Leading article

The AIDS Epidemic: Past, present and future

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A scientific hallmark of the decade of the 1980s was the report published in June 1981 by the Centers for Disease Control of an unexplained cluster of Pneumocystis pneumonia (PCP) in five previously healthy gay men in Los Angeles. In July, the CDC published another report on a rare cancer known as Kaposi's sarcoma. Both pneumonia and cancer symptoms indicated that a never-before-seen infectious disease was destroying the immune systems of many gay men and was called the Acquired Immune Deficiency Syndrome or AIDS[1].

Two years later the causative organism causing the immune deficiency was identified by Luc Montagnier in 1983 and Robert Gallo in 1984 and was named human immune deficiency virus in 1985. In 1989, a second virus named HIV 2 was discovered[2,3]. HIV is composed of five different viral "families": HIV-1 groups M, N, and O and HIV-2 groups A and B. All of these families have descended from SIV (Simian Immunodeficiency Virus, which infects apes and monkeys) — but each is the result of a separate invasion of human hosts[4].

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There are many lines of evidence, to confirm that the causative virus has probably been in existence since 1908 as the year that HIV Group M began its assault. Though 1908 is an approximation, the evidence suggests that the true date almost certainly falls sometime between 1884 and 1924. There were various theories and debates on how the virus entered humans. An early theory was that a simian (monkey) version contaminated a polio vaccine given to Africans in the Congo between 1957 and 1960, but confirmation that the virus appeared in humans much earlier than this has discredited this theory. The reuse of unsterilized needles in vaccination programs has also been rejected now. The best explanation is that during butchering or consumption of monkey flesh the virus entered humans.

Recently a new HIV virus strain was identified in a Cameroonian woman living in France and traced to gorillas, not chimpanzees. The new virus is dissimilar enough from previously known strains that it cannot be detected by standard HIV tests[5]. This demonstrates that HIV evolution is an ongoing process and it cannot be predicted when it will switch host species when it is opportune for such invasions.

The main mode of transmission of HIV 1 & 2 is through unprotected sex between men and women or between two men, by contaminated blood and blood products as during blood transfusions or when sharing of needles and syringes among people who inject drugs and thirdly from an infected pregnant mother to the newborn while in utero or during delivery or from breast milk. HIV-1 spreads more rapidly and produces more severe disease than HIV-2[4].

The American government completely ignored the emerging AIDS epidemic. The watershed event that brought the disease into full view of the public eye was the announcement in 1985 that film star Rock Hudson had the disease. Attitudes of officials and the public that only gays and intravenous drug users (IVDU), underdogs, people who didn't deserve any special attention have AIDS was changed when children with hemophilia like Ryan White developed PCP and other opportunistic infections.

In that era no one could have predicted HIV/AIDS would become a global epidemic, affecting the lives of millions of people. With the rapid spread of HIV-1, in 2011, UNAIDS/WHO estimated that 34.2 million people are living with HIV (PLHIV) giving a global prevalence of 0.8%. This is an 18% increase compared to 28.9 million in 2001. Globally an estimate of 2.7 million children under 15 years of age is currently living with HIV[6].

HIV/AIDS is currently at the top of the list of health problems in Africa, where the poorest countries do not have the money or political organization to

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effectively deal with it. Rates of HIV infection are still extremely high in sub-Saharan Africa, and an estimated 1.8 million people in this region became newly infected in 2011. This means that there are now an estimated 23.5 million people living with HIV (PLHIV) in sub-Saharan Africa. Women are disproportionately at risk, accounting for 58% of all people living with HIV in the region. In Swaziland 26% of adults are now infected with HIV, while in Botswana and Lesotho, prevalence is reported at 23.4% & 23.3% respectively. South Africa despite a lower HIV prevalence of 17.3%has the most number of people living with HIV (5.6 million) than any other country. The situation has been far worse previously. Today, due to the introduction of anti retro viral therapy (ART) deaths are down by 74% in Botswana[7].

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The virus entered the Asia population a little later in the mid eighties and in 2011 the overall HIV prevalence in the adult population in the South East Asia Region was 0.3% and nearly3.5 million people are estimated to be living with HIV which is the second largest group of PLHIV[8]. Annually an estimated 210,00 new infections occur which is translated to 575 people are getting infected daily[8]. In Asia only 30% of pregnant women have access to HIV testing and only 16% have access to treatment to prevent mother to child transmission of HIV[8]. In the early 1990s the lessons of devastation from AIDS in Africa and the Caribbean went unheeded in much of Asia, until extensive spread of HIV was taking place in Cambodia, Vietnam and Thailand. Today with the targeted interventions such as 100% condom use programme, harm reduction programmes such as needle syringe service programmes, opioid substitution therapy and antiretroviral therapy these three countries are showing a marked decline in the number of new infections.

