Chapter 11

The Situation in the Cradle of AIDS: Congo and Central Africa

Marie Laga, Richard Matendo, and Ann Buvé

D.D. Celentano and C. Beyrer (eds.), *Public Health Aspects of HIV/AIDS in Low and Middle Income Countries*,
DOI: 10.1007/978-0-387-72711-0_11,

Introduction

For the Central Africa region, long considered the home of the HIV-1 virus, the decades which have seen the emergence and spread of HIV-1 have been dominated by the demands and upheaval of relentless conflict. Countries within this region which include for the purposes of this chapter, Burundi, Cameroon, the Central African Republic (CAR), the Republic of Congo or Congo Brazzaville, the Democratic Republic of Congo (DRC), Gabon and Rwanda, have had limited resources to focus on this deadly infectious disease and its intriguing epidemiology. Poverty is rampant throughout the region, with many individuals, in some countries close to 90%, living on less than USD 2 a day (UNAIDS, 2007). Life expectancy is uniformly low throughout the region, with no country having an average life expectancy of 60 or higher and some lower than 45 years (CIA, 2007). The median age of each population is also low ranging from as low as 16 to no higher than 19 (CIA, 2007), reflecting the toll of poverty, civil and other wars, and the impact of untreated HIV infections. Persistent conflict has also led to widespread displacement and engendered huge legions of refugees shifting homes from one country to the next, eliminating what employment may have existed, and placing even greater demand on infrastructures that are minimal at best. Within this context, efforts at characterizing and responding to the HIV/AIDS epidemic have been severely challenged. This chapter will discuss the history of the epidemic within this region, and the progress that has been made in understanding the epidemiology of the epidemic and addressing the additional threat it poses to these societies.

Epidemiology

Central Africa: The Cradle of HIV-1

AIDS in patients from Central Africa was first reported in a letter to the editor in the Lancet in 1983, two years after AIDS was first described in homosexual men in North America (Clumeck et al., 1983; Gottlieb et al., 1981). The African patients, who were diagnosed in Brussels, were from the Democratic Republic of Congo (DRC, formerly known as Zaire) and Tchad (also known as Chad), and three of them had been living in Belgium for less than 3 years, suggesting that these patients had not been infected in Belgium but rather in their home country. Subsequent review of patient records revealed that between 1979 and 1984, 18 patients from Central Africa had been admitted to hospital in Brussels with AIDS related problems (Clumeck et al., 1984). These patients did not belong to any of the known risk groups at that time, but appeared to have acquired their infection through heterosexual intercourse.

Around the same time, clinicians in Uganda had noticed the emergence of a new syndrome which they coined “slim disease” and which appears to have been AIDS (Serwadda et al., 1985). Considering the long incubation period from infection with HIV-1 to the development of full blown AIDS, HIV infections must have started to occur in Central Africa at the latest in the early 1970s. Indeed, tests of stored, frozen blood samples revealed HIV infection in a 1959 blood sample from a male resident of Kinshasa, the oldest documented case of HIV infection (Nahmias et al., 1986). Phylogenetic analysis of the RNA

isolated from this sample suggested that introduction of HIV-1 in the human population would have first occurred in the 1940s to early 1950s (Zhu et al., 1998). This evidence suggests that the HIV-1 epidemic in Central Africa is the oldest HIV epidemic in the world and most probably was the source of this infectious disease.

Since the late 1980s evidence has been accumulating that HIV in humans is the result of zoönotic transmission of primate lentiviruses, i.e. simian immunodeficiency viruses. The primate reservoir of HIV-2 was clearly identified as the soothy mangabey, whose natural habitat of West Africa overlaps with the epicentre of the HIV-2 epidemic (Chen et al., 1996). In the late 1990s, a subspecies of the common chimpanzee (*Pan troglodytes troglodytes*) was found to be the reservoir for HIV-1 groups M and N (Gao et al., 1994). The natural habitat of *P. t. troglodytes* extends from the south of Cameroon and the CAR, over Gabon to the northern parts of the Republic of Congo (Brazzaville). More recently the western gorilla (*Gorilla gorilla*) has been found to be infected with an SIV that is closely related to HIV-1 group O (Van Heuverswyn et al., 2006).

Zoönotic transmission of SIV to humans is believed to be due to the handling of monkey meat, that is typically consumed in Central Africa, in both the butchering process and in food preparation (Gao et al., 1994). The first cases of HIV infection probably occurred in isolated, rural communities where epidemic level spread of disease would be inhibited. The construction of roads, exploitation of the rain forest and urbanisation and migration to towns, however, likely provided the necessary conditions for a rapid spread of HIV (Anderson et al., 1991).

A Great Diversity of Strains

So far three major lineages of HIV-1 have been identified through phylogenetic analyses. By far the most common HIV-1 lineage is the HIV-1 group M strain. Within group M, strains are classified into subtypes and so far 11 primary subtypes have been identified (A1, A2, B, C, D, F1, F2, G, H, J and K). In addition there are a growing number of circulating recombinant forms. All known groups and subtypes have been found in Central Africa. Table 11.1 gives a summary of the distribution of HIV-1 group M subtypes, classified according to the *env* fragment, in the DRC, Cameroon, the CAR and Gabon, in the 1990s (Vidal et al., 2000; Morison et al., 2001; Muller-Trutwin et al., 1999; Makuwa et al., 2000). A similar diversity of strains has been found in the Republic of Congo (Bikandou et al., 2000).

In populations with high HIV prevalence where many different HIV strains are co-circulating, one can expect the emergence of recombinants. Indeed, in Cameroon it was found that more than half of the strains classified as subtype A were in fact the circulating recombinant form CRF02_AG (Morison et al., 2001; Ndongmo et al., 2006). Studies conducted in the late 1990s found that more than 25% of strains circulating in DRC and in Cameroon were isolated recombinant forms (Vidal et al., 2000; Ndongmo et al., 2006).

The diversity of strains found in Cameroon, Gabon, the Republic of Congo, DRC and CAR, is consistent with this region having the oldest HIV epidemic in the world and is unique in the world. In Rwanda and Burundi, the situation is quite different. The epidemics in these two countries are dominated by two

Table 11.1 Distribution of HIV-1 subtypes in four countries in Central Africa.

	DRC 1997 N = 247	Cameroon 1997 N = 104	CAR 1991–1997 N = 105	Gabon 1997–1998 N = 92
A*	52% (127)	86% (89)	80% (84)	49% (45)
B	0.5% (1)	–	1% (1)	2% (2)
C	7% (18)	–	1% (1)	3% (3)
D	9% (23)	4% (4)	1% (1)	10% (9)
E (now CRF01_AE)	2% (4)	2% (2)	12% (13)	–
F	4% (10)	2% (2)	–	7% (6)
G	7% (17)	5% (5)	1% (1)	1% (1)
H	7% (18)	1% (1)	2% (2)	7% (6)
J	3% (7)	–	–	–
K	3% (8)	–	–	–
Group O	–	1% (1)	–	–
?	6% (15)	–	4% (4)	22% (20)

*Classification based on the *env* fragment only, so this includes both subtype A and CRF02_AG.

HIV-1 subtypes, subtype A and C, and a minority of A/C recombinants (Gao et al., 1994; Vidal et al., 2007).

Trends in HIV Prevalence

When it became clear that HIV/AIDS could be a major public health problem in Central Africa, several initiatives were taken to study the epidemiology of HIV/AIDS in this region. From 1985 on, in several countries, regular surveys were conducted on HIV prevalence among pregnant women in order to monitor trends in HIV infection in the general population. However during the 1990s these surveillance activities became more irregular in most countries for a variety of reasons. One factor was the lack of resources to maintain the surveillance system, but in a number of countries activities were interrupted because of political upheaval and civil war, including the DRC, Rwanda, Burundi, the Republic of Congo and the CAR. As a result, data for the past 10–15 years are sparse although trends in the epidemics in Central Africa can be discerned.

