

Chapter 30

Zika Virus and HIV/AIDS

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Core Message

The new Zika epidemic has many similarities and parallels with the HIV/AIDS pandemic that commenced more than 30 years ago.

Ignoring the rapidly emerging prevalence of the ZikaV globally has the potential to follow the trends experienced during the HIV/AIDS epidemic on a global scale. The emergence of the ZikaV pandemic has occurred globally and its spread is well documented. Insufficiently addressing the potential global impact could be extremely dangerous.

The unprecedented upsurge of this epidemic stresses the importance for continual monitoring and the incorporation of sustainable public health measures as soon as possible.

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30.1 Introduction

Viral infections are a continued and expanding threat to global public health and are under continual epidemiological and medical scrutiny. Viral infections cause approximately 11 million deaths, annually, of which 1 million were due to HIV/AIDS, for example, in 2010 [1]. These fatalities are heightened with the periodic epidemics and pandemics of various strains of influenza, Ebola, continued HIV and HCV spread, TB, and many other viruses. These emerging and periodically re-emerging epidemic diseases pose an ongoing threat to global health security. At the end of 2016, the World Health Organization (WHO) Department of Pandemic and Epidemic Diseases (PED) was monitoring worldwide viral outbreaks of avian influenza, coronaviruses (MERS-CoV, SARS), Ebola, Hendra, influenza (seasonal, pandemic), Nipah, Rift Valley fever, viral hemorrhagic fevers (including Ebola, Marburg, Lassa, Crimean-Congo hemorrhagic fever), yellow fever, and ZikaV [2]. The global spread of ZikaV has evolved into a global pandemic since its original emergence in the Americas, since 2015; ZikaV has evolved into a highly virulent and pathological virus for children and adults, becoming a current unparalleled pandemic. The spread of viral diseases is generally associated with fear that can hinder public health efforts [3]. This fear response has been evident in the public's reaction to the Zika pandemic. This and many other factors closely mirror the setting that has existed with HIV.

30.2 Virus Descriptions

30.2.1 HIV Virus and AIDS

Human immunodeficiency virus (HIV) can lead to acquired immunodeficiency syndrome (AIDS) if not treated. People are unable to rid themselves of HIV completely, even with treatment, unlike some other viruses. Consequently, once infected with HIV, the infection is for life, as reservoirs of infection remain in various organs [4, 5].

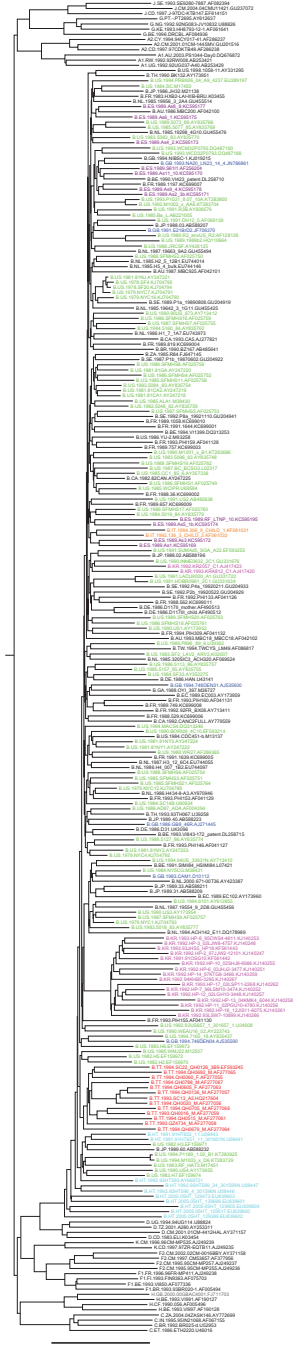
HIV is a retrovirus, lentivirus, which has a lipid bilayer envelope. HIV binds to CD4 T-cell and macrophage receptors and infects these and other cell types. HIV contains an RNA genome that is reverse transcribed into proviral DNA, which is integrated into the host cell's genome [6].

Due to its extreme nucleic acid sequence heterogeneity, HIV consists of several different strains, swarms, clades, and recombinant forms. Individuals may harbor different strains, simultaneously [7–9, 36]. HIV is classified into two overall groups with numeric designations, HIV-1 and HIV-2. HIV-1 is most common and is found globally. HIV-2 is primarily found in Western Africa [10]. Due to its extreme ability to mutate, HIV can escape from immune surveillance and continue infection and proliferation [11].

Figure 30.1: A representative phylogenetic tree for HIV

By infecting blood cells such as CD4 T cells and macrophages, HIV damages the immune system and increases the likelihood of acquiring opportunistic infections [12, 13]. If left untreated, it can take approximately 5–10 years for AIDS to develop

Fig. 30.1 Phylogenetic tree of HIV



[10, 14]. AIDS is considered when the number of CD4 cells falls below 200 cells per cubic millimeter of blood [15]. Without treatment, once diagnosed with AIDS, people typically survive about 3 more years. Life expectancy falls even further due to opportunistic infection, without treatment [7].

30.2.2 *Zika Virus*

Zikavirus (ZikaV) is a flavivirus, which is in the arbovirus group that includes two additional virus subgroups – alphaviruses and bunyaviruses. ZikaV had been considered, originally a relatively mild or benign virus. However, the other related viruses have been known for several years to be associated with several severe and often fatal diseases, including central nervous system disorders, viral meningitis, encephalitis, and many other serious health outcomes. Arboviruses are often in the forefront of discussions regarding public health and their global prominence is a major public health concern. In addition to ZikaV, these viruses include dengue (DEN), Japanese encephalitis (JE), West Nile virus (WNV), chikungunya fever (CHIK), hemorrhagic fevers such as Crimean-Congo hemorrhagic fever (CCHF), and Kyasanur forest disease virus (KFDV) [16–19]. However, since 2015, in the Americas, ZikaV evolved into a highly virulent and pathological virus for children, nearly seven decades after its discovery. ZikaV has further evolved into strains that are more virulent and lethal for adults as well [19, 20]. In fact, this process of evolving toward increased pathogenicity (pathogenization) appears to be ongoing. Globally, there is an increased association of Guillain–Barré syndrome (GBS) with ZikaV infection as well [21–23].

Figure 30.2: A phylogenetic tree for arboviruses with ZikaV highlighted

An individual infected with ZikaV will often manifest only mild symptoms or none. The most common symptoms are fever, rash, joint pain, and conjunctivitis. Occasionally, there can be related muscle pain or headaches. ZikaV manifests itself very much like the common flu, and consequently most people do not seek medical attention when infected. Moreover, like the flu, it can last from several days up to a few weeks. An increased association with Guillain–Barré syndrome, an uncommon disease of the nervous system, has also caused concerns. Death results rarely from ZikaV infection. Be that as it may, at the end of 2016, the most distressing effect of ZikaV infection has been for mothers during pregnancy because ZikaV was associated with a brain birth defect – microcephaly. Additional complications for infants born of ZikaV-infected mothers include defects of the eyes, ears, and growth [16].

