did not enroll those less than 18 years of age, and the treatment of adolescents with PrEP should be done cautiously but can be considered if high risk. In those who decide to begin taking PrEP, less than 90 days’ supply of Truvada once daily should be prescribed, and patients should be re-evaluated at least every 3 months to assess tolerability and adherence, to receive sexual health counseling, to have HIV testing performed, and to have a pregnancy test performed if a female of child-bearing potential. Patients should also receive STI screening for syphilis, gonorrhea, and Chlamydia at least every 6 months, and reassessment for indication for PrEP should be addressed at least annually. In those who develop HIV infection while being prescribed PrEP, Truvada alone should not be continued as HIV-infected patients should receive three-drug antiretroviral therapy (cART).

Payment of Truvada for PrEP is currently one of the more difficult challenges to uninterrupted treatment, although many insurers are now covering PrEP prescriptions and provider services. Also, Gilead Sciences, the manufacturer of Truvada, has developed a drug assistance program to help provide medication, free HIV testing, and free condoms, as well as to help fund provider services, to those who cannot afford PrEP medication and services. Applications can be found at https://start.truvada.com.

Conclusions

The prevention of HIV infection is complex and grounded on altered risk behavior through sexual risk reduction strategies, decreased source of HIV infection by treating HIV-infected individuals, and decreased host susceptibility through treating comorbid STIs and PrEP / PEP. PrEP and PEP as HIV prevention strategies are an effective compliment to other risk reduction efforts that can substantially decrease HIV transmission if administered properly along with effective sexual health education.

Dr. Mena is an associate professor and Dr. Brock is an assistant professor of medicine in the division of infectious diseases at the University of Mississippi Medical Center.

Requests for reprints can be sent to: James B. Brock, MD, University of Mississippi Medical Center, Division of Infectious Diseases, 2500 N. State St., Jackson, MS 39216

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Contact: Wayne Johnson 601-955-5906.
Late Diagnoses of HIV Infection in Mississippi: Implications for Improved Testing Strategies and Treatment

KENDRA JOHNSON, MPH AND THOMAS DOBBS, MD, MPH
ABSTRACT

Introduction: According to the Centers for Disease Control and Prevention, more than 1.1 million people in the United States are living with HIV infection, and approximately 1 in 6 (18%) are unaware of their infection. People living with undiagnosed HIV are more likely to progress to AIDS, transmit the virus to others, and have poorer overall health outcomes. In 2013, Mississippi had the 6th highest estimated AIDS diagnoses rate among adults and adolescents in the United States and when comparing persons living with AIDS, the Jackson, MS metropolitan area had the tenth highest rate among all MSAs.

Objective: The objective of this study is to describe people who are diagnosed with HIV late in their course of illness and to identify characteristics associated with late diagnoses.

Methods: Demographic data was obtained for all Mississippi residents who were diagnosed with HIV infection between January 1, 2004 and December 31, 2014. Late diagnoses of HIV infection is defined as an AIDS diagnosis made within 12 months from an initial HIV diagnosis. Prevalence trends, demographics, and predictors of late diagnoses were measured.

Results: Among 4,864 cases of HIV disease, 35% (1,682) were late diagnoses. Late diagnoses were more likely to occur among males, individuals over the age of 34, and individuals who were diagnosed outside of Mississippi State Department of Health clinics.

Conclusion: A large proportion of individuals had late diagnoses of HIV infection and this proportion has slightly declined in recent years. Routine testing in medical settings and in areas with high morbidity may increase early HIV diagnosis.

Key Words: Late HIV diagnosis, HIV testing

Introduction

Approximately 56,000 persons in the United States are newly infected with HIV each year, which is nearly one new infection every nine and a half minutes. Without treatment, most persons develop acquired immunodeficiency syndrome (AIDS) within 10 years of HIV infection. Antiretroviral therapy delays this progression and increases the length of survival, but is most effective when initiated during the asymptomatic phase. It is estimated that on average, an HIV-positive person aged 25 years who receives high-quality care will survive an additional 39 years. According to the Centers for Disease Control and Prevention, more than 1.1 million people in the United States are living with HIV infection, and approximately 1 in 6 (18%) is unaware of their infection and the percentage of persons with late diagnoses of HIV infection was stable at approximately 37% from 2001 to 2004, decreasing to 32.3% by 2007. Persons with late diagnoses of HIV infection have missed opportunities for treatment during the asymptomatic period and for prevention of transmission to others; they also have a shortened life expectancy. In 2006, the CDC recommended that all health care providers in public and private sectors provide routine screening for HIV infection to all patients aged 13-64 years, regardless of the person’s risk behavior. Testing identifies infected persons, which enables them to seek medical care that can improve the quality and length of their lives and reduce risk for HIV transmission. The National HIV/AIDS Strategy includes goals to reduce infections by increasing the proportion of infected individuals who know their status by 2015. The implementation of routine screening will lead to the earlier detection of disease; thus, improving health outcomes and preventing others from becoming exposed to the virus.

In 2013, Mississippi had the 6th highest estimated AIDS diagnoses rate among adults and adolescents in the United States and when comparing persons living with AIDS, the Jackson, MS metropolitan area had the tenth highest rate among all MSAs.

Methods

In Mississippi, HIV infection, including AIDS is a Class 1 reportable disease. Class 1 diseases should be reported directly to the Mississippi State Department of Health (MSDH) by telephone within 24 hours of first knowledge or suspicion. Laboratory directors have an obligation to report laboratory findings. Mississippi has had mandatory confidential name based HIV reporting by providers and laboratories since 1988 and in January 2013, HIV associated CD4+ (T4) lymphocyte results of any value and HIV viral load results, both detectable and undetectable became a Class 3 reportable condition, which requires laboratories to report by mail, telephone, fax or electronically within one week of completion of laboratory tests. HIV/AIDS patients are reported primarily through passive surveillance activities in which health department personnel receive laboratory reports to identify persons with HIV infection. The information collected includes demographic and risk characteristics, AIDS opportunistic illnesses, the dates and results of the first and subsequent CD4 and viral load tests, and the date of the patient’s first positive HIV test.