Table 11.2 presents the UNAIDS estimates for 2005 of the HIV prevalence in adults in the different countries of Central Africa (UNAIDS, 2006). With the exception of Rwanda and Burundi, the general trend in Central Africa has been one of relatively stable or slowly increasing HIV prevalence in the general adult population. In urban areas of Cameroon and Gabon HIV prevalence of HIV infection in pregnant women increased between the mid 1980s and the late 1990s, but remained below 10%. Among pregnant women in Yaoundé, the capital of Cameroon, the HIV prevalence was 0.7% in 1989, 4.7% in 1996 and 5.5% in 1998 (Sam-Abbenyi et al., 1993; Mbopi Keou et al., 1998; Glynn et al., 2000). In Libreville, the capital of Gabon HIV prevalence increased from 2.1% in 1986 to 4.2% in 1998 (Delaporte et al., 1996; Makuwa et al., 2000).

Table 11.2 Recent HIV prevalence estimates in Central Africa.

	Most recent estimated adult prevalence	HIV prevalence obtained by population based survey [year]>
Burundi	3.3% [2.7–3.8%]	3.6% [2002]
Cameroon	5.4% [4.9–5.9%]	5.5% [2004]
Central African Republic	10.7% [4.5–17.2%]	
Chaad	3.5% [1.7–6.0%]	
Congo (Brazz)	5.3% [3.3–7.5%]	
DRC	3.2% [1.8–4.9%]	
Gabon	7.9% [5.1–11.5%]	
Rwanda	3.1% [2.9–3.2%]	3.0% [2005]

Source: UNAIDS: "2006 Report on the Global AIDS Epidemic".

In Kinshasa, the capital of DRC, the first survey among pregnant women was conducted in 1985 and found a prevalence of 5.9%. In 1997 the prevalence was 3.1% and in 2000 it was 4.1% (N'Galy et al., 1988; Mulanga et al., 2004; Denolf et al., 2001). This suggests that the HIV prevalence in the general population of Kinshasa has remained relatively stable for at least 15 years. Also among female sex workers in Kinshasa there does not appear to have been an increase in HIV prevalence between 1988 and 2002 (Vandepitte et al., 2007). A similar pattern of stable HIV prevalence is seen in Brazzaville, the capital of the Republic of Congo which is across the Congo River from Kinshasa (Bazabana et al., 1995). In Pointe-Noire the port city of the Republic of Congo the HIV prevalence seems to be higher than in Brazzaville, around 10% but no trend data are available. In the CAR, HIV seems to have spread faster than in neighbouring DRC, Cameroon and Congo. At the end of the 1980s the prevalence of HIV among pregnant women in Bangui was similar to what had been found in Kinshasa, around 5%, but by 2001–2002 the prevalence had increased to 15% (Matsika-Claquin et al., 2004).

Rwanda and Burundi

The epidemics in Rwanda and Burundi have run a somewhat different course. While both Rwanda and DRC were Central African countries where AIDS cases were already documented in 1983 (Van de Perre et al., 1984), in the 1980s and early 1990s HIV prevalence rates among pregnant women in Kigali, the capital of Rwanda, were much higher than in cities in the DRC and were in the same range as what was found in Kampala, Uganda. Indeed, sero-surveillance from the 1980s confirmed a severe generalised epidemic, with HIV prevalence among pregnant women increasing from 23–25% in 1989 to 26–31% in 1990 (Bucyendore et al., 1993). HIV rates of 75–88% were found among female sex workers in Kigali in 1983–1984 (Van de Perre et al., 1985). Civil unrest during the early 1990s and the genocide in 1994 resulted in massive displacement (estimated at 4 million persons), an estimated 800,000 deaths and had a devastating impact on the health infrastructure. Data obtained from Sentinal Surveillance during the 1990s are influenced by those factors which makes it difficult to interpret the extant data. Data from sentinel surveillance rounds

between 1998 and 2003, however, do suggest a declining trend in HIV prevalence. In 1998 the median prevalence of HIV infection in pregnant women in Kigali was 16.5% and in 2003 it was 13.2% (Kayirangwa et al., 2006). A national, population based survey conducted in 2005 found a 3.0% prevalence among adults (Garcia-Calleja et al., 2006).

Wide differences were also observed between urban and rural prevalence in Rwanda. In a national household survey conducted in 1986 the urban estimate was 17.8% while the rural prevalence estimate was 1.3% (Bugingo et al., 1988). HIV rates most likely peaked in the early 1990s in urban areas, with significant declines afterwards between 1990 and 2004. The rural/urban divide continues to exist until now, with rural areas experiencing a slow but consistent increase, or stable prevalence, with no signs of significant decline yet.

The HIV epidemic in Burundi is in many ways comparable to its neighbour Rwanda. Burundi also experienced an early, generalised epidemic in the 1980s. In 1991, the HIV prevalence was estimated at 18–20% in Bujumbura and 1% in rural sites (where surveillance was conducted) and in 1991/1992 the prevalence of HIV infection among pregnant women ranged from 8 to 26% (Sokal et al., 1993). Severe political unrest between 1993 and 1997 resulted in massive displacements of people and high mortality making surveillance very difficult. By 2001, HIV rates had stabilised and declined in urban areas, while a steady increase was noted in rural areas (Plan Stratégique National de Lutte contre le SIDA, République du Burundi). In 2002 a population based survey found a prevalence of around 10% in urban areas and 2.5% in rural areas (Niyongabo et al., 2005).

Armed Conflicts and HIV/AIDS Epidemics in DRC, Rwanda and Burundi

Civil unrest and war are considered circumstances that are favourable for a rapid spread of HIV infection. Civilians are exposed to groups of soldiers who are in search of sex. Levels of sexual violence increase and rape may be used as a strategy to terrorize the civilian population. War brings normal economic activities to a halt and poverty may lead women to exchange sex for money as a survival strategy. Large numbers of people are displaced and the social fabric of communities is destroyed leading to higher risk sexual behaviour.

In 1992/1993 DRC plunged into a deepening political crisis. The overthrow of the Mobutu regime in 1998 raised hopes for a new and brighter future for the Congolese population, but these hopes were soon smashed as civil war broke out in the east of the country. The central government lost control over large parts of the country and since the beginning of the 21st century DRC has been a failed state with a complete breakdown of public services, insecurity, civil conflict and deepening poverty for the majority of the population. Despite this seemingly fertile ground for a rapid expansion of the HIV epidemic in DRC, HIV prevalence appears to have remained stable, not only in Kinshasa but also in the war ravaged eastern parts of the country (Mulanga-Kabeya et al., 1998; Mulanga et al., 2004; Programme National de Lutte contre le SIDA, 1997). The reduction in purchasing power and the resulting reduction in access of men to sex workers and extramarital partners have been proposed as explanations for the stable prevalence, in addition to the reduced mobility of people (Mulanga et al., 2004).

In 1994, Rwanda was the scene of a genocide in which an estimated 800,000 Tutsi and moderate Hutus were killed within a time span of three months. Thousands of women and girls were raped and hundreds of thousands of Tutsis and Hutus fled their homes (Donovan, 2002). A survey conducted a few years after the genocide, found that the large gap in HIV prevalence between urban and rural areas that existed in Rwanda before the genocide had substantially narrowed to 12.5% in urban areas versus 10.8% in rural areas (Programme National de Lutte contre le SIDA). Massive displacement of people would have been responsible for this. The findings of this survey however, were not confirmed by results from sentinel surveillance rounds among pregnant women, conducted between 1998 and 2003. In 1998, the median HIV prevalence among pregnant women was 16.5% in Kigali, 10.2% in other urban areas and 3.3% in rural areas (Kayirangwa et al., 2006).

Civil war started in Burundi in 1993 and by 2005, 250,000 people had been killed and more than a million displaced. As in DRC there is no evidence for an enhanced spread of HIV infection since the civil war broke out. A population based study conducted in 2002, found an overall prevalence in the age group above 12 years of 3.6% (Garcia-Calleja et al., 2006).