30.3 Modes of Transmission

30.3.1 *HIV/AIDS Routes*

HIV can be transmitted through several risk factor routes, which disputes the initial assumption in the 1980s that this epidemic was only experienced in limited demographics and/or risk groups.

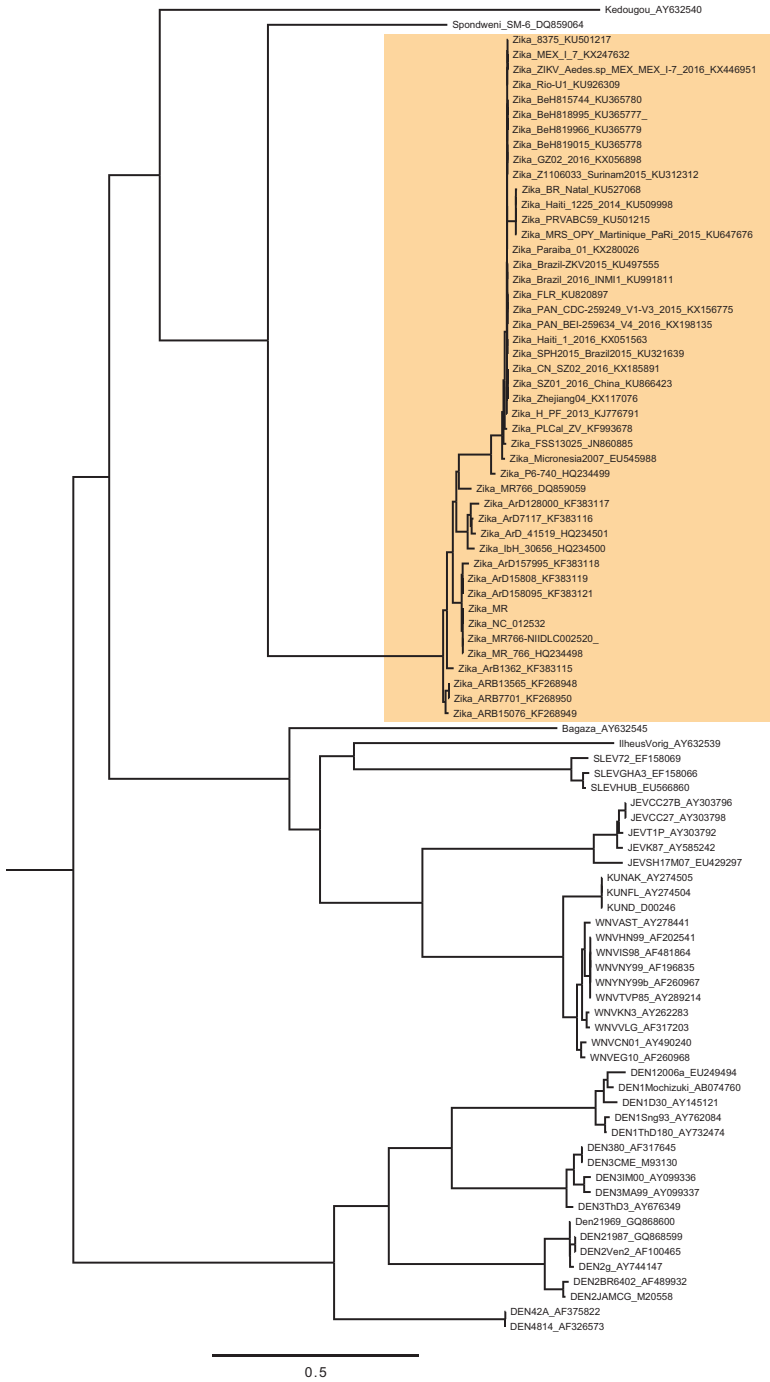


Fig. 30.2 Phylogenetic tree of Zika V

The following are categorical routes for HIV infection and spread.

- High risk sexual contact [24]
 - Anal sex
 - Vaginal sex
 - Oral sex
 - Multiple sexual partners
 - Lack of condom use
 - Deep kissing
- Needle/syringe sharing [24–29]
- Injecting drug user (IDU) paraphernalia including cottons, cookers, and wash waters [24, 26–29]
- Transmission via mother/prenatal [24]
 - Pregnancy
 - Breast feeding
- Medical procedures [24]
 - Blood transfusion
 - Organ transplantation
- Occupational exposure [24]
 - Needle/syringe stab
- Miscellaneous [24]
 - Bites
 - Wound contact

30.3.2 *Zika Virus Vectors*

Recent reviews summarized the status of clinical syndromes involving ZikaV. Issues discussed include ZikaV associated microcephaly, Guillain–Barré syndrome, potential Dengue virus–ZikaV interactions, and the prospects of a future medical establishment response by developing vaccines and other antiviral agents [19, 30].

The following are several risk factors involving ZikaV.

- Mosquito bites

ZikaV is transmitted to people primarily through the bite of an infected *Aedes* species mosquito. These mosquitoes typically lay eggs in standing water, for example, in tires, buckets, bowls, animal dishes, flowerpots, vases, and leaves that trap water in trees. Further, they become infected when they feed on people already infected with ZikaV and then spread the virus to other people through bites [30].

- **Mother/Prenatal**

The ZikaV can be transmitted from the mother to an infant near the time of delivery, if the mother contracted the virus during her pregnancy. No cases of ZikaV have surfaced through mothers’ breastfeeding. Thus, mothers are continually encouraged to breastfeed even in areas where this virus is prevalent [30].

- **Sexual Contact**

A man can spread ZikaV to his sexual partners. It is unknown yet whether women can transmit the virus. Moreover, the virus is present in semen longer than blood, stressing the importance of condom use and other such means that prevent the unnecessary transmittal of the ZikaV [30]. In addition, the issue of viral reservoirs continues as has been found with HIV infection.

- **Blood Transfusions**

- Public health services are considering the risk of transmission of ZikaV during blood transfusions. Although no confirmed cases have occurred, reports have indicated potential cases in Brazil and historical records indicated that blood donors have tested positive for the virus after they had given blood [30]. Several news sources have reported that donated blood has tested positive for the presence of ZikaV [31]
- ZikaV vaccines are on the way from NIH and Walter Reed [30].

30.3.3 A Comparison of Zika Virus and HIV/AIDS Modes of Transmission

Although many modes of transmission for the HIV/AIDS virus are known, graphically presenting these modes will assist in highlighting current and potential mechanisms that can affect the spread of both the HIV/AIDS and ZikaV.