Demographic data including date of diagnosis, stage of infection (Non Late/Late), age, gender, race, mode of exposure, residence at diagnosis, and facility at diagnosis was obtained for all Mississippi residents who were diagnosed with HIV infection between January 1, 2004 and December 31, 2013. This information was exported from Mississippi’s HIV/AIDS reporting system (eHARS). Persons whose initial HIV diagnosis occurred 12 months or less before their AIDS diagnosis were defined as late diagnosis. The date of HIV diagnosis was determined by identifying the earliest date of a documented positive HIV antibody test. The Chi Square (x2) test was used to measure associations between sociodemographic and risk characteristics and late diagnosis. Independent predictors of late diagnoses were measured using multiple logistic regression in which all variables that were significant at a P value of 0.05 or less from the x2 test were entered into the model.
Results
From 2004 through 2013, there were 4,864 cases of HIV disease (mean = 486). During this time frame, 35% (1,682) were late diagnoses (range 29% - 44%). Figure 1 illustrates infection diagnosed from 2004-2013 and the proportion of cases that were diagnosed late. In 2004, 44% were late diagnoses of HIV infection. There was a sharp decrease until 2009. Late diagnoses peaked at 37% in 2010 and have since declined to 32% in 2013. Although the number of overall cases declined from 2009-2010, the proportion of late diagnoses increased (from 29% to 37%).

Among all cases diagnosed from 2004-2013, 71% were males and African Americans represented 76.2% of cases. The mean age was 35± 12.8 years and 26.9% of cases were between the ages of 25-34. Individuals with unidentified risk factors represented 43.1% followed by men who have sex with men (MSM) (41.2%). 65.2% of cases occurred in individuals who resided outside of the Jackson MSA and individuals who lived in urban areas at the time of diagnosis represented over half (52.5%) of cases. 83.3% of cases were diagnosed at non-MSDH clinics (Table 1).

FIGURE 1.
HIV DIAGNOSIS AND PROPORTIONS THAT WERE DIAGNOSED LATE, BY YEAR OF DIAGNOSIS, MISSISSIPPI, 2004-2013

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<th>CASES</th>
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<td>37.0%</td>
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<td>2006</td>
<td>36.3%</td>
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<td>2008</td>
<td>34.7%</td>
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<td>2009</td>
<td>29.1%</td>
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<td>2010</td>
<td>36.9%</td>
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<td>2011</td>
<td>35.4%</td>
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<tr>
<td>2012</td>
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<td>2013</td>
<td>31.7%</td>
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</table>

From 2004-2013, there were 1,682 late infections diagnosed. Table 2 provides the demographic summary of Mississippians who received a late diagnosis. The mean age of individuals who were late diagnoses was 39± 12.7 years and 33.2% of cases were 45 years or older. There were more cases reported in males (76.2%) and African Americans accounted for 73.8% of late diagnoses. Individuals with no risk reported represented 44.3% of late diagnoses followed by men who have sex with men (MSM) (40.5%). 65.2% were non-residents of the Jackson metropolitan area and individuals who lived in urban areas at the time of diagnosis represented 53.8% of cases. 88.2% were diagnosed at non-MSDH clinics.

Factors that were independently associated with an increased likelihood of late diagnosis were age older than 34 at time of diagnosis, males, and individuals who were diagnosed with HIV at a non-MSDH clinic (Table 1).

Conclusion/Implications
The Mississippi State Department of Health has 100 Public Health Clinics, where free and confidential HIV testing is available. Women in health department settings are more likely to be routinely screened for HIV through STD, Family Planning, and Maternal and Child Health clinics. MSDH implemented routing HIV testing in patients receiving family planning, TB, prenatal care and STD services for over a decade ago and this policy may explain why cases are more likely to be diagnosed late if tested outside of a MSDH clinic. Opt-out testing, without using specific written consents for HIV testing, is standard in county health departments and likely contributes to the earlier detections demonstrated. Despite the availability of testing, 35% of individuals throughout Mississippi were diagnosed with HIV infection only 12 months or less before their AIDS diagnosis. The extent of late diagnoses in Mississippi is slightly higher than what has been reported nationally (35% vs. 32%).

Identifying persons early in the course of infection saves lives, reduces morbidity and mortality, prevents new infections, and can reduce healthcare expenditures. In one study, persons unaware of their infection were 3.5 times more likely to transmit HIV than persons aware of their infection. Persons who have been diagnosed can take precautions to avoid transmission and can be treated with appropriate antiretroviral therapy. Such therapy lowers the amount of virus in the blood and genital secretions, reducing the biologic risk for transmission. Every new HIV infection averted saves approximately $367,000 (2009 dollars) in lifetime medical costs. For all these reasons, HIV screening to identify infected persons and linking them to care and prevention services is a cornerstone of the national HIV prevention strategy. These findings underscore the need to continue the expansion of routine HIV testing as a component of normal medical care. Opt-out testing, which foregoes the cumbersome and stigmatizing process of written consents, should be the standard. These findings also highlight the importance of effective programs linking diagnosed individuals to HIV care where they can receive treatment, especially those with late diagnoses.

Limitations
This analysis was based on information reported to the MSDH HIV surveillance system and therefore is subject to several limitations:

1. Due to reporting delays, the actual number of diagnosed cases may actually be higher than what is reported. We did not utilize any form of statistical estimates to adjust for reporting delays in this project.

2. Reporting laws for CD4 and HIV viral loads were recently changed and therefore, historical data may have been underreported. Individuals with CD4 count less than 200 that may not have been reported by their providers as having AIDS were likely misclassified as Non-late diagnosis.
TABLE 1.
COMPARISON OF CHARACTERISTICS OF NON-LATE VS. LATE DIAGNOSES AND INDEPENDENT PREDICTORS OF LATE TESTING, MISSISSIPPI, 2004-2013
* Men who have sex with men  **Injection drug user  ***Metropolitan Statistical Area  ****Mississippi State Department of Health