HIV surveillance activities were hampered by the civil wars in the DRC, Rwanda and Burundi. However the few data from sentinel surveillance rounds that are available and the data from population based surveys that have been conducted in recent years, provide evidence that political upheaval and civil war have not led to explosive epidemics in these three countries. This is contrary to common expectations. Likewise the wars in southern Sudan, Sierra Leone and Somalia seem not to have led to major HIV epidemics, suggesting that we need to revise our thinking about the effects of conflicts and social upheaval on the course of HIV epidemics (Spiegel et al., 2007).

What Explains the Differences in HIV Spread Between Different Countries in Central Africa and Their Neighbouring Countries?

HIV prevalence in urban populations in Cameroon, Gabon, the Republic of Congo and the DRC has increased since the mid-1980s but this increase was relatively slow and did not bear any resemblance to the explosive spread of HIV in some neighbouring countries such as Uganda, Rwanda and Zambia. The most striking contrast was between towns in the Shaba Province (formerly Katanga) in the south-east of DRC and towns in neighbouring Zambia. Lubumbashi, the capital of DRC's Shaba Province, is a mere 200 km from Ndola, the largest town in the Copperbelt Province of Zambia. Both towns are in mining areas and the border between DRC and Zambia has not presented a major barrier to the movement of people. Yet, in 1989/1990, HIV prevalence in cities in the Shaba Province was well below 5%, whereas in urban areas in Zambia it was over 20% (Magazani et al., 1993). Likewise, at the end of the 1980s the HIV prevalence among pregnant women in Kigali was around 30%, whereas in Kinshasa it was below 10%.

A multicentre study conducted in the 1990s explored this issue in four cities in sub-Saharan Africa with contrasting HIV prevalence, including Yaoundé in Cameroon, Cotonou in Benin, Ndola in Zambia and Kisumu in Kenya and offered some insights into regional differences in HIV rates (Buvé, Caraël et al.,

2001a, b). Differences in sexual behaviour could not explain the differences in HIV prevalence. For example, high risk sexual behaviour appeared to be most common in Yaoundé, one of the cities with relatively low HIV prevalence (Ferry et al., 2001). The study concluded that any differences in sexual behaviour were outweighed by differences in prevalence of male circumcision and HSV-2 infection (Buvé et al., 2001b). The important roles that male circumcision and HSV-2 infection play in determining the course of HIV epidemics in sub-Saharan Africa, has recently been explored in mathematical models (Orroth et al., 2007; Freeman et al., 2007). The fact that in West and Central Africa most men are circumcised, may explain to a large degree the relatively slow spread of HIV, notwithstanding high rates of partner change and other risky sexual behaviours.

Responding to the Epidemic in the DRC

The DRC was one of the first countries in Africa where the HIV/AIDS epidemic was recognized publicly. The epidemic in the DRC has been particularly well studied and provides a useful, in depth example of how HIV/AIDS has emerged and progressed in the Central African region. The first AIDS cases were confirmed in 1983 in Kinshasa at the General Hospital, then known as Mama Yemo (Piot et al., 1984) and led to the creation of Project SIDA, a Congolese-American-Belgian research program (Cohen, 1997). This program shed light on the epidemiology of the emerging epidemic and triggered the initiation of the first HIV prevention and care activities. As part of the research program, the first drop in centre for sex workers was set up in 1988 offering peer education, condom promotion and sexually transmitted infection (STI) care. It showed that working with this population of vulnerable and marginalised women was not only feasible, but also effective in slowing the spread of HIV and STIs among this group (Laga et al., 1994). During the same period, Population Services International (PSI) initiated one of its first condom social marketing campaigns on the African continent. Information campaigns were launched in the national media in 1987, and Franco, the most famous Congolese singer at the time, wrote a popular song about AIDS that received widespread playtime on radio, raising public awareness. Authorities responded to these initiatives by creating the national AIDS program (PNLS) within the Ministry of Health. These activities placed Congo, and in particular the city of Kinshasa, at the forefront of fighting the HIV/AIDS epidemic in the 1980s in Africa.

It is plausible that actions by both nongovernmental organizations (NGOs) and the government contributed to the low rates of HIV infection in Kinshasa in the 1980s although this is difficult to confirm, given the multiple factors involved in the spread of HIV. In 1991, Project SIDA suddenly ended, as a result of civil unrest. From 1991 to 1999, the country remained unstable, and HIV prevention and control activities were reduced to a minimum. Bilateral and multilateral cooperation were put on hold although local and international NGOs assured some basic services. Remarkably, the HIV rates in Kinshasa remained low and stable throughout this period, and even in 2006 the prevalence is estimated at 2–3% in pregnant women. Data from the rest of the country are scarce, but indicate the absence of an explosive spread of disease (Figure 11.1).

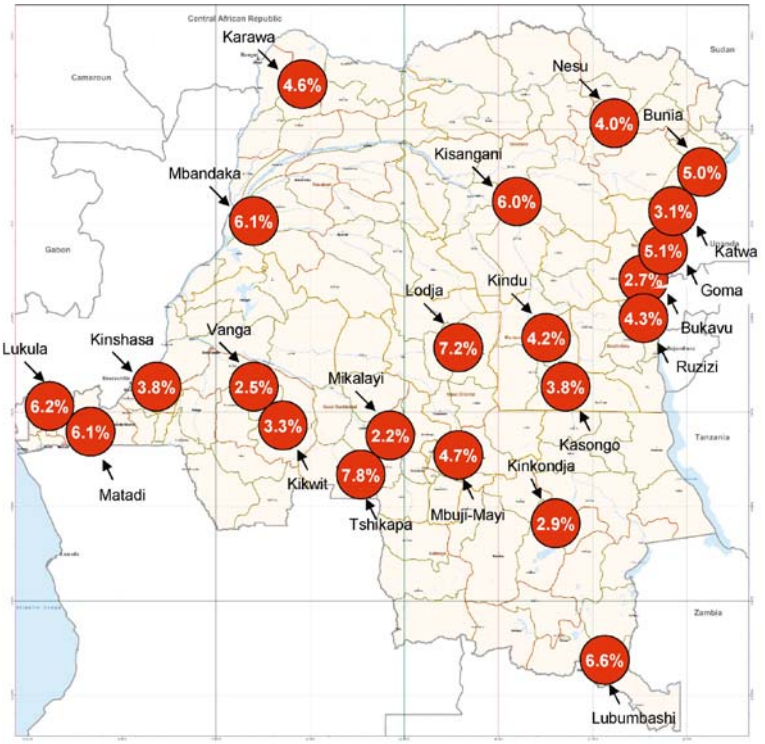

Figure 11.1 HIV prevalence by geographic area in DRC, obtained by sentinel surveillance in pregnant women 2005.
Source: Programme National de Lutte contre le SIDA, DRC.

Since 2000 international donors have been returning to DRC, and more recently significant funding was made available through the World Bank's MAP program and the Global Fund to fight AIDS, Tuberculosis and Malaria. As with many other African countries the focus shifted from prevention to treatment, and the number of AIDS patients receiving antiretroviral treatment (ART) increased from 9,096 in 2005 to 17,561 in 2006, representing a coverage increase from 5.6 to 20.7% of the estimated eligible AIDS patients (Programme national de Lutte contre le SIDA, 2006). Prevention of mother to child transmission (PMTCT) was introduced in 2002, but is mostly limited to urban areas, representing a national coverage of less than 5%.

Due to the state failure, civil society organisations had to compensate or replace the state in domains like health and education. Congolese grass roots organisations like Amo-Congo and Fondation Femmes Plus have been playing an essential role in HIV testing, ARV provision, as well as advocacy and income generating activities. International NGOs like PSI, Family Health International and Medecins Sans Frontiers have been instrumental in scaling up ARV treatment programs, Voluntary Counselling and Testing programs and condom promotion.