Figure 30.3: Modes of transmission for Zika and HIV

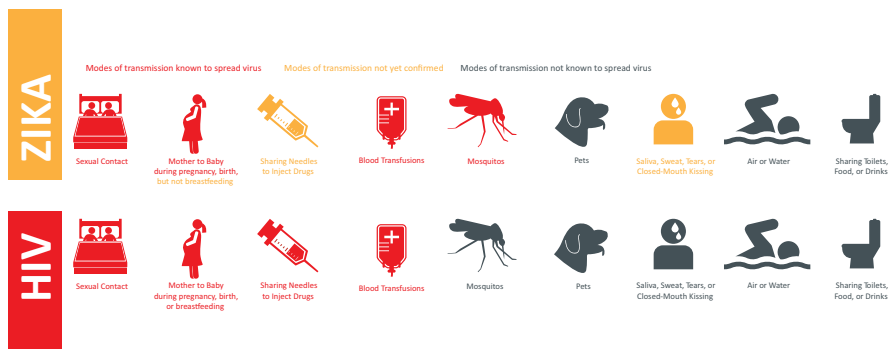


Fig. 30.3 A comparison of the modes of transmission between HIV and Zika

30.4 Pathways

30.4.1 HIV Pathway

Figure 30.4: HIV pathway [32, 33]

30.4.2 AIDS Pathway

Figure 30.5: HIV->AIDS pathway [34, 35]

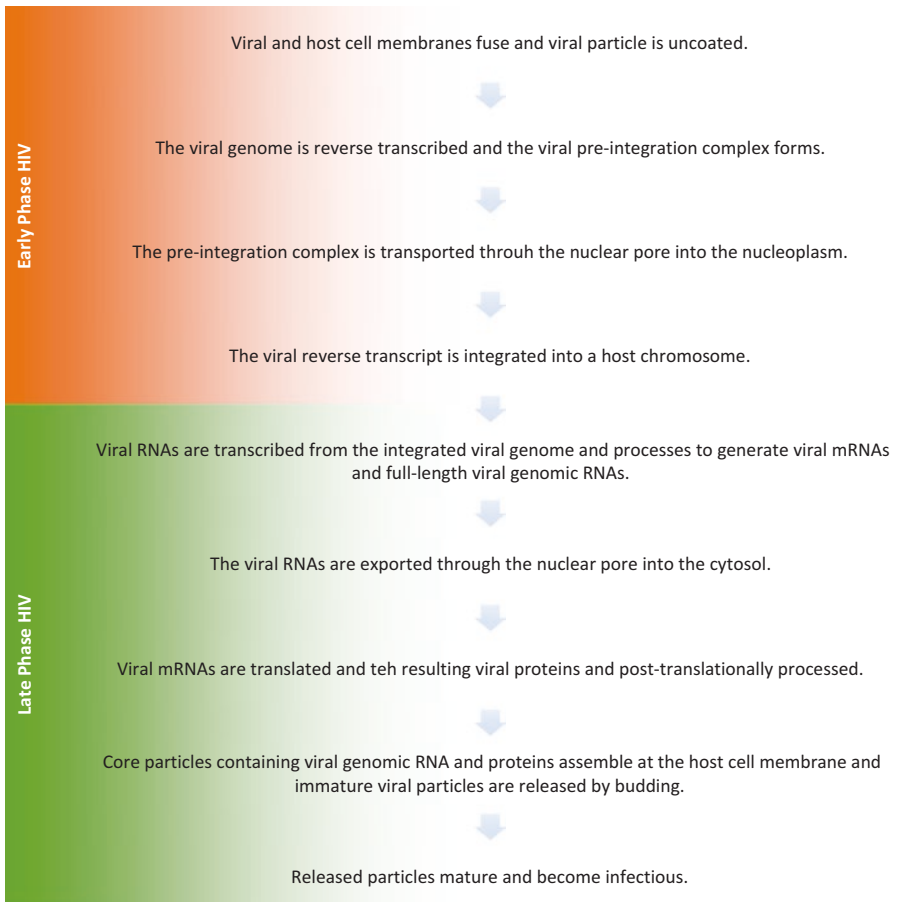


Fig. 30.4 HIV pathway [32, 33]

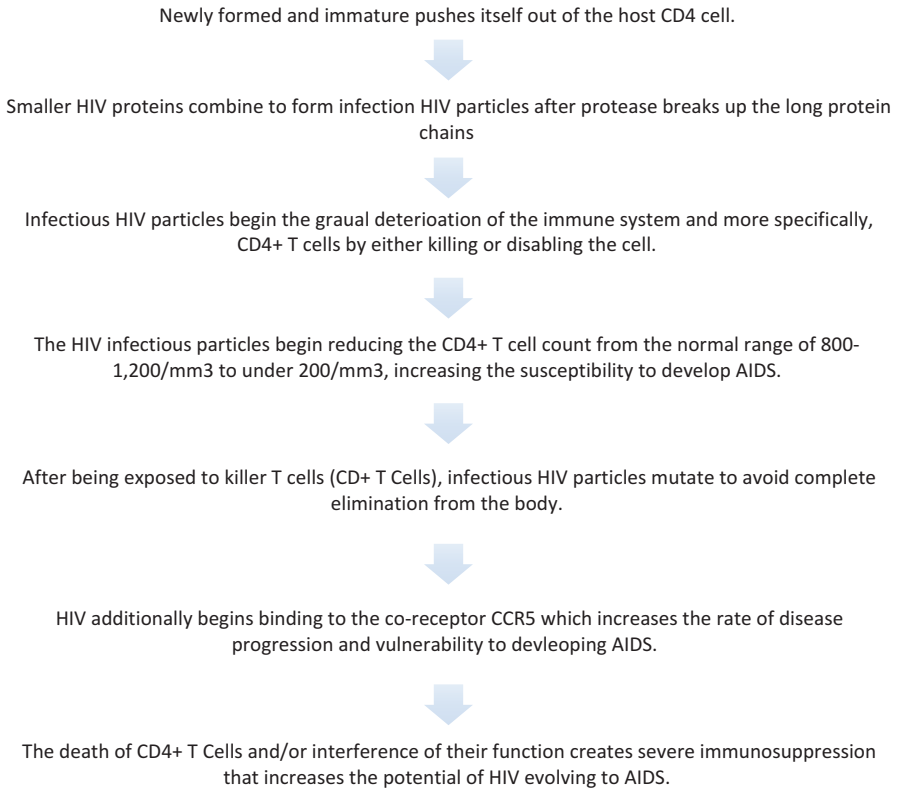


Fig. 30.5 HIV -> AIDS pathway [34, 35]

30.4.3 Zika Virus Pathway

Figure 30.6: Zika virus pathway [36]

30.5 HIV/AIDS Epidemic

The HIV/AIDS epidemic forever changed the health landscape of the United States as well as globally. A lack of understanding of epidemiology in general and of this virus-caused disease created a sense of fear and apprehension for the public.

