

Paul Shapshak · Andrew J. Levine
Brian T. Foley · Charurut Somboonwit
Elyse Singer · Francesco Chiappelli
John T. Sinnott *Editors*

Global Virology II - HIV and NeuroAIDS

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Editors

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 Springer

Editors

Paul Shapshak
Department of Internal Medicine,
Division of Infectious Diseases and
International Health
University of South Florida
Tampa, FL, USA

Brian T. Foley
Theoretical Division
Los Alamos National Laboratory
Los Alamos, NM, USA

Elyse Singer
Department of Neurology
UCLA David Geffen School of Medicine
Los Angeles, CA, USA

John T. Sinnott
Department of Internal Medicine,
Division of Infectious Diseases and
International Health
University of South Florida,
Morsani College of Medicine
Tampa, FL, USA

Andrew J. Levine
Department of Neurology
UCLA David Geffen School of Medicine
Los Angeles, CA, USA

Charurut Somboonwit
Department of Internal Medicine,
Division of Infectious Diseases and
International Health
University of South Florida,
Morsani College of Medicine
Tampa, FL, USA

Francesco Chiappelli
Department of Oral Biology and Medicine
UCLA School of Dentistry
Los Angeles, CA, USA

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Preface

The spread of HIV-1 and associated NeuroAIDS commenced in earnest during the last few decades of the twentieth century, and although better characterized by the start of the twenty-first century, the spread of HIV continues in the current decade. The characteristics of NeuroAIDS and treatments have come within reach of practitioners, clinics, research, and development. Presentations in this book include HIV global view, global views in NeuroAIDS, descriptions of NeuroAIDS in several countries, CNS HIV entry, neuropathology, peripheral nervous system illness, genetics, neuroimmunology, perinatal NeuroAIDS, neurocognition in children, human and drug trafficking, drug abuse, oral manifestations, socioepidemiology, HAND and HAART, chemotherapy, genetics and epigenetics, gene expression, multiscale oscillatory biology, new tools and data mining, DNA sequence and database errors, amyloidogenic pattern prediction, miRNAs, neuronal apoptotic pathways, humanized mouse models, psychiatric comorbidities, cardiovascular disease, HCV, Chagas disease, TB, opportunistic infections, Zika virus, Ebola virus, biostatistics, HIV and SIV evolution, and vaccines.

The presentations in this book are a fraction of all that is being done. In addition, there are many books that review many topics during prior years of which a few are mentioned [1–9].

With all this progress, why produce a book such as this? The progress needs to be summarized and described for the global audience: the “cures” for HIV and NeuroAIDS. Moreover, worldwide, with the plethora of various strains of HIV, the work that has been done serves as a paradigm for the continued quest against HIV disease spread and pathogenesis.

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Acknowledgements

This book, for professionals, students, faculty, and interested readers, brings to bear snapshots of where we are with HIV and NeuroAIDS. Clearly, it took many years of work and debate among physicians, scientists, researchers, and other practitioners, including clinicians, interventionists, virologists, immunologists, and epidemiologists—from molecular levels of analysis to patients and clinics—for progress to occur and thus allow us to comprehend and attack the scope of infection, spread, and damage caused by a 9000 nucleotide-base microorganism, a small virus.

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Tampa, FL, USA
Los Angeles, CA, USA
Los Alamos, NM, USA
Tampa, FL, USA
Los Alamos, CA, USA
Los Angeles, CA, USA
Tampa, FL, USA

Paul Shapshak
Andrew J. Levine
Brian T. Foley
Charurut Somboonwit
Elyse Singer
Francesco Chiappelli
John T. Sinnott

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Chapter 1

Multidisciplinary Approach to HIV/AIDS: Historical Perspective

Clyde B. McCoy, A. Jeanene Bengoa, Duane C. McBride, Brian T. Foley,
Shikha Puri, Alejandro J. Mendez, and Paul Shapshak

Keywords HIV/AIDS • Epidemiology • Risk activity • Sex • Drug abuse • IDU • NIDA • Transmission • Multidisciplinary • Historical perspective

Core Message

The HIV/AIDS epidemic has persisted over the past three decades due to its adaptability, deleterious effect on the immune system, and various modes of transmission. A multi- and interdisciplinary collaborative approach is one of, if not the best, method in combating the HIV/AIDS epidemic. Specific demographics and high-risk groups dominate this epidemic and are a driving force. Therefore, collaborative approaches must continue to evolve to reduce and prevent the spread of HIV/AIDS. Although the HIV/AIDS epidemic has shown signs of improvement, trends continue in the United States, highlighting the overall global impact of this virus.

Clyde B. McCoy and A. Jeanene Bengoa contributed equally to this work.

C.B. McCoy (✉) • A. Jeanene Bengoa • D.C. McBride • S. Puri • A.J. Mendez
Department of Public Health Sciences, University of Miami Miller School of Medicine,
1120 NW 14 Street, CRB 1507, Miami, FL 33136, USA
e-mail: cmccoy@miami.edu

B.T. Foley
Theoretical Division, Los Alamos National Laboratory, Los Alamos, NM, USA

P. Shapshak
Division of Infectious Disease and International Health, Department of Internal Medicine,
Tampa General Hospital, University of South Florida, Morsani College of Medicine,
Tampa, FL 33606, USA

1.1 Introduction

The Body Snatchers, a science fiction novel written in 1954 by Jack Finney set the precedence in portraying the mindset surrounding a plague. Throughout the years, the original novel evolved into subsequent literary works and cinematic movies. In 1994, *Body Snatchers*, a film that starred Meg Tilly and Gabrielle Anwar strangely but accurately portrayed the HIV/AIDS epidemic through a unique perception. The graphic display of individuals who were “normal” and had not yet been subject to the alien seed “pods” clearly depicts the experience of the population throughout the HIV/AIDS epidemic. Those who had not been exposed to those alien “pods” would peer intently at one another, attempting to decipher if they had become alien and fatal. *Body Snatchers* mirrored the feelings and unfortunate fear experienced by those in the forefront of the HIV/AIDS epidemic.