<table>
<thead>
<tr>
<th>CHARACTERISTIC</th>
<th>TOTAL N (%)</th>
<th>NOT LATE N (%)</th>
<th>LATE N (%)</th>
<th>CHI SQUARE P VALUE</th>
<th>ADJUSTED OR (95% CI)</th>
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<td><strong>Sex</strong></td>
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<tr>
<td>Male</td>
<td>3475 (71)</td>
<td>2194 (69)</td>
<td>1281 (76)</td>
<td>.0001</td>
<td>1.58 (1.4-1.8)</td>
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<tr>
<td>Female</td>
<td>1389 (29)</td>
<td>988 (31)</td>
<td>401 (24)</td>
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<tr>
<td>African American</td>
<td>3707 (76)</td>
<td>2466 (78)</td>
<td>1241 (74)</td>
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<tr>
<td>White</td>
<td>803 (17)</td>
<td>502 (16)</td>
<td>301 (18)</td>
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<td>Hispanic</td>
<td>164 (3)</td>
<td>98 (3)</td>
<td>66 (4)</td>
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<td>Other/Unknown</td>
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<td>116 (4)</td>
<td>74 (4)</td>
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<td><strong>Age at HIV Diagnosis</strong></td>
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<td>Mean Age</td>
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<td>33</td>
<td>39</td>
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<tr>
<td>13-17</td>
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<td>59 (2)</td>
<td>17 (1)</td>
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<td>18-24</td>
<td>1235 (25)</td>
<td>978 (31)</td>
<td>257 (15)</td>
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<td>25-34</td>
<td>1306 (27)</td>
<td>892 (28)</td>
<td>414 (25)</td>
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<td>35-44</td>
<td>1035 (21)</td>
<td>600 (19)</td>
<td>435 (26)</td>
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<td>45 and older</td>
<td>1212 (25)</td>
<td>653 (21)</td>
<td>559 (33)</td>
<td>2.8 (1.6-4.9)</td>
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<td><strong>Mode of HIV exposure</strong></td>
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<td>MSM*</td>
<td>2006 (41)</td>
<td>1325 (42)</td>
<td>681 (40)</td>
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<tr>
<td>IDU**</td>
<td>118 (2)</td>
<td>72 (2)</td>
<td>46 (3)</td>
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<tr>
<td>MSM/IDU</td>
<td>59 (1)</td>
<td>32 (1)</td>
<td>27 (2)</td>
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<tr>
<td>Heterosexual</td>
<td>585 (12)</td>
<td>402 (13)</td>
<td>183 (11)</td>
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<td>Other/No Risk Identified</td>
<td>2096 (43)</td>
<td>1351 (42)</td>
<td>745 (44)</td>
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<tr>
<td><strong>Residence at HIV diagnosis</strong></td>
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<tr>
<td>Jackson, MS MSA***</td>
<td>1692 (35)</td>
<td>1107 (35)</td>
<td>585 (35)</td>
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<tr>
<td>Outside of Jackson, MS MSA</td>
<td>3172 (65)</td>
<td>2075 (65)</td>
<td>1097 (65)</td>
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<td>1534 (48)</td>
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<td>Urban</td>
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<td>1648 (52)</td>
<td>905 (54)</td>
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<td><strong>Facility at Diagnosis</strong></td>
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<tr>
<td>MSDH Clinic****</td>
<td>812 (17)</td>
<td>613 (19)</td>
<td>199 (12)</td>
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<td>Non-MSDH Clinic</td>
<td>4052 (83)</td>
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<td>1483 (88)</td>
<td>1.5 (1.3-1.8)</td>
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</table>

5. CDC. Revised Recommendations for HIV Testing of Adults, Adolescents, and Pregnant Women in Health-Care Settings. MMWR Recommendations and Reports. 2006; 55(RR-14); 1-17.
8. Marks G, Crepaz N, Janssen RS. Estimating sexual transmission of HIV from persons who are unaware and aware that they are infected with the virus in the USA. AIDS 2006; 20: 1447–50.
**Introduction**

The landscape of HIV infection has changed dramatically in the last 30 years. Initially a universally fatal outcome with an average prognosis of two years after an AIDS-defining illness, the development of antiretrovirals prescribed as combination therapy known as highly active antiretroviral therapy (HAART) has turned HIV infection into a chronic illness that can usually be treated effectively with once-daily medications, often in single-pill fixed-dose combination (FDC) tablets.

There is currently no cure for HIV infection. Infection with the human immunodeficiency virus results in the integration of its genetic material into the DNA of infected CD4-positive host cells, thereby causing chronic, lifelong infection. An HIV-infected patient will retain a reservoir of latently-infected CD4 cells for the rest of his life due to this process. Effective drug therapy with antiretrovirals is not curative since HAART cannot eradicate HIV from latently-infected CD4 positive cells, but HAART is capable of suppressing ongoing viral replication. This prevents further CD4 cell death resulting in an increase in CD4 cell number, improved immune system function, and the prevention of opportunistic infections. HAART is associated with a significant decrease in the morbidity and mortality associated with HIV infection, and many HIV-infected patients are now living nearly normal life spans.¹

There has been a paradigm shift in the approach to treatment of HIV infection in recent years. The initiation of HAART was previously recommended only for HIV-infected persons with lower CD4 counts. However, the current guidelines by the US Department of Health and Human Services (DHHS) recommend offering HAART to all HIV-infected patients regardless of CD4 count.² The rationale for this approach is based on the availability of newer, relatively simple, minimally toxic HAART regimens and emerging data showing that earlier therapy leads to a more robust immune recovery and can prevent HIV-related comorbidities such as coronary artery disease,³ chronic kidney disease,⁴ malignancies,⁵ and neurocognitive abnormalities, including dementia.⁷ In addition and equally important, viral suppression with HAART substantially decreases the sexual transmission of HIV to uninfected partners, providing a public health benefit.⁸ In fact, HAART is currently the most effective method of prevention of HIV transmission, other than abstinence. Early diagnosis of HIV disease with subsequent linkage to care and early initiation of treatment with antiretrovirals is now an important public health goal. HAART is also recommended for all pregnant HIV-infected women to decrease the perinatal transmission of HIV.¹⁰

**Antiretroviral Drugs**

There are currently six classes of antiretroviral drugs available for use in the U.S. (see Figure). The four classes most commonly used in treatment are the nucleoside reverse transcriptase inhibitors (NRTI), non-nucleoside reverse transcriptase inhibitors (NNRTI), protease inhibitors (PI), and integrase strand transfer inhibitors (INSTI).² They each function to inhibit enzymes essential in the viral replication process. Nucleoside reverse transcriptase inhibitors (NRTI) are analogues of nucleosides/nucleotides that inhibit HIV’s reverse transcriptase, an enzyme that converts viral RNA into DNA. Commonly used NRTIs include tenofovir (TDF), abacavir (ABC), lamivudine (3TC), and emtricitabine (FTC). These medications form the backbone of many HAART regimens and are included in every combination pill available. Tenofovir can cause nephrotoxicity that may only be partially reversible after cessation of the drug. This can vary from mild renal impairment to Fanconi syndrome, a condition of severe electrolyte wasting. Abacavir can cause a hypersensitivity syndrome in those with the HLA-B*5701 allele, manifesting as fever, rash, and gastrointestinal upset. Rechallenge of the drug in those with abacavir hypersensitivity can be fatal. All patients should be screened for the HLA-B*5701 allele prior to starting abacavir, and patients positive for this allele should not receive abacavir.