The first reported case in 1981 at the University of Miami School of Medicine Grand Rounds involved a young Caucasian man of north European descent diagnosed with *Kaposi's* sarcoma. The physician reporting this case noted how unusual and unique the symptoms were as *Kaposi's* sarcoma was unknown in the patient's

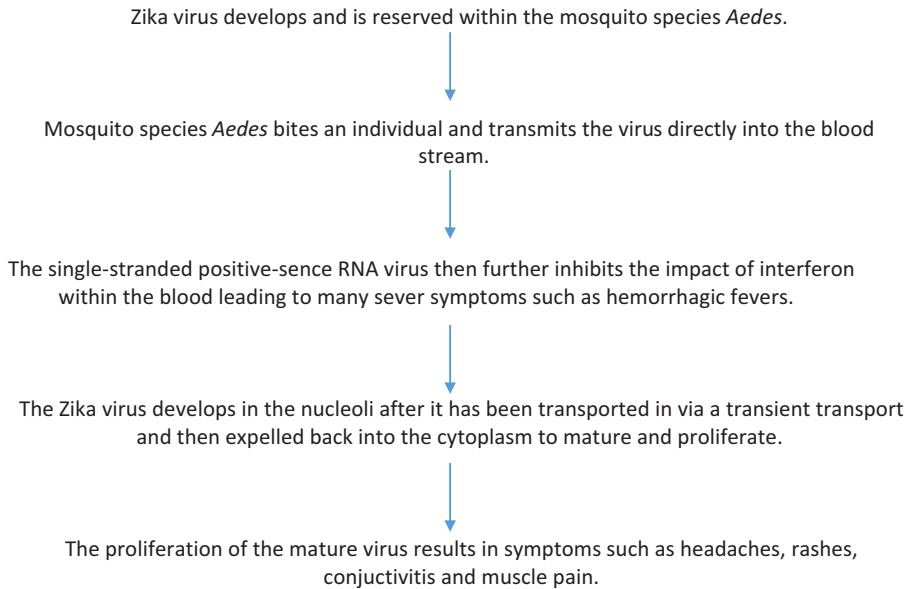


Fig. 30.6 Zika pathway [36]

age group or among those of north European decent. In addition, a second unusual case was also reported. This time, the young man had been diagnosed with *Pneumocystis carinii pneumonia* (PCP) – a disease that usually occurred among the very old and those living in nursing homes. These cases were puzzling and many questions arose including where the patients lived, traveled, what acute or chronic diseases they had, and with whom they interacted. It was further reported 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 [37].

Figure 30.7: Map of HIV spread [2]

The public misconceptions and misinterpretations of the HIV/AIDS epidemic did not help the scientific attack on this disease; it resulted in a limited embracing of the scientific approach by communities to solve medical issues. Early on, after this virus was discovered, immunologists speculated that HIV infection could perhaps be managed through a vaccine approach [38]. Because of further molecular research, it was ascertained that HIV underwent a high mutation rate making the development of vaccines highly difficult [24]. This fundamental molecular understanding of the mutation rate, gene structure, and evolution of HIV and the AIDS epidemic at the county, state, and national levels is still at the forefront of current concern as well.

Figure 30.8: Multidisciplinary risk framework

The HIV-associated novel agglomeration of signs and symptoms was frequently referred to as (1) Gay-Related Immune Deficiency (GRID) and (2) Gay Disease, which indicated a widespread misunderstanding and misconception of HIV epidemiology. The HIV/AIDS epidemic was thought to be primarily transmitted through

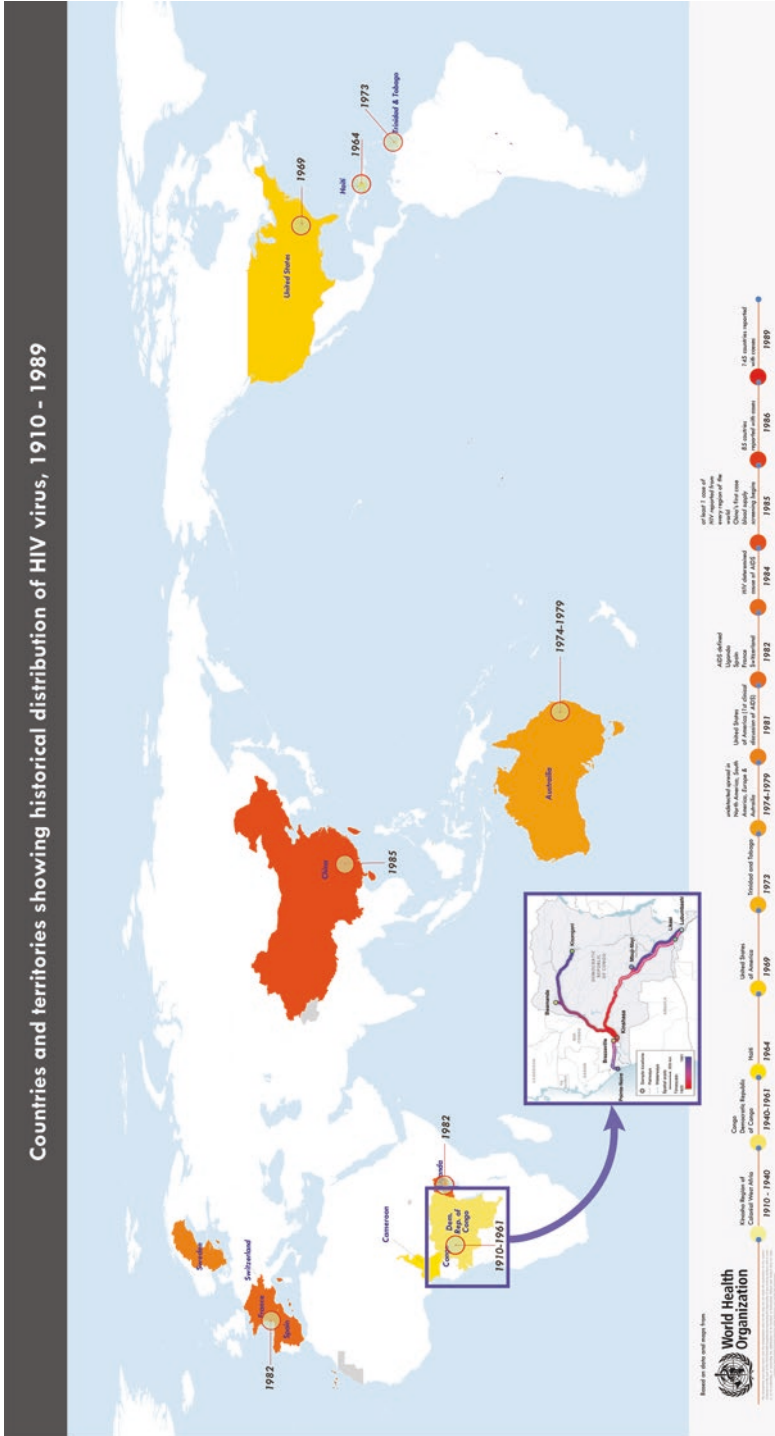


Fig. 30.7 Proliferation of HIV [2]