In recent years, leadership from the president has become more visible. A multisectoral response has been encouraged, and with money from the World Bank, the National Multisectoral AIDS control program, which reports

directly to the office of the president, was created. The PNLS and increasingly the National Multi-Sector Program against HIV/AIDS (PNMLS) have been decentralised with coordination units now in all 11 provinces. Private sector involvement in AIDS control has become an important component of DRC's multisectoral response. For example, the brewery Bralima (Heineken) initiated HIV/AIDS related activities in 1998 and is now providing PMTCT and ARV to all their employees who need it.

Prevention Efforts in Neighbor States

Prevention efforts in other states in the region (Burundi, Cameroon, CAR, Republic of Congo, Gabon and Rwanda), have been characterized by broad population based programs which are best suited to epidemics where the general heterosexual population is the most affected group. These kinds of efforts, however, can be challenging in societies disrupted by civil conflict, where large percentages of the population live in rural areas and where at least one fifth and sometimes nearly one half of the population is illiterate (CIA, 2007). Examples of broad prevention efforts which have had some measure of success within these societal contexts are reviewed in this section.

Governmental Response

Despite the many challenges faced by governments in this region, some have been able to support the implementation of prevention programs. In Burundi, an early national response (1997/1998) focused on prevention and ongoing political commitment let to the formation in 2002 of an AIDS ministry and a national AIDS Control Council (UNAIDS, 2007). Civil societies are also well established and organized in Burundi with the Burundian Alliance for AIDS Control overseeing 150 NGOs. Organizations such as the Association for Young People and the Network of Women's Association's for AIDS control are located throughout the country and are well known (UNAIDS, 2007). In 2006, governmental and civil society supported many prevention activities including 972 Stop AIDS clubs which provided HIV/AIDS information and education to 23,354 school children, and supported efforts aimed at target groups such as young people and military personnel and improving the distribution of condoms (UNAIDS, 2007).

The Rwandan government was also instrumental in that country's early response to the HIV/AIDS epidemic. The government's response was coordinated by the Ministry of Health and included: establishment of a blood donor screening programme, Information, Education and Communication (IEC) activities using radio and public educators and sero-surveillance activities. Responding to the epidemic has been incorporated into all sectors of the government and increasing access to a comprehensive prevention package was a priority for 2007 (UNAIDS, 2007).

The government of Cameroon has also developed structured responses to the epidemic. Cameroon's National Strategic Plan 2006–2010 which was approved by all partners has a series of ambitious goals including cutting the cost of HIV

testing by almost half and increasing the number of mobile testing units. HIV control has also been included as a priority programme in Cameroon's Poverty Reduction Strategy Paper (UNAIDS, 2007).

Voluntary Counselling and Testing

Many barriers to HIV testing remain in sub-Saharan Africa. Limited access to free testing, worries about stigma and discrimination, a lack of qualified counsellors and difficulties obtaining rapid results have all contributed to exceedingly low percentages of individuals being tested (12%) and being aware of their status (10%) (Matovu & Makumbi, 2007). Despite these barriers, some countries in the Central Africa region are making progress in expanding access to Voluntary Counseling and Testing (VCT). In Burundi, the number and quality of VCT centers continues to improve. In 2003, there were 80 VCT centers and by 2006 there were 135 VCT centers with more than 70,000 people tested that year (UNAIDS, 2007). Adoption of norms and standards and the provision of training for over 300 service providers has increased the quality of care provided at these centers as well (UNAIDS, 2007). Access to VCT is also increasing in Rwanda. In 2006, a total of 251 health centers were able to provide VCT (UNAIDS, 2007). In Cameroon, there are now VCT centers in every province. These centers are linked to treatment centers and have involved people living with HIV/AIDS (PLWHA) as counsellors and advisors which has encouraged their acceptability (Bassirou et al., 2004; Zekeng et al., 2004).

In the CAR and the Republic of Congo, where there is less centralized organization of prevention activities, innovative approaches to providing VCT have had some success. In Bangui, in the CAR, the French NGO Médicins du Monde provided technical assistance to an established STD center to expand its services to provide anonymous HIV counselling and testing. The European Union provided support for these activities which allowed the center to charge a relatively minimal fee for testing. Free testing provided in conjunction with annual AIDS day in the CAR was particularly successful. Incorporating anonymous VCT into an existing health venue increased its acceptability and demonstrated that this approach to providing VCT can be a practical one in challenging environments (Grésenguet et al., 2002).

In the Republic of Congo and also Rwanda, Burundi, and as mentioned earlier in the DRC, Heineken International has implemented a VCT program for its employees and their families and has linked testing to the provision of ART for anyone who tests positive (IFC Against AIDS, 2003). By providing prevention services including not only VCT but also STI detection and treatment, prevention of mother to child transmission (PTMCT) and condom distribution in the context of provision of care, Heineken has seen a significant increase in uptake of VCT by employees and their spouses (Rijckborst et al., 2004). Through this effort, Heineken has demonstrated that successful prevention and care can occur in the absence of a stable medical infrastructure (Rijckborst et al., 2004).

Prevention of Mother to Child Transmission

For most countries in this region, barely 1% of HIV exposed newborns had received ART prophylaxis in 2004 (UNICEF, 2005). While the rates in the

Republic of Congo (3.7%) and Rwanda (12.3%) were higher, the region as a whole remained severely challenged in its ability to provide preventive care for its infants. Fundamental difficulties in providing this care still remain. Limited antenatal care, poor health infrastructure, a dearth of personnel and supplies and stigma associated with seeking care still thwart successful interventions (Druce & Nolan, 2007). At the same time, in the last several years, there have been examples of programs which have had appreciable success in PTMCT.

One program, in Cameroon, offered PTMCT as a routine and free part of antenatal care, provided same day results and pre and post test counselling given by the same counsellor (Welty et al., 2005). The program which was initiated in 2000 at two hospitals in the Northwest Province of Cameroon was operating in 115 health facilities in 6 of Cameroon's 10 provinces four years later. In an extension of this program, birth attendants from 20 rural villages were also trained in PMTCT. The birth attendants were able to test 99.1% of the women they encountered and to provide 85.7% of the HIV exposed newborns they delivered with single dose nevirapine prophylaxis (Wanyu et al., 2007). Even with these successes, many challenges remain to this program including having adequate supplies and achieving adequate prevention in terms of breastfeeding (Wanyu et al., 2007). Throughout Cameroon, the number of sites implementing PTMCT programs has grown from 3 in 2000, to 420 in 2005 (Tsague, 2005). Support and commitment from the Ministry of Public Health and the religious private sector and adopting a "bottom-up", "district approach" have been essential elements in this growth. Despite this progress, however, it is estimated that only 4.2% of pregnant women in Cameroon receive treatment to reduce mother-to-child transmission (UNAIDS, 2007).

Support from the central government and NGOs has also fostered progress in PTMCT in Burundi and Rwanda. In Burundi, a national policy calling for the extension and decentralization of PTMCT has meant that 18 sites are now providing PMTCT care and an increasing number of HIV positive women and infants are receiving care (UNAIDS, 2007). Rwanda's strong political commitment to PTMCT has been strengthened by several specific efforts. For example, Family Health International's (FHI) support of PTMCT at eight health centers was associated with high levels of accepted testing (80%) and receiving test results (93%) and high levels of HIV positive women receiving nevirapine at the start of labor (91%), giving birth in a medical setting (74%) and choosing exclusive breastfeeding (89%) which limits the possibility of transmission (Bangendanye, Ngabonziza & Murray, 2004). Researchers observed that low maternity costs encourage more women to choose medical centers which allowed for much greater monitoring of all PTMCT efforts and greater overall nutritional care for women and their babies (Bangendanye et al., 2004). A PEPFAR funded initiative has encouraged men to accompany their pregnant partners on PTMCT visits so that they can also receive testing and counselling. In 2002, the first year of the program, only 3% of men participated, but by the end of the third quarter of 2006, male involvement had increased to 74% (USAID, 2006). Rwanda's ongoing efforts have led to an improvement in PTMCT coverage, with PTMCT services available at over half of all facilities and two thirds of women who have tested HIV positive receiving preventive prophylaxis (Druce & Nolan, 2007).