Non-nucleoside reverse transcriptase inhibitors (NNRTI) inhibit the reverse transcriptase enzyme at a site distinct from the NRTIs and include efavirenz (EFV) and rilpivirine (RPV). The most common adverse effects of NNRTIs are neuropsychiatric, which are broad and
<table>
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<tr>
<th>Generic Drug (listed alphabetically)</th>
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<td>Prezista</td>
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<td>Combivir</td>
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Nominations now being accepted for 2015-2016

Take your leadership skills to the next level! Physicians by definition are leaders, but they are not formally trained in leadership. The MSMA Physician Leadership Academy seeks to prepare MSMA members for future leadership positions as physicians with leadership skills are uniquely positioned to play a major role in today’s healthcare changes to better the lives of their patients.

MSMA’s Physician Leadership Academy is an intensive leadership development program designed to train MSMA members in the core aptitudes to excel in leadership positions within organized medicine, medical practice and community.

This in-depth program will enable physicians to enhance leadership skills and provide training in core aptitudes to excel as future leaders, in their own practices, and in organized medicine and the public policy arena.

For more information, contact Phyllis Williams at 601-853-6733 ext 322 or via email at PWilliams@msmaonline.com
New HIV Infections  
Mississippi 2013

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Route of Transmission

- Other/unknown: 26%
- Injection Drug Users: 2%
- Heterosexuals: 21%
- Gay and Bisexual men: 51%

All other routes account for 1% of new infections.

Race/Ethnicity

- African Americans: 78% of all new infections
- Whites: 7.5
- Hispanics: 25.9

Number of infections per 100,000 people in 2013.
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African Americans: 78% of all new infections

Whites: 17.9

Hispanics: 7.5

Number of infections per 100,000 people in 2013.

All other races account for less than 4% of new transmissions.

Teens and Young Men

- 33% of all new infections were among teens and adults ages 13-24
- 23% of all new infections were among young men who have sex with men
- 20% of all new infections were among young black men who have sex with men
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range from sleep disturbance to increased risk of suicide. Given the availability of other classes of antiretrovirals, NNRTIs should be avoided in those with psychiatric comorbidities. Efavirenz has been associated with neural tube birth defects and should not be used in pregnancy.

Protease inhibitors (PI) inhibit the viral protease enzyme, the normal function of which is critically important during the viral replication process. These include atazanavir (ATV) and darunavir (DRV). PIs should be prescribed with a low dose of ritonavir, known as “ritonavir boosting.” The co-use of ritonavir slows the hepatic breakdown of the PI and increases the half-life and the serum concentration of the other drug, improving potency and allowing for once-daily administration. The major adverse effects of PIs are gastrointestinal and include bloating, nausea, and diarrhea, which often limit their tolerability. PIs are also potent inhibitors of the hepatic cytochrome P450 3A4 enzyme, a metabolic pathway for many other classes of pharmaceuticals, and thus any current and new medications that are also hepatically-metabolized should be screened for drug-drug interactions and dose-adjusted or withheld as indicated.

Integrase strand transfer inhibitors (INSTI), commonly called integrase inhibitors, block the HIV integrase enzyme, which incorporates viral DNA into the human host cell DNA following viral infection of the host cell. These drugs include raltegravir (RAL), elvitegravir (EVG), and dolutegravir (DTV). Raltegravir is the only first-line antiretroviral that must be given twice a day, and it has been uncommonly-associated with myalgia and myopathy. Elvitegravir is administered in an FDC with the boosting agent cobicistat to allow for once-daily administration, and cobicistat has the potential for drug-drug interactions with many medications, similar to protease inhibitors. Dolutegravir is the newest INSTI, is well-tolerated and very effective as part of a once-daily initial HAART regimen.

Viral resistance, efficacy, adherence
The reverse transcriptase enzyme, which transcribes viral RNA into DNA, does not possess any error-checking mechanisms and thus regularly allows for mutations. This can benefit the virus in the presence of suboptimal drug therapy if a mutation creates a new virus that is resistant to the currently prescribed antiretroviral drugs. Antiretroviral therapy with a single agent is known to result in the rapid emergence of resistance due to this phenomenon. To prevent the emergence of viral resistance, three antiretroviral drugs should be prescribed in every HAART regimen (except in the uncommon instance of profound viral resistance with only two active drugs available on the market), and they must represent more than one class of antiretroviral drug. If taken as prescribed, three-drug HAART regimens have a very low risk of development of viral resistance. The medications are very potent and result in rapid declines in viremia, reaching undetectable levels typically within a few weeks.

Viral resistance can develop from two mechanisms. First, patients infected with drug resistant virus can transmit the mutant virus to an HIV-uninfected person. About 10-15% of patients will be infected with drug resistant virus prior to ever receiving antiretroviral therapy through this mechanism. Likewise, HIV-infected patients with viral suppression on a HAART regimen can be superinfected with another person’s drug resistant virus. More common, however, drug resistance emerges due to poor adherence. Regular exposure of the virus to subtherapeutic drug levels as a result of inconsistent adherence reliably and frequently results in virologic failure and the emergence of drug resistance, and even infrequently-missed doses can result in the same outcome. Impressing the importance of adherence to patients receiving HAART cannot be overemphasized. When assessing a patient for the initiation of HAART, a provider should take some time to evaluate whether that patient is ‘ready’ to start therapy and educate that patient on the risk of the occurrence of drug resistance if adherence is not good.

Laboratory analysis
Patients with a confirmed diagnosis of HIV infection should have several follow-up laboratory studies obtained to further guide therapy and prognosis. A quantitative viral PCR, called a viral load, measures viremia in the peripheral blood. Patients with higher viral loads tend to have more rapid progression to AIDS and are also more likely to develop viral resistance when starting therapy if adherence to HAART is poor. After starting HAART, the viral load should continue to be monitored and should decrease several log10 copies/mL within a few weeks and reach undetectable levels within a few months. Occasionally, patients with very high viral loads prior to starting treatment may take up to six months to achieve full virologic suppression. Once patients have undetectable viral loads on HAART and are stable clinically, their viral load can be monitored every 3-6 months. After starting HAART and achieving virologic suppression, consistently undetectable viral loads confirm successful therapy, and a persistently positive viral load more than 200 copies/mL is the definition of treatment failure.

The CD4+ T cell count is used to stage the degree of immunologic suppression, and the absolute CD4 count is clinically the most useful value. AIDS is defined by the occurrence of an opportunistic infection at any CD4 count or a CD4 count less than 200 without an opportunistic infection. While HAART is now recommended for all patients with HIV infection regardless of CD4 count, those with defined AIDS and low CD4 counts have the strongest indication for HAART and the greatest urgency to start therapy as soon as possible.