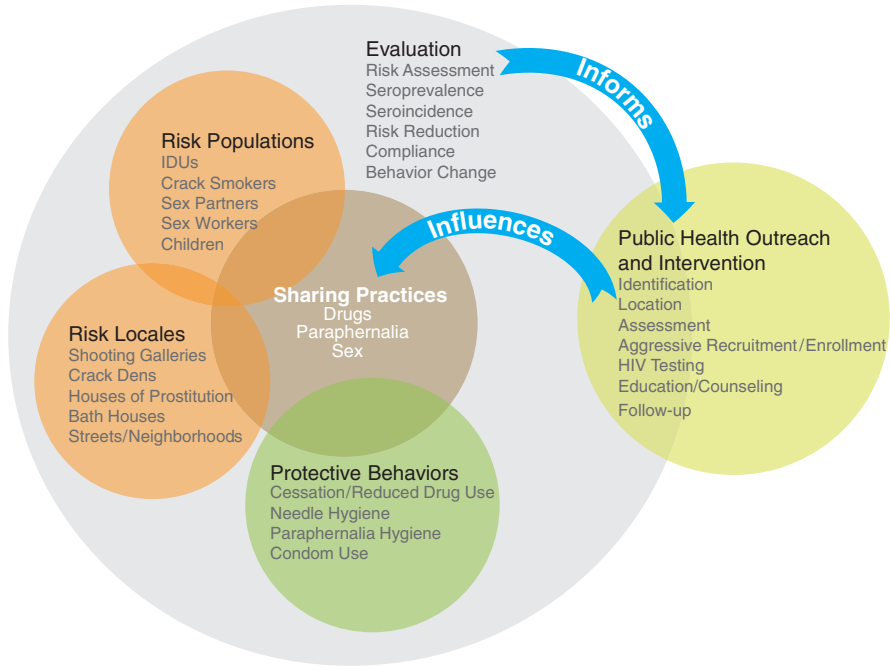


Fig. 30.8 Multidisciplinary risk framework. This chart was developed to graphically display risk populations, HIV risk, evaluation methods, and various other components that directly impact the HIV/AIDS epidemic

Caucasian and/or homosexual males. Moreover, the lifestyles within the United States during this disease's initial phase were not supportive of practices that could help contravene the emerging epidemic. It was a period of substantially increased urbanization, rapidly increased human trafficking and prostitution, venereal diseases, and drug abuse, including the use of hypodermic needle/syringes [39, 40]. Additionally, the sexual "revolution" that occurred during the 1960s and the gay liberation movement in the 1970s enhanced the severity of this new epidemic [38]. These specific manifestations combined with a dearth of scientific knowledge regarding HIV/AIDS further delayed foundation of the most rapid and preventable approaches against acquiring and transmitting HIV.

30.6 Zika Virus Epidemic

On April 18, 1947, the first documented case of the ZikaV emerged in the Zika forest of Uganda [31]. This information only surfaced as the monkey, Rhesus 766 was being observed and studied for research on yellow fever, which is an arbovirus related to the ZikaV [24]. Within a year, the virus was isolated from *Aedes*

africanus mosquitoes and serological studies commenced, examining the impact of this virus [41].

Since its discovery, ZikaV global spread was methodically tracked as follows: 1947 – Zika forest, Uganda, Nigeria, east Africa; 1954 – India; 1978 – Indonesia, Malaysia; 1999 – Ivory Coast; 2001 – Sabah, Malaysia; 2007 – Micronesia, Yap Islands, Easter Islands, Nepal, New World, Argentina, Hawaii, Scandinavia, and Saudi Arabia; 2008 – Southeastern Asia and Australia; 2008 – Senegal, Egypt, Pakistan, North Vietnam, Indonesia, the Philippines, and Borneo/Java, USA; 2012 – Singapore, Australia, Tahiti, and Germany. Tracking ZikaV highlights the ability of an initially, supposedly innocuous virus to spread globally [19, 41, 42].

In 2011, ZikaV was first detected in the United States (Colorado), where it was spread by sexual risk, having been brought to the United States by an infected health care worker, who had been in Indonesia [43].

Later, additional cases of ZikaV infection were reported within the United States and its territories, including Puerto Rico, US Virgin Islands, and American Samoa – 274 cases had occurred as of March 2016 [44]. As of November 16, 2016, every state and territory (other than Guam and Alaska) had reported cases of Zika totaling 36,323. Locally acquired cases were restricted to South Florida, Samoa, US Virgin Islands and Puerto Rico. Puerto Rico accounted for 86% of these cases [44, 45]. It is interesting to note that as of February 2016, according to WHO, there was no ZikaV detected yet in Sierra Leone (a medium risk country); however, by September 2016, ZikaV was detected in another medium risk area, Cape Verde islands, off the west African coast. (There are 195 countries in the world [46].) As of the latest report, March 10, 2017, ZikaV has spread to 184 countries, 13 countries report person-to-person spread, 31 countries report CNS malformations including microcephaly, and 23 countries report GBS – all specifically related to ZikaV infection. The spread of ZikaV, therefore, has rapidly expanded its domain. Thus, local and global public health services, in concert, continue to monitor ZikaV infection [21–23, 47, 48].

Figure 30.9: The map indicates the proliferation of the ZikaV [2]

Figure 30.10: ZikaV in the United States, November 16, 2016 [17]

30.7 Urbanization and Globalization

Several factors probably contributed to the global expansion of ZikaV (as well as many other viruses), including increased urbanization, economic expansion, swelled human populations and migrations, international travel, wars, and global warming. The rapid expansion of the global landscape as well as major climate changes (global warming) augmented the vector of transmission, the *Aedes aegyptus* and *Aedes albopictus* mosquitoes (including in Florida). Moreover, increased temperatures not only increase the transmission vectors but also additional health outcomes that can negatively heighten the effects of ZikaV infection. Moreover, there has not been a corresponding increase in quality and quantity of sanitation and healthcare,