While countries can monitor the provision of preventive prophylaxis at the time of delivery, breastfeeding practices are more difficult to measure and control. Using infant formula is often impractical and even dangerous in situations where access to clean water is unreliable. Cultural norms may also make it difficult for women to choose formula to feed their newborns. Following recommended practices for breastfeeding and early weaning which limit the transmission of HIV can also be culturally or practically difficult. Addressing these issues in countries in Central Africa remains a major task.

Access to Care

Between 2003 and 2006, the prices of ART for most "first line" medications decreased by between 37 and 53% in low- and middle- income countries (WHO, 2007). For most low-income countries this meant that in 2006, the average cost for first-line treatment ranged from USD 123 per person per year to USD 493 per person per year (WHO, 2007). In countries where many are living on less than USD 2 a day and where the ability of the government to subsidize care is extremely limited, even these very low costs can be simply too high. Access to treatment is also impacted by the availability of established health services. Provision of treatment has been easier to accomplish in urban areas where existing health infrastructure may be better equipped to provide ART than in rural areas (WHO, 2007). Issues of cost and infrastructure underlie efforts to provide ART in Central Africa, where estimated coverage rates in Burundi, Cameroon, CAR, the Republic of Congo and Gabon range from a high of 35% (Gabon) to a low of 6% (CAR) (WHO, 2007). Rwanda whose estimated coverage rate of 72% is an exception in the region is discussed in detail in the box below.

Rwanda's HIV Treatment Program: Signs of Hope (Kathryn Anastos)

Although Rwanda is most often discussed internationally in the context of its 1994 genocide, which left a deeply traumatized population, its current commitment to economic development, education and health care make it an important example of the successes that can be achieved in resource-limited settings by developing an infrastructure for delivery of services in a planned, systematic and logical manner. Healthcare services are a critical component of Rwanda's integrated approach to overall development, in which healthcare is a part of a larger whole that includes improving the quality and availability of education at all levels, investing in information and communication technology, and fostering economic development. The government of Rwanda has developed its programs for HIV/AIDS services with careful attention to policies that will promote success, with an explicit commitment to using resources efficiently to improve the health of HIV-infected Rwandans, and where possible, create an infrastructure for HIV services that also improves the public health infrastructure generally. Rwanda was the recipient of the 2005 PEPFAR commendation for excellence in implementing programs to deliver antiretroviral therapy effectively—meaning, a sustainable set of services resulting in improvements in AIDS-related morbidity and mortality. The World Bank has reported that the median life expectancy in Rwanda increased from just less than 40 years in 2001 to 52 years in 2007—an improvement in public health that is rarely achieved.

There are several keys to this success—not least the government's focus on improving the lives of Rwandans, including a commitment to provide to all HIV-infected Rwandans the full spectrum of care, including provision of medically indicated antiretroviral treatment (ART). As in many African countries, the

rate-limiting steps in achieving this goal quickly are the development of the infrastructure for the effective delivery of healthcare services, and increasing the size and scope of the healthcare workforce, especially physicians. Thus, simultaneous with building the health care infrastructure, the government is expanding and improving medical education, and developing new educational initiatives targeting the leading causes of mortality, for example public university-level training of nurse-midwives to impact favorably on the high maternal mortality rate.

Prevalence of HIV infection in Rwanda is 3 to 5%, with higher rates in urban areas and some specific provinces, and in women. As in most of sub-Saharan Africa, women are more likely than men to seek HIV-testing and to access treatment services. Nearly all HIV services in Rwanda, both prevention and treatment, are developed with the guidance of the public health system (the exception are small private clinics), which has implemented several mechanisms for optimizing the use of resources. The government maintains strict control over the allocation of HIV-related aid dollars to prevent duplication, ensure broad reach across the country rather than a concentration of resources in a few areas, and optimize the public health benefit. The approach is evidence-based, including evaluation of current practice for both medical effectiveness and cost-effectiveness. No provider is able to prescribe a suboptimal regimen, and all patients initiating ART are required to attend a 2 to 3-day education program, and must identify a "buddy" who attends the training with them. Thus for both patient and provider some monitoring mechanisms are in place, designed to foster both individual and population-based effectiveness.

Special Challenges in Post-conflict Settings

The Rwandan genocide is one of the most commonly cited, and indeed one of the worst, examples of rape and other extreme forms of genital violation specifically wielded against women as a weapon of war. In the 100-day 1994 genocide, an estimated 250,000 Rwandan women experienced multiple episodes of brutal rape, with HIV infection planned by the perpetrators and deliberately used as a genocidal tool ("slow poison"). It was the International Criminal Tribunal for Rwanda that revolutionized the legal treatment of sexual violence by recognizing rape as an instrument of war and a crime against humanity. However, in 2007, the groups who perpetrated these rapes continue their crimes in the eastern Democratic Republic of the Congo, along the Rwandan border.

The prevalence of HIV infection is higher in women survivors than in the country as a whole, and their needs are far broader. They experience a high prevalence, as high as 50%, of depression and post-traumatic stress (PTS) symptoms, or both, and HIV-infection itself is experienced as a traumatic event. Many avoid public settings for several reasons, including fear of encountering the perpetrator(s) of their rape(s). Among those with PTSD, the most common PTS symptom is reliving of the traumatic events, and can be precipitated by entering some public settings. The effects of these conditions on the survivors' lives are profound, and some, even many, women avoid receiving necessary healthcare services for HIV-infection.

Thus in addition to the already large challenge of delivering needed care to the general population with very limited resources, there is an additional challenge in post-conflict settings: to ensure care to those too traumatized to engage in the general healthcare system. One mechanism that is working in Rwanda is the placement of services in community-based settings that feel safe to the survivors, for example grassroots associations of genocide "widows". Of interest, there is some evidence that treating their HIV-infection decreases the women's PTS and depressive symptoms. There is no evidence that their adherence to therapy is less. In fact, in nearly all available studies, self-reported adherence to ART among treated Rwandans, both women and men, and including genocide survivors, is close to 100%.

However, in all resource-limited settings, the most effective pharmacologic treatments for the mental health conditions resulting from trauma, for example selective serotonin reuptake inhibitors, are not available or are available only in rare

circumstances. For post-conflict settings, attention should be paid to funding mechanisms that will foster treatment of PTSD and depression.

On a broader scale, Rwanda has directly addressed the issue of gender inequality through its constitution and explicit policies in its legal system. As part of their commitment to economic development and "never again"—preventing future genocide—Rwanda has integrated women into positions of power and authority, with the belief that having women integrated more fully into political life can prevent the extremism that allowed the genocide. One example is that Rwanda has the highest proportion in the world of women in parliament (48%) and all decision-making organs must have a minimum representation of 30% women. However, one can assume that it will take some time for this to trickle down effectively to the day to day lives of all women, especially deep in the country-side.

In the midst of its struggle to overcome the legacy of a brutal genocide, Rwanda's mission-driven, non-corrupt government is developing one of the best HIV care delivery systems in the world, and is addressing the additional challenge of a traumatized population in general, and a large group of severely traumatized women victims of genocidal rape. We have much to learn from this example.

Other countries have also been able to make strides in providing care. In Burundi, access to ART is increasing rapidly. In 2006, more than 7,000 people received ART (UNAIDS, 2007) for an estimated coverage rate of 26% (WHO, 2007). Burundi also has more women on ART than would be expected by the percentage of individuals who are infected (WHO, 2007). Burundi's success may be attributed to a home based treatment and care programme which has improved access to care by bringing treatment, care and support activities into affected communities (IRIN, 2007).