The forefront of the HIV/AIDS epidemic in the Americas was seen in the manifestations of diseases in unusual populations and with no clear explanations of Kaposi’s sarcoma and *Pneumocystis carinii* pneumonia (PCP) in the populations that were being seen in major cities such as New York, Los Angeles, and Miami. It is hard to imagine how quickly this epidemic spreads, and it is even more difficult to understand what would have happened if not for global scientific efforts that quickly launched research on these populations using multiple strategies. Among institutes commending such works were the Centers for Disease Control (CDC) and the National Institutes of Health (NIH). The NIH included the National Institute on Drug Abuse (NIDA), which had only become an institute in 1974. NIDA quickly established several research centers that happened to be in the very cities where these populations were being studied clinically. Miami received one of these first centers beginning in 1974 [1].

Furthermore, beginning in 1974 in Miami, there was an additional funded NIH institute center, the Comprehensive Cancer Center. At the advent of the study of this epidemic, there were multidisciplinary and interdisciplinary research teams, including some of this chapter’s authors, who worked at both NIH-sponsored centers.

It is unfathomable to imagine the rate at which the HIV/AIDS epidemic would have spread if it were not for the creation of research organization such as NIDA under the umbrella of NIH in 1974 [1]. The first part of the twentieth century saw little to no drug abuse research until the 1960s and 1970s, when the drug epidemic ran rampant [1]. The abuse of drugs provided the need and platform to develop strategies, establish metrics, and institutionalize drug abuse research and prevention to promote multidisciplinary collaboration both domestically and abroad.

The multidisciplinary and interdisciplinary foci that developed throughout the institutionalization of drug abuse research assisted in implementing research priorities within both clinical and research settings [1]. Through this approach, disciplines such as demography, psychiatry, neurology, pediatrics, psychology, sociology, immunology, viral epidemiology, molecular biology, anthropology, ethnography, biostatistics, and public health provided the basis for providing the highest quality of research regarding HIV/AIDS among drug abusers. In addition, development and testing the efficacy of interventions to reduce high-risk behaviors included field

studies regarding drug abuse paraphernalia, efficacy of bleach in eliminating HIV and HCV from needles, as well as many other pertinent vectors of this epidemic [4–8]. This evolutionary process provided the means for extensive community outreach and the acquisition of funding that would allow for crucial information regarding the pathways of transmission, acquisition, and proliferation that manifest within the individual and society [1].

NIDA and other similar agencies at the local, state, and national level through funded infrastructure provided the sustainable foundation for research to progress structure and collaborative support. Unbeknownst to researchers globally, developing NIDA and other scientific oversight would allow for research to develop an understanding of this “strange and pernicious disease” [4, 9]. Although this virus was not studied until the 1980s, the foundation to reduce the impact of the HIV/AIDS epidemic began a decade earlier.

1.1.1 The Initial Years of Fears

Retrospectively, HIV infected humans in the 1920s in the Kinshasa region of what became the Democratic Republic of the Congo and Zaire. In the 1950s and 1960s, the virus embarked on its path as a global pandemic [2, 3]. Once reaching the United States, the HIV/AIDS epidemic forever changed the landscape of the United States. Attempting to understand this inexplicable disease and phenomenon created a sense of fear and apprehension. This virus was first presented to the University of Miami School of Medicine Grand Rounds in 1981, which puzzled physicians as to the cause and effect as well as the potential outcomes and risks associated therewith.

The first reported case in Florida involved a young Caucasian man of Northern European descent who was diagnosed with Kaposi’s sarcoma. The physician reporting this case noted how unusual and unique the symptoms were as Kaposi’s sarcoma was not known to exist in the age group of the patient or among those of Northern European descent. A second unusual case was also introduced. This time, the young man had been diagnosed with PCP – a disease that, according to the attending physician, usually occurred among the very old who were living in a nursing home. These cases puzzled the group in attendance at the University of Miami School of Medicine Grand Rounds in 1981, and many questions arose from these two cases at hand such as where the patients lived, where they had been, what acute or chronic diseases they had, and with whom they interacted [4]. It was further reported that there was little in the patients’ background information that indicated any major acute or chronic diseases that would suggest they would be susceptible to these illnesses.

In the search for the explanation of “this strange and pernicious disease,” the University of Miami research centers, departments, and schools had attracted and organized a very effective, multidisciplinary, and interdisciplinary group [1]. This allowed for a very synergistic approach to determining what the origins, consequences, and interventions should be for this “new thing” that initially went by several nomenclatures, such as [1] Gay-related immune deficiency (GRID) and [2] Gay disease. Further, the virus causing AIDS was given various names such as lymphade-

nopathy-associated virus and HTLV-III and even the 4H club which led to increased stigmatization and unnecessary stereotyping [4, 9]. Soon after, AIDS was used to describe this new syndrome that moderately caused a defect in cell-mediated immunity within individuals that had no other known diminished resistance to opportunistic infections such as organ transplant or inherited immune deficiency [10].

The misconception and misinterpretation of the HIV/AIDS epidemic was one of the main reasons for such a rapid increase in the proliferation of this disease. Immediately after this virus surfaced, immunologists were confident that HIV/AIDS could be managed through a simple vaccine and eventually as treatable as other chronic diseases such as asthma and diabetes [4]. Unknown to these scientists was that the AIDS virus was not capable to be overcome by a vaccine that would attempt to trick the immune system into producing effective antibodies [4].

1.1.1.1 AIDS Cases 1981–1991

Misdirection and a lack of scientific understanding led to the rapid increase in the prevalence of HIV/AIDS not only among individuals in the United States, but globally. The exponential rise of HIV/AIDS cases during the first decade of this epidemic shows that although agencies such as NIDA were available to combat drug abuse, the specificity and means by which HIV progresses and becomes AIDS were a mystery to all researchers and healthcare practitioners. Four cases of AIDS were documented in 1981, and by 1991, there were over 261,159; 23,162 and 7488 cases in the United States, Florida, and Miami-Dade County (MDC), respectively [11].