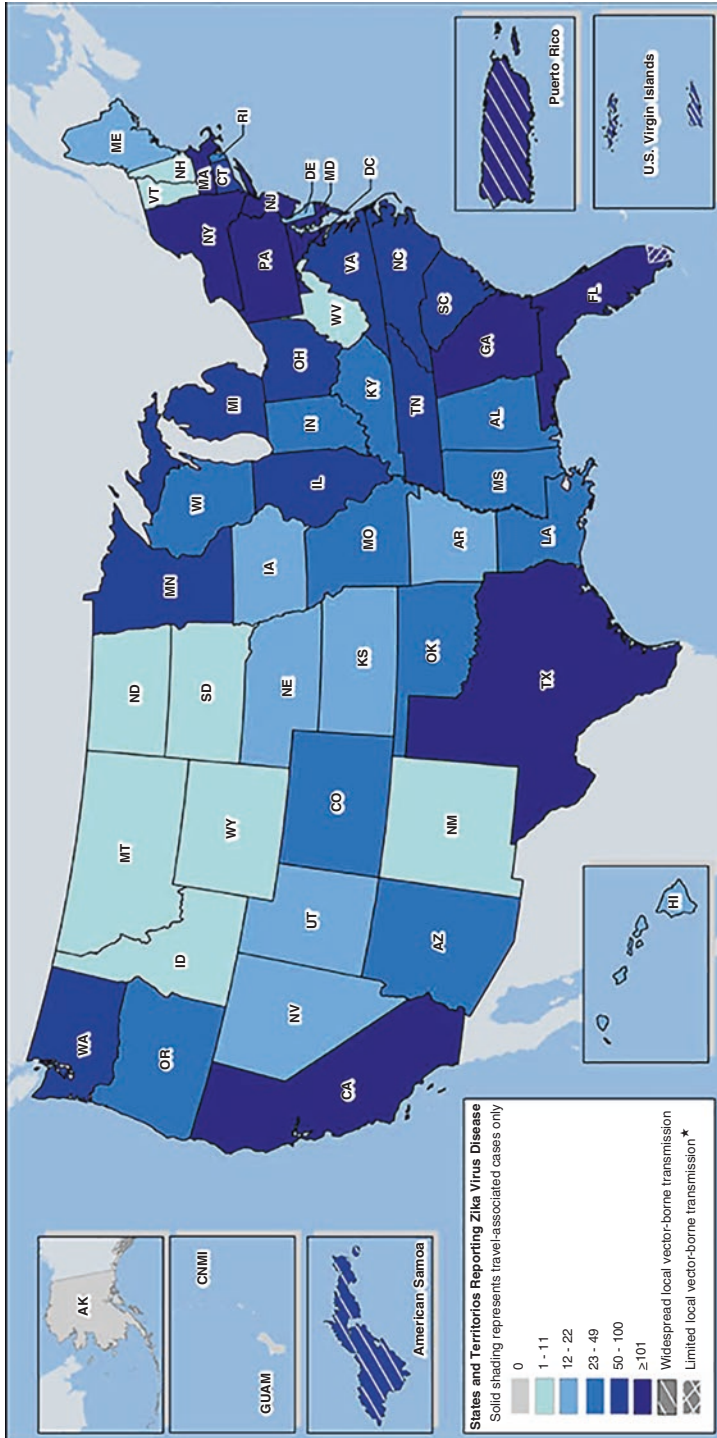


Fig. 30.10 ZikaV in the United States, November 16, 2016 [17]

which further contributes to the problem. Sanitary infrastructure and practices are necessary to address the rapid spread of the epidemic; however, pleas for funding of such efforts are underway [19, 20, 49].

30.8 Zika Virus and HIV/AIDS

The expansion of the ZikaV pandemic has been disturbingly like the HIV/AIDS epidemic. Initially, the HIV/AIDS epidemic was difficult to diagnose, the modes of transmission were not understood and the risk groups were unknown, thus, in retrospect, making the proliferation of this disease all but certain. The recent emergence of ZikaV mirrors similar delays in public health action and understanding that initially accelerated the spread of HIV/AIDS globally. Without a comprehensive and collaborative approach, ZikaV will have a similar damaging effect, globally, as the HIV/AIDS epidemic has had during the past decades.

The ZikaV pandemic reinforced that there is global human domination, urban crowding, expanded international travel, disruption of environmental equilibria, and other human behaviors combined with human-caused perturbations in ecologic balance that have promoted several latent infectious agents to emerge so unexpectedly [19, 44]. It is urgent to approach this epidemic through a multidisciplinary and collaborative approach to minimize the spread of the ZikaV [44]. The implementation of a global framework is needed in which collaborative efforts drive the research and clinical efforts for containing and eliminating this new epidemic and to anticipate other epidemics to come [44, 45].

It should be noted that the current damage caused by the ZikaV pandemic was predicted as likely to occur in a 2015 publication [19]. The reasons provided at that time are as follows: global warming and mosquito spread; war, pestilence, and malnutrition; relatedness of clinical symptomatic and immune relatedness to other diseases and their viruses; the proximity of ZikaV molecular and viral properties to all the other related viruses that are well-known to be pathogenic; viral superinfection issues; and lack of support from global economic and social structures.

Further, the impact of the ZikaV on pregnancy and newborn infants is different compared with HIV/AIDS. Both viruses can have deleterious effects on mothers and newborn children and have the potential to produce major health challenges and negative birth outcomes. Unlike HIV/AIDS for which manageable chronic interventions have been developed over the decades for both adults and children growing up HIV positive, ZikaV causes additional outcomes including intrauterine growth constraints, eye defects, congenital brain abnormalities, and microcephaly risks for infants, and GBS risk for adults [50–52]. The immediacy and relationship between ZikaV and pregnancy highlights the viruses' virulence and capability to cause major health challenges for future generations if it is not immediately controlled (Table 30.1).

Table 30.1 Comparison of HIV and ZikaV

HIV	ZikaV
Retrovirus	Arbovirus closely related to dengue, chikungunya, and West Nile viruses
Effects children and adults alike, yet with treatment children are living to adulthood	Highly virulent and pathologically disastrous for children
Most people are asymptomatic for long durations (years) before displaying disease and contracting other rare diseases (<i>Kaposi's</i> sarcoma)	Symptoms are rash and/or fever for 2–7 days but many are asymptomatic
Primary transmission is via sexual contact. Effective HIV prevention targets safe sex	Primary transmission is via mosquitoes, <i>Aedes aegypti</i> and <i>Aedes albopictus</i>
Most eventually require long-term expensive medical care for duration of life. Death from AIDS still occurring globally	Four-fifths of those with disease never need or receive medical care
Transmission still occurring in the United States yet threats continue in Africa and India	Local transmission just beginning in the United States though disease is now worldwide
No vaccine but many regimens of medication treatment in use	No vaccine or medication currently (4–2017)
Originated in Africa, Kinshasa, in the early 1900s, years before adverse health seen because of infection	Originated in Africa, Zika Forest in 1950s, years before adverse health seen because of infection

30.9 Conclusions

During the initial phases of the HIV/AIDS epidemic, an accurate diagnosis could not be made and neither were there clinical and/or therapeutic treatments available that were efficient and effective. It is similarly very difficult to discern a “pure” ZikaV diagnosis as it is closely related to dengue and other arbovirus diseases and many of the clinical tests cannot readily distinguish among the viruses [44]. A modern highly diagnostic technique in widespread use for neuroAIDS is brain imaging. Neuroimaging has also become important in ZikaV infection-related microcephaly, GBS, and acute disseminated encephalomyelitis (ADEM) [53, 54].

From the viewpoint of evolution and at the molecular level, HIV and ZikaV are widely divergent although they entered the human framework near each other in tropical Africa. For example, their mutation rates are divergent. The mutation rate of HIV is $4.1 \pm 1.7 \times 10^{-3}$ mutations per base in a viral genome of 9749 bp. That means that there are about 39.97 mutations per genome for HIV-1. This is the most rapid mutation rate of any living organism on planet Earth. However, in comparison, the mutation rate of ZikaV, in vivo, is 12–25 bases a year, in a viral genome of 10,272 bp. However, comparisons of HIV-1 and ZikaV mutation rates are made difficult because their mutation rates are not measured or reported under identical laboratory or epidemiological conditions [55, 56].