Cameroon, which also has more women on ART than might be expected by the percentage of infected individuals overall (WHO, 2007) also has strong government commitment to providing widespread access to ART. Its 2004/2005 multisectoral plan for decentralizing the provision of ART has been hampered by weaknesses in health system infrastructure and personnel, particularly at the district level (IRIN, 2007). Problems with procuring and managing supplies of drugs and diagnostics have also been identified (IRIN, 2007). Technical assistance with these problems along with additional and sustained financial resources are needed to improve Cameroon's current estimated coverage rate of 25% (WHO, 2007). Similar problems plague CAR where years of political instability have had a critical impact on the basic health infrastructure (WHO, 2005) and the Republic of Congo where treatment and care are constrained by severely limited services, a shortage of trained staff, and an insufficient legal framework and funding mechanism (UNAIDS, 2007).

Higher estimated coverage in Gabon (35%) may be the result of the commitment of Gabon's head of state and the fact that the government's principal HIV/AIDS focus has been on providing care for PLWHA (UNAIDS, 2007). An annually renewable Treatment Solidarity Fund and the establishment of outpatient treatment centres in each of the country's provinces has also made the extension of treatment and care possible (UNAIDS, 2007).

Access to care in the Central African states underscores again the importance of political will and the basic resources of infrastructure, trained personnel

and secure, ongoing funding. While many of these countries have made impressive gains in coverage despite these challenges, scaling up to universal coverage will only be possible when these issues have been addressed.

Conclusion

Countries in the central African region host some of the oldest HIV epidemics on the African continent, indeed in the world. These epidemics which feature multiple HIV subtypes are an ideal focus for research on the epidemiology of the epidemic as well as potential approaches for vaccinating against it. While there are intriguing vagaries in the spread of this epidemic, the result for this region, so burdened by other miseries, has been devastating. In every instance the generalized epidemics of the central African region have targeted the heterosexual population in the prime of their reproductive years. Women are disproportionately infected and their children remain at tremendous risk. The complexities of the epidemic present nearly insurmountable challenges for barely established political systems. The requirements of surveillance systems, prevention programs and treatment delivery are inconsistent with existing health and information networks. At the same time, the costs required for adequately assessing and addressing generalized epidemics are difficult to fathom in countries where subsistence is still a struggle. Despite all of this, however, countries in this region are, albeit to different degrees, struggling to mount an effective response to the epidemic. The success of these efforts will require substantial political, technical and economic support.

References

Anderson, R.M., May, R.M., Boily, M.C., Garnett, G.P., & Rowley, J.T. (1991). The spread of HIV-1 in Africa: sexual contact patterns and the predicted demographic impact of AIDS. *Nature, 352*, 581–9.

Bangendanye, L., Ngabonziza, M., & Murray, D. (2004). Increasing the success of PMTCT programs: an experience from Rwanda. *International Conference on AIDS*, July 11–16;15: abstract no. ThPeB7101.

Bassirou, B, Tsague, L., Menyeng, L., Eyong, C., Engozo'o, A., Bungo, J.P., Koulla, S., Tardy, M., Mbitongui, M., Totouom, A., & Zekeng, L. (2004). Synergy between VCT and HAART availability across Cameroon success and challenges. *International Conference on AIDS*, July 11–16;15: abstract no. TuPeE5386.

Bazabana, M., Loukaka, J.C., & M'Pele, P. (1995). Evolution de la sérosurveillance de l'infection à VIH chez les femmes enceintes au Congo de 1990 à 1993. IXth International Conference on AIDS and STD in Africa. Kampala, Uganda, 10–14 December 1995. Poster MoC497.

Bikandou, B., Takehisa, J., Mboudjeka, I., Ido, E., Kuwata, T., Miyazaki, Y., Moriyama, H., Harada, Y., Taniguchi, Y., Ichimura, H., Ikeda, M., Ndolo, P.J., Nzoukoudi, M.Y., M'Vouenze, R., M'Pandi, M., Parra, H.J., M'Pele, P., & Hayami, M. (2000). Genetic subtypes of HIV type 1 in Republic of Congo. *AIDS Research and Human Retroviruses Journal, 16*, 613–9.

Bucyendore, A., Van de Perre, P., Karita, E., Nziyumvira, A., Sow, I., & Fox, E. (1993). Estimating the seroincidence of HIV-1 in the general adult population in Kigali, Rwanda. *AIDS, 7*, 275–7.

Bugingo, G., Ntilivamunda, A., Nzaramba, D., et al. Nog auteurs toevoegen (1988). Etude sur la séropositivité liée à l'infection au virus de l'immunodéficience humaine au Rwanda. *Revue Médicale Rwandaise, 20*, 37–42.

Buvé, A., Caraël, M., Hayes, R.J., Auvert, B., Ferry, B., Robinson, N.J., Anagonou, S., Kanhonou, L., Laourou, M., Abega, S., Akam, E., Zekeng, L., Chege, J., Kahindo, M., Rutenberg, N., Kaona, F., Musonda, R., Sukwa, T., Morison, L., Weiss, H.A., & Laga, M. (2001a). Multicentre study on factors determining differences in rate of spread of HIV in sub-Saharan Africa: methods and prevalence of HIV infection. *AIDS, supplement 4*, S5–S14.

Buvé, A., Caraël, M., Hayes, R.J., Auvert, B., Ferry, B., Robinson, N.J., Anagonou, S., Kanhonou, L., Laourou, M., Abega, S., Akam, E., Zekeng, L., Chege, J., Kahindo, M., Rutenberg, N., Kaona, F., Musonda, R., Sukwa, T., Morison, L., Weiss, H.A., & Laga, M. (2001b). Multicentre study on factors determining differences in rate of spread of HIV in sub-Saharan Africa: summary and conclusions. *AIDS, supplement 4*, S127–S131.

Central Intelligence Agency (2007). CIA- The World Factbook (Accessed December 30, 2007). https://www.cia/gov/library/publications/the-world-factbook/

Chen, Z., Telfier, P., Gettie, A., Reed, P., Zhang, L., Ho, D.D., & Marx P.A. (1996). Genetic characterization of new West African simian immunodeficiency virus SIVsm: geographic clustering of household-derived SIV strains with human immunodeficiency virus type 2 subtypes and genetically diverse viruses from a single feral sooty mangabey troop. *The Journal of Virology, 70*, 3617–27.

Clumeck, N., Mascart-Lemone, F., De Maubeuge, J., Brenez, D., & Marcelis, L. (1983). Acquired immune deficiency syndrome in black Africans. *Lancet, 1*, 642.

Clumeck, N., Sonnet, J., Taelman, H., Mascart-Lemone, F., De Bruyere, M., Vandeperre, P., Dasnoy, J., Marcelis, L., Lamy, M., & Jonas, C. (1984). Acquired immunodeficiency syndrome in African patients. *New England Journal of Medicine, 310, 8*, 492–7.

Cohen, J. (1997). The rise and fall of Project SIDA. *Science, 278, 5343*, 1565–8.

Delaporte, E., Janssens, W., Peeters, M., Buvé, A., Dibanga, G., Perret, J.L., Ditsambou, V., Mba, J.R., Courbot, M.C., Georges, A., Bourgeois, A., Samb, B., Henzel, D., Heyndrickx, L., Fransen, K., van der Groen, G., & Larouze, B. (1996). Epidemiological and molecular characteristics of HIV infection in Gabon, 1986–1994. *AIDS, 10, 8*, 903–10.

Denolf, D., Musongela, J.P., Nzila, N., Tahiri, M., & Colebunders, R. (2001). The HIV epidemic in Kinshasa, Democratic Republic of Congo. *International Journal of STD and AIDS, 12*, 832.

Donovan, P. (2002). Rape and HIV/AIDS in Rwanda. *Lancet, 360*, supplement, S17–8.

Druce, N., & Nolan, A. (2007). Seizing the big missed opportunity: Linking HIV and maternity care services in Sub-Saharan Africa. *Reproductive Health Matters, 15*, 190–201.