The surveillance systems that had been established in MDC prior to the rise of the HIV/AIDS epidemic enabled vital data to be collected regarding this virus from the first documented cases. Beginning with four AIDS cases that were presented at the University of Miami Medical Grand Rounds in 1981, there was an exponential increase in the number of HIV/AIDS cases in the following decades [12]. By 1991, nearly 7500 cases were identified in Miami, Florida, which more than tripled to 25,000 in the next decade [7]. The cumulative incidence of AIDS in MDC during 1981–1991 was 85 per 100,000 individuals, the highest rate reached in any decade (see Fig. 1.1) [7].

The first decade (1981–1991) of the HIV/AIDS epidemic in MDC, with 7488 AIDS cases, resulted in ranking only behind the much larger Los Angeles and San Francisco metropolitan areas [12]. Further, MDC was ranked second among US metropolitan areas, with 706 cases attributed to heterosexual contact, third in cumulative AIDS cases among women, and second in the cumulative AIDS cases among pediatric cases [12] (Table 1.1).

The rankings and impact of the HIV/AIDS epidemic within MDC were driven by specific demographics and risk groups which were unknown during the advent of this disease [7]. Men had a higher cumulative incidence when compared to women, and when observed by race/ethnicity, Black/African American had the highest cumulative incidence followed by White/Caucasian and the Hispanics [7]. Although understanding the demographics was essential to understanding and

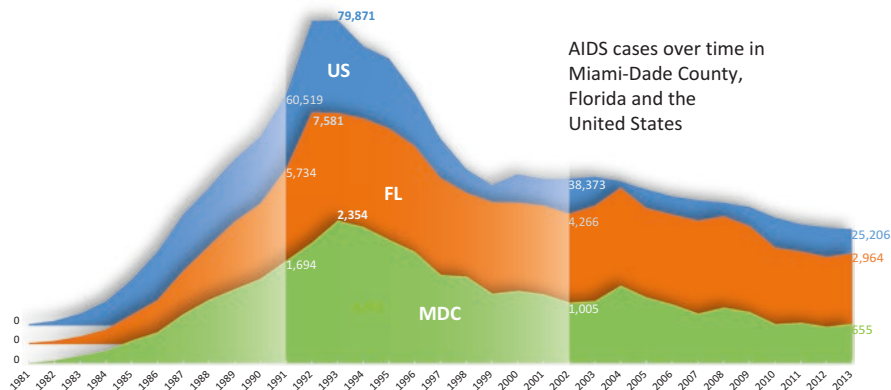


Fig. 1.1 Miami-Dade County vs. State of Florida vs. United States of America. This chart represents the number of AIDS cases per year from 1981 to 2013 [14, 33]

Table 1.1 Cumulative AIDS cases by year for United States, Florida, and Miami-Dade County [14, 33]

		Year		
		1991	2002	2013
Geography	United States	261,159(23)	866,590(16)	1,214,305(10)
	FL	23,162(43)	87,666 (26)	130,099(15)
	MDC	7,488(85)	25,347(43)	34,903(25)

developing methodologies to combat this epidemic, gaining valuable data regarding specific risk groups served as a major contributor in preventing the uncontrollable spread of HIV/AIDS, especially before serological testing for asymptomatic infection became available.

However, the category that accounted for the largest risk group was male-to-male sexual contact (MSM), which represented 45% of the cases irrespective of race/ethnicity [7]. Injecting drug users (IDU) were the next highest group at 23%, followed by heterosexual contact at 20%, unrelated/other causes at 6%, MSM/homosexual/bisexual/IDU at 4%, and blood transfusions at 2% [7]. Once the race/ethnicity was incorporated into the major risk groups, the percentage of high-risk practices differed. Like the overall trend, Hispanics primarily contracted AIDS through MSM at 70% followed by IDU at 10%, while Black/African Americans contracted AIDS predominantly through heterosexual contact and IDU at 37% [7]. Southern Florida was particularly influenced by its proximity to Haiti and thus its influx of Haitian immigrants. It is now well understood that the HIV-1 subtype B epidemic was simmering in Haiti for at least a decade before spreading to the United States and Europe [13].

MDC is an indicator, reflecting the total number of AIDS cases and the impact that HIV/AIDS had in the state of Florida. Although MDC has been one of the major epicenters for the HIV/AIDS epidemic, Florida has experienced its own

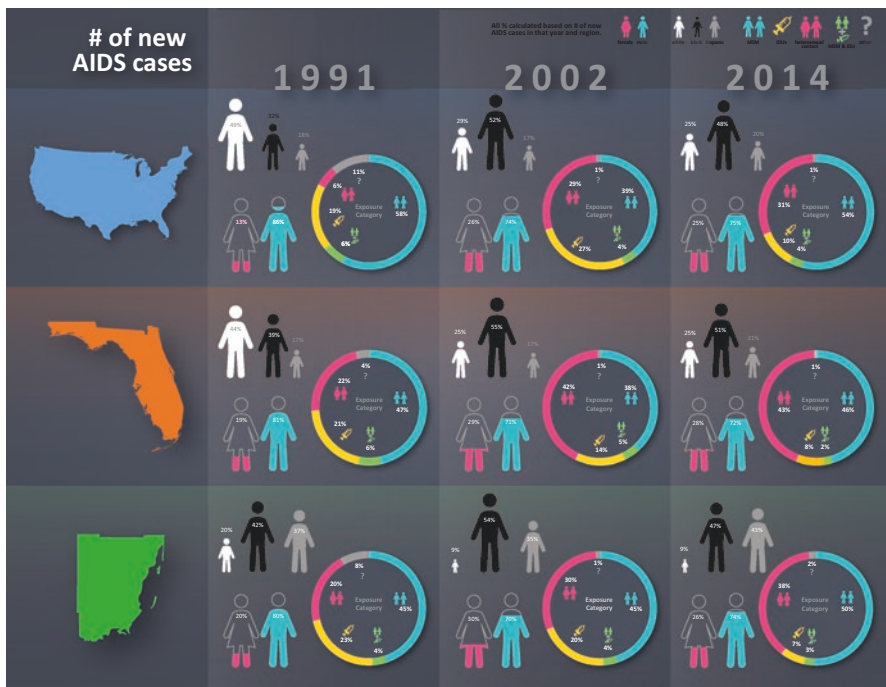


Fig. 1.2 Demographic breakdown of AIDS cases by decade and location [14, 33]

unique challenges distinct from MDC. Like the impact of this epidemic on MDC, individuals who were not white, male, and/or gay had a false sense of security that this virus could not affect them [14]. This misconception, coupled with the initial lack of scientific information, provided the mode for this virus to proliferate among risk groups that were thought to be safe from this epidemic.