The risk groups, lifestyles, and poor accessibility to preventive measures and healthcare enhanced the spread of the HIV/AIDS epidemic and this trend appears to

be paralleled by ZikaV. The different modes of transmission coupled with the rapid spread of ZikaV stresses the importance of being alert, pre-emptive, and proactive rather than reactive to prevent this virus from continuing its pandemic trajectories and trails.

Conflict of interest The authors report no conflicts of interest.

References

1. Dye C (2014) After 2015: infectious diseases in a new era of health and development. *Philos Trans R Soc Lond Ser B Biol Sci* 369(1645):20130426. doi:10.1098/rstb.2013.0426. PMID: PMC4024220
2. World Health Organization Zika virus [Internet] World Health Organization [Cited 2016 Nov 22]. Available from: <http://www.who.int/mediacentre/factsheets/zika/en/>
3. Shultz JM, Cooper JL, Baingana F, Oquendo MA, Espinel Z, Althouse BM et al (2016) The role of fear-related behaviors in the 2013–2016 West Africa Ebola virus disease outbreak. *Curr Psychiatry Rep* 18(11)
4. Centers for Disease Control and Prevention (2016) About HIV/AIDS [Internet] Centers for Disease Control and Prevention [Cited 2016 Nov 21] Available from: <http://www.cdc.gov/hiv/basics/whatishiv.html>
5. Joseph J, Cinque P, Colosi D, Dravid A, Ene L, Fox H, Gabuzda D, Gisslen M, Joseph SB, Letendre S, Mukerji SS, Nath A, Perez-Valero I, Persaud D, Price RW, Rao VR, Sacktor N, Swanstrom R, Winston A, Wojna V, Wright E, Spudich S (2016) Highlights of the global HIV-1 CSF escape consortium meeting, 9 June 2016, Bethesda, MD, USA *J Vir Erad* 2:243–250
6. HIV is a retrovirus [Internet] HIV is a retrovirus [Cited 2016 Nov 21] Available from: <http://www.chm.bris.ac.uk/webprojects2002/levasseur/hiv/hiv3.htm>
7. Joy JB, Liang RH, Nguyen T, McCloskey RM, Poon AFY (2015) Origin and evolution of HIV. In: Shapshak P, Sinnott JT, Somboonwit C, Kuhn JH (eds) Chapter 23 in *Global virology I – identifying and investigating viral diseases*. Springer Publications, New York, pp 587–612
8. Balaji S, Sneha P, Rama M, Shapshak P (2015) Global protein sequence variation in HIV-1B isolates derived from human blood and brain In: Shapshak P, Sinnott JT, Somboonwit C, Kuhn JH (eds) Chapter 24 in *Global virology I – identifying and investigating viral diseases* Springer Publications, New York, pp 613–666
9. Foley BT HIV and SIV evolution. In: Shapshak P, Sinnott JT, Somboonwit C, Singer E, Levine AJ, Foley BT, Chiappelli F (eds) *Global virology II – HIV and NeuroAIDS*. Springer Publications, New York, p 2017
10. What is HIV/AIDS? [Internet] Welcome to [AIDSGov](http://www.aids.gov) [Cited 2016 Nov 21] Available from: <https://www.aids.gov/hiv-aids-basics/hiv-aids-101/what-is-hiv-aids/index.html>
11. Shahid A, Brumme ZL (2015) Mutational immune escape in HIV-1 infection. In: Shapshak P, Sinnott JT, Somboonwit C, Kuhn JH (eds) Chapter 25 in *Global virology I – identifying and investigating viral diseases*. Springer Publications, New York, pp 667–706
12. Dixit D, Vatakis DN (2015) The biology of quiescent CD4 T cells, their role in HIV-1 infection and cocaine drug abuse. In: Shapshak P, Sinnott JT, Somboonwit C, Kuhn JH (eds) Chapter 26 in *Global virology I – identifying and investigating viral diseases*. Springer Publications, New York, pp 707–722
13. Flynn JK, Gorry PR (2015) Role of macrophages in the immunopathogenesis of HIV-1 infection. In: Shapshak P, Sinnott JT, Somboonwit C, Kuhn JH (eds) Chapter 27 in *Global virology I – identifying and investigating viral diseases*. Springer Publications, New York, pp 723–744
14. HIV/AIDS. www.dhhr.wv.gov/oeps/std-hiv-hep/hiv_aids/pages/hivaidinformation.aspx

15. WHO HIV/AIDS Laboratory diagnosis manual Laboratory guidelines for enumerating CD4 T lymphocytes in the context of HIV/AIDS World Health Organization Regional office for Southeast Asia, New Delhi June 2007 NLM classification: WH200 ISBN 978-92-9022-298-9
16. Dash AP, Bhatia R, Sunyoto T, Mourya DT (2013) Review Article Emerging and re-emerging arboviral diseases in Southeast Asia. *J Vector Borne Dis* 50:77–84
17. Centers for Disease Control and Prevention [Internet] (2016) Centers for Disease Control and Prevention Centers for Disease Control and Prevention [Cited 2016 Nov 21] Available from: <http://www.cdc.gov/zika/about/overview.html>
18. van Vreden C, Niewold P, vu Dinh L, Munoz-Erazo L, Getts D, King NCJ (2015) Flavivirus encephalitis immunopathogenesis of disease and immunomodulation. In: Shapshak P, Sinnott JT, Somboonwit C, Kuhn JH (eds) Chapter 16 in *Global virology I – identifying and investigating viral diseases*. Springer Publications, New York, pp 425–455
19. Shapshak P, Somboonwit C, Foley BT (2015) Zika virus In: Chapter 18 in *Global virology I – identifying and investigating viral diseases* Springer Publications, New York, pp 477–500. doi: [10.1007/978-1-4939-2410-3_18](https://doi.org/10.1007/978-1-4939-2410-3_18)
20. Braks MAH, Honório NA, Lounibos LP, Lourenço-De-Oliveira R, Juliano SA (2004) Interspecific competition between two invasive species of container mosquitoes, *Aedes aegypti* and *Aedes albopictus* (Diptera: Culicidae), in Brazil. *Ann Entomol Soc Am* 97(1):130–139. doi: [http://dx.doi.org/10.1603/0013-8746\(2004\)097\[0130:ICBTIS\]2.0.CO;2](http://dx.doi.org/10.1603/0013-8746(2004)097[0130:ICBTIS]2.0.CO;2)
21. WHO Situation Report (2017) Zika virus, microcephaly, Guillain-Barre Syndrome (GBS). <http://www.who.int/emergencies/zika-virus/situation-report/en/>
22. Krauer F, Riesen M, Reveiz L, Oladapo OT, Martinez-Vega R, Porgo TV (2017) Zika virus infection as a cause of congenital brain abnormalities and Guillain–Barre syndrome: systematic review. *PLoS Med* 14(1):e1002203. doi:[10.1371/journal.pmed.1002203](https://doi.org/10.1371/journal.pmed.1002203)
23. WHO Situation Report (2016) Zika virus, microcephaly, Guillain-Barre Syndrome (GBS). <http://www.who.int/emergencies/zika-virus/situation-report/en/> <http://apps.who.int/iris/bitstream/10665/254714/1/zikasitrep10Mar17-eng.pdf?ua=1>
24. Centers for Disease Control and Prevention (2015) HIV transmission – HIV basics Last accessed 1 Apr 2017 <https://www.cdc.gov/hiv/basics/transmission.html>
25. McCoy CB, Shapshak P, Rivers JE, McCoy HV, Weatherby NL, Chitwood DD, Shah SM, Inciardi JA, McBride DC, Watters JK (1994) The risks of injection practices and compliance to risk reduction protocols in the prevention of HIV-1 among injecting drug users. *J AIDS* 7:773–776
26. Page JB, Shapshak P, Duran EM, Even G, Moleon- Borodowski I, Llanusa-Cestero R (2006) Detection of HIV-1 in injection paraphernalia: risk in an era of heightened awareness. *AIDS Patient Care STDs* 20:576–585
27. Shapshak P, McCoy CB, Rivers J, Mash DC, Chitwood DD, Weatherby N, Shah SM (1993) Bleach effectively inactivates HIV-1 at short time intervals. *J AIDS* 6:218–219
28. Shah SM, Shapshak P, Rivers JE, Weatherby NL, Xin KQ, Stewart RV, Chitwood DD, Page JB, Mash DC, Vlahov D, McCoy CB (1996) Detection of HIV-1 DNA in needle/syringes, paraphernalia, and washes from shooting galleries in Miami: preliminary laboratory results. *J AIDS* 11:301–306
29. McCoy CB, Metsch LR, Chitwood DD, Shapshak P, Comerford ST (1998) Parenteral transmission of HIV among injection drug users: assessing the frequency of multi-person use of needles, syringes, cookers, cotton, and water *J Acquir Immune Def Syn Human Retrovirol* 18:S25–S29
30. Centers for Disease Control and Prevention (2016) Zika virus – transmissions and risk. <https://www.niaid.nih.gov/diseases-conditions/zika-vaccines>
31. Powell J (2016) <http://www.wptv.com/news/region-c-palm-beach-county/west-palm-beach/blood-donated-in-florida-tests-positive-for-the-zika-virus>
32. Frankel AD, Young JA (1998) HIV-1: fifteen proteins and an RNA. *Annu Rev Biochem* 67:1–25
33. Miller MD, Farnet CM, Bushman FD (1997) Human immunodeficiency virus type 1 preintegration complexes: studies of organization and composition. *J Virol* 71(7):5382–5390