Ferry, B., Carael, M., Buvé, A., Auvert, B., Laourou, M., Kanhonou, L., de Loenzien, M., Akam, E., Chege, J., & Kaona, F. (2001). Comparison of key parameters of sexual behaviour in four African urban populations with different levels of HIV infection. *AIDS*, supplement *4*, S41–S50.

Freeman, E.E., Orroth, K.K., White, R.G., Glynn, J.R., Bakker, R., Boily, M.C., Habbema, D., Buvé, A., & Hayes, R. (2007). Proportion of new HIV infections attributable to HSV- 2 increases over time: simulations of the changing role of sexually transmitted infections in sub-Saharan African HIV epidemics. *Sexually Transmitted Infections, 83*, i17–i24.

Gao, F., Yue, L., Craig, S., Thornton, C.L., Robertson, D.L., McCutchan, F.E., Bradac, J.A., Sharp, P.M., & Hahn, B.H. (1994). Genetic variation of HIV type 1 in four World Health Organization-sponsored vaccine evaluation sites: generation of functional

envelope (glycoprotein 160) clones representative of sequence subtypes A, B, C, and E. WHO Network for HIV Isolation and Characterization. *AIDS Research and Human Retroviruses Journal, 10*, 1359–68.

Garcia-Calleja, J.M., Gouw, E., & Ghys, P.D. (2006). National population based HIV prevalence surveys in sub-Saharan Africa: results and implications for HIV and AIDS estimates. *Sexually Transmitted Infections, 82*, supplement *3*, iii64–iii70.

Glynn, J.R., Buvé, A., Caraël, M., Kahindo, M., Macauley, I.B., Musonda, R.M., Jungmann, E., Tembo, F., & Zekeng, L. (2000). Decreased fertility among HIV-1 infected women attending antenatal clinics in three African cities. *Journal of Acquired Immune Deficiency Syndrome, 25, 4*, 345–52.

Gottlieb, M.S., Schroff, R., Schanker, H.M., Weisman, J.D., Fan, P.T., Wolf, R.A., & Saxon, A. (1981). *Pneumocystic carinii* pneumonia and mucosal candidiasis in previously healthy homosexual men. Evidence of a new acquired cellular immunodeficiency. *New England Journal of Medicine, 305*, 1425–1431.

Grésenguet, G., Séhonou, J., Bassirou, B., de Dieu Longo, J., Malkin, J., Brogan, T., & Belec, L. (2002). Voluntary HIV counseling and testing: Experience among the sexually active population in Bangui, Central African Republic. *Journal of Acquired Immune Deficiency Syndrome, 31*, 106–114.

IFC Against AIDS 2003. Congo Brazza. (Accessed December 28, 2007). http://www.ifc.org/ifcext/aids.nsf/AttachmentsByTitle/Congo+Brazza/$FILE/Congo+Brazza.doc

IRIN (2007). Country Profile: Burundi, Cameroon. (Accessed December 30, 2007). http://www.plusnews.org/country-profile.aspx

Kayirangwa, E., Hanson, J., Munyakazi, L., & Kabeja, A. (2006). Current trends in Rwanda's HIV/AIDS epidemic. *Sexually Transmitted Infections, 82*, supplement *1*, i27–31.

Laga, M., Alary, M., Nzila, N., Manoka, A.T., Tuliza, M., Behets, F., Goeman, J., St Louis, M., & Piot, P. (1994). Condom promotion, sexually transmitted diseases treatment, and declining incidence of HIV-1 infection in female Zairian sex workers. *Lancet, 344*, 246–8.

Magazani, K., Laleman, G., Perriens, J.H., Kizonde, K., Mukendi, K., Mpungu, M., Badibanga, N., & Piot, P. (1993). Low and stable HIV seroprevalence in pregnant women in Shaba province, Zaire. *Journal of Acquired Immune Deficiency Syndrome, 6*, 419–23.

Makuwa, M., Souquiere, S., Apetrei, C., Tevi-Benissan, C., Bedjabaga, I., & Simon, F. (2000). HIV prevalence and strain diversity in Gabon: the end of a paradox. *AIDS, 14*, 1275–6.

Matovu, J.K.B., & Makumbi, F.E. (2007). Expanding access to voluntary HIV counselling and testing in sub-Saharan Africa: alternative approaches for improving uptake, 2001–2007. *Tropical Medicine and International Health, 12*, 1315–1322.

Matsika-Claquin, M.D., Massanga, M., Menard, D., Mazi-Nzapako, J., Tenegbia, J.P., Mandeng, M.J., Willybiro-Sacko, J., Fontanet, A., & Talarmin, A. (2004). HIV epidemic in Central African Republic: high prevalence rates in both rural and urban areas. *Journal of Medical Virology, 72, 3*, 358–62.

Mbopi Keou, F.X., Mbu, R., Mauclere, P., Andela, A., Tetanye, E., Leke, R., Chaouat, G., Barre-Sinoussi, F., Martin, P., & Belec, L. (1998). Antenatal HIV prevalence in Yaounde, Cameroon. *International Journal of STD and AIDS, 9*, 400–2.

Morison, L., Buvé, A., Zekeng, L., Heyndrickx, L., Anagonou, S., Musonda, R., Kahindo, M., Weiss, H.A., Hayes, R.J., Laga, M., Janssens, W., & Van der Groen, G. (2001). HIV-1 Subtypes and the HIV Epidemics in four cities in sub-Saharan Africa. *AIDS*, supplement *4*, S109–16.

Mulanga-Kabeya, C., Nzilambi, N., Edidi, B., Minlangu, M., Tshimpaka, T., Kambembo, L., Atibu, L., Mama, N., Ilunga, W., Sema, H., Tshimanga, K., Bongo,

B., Peeters, M., & Delaporte, E. (1998). Evidence of stable HIV seroprevalences in selected populations in the Democratic Republic of the Congo. *AIDS, 12*, 905–10.

Mulanga, C., Bazepeo, S.E., Mwamba, J.K., Butel, C., Tshimpaka, J.W., Kashi, M., Lepira, F., Caraël, M., Peeters, M., & Delaporte, E. (2004). Political and socioeconomic instability: how does it affect HIV? A case study in the Democratic Republic of Congo. *AIDS, 18*, 832–4.

Muller-Trutwin, M.C., Chaix, M.L., Letourneur, F., Begaud, E., Beaumont, D., Deslandres, A., You, B., Morvan, J., Mathiot, C., Barre-Sinoussi, F., & Saragosti, S. (1999). Increase of HIV-1 subtype A in Central African Republic. *Journal of Acquired Immune Deficiency Syndrome, 21*, 164–71.

Nahmias, A.J., Weiss, J., Yao, X., Lee, F., Kodsi, R., Schanfield, M., Matthews, T., Bolognesi, D., Durack, D., & Motulsky, A. (1986). Evidence for human infection with HTLV III/LAV-like virus in Central Africa. *Lancet, 2*, 1279–1280.

Nationwide community-based serological survey of HIV-1 and other human retrovirus infections in a central African country. Rwandan HIV Seroprevalence Study Group. (1989). *Lancet, 1*, 941–3.

Ndongmo, C.B., Pieniazek, D., Holberg-Petersen, M., Holm-Hansen, C., Zekeng, L., Jeansson, S.L., Kaptue, L., & Kalish, M.L. (2006). HIV genetic diversity in Cameroon: possible public health importance. *AIDS Research and Human Retroviruses Journal, 22*, 812–6.

N'Galy, B., Ryder, R., Francis, H. et al. (1988). IVth International Conference on AIDS. Stockholm, Sweden, 13–14 June 1988. Poster 5632.

Niyongabo, T., Ndayiragije, A., Larouzé, B., & Aubry, P. (2005). Burundi: l'impact de dix années de guerre civile sur les endémo-épidémies. *Médecine Tropicale, 2005, 65*, 305–312.