The state of Florida saw a consistent increase in the total number of AIDS cases from 0.1 per 100,000 people in 1981 to 43 per 100,000 in 1991 [14]. Like MDC, men dwarfed women in the total number of AIDS cases (see Figs. 1.1 and 1.2) [14]. Further, the greatest number of AIDS cases occurred within White/Caucasian, followed by Hispanics and African Americans [14]. Also, MSM and IDUs served as the largest cluster among all high-risk groups [14]. The proliferation of this virus in MDC and Florida and the widespread increased incidence of AIDS signaled Florida as a major epicenter in the HIV/AIDS epidemic within the United States.

The impact and fear because of the HIV/AIDS epidemic was daunting nationwide. The total number of AIDS cases reported during the first decade showed the proliferation of this virus throughout the United States [15]. The trends experienced within MDC and Florida were also seen in the United States regarding gender. Men accounted for 86% of the total number of AIDS cases when compared to women, which was slightly a larger gap when compared to both MDC and Florida. Further, White/Caucasian individuals accounted for 49% of the total AIDS cases from 1981 to 1991 followed by Black/African Americans with 32% and Hispanics with 18%

[15]. The greatest impact of this epidemic within the United States was among MSM (58%), followed by IDUs (19%) and heterosexual contact (6%) [15].

1.1.1.2 Interventions and Progressive Movements 1981–1991

Social structures within the United States were not necessarily supportive of practices that could help combat an emerging epidemic. Indeed, increased urbanization reduced social structures that constrained sexual behavior [7, 5]. During this initial period of this epidemic, prostitution and venereal diseases increased alongside the abuse of hypodermic needles which became more widespread [1]. Further, changes in sexual mores in the 1960s reduced barriers within the heterosexual population, as also the Gay Liberation Movement in the 1970s presented new and unexpected losses of barriers and an increased severity of this new epidemic [9]. In addition, civic and legal policies produced severe limitations of the availability of clean legally acquired hypodermic needle/syringes, enhancing the conditions for acquiring and transmitting HIV/AIDS among IDUs [4, 5, 16, 17].

Prior to 1981, surveillance tools and agencies such as the Florida Department of Health had been established both within MDC and Florida, which allowed for the prompt documentation of the first AIDS cases. The first AIDS surveillance began within the Florida Department of Health and Rehabilitative Services, and the Centers for Disease Control and Prevention (CDC) declared AIDS a reportable disease in 1983, resulting in a lapse in the reporting of crucial information in the initial years [11]. The delay in recording AIDS as a reportable disease missed the opportunity in documenting the initial cases of IDU, heterosexual contact, transfusions, and infants [11]. In 1983, the HIV/AIDS epidemic was declared a “public health emergency” by the Florida State Health Officer which enforced the responsibility of physicians to report diagnosed cases, which actively began in 1984, mostly in South Florida [11].

In 1984, HIV was determined to cause AIDS with a major impact on the way hospitals, clinics, public health practitioners, and various other healthcare entities in Florida approached this epidemic. This fundamental knowledge directed active surveillance within Florida, and especially in South Florida, which was one of the epicenters for this epidemic [11]. The progression of programs and initiatives continued, and in 1985, the Food and Drug Administration (FDA) approved the first HIV antibody test, and national screening of blood commenced [11]. Further, 26 anonymous HIV counseling and testing sites were established with a statewide toll-free AIDS hotline [11].

After implementing these programs, Jackson Memorial Regional Medical Center, serving as a public hospital and the medical center for the University of Miami, was the primary hospital to deliver comprehensive care to HIV/AIDS patients [11]. Because 75% of all AIDS cases in Florida, health education, and risk reduction programs were established in Miami-Dade, Broward, Monroe, and Palm Beach counties [11]. Statewide public information programs were established to provide vital information and education regarding the HIV/AIDS epidemic to all households in Florida [4]. Six years after the first cases of this epidemic, the first antiretroviral drug, Retrovir, was developed to assist in combating this disease [12].

The expansion of the initial programs and availability of antiretroviral therapy used in AIDS treatment and prevention, coupled with the required notifications to partners of individuals with HIV/AIDS, began the movement in working to contain the impact of this virus.

As the late 1980s approached, new laws, interventions, and programs surfaced and were implemented statewide. In 1987, the World Health Organization (WHO) launched the Global Program on AIDS [11]. The Joint United Nations Program on HIV/Acquired Immune Deficiency Syndrome (UNAIDS) was developed and resulted in more impactful initiatives such as the Multi-Country AIDS Program (MAP) launched by the World Bank, which gave rise to most nations worldwide agreeing to global goals to reverse the spread of HIV [18]. As a result, 700 individuals were enrolled to receive antiretroviral therapy in 1988, which saw one of the first prominent movements in preventing the excessive spread of this virus [11]. In 1989, Project AIDS Care was established by Medicaid, and the FDA approved the use of antiretroviral therapy in mothers, which provided a new mode of preventing the transmission of HIV/AIDS to infants [18]. Although an overall improvement in treatment options occurred just before the start of the 1990s, the 1990s also brought the epidemic of “crack” cocaine in South Florida which led to a substantial increase in the risk factor for AIDS and other related sexually transmitted infections, such as needle-sharing and prostitution in exchange for drugs [19–21].

The Ryan White Comprehensive AIDS Resource Emergency Act was passed in 1990 by the US Congress; this Act provided essential services to those infected with HIV who lacked health coverage. This resulted in Florida obtaining seven million dollars to provide care and support to those living with HIV/AIDS [12]. Also, the second antiretroviral drug was approved by the FDA, and soon after, a combination antiretroviral drug was created that would provide a mechanism that would further assist in preventing the uncontrollable spread of HIV/AIDS. The introduction of Videx in 1991 further enhanced the ability to reduce the impact of the HIV/AIDS epidemic nationwide [12].