Testing for HIV drug resistance is also an important part of ongoing HIV care. This can be done by obtaining an HIV genotype, which involves the sequencing of those parts of the viral DNA that code for the reverse transcriptase, protease, and integrase enzymes. Certain viral mutations are known to confer resistance to specific medications or entire classes of antiretrovirals, and these mutations can typically be detected with a genotype. An HIV genotype is recommended prior to starting HAART to assess for any baseline drug resistance and whenever a positive viral load is detected while taking HAART to see if drug resistance has emerged. Patients with drug resistance can still be treated effectively with alternative, salvage HAART regimens based on genotype results. However, some resistance patterns can be complicated, and the interpretation of genotypes may sometimes be confusing, therefore consultation with an experienced HIV provider to assist with genotype interpretation is advised.

Choosing a HAART regimen
There are several expert guidelines available pertaining to antiretroviral
therapy and these continue to evolve and be updated, but the general principles of antiretroviral therapy remain the same: prescribe three active drugs in combination, preferably two NRTIs plus a third drug from a different class. The individual drugs are chosen for each patient based on previous viral resistance patterns, patient comorbidities, and the potential for drug-drug interactions, and should be tailored for each individual patient. Ideally, the chosen regimen would be convenient (once a day), and if possible for the greatest simplicity, one pill once a day. All these factors are taken into account to optimize adherence, which is truly the most important factor in the long-term success of any HAART regimen other than preexisting drug resistance.

When choosing a two-drug NRTI “backbone” as part of an initial HAART combination, emtricitabine or lamivudine (never together as they have the same parent nucleoside and identical resistance mechanisms) are typically included in the HAART regimen as they exhibit minimal side effects and convenient dosing, and the second NRTI chosen is usually tenofovir or abacavir. Most FDC pills include tenofovir and emtricitabine, but there are also FDCs composed of abacavir and lamivudine, and zidovudine and lamivudine.

The third drug of the HAART combination is chosen from the NNRTI, PI, or INSTI class. NNRTIs such as efavirenz and rilpivirine may have CNS side effects or exacerbate depression and should be used with caution in patients with psychiatric comorbidities. Also, efavirenz is not recommended in those of child-bearing potential due to concern for neural tube defects. PIs are not used by some HIV providers as first-line therapy due to common gastrointestinal side effects, and drug interactions may complicate their administration. Integrase inhibitors are emerging as highly effective agents with good tolerability profile and are becoming widely-used. As of this writing, the DHHS Guidelines for the Use of Antiretroviral Agents in HIV-1-Infected Adults and Adolescents recommend five preferred regimens, four of which contain an integrase inhibitor. Among the FDC single pill regimens, tenofovir/emtricitabine/efavirenz (Atripla) was the first available and has demonstrated good tolerability and excellent efficacy a decade. Tenofovir/emtricitabine/rilpivirine (Complera) is another NNRTI-based FDC that can be used in those of child-bearing potential, although it is not recommended in those with baseline viral loads > 100,000 due to decreased efficacy. Tenofovir/emtricitabine/cobicistat/elvitegravir (Stribild) is an integrase inhibitor-based FDC that is well-tolerated and potent, although there may be drug interactions with cobicistat. Lastly, abacavir/lamivudine/dolutegravir (Triumeq) is an integrase inhibitor-based FDC with excellent tolerability and efficacy. A more detailed, thorough review of antiretroviral drug therapy is beyond the scope of this article. The reader is referred to the DHHS guidelines for a more detailed review of each individual regimen.

HAART regimens are not cheap, and cost is often cited as a barrier to therapy. All third party payers in the United States pay for HAART medications, and special drug assistance programs are available to help patients afford high co-pay charges if present. Patients with no insurance at all are eligible to be enrolled into the Mississippi AIDS Drug Assistance Program (ADAP). All 50 states have an ADAP program, and these are funded by the federal Ryan White Care Act and administered by the Health Department. ADAP provides all of the available HAART meds at no cost to HIV-infected persons who have no insurance, so cost should not be an insurmountable barrier to providing HAART therapy to an HIV-infected person in the United States.

Conclusions
The natural history of HIV infection has changed dramatically since the advent of the HAART era. A once universally fatal infection has become an often easily-managed chronic illness. "Cocktails" consisting of many pills administered several times a day with significant toxicities have made way for contemporary regimens consolidated into single pills administered once daily that are well-tolerated and highly effective. Early diagnosis and treatment not only leads to improved immunologic recovery but also prevents conditions as varied as cardiovascular disease, chronic kidney disease, and dementia, and HAART has now been demonstrated to markedly decrease person-to-person viral transmission. Persons living with HIV can now live long, productive, healthy lives.

Requests for reprints should be addressed to Harold Henderson MD, Division of Infectious Diseases, University of Mississippi Medical Center, 2500 N. State Street, Jackson, MS 39216.

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CLAUDE D. BRUNSON, MD  ~  2014-15 MSMA PRESIDENT

MEDICAL BREAKTHROUGHS – and on occasion, miracles – happen every day. For example, the Cleveland Clinic polled 110 of its medical experts and compiled a list of the Top 10 Medical Innovations of 2015 (Figure).¹

The annual list never disappoints. It is always composed of amazing medical breakthroughs that promise to dramatically improve the landscape of healthcare. Even more exciting, these innovations are transforming patients’ lives, sometimes with the touch of a button.

As a physician, I am fascinated by the medical miracles occurring during my lifetime and medical career. Just a few short years ago, I could never have imagined a bionic eye would restore sight in patients with inherited retina disease, the number one innovation on the 2014 list. Spending time in the OR with a bionic arm is not something I envisioned in medical school.

These and many other breakthroughs are met with excitement by those of us who’ve practiced medicine long enough to remember numerous cases in which there was simply no way to improve a patient’s quality of life – or even extend their life.

While I applaud these and other medical breakthroughs on the horizon, I often wonder why more is not being done to stem the rising tide of Human Immunodeficiency Virus (HIV) and Acquired Immunodeficiency Syndrome (AIDS) cases in our state, country, and world. With an estimated 2.1 million new cases of infection around the world and more than 39 million deaths from AIDS, something must be done.

Mississippi has the highest rate of AIDS-related mortality of all states and territories.² The state ranks 9th for HIV diagnoses with an overall case rate of 21.8 per 100,000. Among U.S. metropolitan areas, Jackson ranks 8th for HIV infection rates, 2nd for AIDS diagnosis rate, and 3rd for HIV infection rate among African American men under age 25.