34. National Institute of Health (2012) How HIV cause AIDS <http://www.niaid.nih.gov/topics/hiv/aids/understanding/howhivcausesaids/Pages/cause.aspx>
35. National Institutes of Health (2010) The evidence that HIV causes AIDS <http://www.niaid.nih.gov/topics/HIVAIDS/Understanding/howHIVCausesAIDS/Pages/HIVcausesAIDS.aspx>
36. Shapshak P, Somboonwit C, Foley BT, Alrabaa SF, Wills T, Sinnott JT (2015) Zika virus In: Global virology I Springer Publications, pp 477–500
37. McCoy CB, McBride DC, Bengoa AJ (in press) From the many one: a collaborative approach In: Wechsberg WM (ed) Lives lost, careers changed, and survival 30 years on: narratives from HIV pioneers Copublished RTI Press, Research Triangle Park and The Johns Hopkins University Press, Baltimore
38. Lazear HM, Diamond MS (2016) Zika virus: new clinical syndromes and its emergence in the Western Hemisphere. *J Virol* 90:4864–4875. doi:10.1128/JVI.00252-16
39. McCoy CB, Inciardi J (1995) Sex, drugs, and the continuing spread of AIDS. Roxbury, Los Angeles
40. McCoy CB (2009) Institutionalization of drug abuse research in academia—One professor’s view *J Drug Issues* 39(1) reflections
41. Mirko DG (1990) History of AIDS: emergence and origin of a modern pandemic Princeton University Press
42. Hayes EB (2009) Zika virus outside Africa. *Emerg Infect Dis* 15(9):1347–1350. PMID: PMC2819875 PMID: 19788800
43. Foy BD, Kobylinski KC, Foy JL, Blitvich BJ, Travassos A, Haddow AD, Lanciotti RS, Tesh RB (2011) Probable non-vector-borne transmission of Zika virus, Colorado, USA. *Emerg Infect Dis* 17(5):880–882
44. Centers for Disease Control and Prevention (2016) Zika virus in the United States, 2015–2016
45. Anthony S, Morens DM (2016) Zika virus in the Americas – yet another arbovirus threat. *N Engl J Med* 374:601–604. doi:10.1056/NEJMp1600297
46. <http://www.infoplease.com/ipa/A0932875.html>
47. <http://www.afro.who.int/en/sierra-leone/health-topics/5104-zika-virus-disease.html>
48. Moore DL, Causey OR, Carey DE, Reddy S, Cooke AR, Akinkugbe FM et al (1975) Arthropod-borne viral infections of man in Nigeria, 1964–1970. *Ann Trop Med Parasitol* 69:49–64
49. Juliano SA, Lounibos LP (2005) Ecology of invasive mosquitoes: effects on resident species and on human health. *Ecol Lett* 8(5):558–574
50. Heymann DL, Liu J, Lillywhite L (2016) Partnerships, not parachutists, for Zika research. *N Engl J Med* 374(16):1504–1505. doi:10.1056/NEJMp1602278
51. Brasil P, Pereira JP Jr, Raja Gabaglia C et al (2016) Zika virus infection in pregnant women in Rio de Janeiro—preliminary report. *N Engl J Med* NEJMoa1602412. Published online 4 Mar 2016 <http://dx.doi.org/10.1056/NEJMoa1602412>
52. Meaney-Delman D, Rasmussen SA, Staples JE et al (2016) Zika virus and pregnancy: what obstetric health care providers need to know. *Obstet Gynecol* Published online 17 Feb 2016
53. Thompson PM, Alger JR, Jahanshad N (2015) Brain imaging in people with HIV. In: Shapshak P, Sinnott JT, Somboonwit C, Kuhn JH (eds) Chapter 28 in *Global Virology I – Identifying and investigating viral diseases*. Springer Publications, New York, pp 745–759
54. Mehrjardi MZ, Keshavarz E, Poretti A, Hazin AN (2016) Neuroimaging findings of Zika virus infection: a review article. *Jpn J Radiol*. doi:10.1007/s11604-016-0588-5
55. Cuevas JM, Geller R, Garijo R, Lopez-Aldeguer J, Sanjuan R (2015) Extremely high mutation rate of HIV-1 *in vivo*. *PLoS Biol* 13(9):e1002251. doi:10.1371/journal.pbio1002251
56. Logan IS (2016) ZIKA-How fast does this virus mutate? *Dongwuxue Yanjiu* 37(2):110–115. Published online 2016 Mar 18. doi: 10.13918/j.issn.2095-8137.2016.2.110. PMID: PMC4876826