The AIDS epidemic provided the platform for many initiatives to be developed prior to all the factors associated with HIV/AIDS. For example, the CDC established the National AIDS Information Line (1983), National AIDS Clearinghouse (1987), institution of the nationwide America Responds to AIDS public information campaign (1987), and distributed *Understanding AIDS* (1988), which was the first mailed information regarding a major public health problem delivered to every residential mailing address in the United States [20]. Throughout the advent of these successful programs, the identification of HIV as a root cause of AIDS created the platform to develop serological tests that could detect HIV in the blood [20, 21].

1.1.1.3 Molecular Epidemiology

Beginning with the first infectious molecular clone of HIV-1 to be sequenced in 1985, many more clones from the United States, Europe, and Africa were also sequenced soon, and it became obvious that HIV was a diverse and rapidly evolving

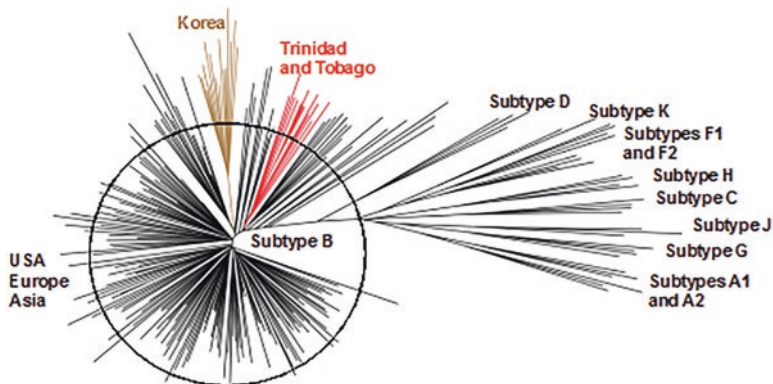


Fig. 1.3 Maximum likelihood phylogenetic tree constructed from HIV-1 subtype B [23]

virus [20, 22]. The rapid rate of evolution of HIV coupled with the knowledge that the virus spreads by direct intimate contact with an infected person allowed the development of a new field now known as molecular epidemiology. Many studies showed that analyzing the virus gene sequences could provide an accurate reconstruction of the spread of HIV within a local group or transmission cluster, and that the same methods can be applied to larger data sets and the study of larger portions of the pandemic [23]. One of the first widely publicized transmission cases solved in part by molecular methods is known as “the Florida dentist case,” in which one dentist evidently infected six patients [24].

Misreporting and the resulting lack of public understanding of HIV and AIDS in general, especially during the early years of the pandemic, have resulted in some misreporting and confusion. Although the Florida dentist case was a doctor-to-patient spread of HIV, it was equally clear that this case was very highly unusual, and that dentists and other doctors could continue to work with reduced risk to their patients, assuming appropriate medical precautions.

Although HIV-1 subtype B was present in Haiti before it arrived in the United States and Europe, neither Haiti nor individuals from Haiti are to blame for the US epidemic. Figure 1.3 is a maximum likelihood phylogenetic tree constructed using HIV-1 subtype B complete envelope gene sequences sampled before 1999. Although there are some local subepidemics detectable in such a data set, for the most part the United States and European sequences are intermingled with each other.

Although it is possible to use molecular epidemiology to study HIV transmission patterns in geographical regions such as Florida, the process is fraught with many problems. One of the main problems is detecting and sampling recently infected individuals if the purpose is to study the current trends rather than infections that may have taken place a decade or more prior. Another problem is patient confidentiality and privacy, and the possibility of doing more harm than good by discouraging people from seeking diagnosis and treatment if they fear invasion of privacy or being identified as an IDU.

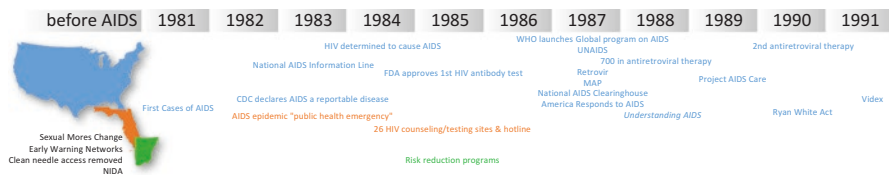


Fig. 1.4 First 10 years of AIDS timeline for key moments [11]

1.1.2 AIDS Cases 1992–2001

The second decade (1992–2001) of the HIV/AIDS epidemic not only saw an increase in the total number of AIDS cases but also new programs, interventions, and initiatives while obtaining crucial knowledge to combat this disease. Although different programs and laws were enacted during this epidemic, comprehensive approaches were not established effectively for targeting and serving the highest risk groups to stem the peaking of the epidemic. This misstep led to an increase in the total number of AIDS cases in the United States, Florida, and Miami-Dade County to more than 260,000; 23,000; and 7500, with new cases peaking: new 80,000; 7500; and 2500 [11, 14].

The total number of AIDS cases within Miami-Dade County continued to rise at an exponential pace throughout the time from 1982 to 1994, with a leveling off in the number of new AIDS cases diagnosed each year in the 1994–2001 time period, mainly due to the development of highly active antiretroviral therapy cocktails. Although Miami, Florida, only accounted for less than 1% of the US population in the early 1990s, it contributed over 3% of all AIDS cases [25]. Miami-Dade County continued to serve as one of the major epicenters during the 1992–2001 time period. AIDS and its impact were ever so present among South Florida and its respective risk groups (see Figs. 1.2 and 1.4). The cumulative HIV incidence of men was 1,703 and for women, 445 per 100,000 [25]. These rates rose exponentially for the first ten years after 1981. Further, African Americans accounted for the largest cumulative incidence of AIDS in MDC at a rate of 2,647 per 100,000, followed by Hispanics at 696 per 100,000 and White/Caucasian at 657 per 100,000 now had a larger incidence of AIDS when compared to White/Caucasian [25].