In 2013, Mississippi reported 556 new HIV infections (18.6 per 100,000 persons), according to the Mississippi State Department of Health’s STD/HIV Office. HIV infection rates were the highest among those aged 25-44, followed closely by those ages 13-24 (35.9 and 32.9, respectively), with 25-44 year olds accounting for 49% of newly reported HIV disease infections.

And here’s another sobering fact. The rate of infection among males was four times higher than females (30.4 per 100,000 compared to 7.4 per 100,000 persons). Statewide, males accounted for 79% of newly reported HIV disease infections.

From 2004 to 2013, the total percentage of new HIV infections in men who have sex with men (MSM) ages 13 to 24 years increased from 35% to 72%. The total percentage of HIV infections attributed to African American men who have sex with men (AAMSM) increased from 37% to 62%.

But not all of the news is negative. Progressive strides have been made in Mississippi and the nation. HIV transmission via blood transfusions and from mother to child have been virtually eliminated. New infections from intravenous drug use have been reduced in record numbers. The Centers for Disease Control and Prevention (CDC) and United States Preventive Health Task Force have issued recommendations for HIV testing of patients in all health care settings in an attempt to identify those with HIV infection so they can be linked to HIV care. And the progression of modern antiretroviral drugs in treating HIV means a new infection is no longer a death sentence; a 25 year old infected with HIV on treatment should have the same life expectancy as an uninfected 25 year old.

However, more than three decades after the AIDS pandemic swept into the U.S. and Mississippi, there’s still no cure or vaccine. The CDC estimates that there are still 50,000 new annual infections in the U.S.³ This number has remained unchanged for more than a decade, demanding an expansion of our prevention efforts.

One glimmer of hope comes in the form of a small pill. The FDA approved the use of tenofovir/emtricitabine (Truvada®) for pre-exposure
Prophylaxis or PrEP in July 2012. PrEP is a novel HIV prevention strategy recommended by the CDC and the U.S. Public Health Service. Practice guidelines to help clinicians implement its use were released in June 2014.

If physicians know about PrEP and prescribe it to at-risk patients, this pill, in conjunction with other prevention measures, could have a major impact on ending or at least slowing down the HIV epidemic in Mississippi.

There is extensive data from clinical trials demonstrating the effectiveness of PrEP preventing HIV infections. When those who aren’t infected take the pill once a day, PrEP is more than 90% effective in blocking HIV transmission. The new guidelines recommend the clinician evaluate their male and female HIV negative patients who are sexually active or who are injecting illicit drugs. They should consider offering PrEP to those whose behaviors place them at substantial risk of acquiring HIV. The CDC warns that PrEP isn’t meant to replace other prevention tools like condoms and that it doesn’t prevent transmission of other sexually transmitted infections. But if physicians know about PrEP and prescribe it to at-risk patients, this pill, in conjunction with other prevention measures, could have a major impact on ending or at least slowing down the HIV epidemic in Mississippi.

Educating our members about PrEP and many other factors related to the growing HIV and AIDS crisis is the reason MSMA partnered with MSDH on an initiative called “Mississippi Physicians HIV/AIDS Prevention Plan.” It’s a multi-faceted educational program that includes the printing of this special HIV issue of the Journal; a comprehensive tool-kit of HIV and AIDS-related resources that will be provided to all members; HIV CME events and speakers; free HIV testing and follow-up services offered to physicians upon request and other components to be rolled out in coming months.

Lastly, despite the advances in prevention and treatment, there is still no cure for HIV or AIDS. But as physicians, we’re trained to do everything in our power to improve the lives of our patients and others in need of care. HIV screening of all patients, prompt linkage to care for those diagnosed with HIV, and PrEP for those HIV-negative at high risk of infection are important steps in improving the health of all Mississipians.

What is Better than “Curing” an HIV-Infected Child?

HANNAH GAY, MD
Children’s Infectious Diseases, University of Mississippi Medical Center
In 2013 the Pediatric/Perinatal HIV Program at Children’s of Mississippi, The University of Mississippi Medical Center, garnered much international attention following our report of the discovery of a child with perinatally-acquired HIV infection who had achieved “functional cure” or remission. Although the child relapsed after at least 27 continuous months of remission, this child, dubbed the “Mississippi Baby”, remains a unique and very instructive case of suppression of viral reservoirs by very early initiation of antiretroviral therapy. This celebrated case may seem to many to represent the height of the success of pediatric HIV care in Mississippi. As someone who has been involved in our state’s pediatric treatment for over 20 years, I would disagree. I think that we should celebrate with much greater enthusiasm the many babies who have been born exposed to HIV but without acquiring the infection.

Prior to 1994, nationally the transmission rate of the HIV virus from mother to child (MTCT) near the time of birth was about 25%. In Mississippi our rate of MTCT was generally closer to 30% due to the high number of comorbidities in our patient population including preterm birth and other sexually transmitted infections during pregnancy. In 1994, however, interim results from a large study of the Pediatric AIDS Clinical Trials Group (PACTG) changed everything for perinatally exposed infants. This study, known as PACTG 076, showed that a 3-pronged approach using zidovudine treatment of the mom during pregnancy, intravenous zidovudine during labor, and oral zidovudine for 6 weeks as post-exposure prophylaxis for the baby, was highly effective at preventing the establishment of HIV-infection in the infants of infected mothers.

In August, 1994 the US Public Health Service recommended that zidovudine therapy should be given in all cases of maternal HIV infection and in September of 1994 the Mississippi State Department of Health and UMMC’s Pediatric HIV Program partnered to begin implementation of this new form of treatment across our state. Our success over the past 20 years is graphically represented in Figures 1 and 2.

There was obviously not an immediate fall to zero in mother-to-child-transmission rates in 1994. We saw a dramatic decline in MTCT within the first three years after beginning the prevention program even though we were using only zidovudine monotherapy at that time. During the remaining years of the 1990’s combinations of antiretroviral medicines were found to be highly successful at controlling viral replication in HIV-infected adults and children. Because maternal viral load at the time of delivery is the greatest independent predictor of viral transmission to the infant, it was not surprising that, as soon as these combination treatment regimens were shown to be safe during pregnancy, we saw a further fall in transmission rates to <2% nationwide.
In Mississippi only 8 babies have been vertically infected in the years 2001-2014 inclusive. In each of those 8 cases, the mother did not receive prenatal care and, thus, was not offered antiretroviral therapy during pregnancy.6

How has this success been achieved?