Orroth, K.K., Freeman, E.E., Bakker, R., Buvé, A., Glynn, J.R., Boily, M.C., White, R.G., Habbema, J.D., & Hayes, R.J. (2007). Understanding the differences between contrasting HIV epidemics in east and West Africa: results from a simulation model of the Four Cities Study. *Sexually Transmitted Infections, 83*, i5–i16.

Piot, P., Quinn,T.C., Taelman, H., Feinsod, F.M., Minlangu, K.B., Wobin, O., Mbendi, N., Mazebo, P., Ndangi, K., & Stevens, W. (1984). Acquired Immunodeficiency Syndrom in a heterosexual population in Zaïre. *Lancet, 2*, 65–9.

Plan Stratégique National de Lutte contre le VIH/SIDA et les MST, République du Burundi, 1999–2003.

Programme National de Lutte contre le SIDA, 1997. Population based serosurvey. Kigali: Ministry of Health, PNLS.

Rijckborst, H., Wesseling, J.L., Van der Borght, S.F., Van Mameren, J.H., De Man, T.A., Lange, J.M., Home, J.L., & Ruys, A. (2004). Heineken's HIV/AIDS policy, the contribution of a private company. *International Conference on AIDS*, July 11–16;15: abstract no. MoPeE4155.

Sam-Abbenyi, A., Garcia Calleja, J.M., Zekeng, L., et al. Welke auteurs nog? (1993). HIV sentinel surveillance among pregnant women in six provinces in Cameroon, 1989–1992. VIIIth International Conference on AIDS in Africa. Marrakech, Morocco, 12–16 December 1993. Abstract Th.P.C.069.

Serwadda, D., Mugerwa, R.D., Sewankambo, N.K., Lwegaba, A., Carswell, J.W., Kirya, G.B., Bayley, A.C., Downing, R.G., Tedder, R.S., & Clayden, S.A. (1985). Slim disease: a new disease in Uganda and its association with HTLV-III infection. *Lancet, 2*, 849–852.

Sokal, D.C., Buzingo, T., Nitunga, N., Kadende, P., & Standaert, B. (1993). Geographic and temporal stability of HIV seroprevalence among pregnant women in Bujumbura, Burundi. *AIDS, 7*, 1481–4.

Spiegel, P.B., Bennedsen, A.R., Claass, J., Bruns, L., Patterson, N., Yiweza, D., & Schilperoord, M. (2007). Prevalence of HIV infection in conflict-affected and displaced people in seven sub-Saharan African countries: a systematic review. *Lancet, 369*, 2187–2195.

Tsague, L. (2005). Can we scale up PMTCT programs in low resource settings?: Lessons learned and challenges from Cameroon's experience. *Third International IAS Conference on Pathogenesis and Treatment,* July 24–27. (Accessed December 29, 2007) http://www.ias-2005.org/planner/Presentations/ppt/2381.ppt

UNAIDS (2006). *Report on the global HIV/AIDS epidemic. A UNAIDS 10th anniversary special edition*. Geneva, UNAIDS, 2006.

UNAIDS (2007). *Country Situation Analysis- Burundi, Cameroon; Central African Republic; Congo (Republic of); Gabon; Rwanda* (Accessed December 30, 2007); http://www.UNAIDS.org/en/CountryResponses.

UNICEF (2005). *PMTCT Report Card: Monitoring Progress on the Implementation of Programs to Prevent Mother to Child Transmission of HIV* (Accessed December 30, 2007). http://www.uniteforchildren.org/knowmore/files/ufc_PMTCTreportcard.pdf

USAID (2006). *Men are the "secret ingredient" in Rwandan PMTCT Program*. (Accessed December 29, 2007). www.usaid-rwanda.rw

Van de Perre, P., Rouvroy, D., Lepage, P., Bogaerts, J., Kestelyn, P., Kayihigi, J., Hekker, A.C., Butzler, J.P., & Clumeck, N. (1984). Acquired immunodeficiency syndrome in Rwanda. *Lancet, 2*, 62–5.

Van de Perre, P., Clumeck, N., Carael, M., Nzabihimana, E., Robert-Guroff, M., De Mol, P., Freyens, P., Butzler, J.P., Gallo, R.C., Kanyamupira, J.B. (1985). Female prostitutes: a risk group for infection with human T-cell lymphotropic virus type III. *Lancet, 2*, 524–6.

Vandepitte, J.M., Malele, F., Kivuvu, D.M., Edidi, S., Muwonga, J., Lepira, F., Abdellati, S., Kabamba, J., Van Overloop, C., & Buvé, A. (2007). HIV and other sexually transmitted infections among female sex workers in Kinshasa, Democratic Republic of Congo, in 2002. *Sexually Transmitted Diseases, 34*, 203–8.

Van Heuverswyn, F., Li, Y., Neel, C., Bailes, E., Keele, B.F., Liu, W., Loul, S., Butel, C., Liegeois, F., Bienvenue, Y., Ngolle, E.M., Sharp, P.M., Shaw, G.M., Delaporte, E., Hahn, B.H., & Peeters, M. (2006). Human immunodeficiency viruses: SIV infection in wild gorillas. *Nature, 444*, 164.

Vidal, N., Peeters, M., Mulanga-Kabeya, C., Nzilambi, N., Robertson, D., Ilunga, W., Sema, H., Tshimanga, K., Bongo, B., & Delaporte, E. (2000). Unprecedented degree of human immunodeficiency virus type 1 (HIV-1) group M genetic diversity in the Democratic Republic of Congo suggests that the HIV-1 pandemic originated in Central Africa. *The Journal of Virology, 74*, 10498–507.

Vidal, N., Niyongabo, T., Nduwimana, J., Butel, C., Ndayiragije, A., Wakana, J., Nduwimana, M., Delaporte, E., & Peeters, M. (2007). HIV type 1 diversity and antiretroviral drug resistance mutations in Burundi. *AIDS Research and Human Retroviruses Journal, 23*, 175–80.

Wanyu, B., Diom, E., Mitchell, P., Tih, P.M., & Meyer, D.J. (2007). Birth attendants trained in "Prevention of Mother-to-Child HIV Transmission" provide care in rural Cameroon. *Journal of Midwifery and Women's Health, 52*, 334–341.

Welty, T.K., Bulterys, M., Welty, E.R, Tih, P. M., Ndikintum, G., Nkuoh, G., Nkfusai, J., Kayita, J., Nkengasong, J.N., & Wilfert, C. (2005) Integrating prevention of mother-to-child HIV transmission into routine antenatal care. *Journal of Acquired Immune Deficiency Syndrome, 40*, 486–493.

World Health Organization (2005). *Summary Country Profile for HIV/AIDS Treatment Scale-Up: Central African Republic*. (Accessed December 31, 2007) http://www.who.int/hiv/HIVCP_CAF.pdf

World Health Organization (2006). *Rwanda Epidemiological Fact Sheet* (Accessed December 30, 2007); www.who.int/globalatlas/predefinedReports/**EFS2006/EFS**_PDFs/**EFS2006**_RW.pdf

World Health Organization (2007). *Towards universal access: Scaling up priority HIV/AIDS interventions in the health sector. Progress Report, April, 2007*. Geneva, Switzerland: World Health Organization.

Zekeng, L., Affana, G., Bela, M., Ateba, A., Mossoko, J.J., Njom Niend, A., Tsague, L., Bassirou, B., Menyeng, L., Gnaore, E;, Dillow, A., & Atangana, N. (2004). Scaling-up HIV/AIDS prevention and care in Cameroon: Lessons learned by the National AIDS Control Committee (NAC). *International Conference on AIDS*, July 11–16;15: abstract no. TuPeE5320.

Zhu, T., Korber, B.T., Nahmias, A.J., Hooper, E., Sharp, P.M., & Ho, D.D. (1998). An African HIV-1 sequence from 1959 and implications for the origin of the epidemic. *Nature, 391, 6667*, 594–7.