As more data was acquired and a better understanding of the epidemic emerged, an understanding of the major risk factors among the demographics in South Florida became more evident. As seen during the first decade, MSM accounted for the largest percentage of AIDS accumulative cases [25]. Further, IDUs followed with the next highest percentage of cases attributed to these high-risk practices at 23% (3,745/19,864) followed by heterosexual risk at 20% [25].

The largest increase in the number of AIDS cases in Miami-Dade County occurred from 1993 to 1996, with the total AIDS cases averaging more than 2000 new cases peaking at 2354 [26]. Following this substantial increase of AIDS cases, a reduction in the total number of new cases began in 1997. From then on, the number of AIDS cases continued to decrease yearly and fell to 1,136 total cases in 2001

[26]. It took nearly two decades to observe a prominent decrease in the number of AIDS cases in the late 1990s, and this was primarily due to effective antiretroviral therapies making HIV treatable, rather than a large reduction in new infections.

Yet, even with the reduction in the total number of AIDS cases that occurred during the latter part of the 1990s, MDC still ranked in the top ten of nearly every AIDS statistic. MDC ranked second in per-capita MSM AIDS cases, seventh among IDU, and fourth in total per-capita AIDS cases among adults/adolescents [25]. As stated above, MDC accounted for <1% of the US metropolitan population yet ranked excessively high among the nation and major metropolitan areas regarding the HIV/AIDS epidemic.

The impact of MDC on Florida exemplified the influence a region can have on its respective state. The number of AIDS cases in Florida rose each year *vis-a-vis* MDC rates of 36.7 per 100,000, 55.1 per 100,000, and 63.7 per 100,000 in 1992, 1993, and 1994, respectively [14]. Males continued to dwarf women in the total number of AIDS cases from 1992 to 2001. For example, in 1994, men had a cumulative incidence of 101.3 per 100,000, whereas women only had an incidence of 28.3 per 100,000. These rates increased during the first half of the 1990s and then saw a prominent reduction in the total number of AIDS between men and women (Fig. 1.4). The epidemics as reviewed by the number of new AIDS cases each year peaked in the early 1990s for the United States, Florida, and MDC. There was a sharp and continuous decline, except for a smaller peak in early 2000s, especially for Florida and MDC (Fig. 1.4).

1.1.2.1 Interventions and Progressive Movements 1992–2001

There were major improvements in both prevention and treatment during the first decade of this epidemic. The evolution of prevention programs continued to progress to combat this epidemic. Further, it was through all these programs and the acquisition of information and knowledge that helped assist in the development of a combination antiretroviral therapy in 1992, and protease inhibitors in 1997, which led to a substantial decrease in AIDS-related deaths while improving the quality of life with those infected with this virus [12]. Preventive strategies continued to be developed, and the fight against this disease had immense momentum as seen by the CDC Serostatus Approach to Fighting the HIV Epidemic (SAFE), providing a framework for improving the health of persons living with HIV and preventing transmission to others [26]. Additional initiatives continued to advance the treatment and prevention of the HIV/AIDS virus [4, 5, 16] (Fig. 1.5).

Finally, in 1993, the CDC recognized and expanded its AIDS case definition to include a CD4 count of <200, and having diseases such as tuberculosis (TB), cervical carcinoma, and bacterial pneumonia if HIV were present [11]. This change in definition resulted in a great increase in reported cases in MDC, Florida, and the United States [11]. The OraSure saliva HIV test was approved by the FDA and supplemented the existing blood tests that provided crucial information regarding the epidemic [11]. The Comprehensive Drug Research Center (CDRC) took a lead

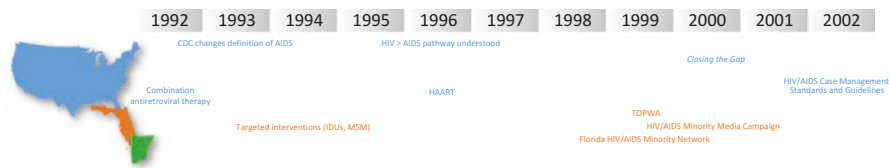


Fig. 1.5 Timeline of the second decade of AIDS [11]

in testing this new tool in our outreach programs. The success of surveillance tools coupled with an extensive classification of this virus provided vital epidemiological profiles that assisted in developing community and specific high-risk group prevention initiatives [11].

Continued acquisition of comprehensive epidemiological profiles nearly 15 years after the first AIDS cases provided the ability to create unique and specific interventions. Combating the impact of IDU within this epidemic was vital as this high-risk group continued to expose themselves to lifestyles that enhanced their probability of acquiring and transmitting AIDS [19–21]. Prevention protocols were then developed regarding the cleansing of needles shared and used by IDUs with bleach in MDC [17, 21].

It was through programs such as these that helped decontaminate needles in an effective and efficient manner. Exemplifying the effectiveness of such programs was highlighted by a study conducted by the CDRC and Health Services Research Center (HSRC) in which needle/syringes from shooting galleries around the Miami, Florida, area were collected and tested without and with cleaning by bleach treatment [4–6, 18, 19]. The study indicated that use of household bleach and proper cleaning techniques by laboratory studies proved that bleach-treated needle/syringes tested negative for HIV whereas those that were not cleaned by bleach tested positive [4–6, 18, 19].

It was innovative and continually developing interventions such as needle/syringe-cleansing programs that promoted cleaning of paraphernalia with bleach and sustained the momentum positively impacting this epidemic. In addition, ancillary paraphernalia were tested for the presence of HIV that included cottons, cookers, and wash-waters used at shooting galleries, which were shown to contain the presence of HIV [17]. In addition, laboratory results indicated that bleach should be utilized for 30 s, which was added to the intervention protocol [6, 7]. Programs and preventive services such as the bleach cleaning of used needle/syringes demonstrated the utility and effectiveness of science-based interventions.