The details of the best medical practices for the prevention of perinatal transmission have changed many times over the years as new information has been gained and new medications discovered. Those best practices are described in guidelines developed and regularly updated by a panel of experts for the US Department of Health and Human Services, and those guidelines have grown to be 300+ page documents.7,8 The basic principles of prevention have, however, remained relatively steady:

Applying these principles to individual cases, even with the myriad details requiring consideration as discussed in guidelines, turns out to be the easy part of providing perinatal HIV care. The harder part is the intensive case management which is required to help infected women cope with the fears and uncertainties surrounding the diagnosis of HIV and to help them overcome the sometimes immense barriers to the complete adherence to therapy that she and her baby need.

How can perinatal prevention be continued in Mississippi?

It is obviously important that our state continue to keep perinatal HIV transmission at as low as possible and this requires the efforts of all healthcare providers in our state. Every practitioner in our state should be diligent in identifying HIV-infected persons in all care settings as recommended by CDC.9 Particularly for women of child-bearing potential who have confirmed positive tests, expert treatment and planning before conception should be encouraged. Every woman should be tested for HIV during the first and third trimesters of every pregnancy regardless of her previous testing history.10 Tests that are confirmed positive for HIV are required to be reported to the State Department of Health. New pregnancies in known HIV-infected women are legally mandated to be reported to the Mississippi State Department of Health. Mississippi providers should ensure that appropriate medications are available in hospital pharmacies for mothers and babies in anticipation of unexpected deliveries, and UMMC and Department of Health staff are available 24 hours a day for consultation.

The Pediatric/Perinatal HIV Program at Children’s of Mississippi welcomes calls for assistance with the care for any pregnant HIV-infected woman or exposed newborn in our state. We have expert medical case managers, social work case managers as well as medical providers who specialize in this field and are willing to help Mississippi providers by accepting referrals, doing distance consultations, providing case management or simply answering questions.

BASIC PRINCIPLES OF PERINATAL PREVENTION

1. Identify infected women as early as possible during pregnancy.
2. Provide antiretroviral therapy that optimally controls maternal viral replication throughout pregnancy both for the health of the mother and protection of the baby, and monitor viral load frequently.
3. Consider cesarean delivery prior to the onset of labor if maternal viral load remains high near the time of delivery.
4. Avoid invasive procedures such as amniocentesis or fetal scalp electrodes.
5. Provide appropriate antiretroviral medications as post-exposure prophylaxis for the baby beginning within the first few hours of life and continuing for 4-6 weeks.
7. Provide appropriate follow-up HIV testing for the baby.
8. Unconfirmed positive HIV screening at the time of labor should be treated as infected until results of confirmatory tests are available.

Contact

Pediatric/Perinatal HIV Program
The University of Mississippi Medical Center
2500 North State Street, Jackson, MS 30216
601-815-1119 • Fax 601-815-3736
Office of HIV and STD, Mississippi State Department of Health
570 East Woodrow Wilson, Jackson, MS 30216
601-576-7723 • After Hours 601-576-7400

6. Unpublished data taken from the database of the Pediatric/Perinatal HIV Program, Children’s of Mississippi, The University of Mississippi Medical Center.
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Hugh Durrence, M.D.  PHC Health  Get the whole story at regions.com/phchealth

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Top Ten Facts
You Need to Know about HIV

1. HIV testing rates are low! Surveillance data shows 45% of Americans haven’t been tested. CDC estimates 1 in 6 people are unknowingly infected with HIV. This means almost 16% of those who have the virus don’t even realize it. Mississippi physicians can help our citizens know their status. MSDH encourages all health providers to offer HIV testing as part of routine preventive care. HIV infection is a Class I Reportable Condition, requiring immediate (<24 hours) notification to the Mississippi State Department of Health (MSDH).

2. HIV testing is quick and easy. New HIV testing technologies can be performed in-office using a finger-prick or oral fluid sample to detect HIV antibodies in 1 to 20 minutes. Current available testing technology (4th generation testing) is able to detect HIV soon after the acquisition of the disease, as early as two weeks after infection. Tests performed very soon after infection may yield false negative results; individuals at high risk or with a recent exposure should be retested at a later date (three or four weeks). Positive screening tests require validation with an approved confirmatory test as false positive results may occur.

3. Most HIV testing is reimbursable. Due to the Affordable Care Act, most health insurance plans now must provide free HIV screenings for anyone ages 15 to 65 with no copayment or coinsurance. Therefore HIV testing is free to most patients. Did you also know that Mississippi Medicaid will cover HIV testing for beneficiaries? The 2015 Medicaid reimbursement rate is $10.91 for an HIV-1 test (CPT 86701) and $16.83 for an HIV 1-2 antibodies test (CPT 86703).

4. HIV/AIDS can be treated with just one pill a day. In most patients, HIV can be controlled with one pill a day. Each pill combines several medications that used to be taken separately. But good medication adherence is essential; those taking HIV medication cannot skip a day. The newer pills also tend to have fewer side effects, making the daily routine even easier.

5. New HIV drugs are released frequently. More one-a-day pills will continue to enter the market, while drugs that can be taken even less frequently may be coming soon. New drugs that need to be taken even less often than every day will also be available. The reason is newer drugs act at different points in the virus life cycle; therefore medications with longer half-lives are not required every day.

6. One pill a day can also prevent HIV infection! In 2012, the FDA approved Truvada as the first pharmaceutical to prevent HIV infection in uninfected individuals, known as Pre-exposure Prophylaxis (PrEP). Truvada is a combination drug pill containing emtricitabine and tenofovir disoproxil fumarate. The CDC recommends PrEP as a prevention option for sexually active HIV-negative men who have sex with men (MSM) and heterosexual men and women who are at “substantial risk” due to a serodiscordant relationship (e.g., an HIV-positive sex partner), high number of sex partners, inconsistent or no condom use, or recent bacterial sexually transmitted infection such as syphilis or gonorrhea. The CDC also
recommends PrEP as a prevention option for HIV-negative injection drug users. Truvada will protect against HIV but it won’t prevent other sexually transmitted diseases. Studies have found that daily PrEP use does not lead to promiscuity and other high-risk behaviors. Physicians should provide counseling about PrEP to individuals at risk for acquiring HIV. Clinicians seeking advice and consultation on PrEP can call the hotline funded by CDC at 855 HIV PrEP (855-448-7737). For more information on the services offered through the PrEPline, visit the National Clinicians Consultation website at http://nccc.ucsf.edu.