In 1996, the FDA approved a new regiment of antiretroviral therapy that ushered in the era of highly active antiretroviral therapy (HAART) [11]. The implementation of HAART coupled with innovative programs and initiatives resulted in the first major decrease in the prevalence of AIDS nationwide. Continual efforts promoted development of new therapeutic options including Nelfinavir (Viracept), Delavirdine (Rescriptor), Saquinavir (Fortovase), and Zidovudine (AZT), which provided powerful pharmaceutical and clinical options for combating HIV/AIDS [11].

It was also during this time that the HIV/AIDS pathways were established and explained in a detailed and scientific manner, which allowed for a more precise understanding of the epidemiology and pathogenesis of HIV/AIDS [27, 28–31]. The HIV/AIDS pathways were distinctive; understanding their complexity allowed for a more comprehensive epidemiological profile to be developed of all demographics and high-risk groups. This crucial scientific data further promoted the development of new programs such as Florida’s Targeted Outreach for Pregnant Women Act (TOPWA) program (1999), Florida HIV/AIDS Minority Network (1999), and “Closing the Gap” (2000). Additionally, media campaigns were developed to promote and increase awareness of HIV/AIDS throughout the county, state, and national level [5].

A significant shift in the HIV/AIDS epidemic occurred post-1990s. Prevention became more prominent than treatment, which had driven the approach for the first 20 years of this epidemic. HIV/AIDS information, protocols, and interventions were then translated in multiple languages, while increasing the networks and programs for all individuals exposed to this epidemic. Challenges continued to arise and cause barriers within the county, state, and national level, but there was an increasing scientific platform to overcome obstacles. The wealth of scientific information of the HIV facilitates current and future policies and programs.

1.1.3 AIDS Cases 2002–2013 (Figs. 1.1, 1.2, and 1.4)

The trends experienced during the 2002–2013 period of the HIV/AIDS epidemic were evidence that the epidemic was not over and was to be very resistant to the remarkable decline that started in the last half of the 1990s. As matter of fact, both Florida and MDC witnessed increases in new cases at various times during the decade (Fig. 1.2).

The impact of AIDS within the county, state, and national level continues into the third decade (2002–2013) of this epidemic. Even with the newly implemented programs, interventions, and access to antiretroviral drugs, the number of new AIDS cases continued. The total decline in AIDS cases in MDC began in the late 1990s and fell under 1,000 total cases in 2007 [14]. The total number of AIDS cases increased in 2008, but then, once again, fell under the 1,000 mark and has continued this trend ever since. Compared to the previous two decades, MDC continues to experience new cases ranking among the highest in the country [14].

Addressing the major demographics and risk groups has served as one of the most important epidemiological tools. Males continued to have a higher incidence of AIDS when compared to females. The trend persisted throughout the first two decades of this epidemic with men accounting for more than 70% in each decade compared to women [14]. Further, Black/African Americans accounted for the largest percentage of AIDS cases followed by Hispanic/Latino [14].

The incidence of specific high-risk groups, such as MSM and IDU, continued into the third decade of the HIV/AIDS epidemic, with MSM as the largest group

battling AIDS with a total 50% cases, followed by adult heterosexual contact with 38% of these cases [14]. The major shift was that IDU decreased to 7% from more than 20% in the first two decades. Although the overall change was not enormous, occurrences such as these indicate the potential success of current interventions and programs while highlighting the need for implementing new initiatives that adapt to the current needs. With the declines, in new AIDS cases over the third decade, especially in the IDU category, we undoubtedly see the results of the role that NIDA and drug researchers and drug interventions have had in developing the science and interventions directly targeting this major risk group.

However, Florida continues to rank in the top ten in nearly every category regarding HIV/AIDS. As of 2013, Florida ranked first in both newly diagnosed HIV infections and AIDS cases (110,000) [14]. Also, Florida ranked third in the nation for people living with HIV through 2014. Further, consistent with the two prior decades, men accounted for the clear majority of AIDS cases with more than 70% of all cases [32]. Black/African Americans were the largest race/ethnic group living with AIDS at 51% of all cases, followed by White/Caucasian at 25% and Hispanics at 21% [32]. Further, of those living with AIDS in Florida, the greatest transmission mode occurred among MSM (46%), heterosexual contact (43%), and IDU (8%) [32].

The trends experienced during the period between 2002 and 2014 in MDC and Florida differed from that of the United States. That is, the total number of AIDS cases within the United States has continued to see a rise throughout this period and culminated with 1,200,000 estimated cases in 2014 [32]. African Americans account for approximately 48% of all AIDS cases followed by Hispanics at 25% [33]. The rate of new cases for Hispanic males was 2.9 and 4.2 times that for White males and females, respectively [32]. Further, MSM were most severely impacted by AIDS at 54% of all cases followed by heterosexual contact at 31%, IDU at 10%, and MSM + IDU at 4% [33].

The earliest association of AIDS resulted in a stigmatization that those with this disease were considered “untouchable” due to misinformation and prejudice [4]. Irrational fear and paranoia often led to an increase in the discrimination of those battling HIV infection and AIDS throughout the United States. The rapid progression of AIDS led to greater uncertainty and uneasiness among the populations combating this new epidemic. The health inequities present among the different race/ethnicities and risk groups within the United States were the result of the misunderstanding and lack of treatment and care for HIV/AIDS during the decades of this epidemic.

1.1.3.1 Interventions and Progressive Movements 2002 to Present

There were major improvements and progress during the first three decades of the HIV/AIDS epidemic; the evolution of prevention programs must continue to ensure a strong platform to combat this epidemic. Many interventions, testing, and medical advances were and are essential for national initiatives to be effective in treating and managing those who have contracted HIV/AIDS [10, 14] (Fig. 1.6).



Fig. 1.6 Timeline of the third decade of AIDS [11]

After three decades in battling the HIV/AIDS epidemic, complacency settled in among individuals, communities, and the media at the county, state, and national levels. The first HIV/AIDS Case Management Standards and Guidelines were developed with the CARE Act Titles in 2002 [14]. Additionally, the first “entry inhibitors” were introduced into the HIV/AIDS epidemic. Nearly 25 years after the advent of this epidemic, over 500 case managers, supervisors, and other interested staff from the Ryan White Titles I, II, III, IV, and HOPWA were trained in the first statewide HIV/AIDS Case Management Training referred to as the “Nuts and Bolts” [34, 35]. The time it took to fund and conduct scientific research, and turn the science to policy statewide initiatives across the nation highlights one of the main reasons the prevalence of AIDS has continued over time.

These prominent and impactful programs that took nearly 30 years to develop assisted in combating this devastating epidemic [14]. The CARE Act Title program, which was passed by the US government provided substantial support to public programs that combat chronic diseases through various laws and legislation. Additionally, the Ryan White Titles (I, II, III, and IV) provide funding for healthcare entities to provide care and treatment. Initiatives such as these provide those with AIDS or HIV infection the ability to obtain the treatment required to prevent the spread and eventually diminish the prevalence of AIDS worldwide.

Early in 2001, one-on-one capacity building activities and initial prevention programs for individuals testing positive were funded that minimized the unnecessary transmission of HIV. Rapid HIV testing was then developed, and the AIDS Drug Assistance Program (ADAP) continued to proliferate and provide funds for drugs and other essential services. The success of ADAP led to new initiatives which targeted the HIV/AIDS crisis among MSM and other high-risk groups in Florida [14].

Community-based organizations and other similar entities continued which assisted in reducing the prevalence of AIDS and the health gaps present within different race/ethnicities and risk groups. Extensive community mobilization began throughout the nation which provided individuals with the care and access to treatment that could assist in preventing the continual spread of this disease. Further, media and social outreach strategies were improved which provided a means that would contribute to spreading vital information regarding AIDS. Also, programs such as Out in the Open (2007), Organizing to Survive (2008), and Man Up (2009) delivered interventions that assisted groups at the highest risk for contracting and transmitting AIDS [14]. Although there were substantial increases in programs and interventions to combat the HIV/AIDS epidemic, funding constraints

and accessibility prevented critical services to be efficiently and effectively delivered to all needed persons. For example, beginning in 2010, the ADAP saw its first wait list created for services and continued to exist until 2012 when the list was eliminated.

In 2011, world leaders adopted a new declaration that reaffirmed commitments and called for an intensification of efforts to combat the epidemic through new commitments and targets through the United Nations General Assembly and a Special Session (UNGASS) [36]. Most recently, UNAIDS set specific goals and targets to control the HIV/AIDS epidemic by 2020; by 2030 to ensure that 90% of people living with HIV know their HIV status; that 90% of people who know their HIV-positive status are on consistent treatment; and that 90% of people on treatment have suppressed viral loads [36].

Over \$30.0 billion is being allocated to AIDS research and programs, prevention initiatives, housing assistance, care, and many other components essential in reducing the impact of the HIV/AIDS epidemic [36]. The momentum to eliminate this disease is in full force and must continue to proactively and aggressively reduce the incidence of new HIV infections. The major impact of AIDS has been consistent among US metropolitan areas with New York, Los Angeles, and Miami topping the list, stressing the importance of improving current programs, initiatives, and interventions to eliminate the spread of the disease [37].

1.1.4 Global Movement

The combined evolution and improvement of the world economy with subsequent increased efficiency and development of the international transport and travel technology has been a major driving force in the global spread of HIV/AIDS [4]. The HIV/AIDS epidemic has affected global populations through many avenues, with MSM, IDU, and heterosexual contact being the predominant risk groups. In addition, newborns and children suffer as well with this disease [38]. This epidemic has spread rapidly among the risk populations around the world, although in some areas it has spread slower and without such a profound impact [36].

Different parts of the world have experienced substantial discrepancies on the progression of HIV/AIDS. Moreover, 95% of HIV cases worldwide are concentrated in developing countries [38]. Further, HIV/AIDS disproportionately impacts distinct demographics and social groups throughout the world. Of the 36.9 million people living with AIDS around the globe, Sub-Saharan Africa accounts for nearly 70% of the cases [39]. Understanding the global network and its unprecedented reach provides the framework for approaching the HIV/AIDS epidemic by developing interventions by focusing on the highest risk networks [40].

Population-based interventions have been very effective in combating the HIV/AIDS epidemic globally [40]. Developing global population-based initiatives through international collaboration has provided a comprehensive approach that recognizes different lifestyles and information regarding this disease which continues to spread, albeit at a slower rate [40]. The specific programs developed throughout

the world provide an expansive resource of enlightened scientific information regarding risk factors such as sex and drug practices, provides better education, health and economic access, and other service components that could have a profound global impact on this epidemic [40]. The success of international programs depends upon a concise understanding and sustainability of modifying interventions to local institutions and communities with distinct cultures and lifestyle practices [40]. It has been consistent international collaboration in striving to break down all the barriers associated with the HIV/AIDS epidemic that led to improved programs and influencing global initiatives. Further, these initiatives have been a major portion of the fight against HIV/AIDS since 1987, when the World Health Organization (WHO) launched the Global Program on AIDS. UNAIDS developed the UN Millennium Development Goals (MDGs) which gave rise to every nation agreeing to global goals to reverse the spread of HIV and AIDS [41]. In the early years of HAART, there was much concern about detrimental side effects of long-term treatment, and thus much study of delaying treatment until CD4 counts fell below some threshold. Recent studies such as the START trial have now proven beyond doubt that treatment should begin as soon as possible [41].

1.1.5 Conclusion

Acquiring a comprehensive scientific understanding of the HIV/AIDS epidemic from a county, state, and national level leads to scientific progress in reducing the prevalence of this disease worldwide. Incorporating a global approach as detailed in this chapter provides a well-defined basis for understanding global epidemics.

Without continued and sustainable funding, initiatives cannot progress, and the HIV/AIDS epidemic will continue to unnecessarily impact millions of people worldwide. Much increased funding at all levels is needed to ensure preventive and treatment services for those affected by HIV/AIDS [36]. The progress of scientific knowledge and a thorough understanding of this epidemic and solid actions taken around the world will be needed to reach the future goal of eliminating this destructive disease, as we have done with other diseases, such as polio and small pox, with global consequences.

Conflict of interest The authors report no conflicts of interest.

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