Even after an exposure, HIV infection can be prevented.
A cocktail of antiretroviral medications taken for one month can prevent individuals who are exposed to HIV infection through sexual contact or other transmission factors from contracting the virus infection. This preventive strategy is called non-occupational post-exposure prophylaxis (nPEP). nPEP isn’t 100% effective, but it can be close if it’s started within 72 hours of exposure. Medications must be prescribed by physicians and are not available through the health department. Emergency rooms, domestic violence shelters, and urgent-care clinics should consider adopting emergency protocols for those with an exposure. Patients without health insurance can access medications through patient assistant programs established by the drug manufacturers.

Early treatment is important and drug resistance is less common.
Studies show that early treatment is prevention. Starting HIV medications early reduces HIV viral load to undetectable levels and decreases the risk of infecting others. It is also easier than ever before for primary care health providers to manage patients with HIV infection instead of referring to a specialist. Previous HIV/AIDS medication options would work only for so long before the patient would no longer respond to the treatment and would need to switch to a different drug. Now HIV drug resistance is less of a problem and HIV genotyping and other technologies allow health care providers to better manage these medication regimens with their patients. Most Affordable Care Act insurance plans will cover HIV treatment and care. With improvements in treatment and expanded health insurance coverage, many people with HIV will never develop AIDS. The Mississippi State Department of Health also receives federal Ryan White funds for HIV medical care. Physicians interested in participating in this program may call Dr. Karen Maccarone at 601-362-4879 or send email to karen.maccarone@msdh.ms.gov.

Hepatitis C infection occurs in HIV/AIDS patients.
About a quarter of all HIV-positive people also have hepatitis C infection. Every one diagnosed with HIV should be screened for chronic hepatitis (C and B). The rate of co-infection is even higher among HIV-positive IV drug users, as high as 90%. In 2013, the FDA approved the first antiviral treatment options for hepatitis C. The medications Olysio (simeprevir) and Solvadi (sofosbuvir) may cure up to 80% of cases.

The AIDS Education Training Center provides comprehensive education and training for clinicians and other healthcare providers on HIV/AIDS prevention, care and treatment practices throughout the state of Mississippi. Training can be customized to meet the specific needs of any agency, clinic, or other group or individual health care provider. For more information and to inquire about upcoming trainings contact Mauda Monger at 601-984-5542 or email mmonger@umc.edu.
This month, we print a poem by the gifted Mississippi-born physician/poet Dwaine Rieves, who won the Tupelo Press Judge’s Prize for “When the Eye Forms,” his 2006 collection of poetry. He states: “The poems, to a large extent, honor the time I spent in Natchez as a public health officer for the Mississippi Department of Health … from 1983-1985.” Among these lovely poems is “Thrush, at 23,” printed above and written during that period at the beginning of the AIDS epidemic when young men were dying from an unknown virus. Oral candidiasis, commonly known as oral thrush, is an infection of the buccal cavity most commonly associated with Candida albicans. It was first described by French pediatrician Francois Valleix in 1838. A number of factors predispose patients to develop thrush: infancy, old age, antibiotic therapy, steroid and other immunosuppressive drugs,

Thrush, at 23

— Dwaine Rieves, MD

Washington, D.C. (Native of Amory)
Today’s last patient comes with his mother, with fever, a throat on fire, the look of someone locked away, smelling smoke. We don’t know this is the year of answers – a virus.

His mother says he came home, moved back in. I’m learning how it works when mothers bring their adult kids – and this evening, I probe the young man’s throat, his mother over my shoulder, looking down him.

“Open wider.”

Maybe she sees it, the white coral crust, cobbled and glistening, as if its lumpy parts must toss their silver before collapsing, sexless atop pearl beds. And caught by the light, the patch of thrush is wet and full, like the fungus bodies were found, parked and hugging each other, mid-swoon on a summer night.

Maybe she hears it, the tactile sounds, suspended within his jaws – a rustle, the slow collecting of thrush; its plaster ghosts mumbling, stunned. She leans as if she must go to the tip of the light and see for herself what distance contains – crystal hills, unmade beds, voices and names.

Then she stops and backs away and he closes his mouth and they are silent and fixed – in a new place and waiting for me.

Xerostomia, anemia, endocrine disorders, and primary and acquired immunodeficiency. Thrush is frequently the first sign of human immunodeficiency (HIV) infection, with reports describing its appearance during the acute stage of HIV infection. However, thrush usually occurs with a falling CD4 (or T-cell) count in the middle and late stages of HIV disease. Although thrush is the least serious of the fungal infections associated with HIV, it may omen that a patient’s HIV disease is worsening and can progress to esophageal candidiasis, which occurs typically when the patient’s CD4 counts are 200 or less. Esophageal candidiasis is the only type of candidiasis that is considered an AIDS-defining illness. Any physician is invited to submit poems for publication in our Journal MSMA, attention: Dr. Lampton or email me at lukelampton@cableone.net. — ED.
Our current issue presents a special series of articles on the current status of HIV/AIDS care in our state. However, this issue is not the first to focus on that disease. Almost three decades ago, on October 13, 1987, Central Medical Society held an AIDS forum in Jackson, and the four presentations were gathered as a special issue of our Journal in January 1988. To the right is that special issue’s cover. That issue’s four part “Seminar on AIDS” featured: Dr. Ed Thompson, then state epidemiologist, discussing “Incidence of AIDS and Prevalence of HIV in Mississippi,” Dr. Eric A. McVey, III discussing “Transmission of Human Immunodeficiency Virus Infection,” Dr. John D. Wofford, Jr. discussing “Testing for HIV Infection,” and Dr. William Causey discussing “AIDS in the Workplace.” Dr. Joseph Burnett, MSMA President 1986-87, had written in a President’s Page in April 1987 of the formation of a “Bureau of Physician Spokespersons” to work toward educating the general public about AIDS, with the hopes of controlling the spread of AIDS and also to “allay public anxiety.” MSMA and the Board of Health were also involved with the formation of an AIDS Task Force which made important legislative recommendations in October 1987. Then followed the JMSMA “AIDS: Special Issue,” edited by Drs. Myron Lockey, Arthur Derrick, and Joseph Johnston. The issue reveals that MSMA physicians were proactively engaging the AIDS epidemic and seeking ways to improve the treatment of HIV disease in the state.

Certainly, the January 1988 AIDS issue is a high point in the history of our Journal. Hopefully, this current special issue will have a similar impact on the health of Mississippians. If you have an old or even somewhat recent photograph which would be of interest to Mississippi physicians, please send it to me at lukelampton@cableone.net or by snail mail to the Journal.

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