Sri Lanka recognized the impending threat of HIV/AIDS quicker than some of the countries in the region and prioritized strategies, allocated resources effectively, mobilized a multi sectoral approach and took courageous decisions based on evidence. In 1985, the STD service was upgraded as the National STD/AIDS Control Programme[9]. The first AIDS case was discovered among a foreigner in 1986 and the first Sri Lankan AIDS case was diagnosed in 1987. Authorities moved fast and with W.H.O support a Short Term Plan was floated. The main objective was to create awareness and strengthen facilities for STD/HIV services including diagnostic facilities. By 1988, ELISA and SERODIA testing facilities were established and within a few years confirmatory tests were in place. A Medium Term Plan was launched in 1992. There was high level political leadership with HIV/AIDS being discussed at the National Health Council chaired by the Hon Prime Minister. A National AIDS Committee was established to plan prevention & control strategies and oversee the national response[9]. HIV has slowly crept into the country and as of end June 2013 a cumulative total of 1739 HIV cases were detected in the country in a background of an estimated 4200 people living with HIV[10]. In the year 2012, a total of 186 new infections were detected which is a 27% increase compared to the previous year. In the year 2013 during the first two quarters a total of 90 new cases were diagnosed which means almost one diagnosis every other day. Sexual transmission is the main mode of spread in the country accounting to around 85% of the reported cases and 4% and 0.1% has been due to mother to child transmission and blood and blood products related transmission[10]. It is strikingly important to note that since year 2000, there have not been any transfusion related HIV infections in the country this is due to the unwavering decision taken by the Ministry of Health in 1988 to educate blood donors on HIV and screen donated blood for HIV in addition to the existing screening for malaria, syphilis and hepatitis B infections[11].

Over the years, STD services were strengthened. New clinics were opened. Comprehensive STD management was introduced and the capacity of the service providers was developed. Another strong policy decision was made to establish the HIV sentinel surveillance system in Sri Lanka to track the

trend of the HIV epidemic in the country[11].Results of the last few surveys are signaling an impending HIV threat in the country as the HIV prevalence among men who have sex with men (MSM) has increased from 0.1% in 2008 to 0.9% in 2012. To substantiate this evidence it is observed that in year 2012 of the total 186 cases detected 17% have been due to MSM[10]. Unless the quality and coverage of targeted interventions for MSMs are scaled up the HIV landscape in the country will take a different contour.

Integration of prevention of Mother to child transmission of HIV into the existing Maternal & Child Health services has taken place and it will help preventing paediatric HIV infections especially by providing ART to mothers[11]. Already 68 infants have acquired HIV from their infected mothers and some have succumbed to AIDS[10].

The vulnerability of external migrants to HIV infection is a global phenomenon. Available data shows that among the women who have been tested positive in the country, the majority have probably acquired the infection while being overseas. In year 2012, almost a third of new male infections and half of female new infections were among external migrants[10]. It has to be noted that external migrants are tested more than other populations.

HIV disease progression depends on host and virus factors. In the absence of treatment the median time to develop AIDS is about 10-12 years[12]. There are also individuals with no disease progression and they are called long term non progressors: by definition are those who have survived for > 10 years without symptoms and without ART, their CD4 counts are more than 500. There are also people who maintain undetectable HIV viral loads in the absence of ART. Approximately 0.6% of PLHIV are considered to be these "elite controllers". Such people have stronger HIV specific immune responses compared with people who do not have the ability to control viral replication. Genetic factors are believed to be associated with slow progression[12].

In 1996, David Ho of Rockefeller University in New York presented his research on a combination drug therapy, a treatment cocktail that rendered the virus undetectable in blood. With this approach the global HIV/AIDS landscape was completely changed[13]. Clinicians were witnessing a miracle, HIV/AIDS with a tag of a death sentence turned from a killer disease into a chronic disease almost overnight. The first drug to be approved for use by the Food & Drugs Administration (FDA) against HIV was AZT (zidovudine) in 1987, and since then, dozens of other anti retroviral agents have been added to the HIV arsenal.

The recommendation was "to hit early and hit hard with ART" even to start ART during sero-conversion. However, taking into consideration the inability of developing countries to bear the high cost of ART and the evident adverse effects the recommendations were changed and the requirement was to initiate ART when CD4 cells drops to 200. The combination therapy which consists of at least three to four drugs which had to be taken as multiple pills have been improved today as fixed dose combinations (FDC) which is given as a daily single pill.

In 2010, W.H.O recommended to initiate treatment when CD4 count reach 350[14]. Consequently 4.2 AIDS related deaths in low and middle income countries were averted[15]. ART has increased survival rates of PLHIV: starting HIV treatment at age 20 could expect to live to 49, a reduction of 27 years compared with those without the disease. Globally although 14.8 million are eligible for ART by 2012 almost 9.7 million were on ART[15].An estimated 3.3 million children (<15 years old) live with HIV/AIDS, but BY 2012 only 34% of those in need of treatment were receiving it, compared with 68% of adults[15]. Without treatment, half of all HIV-positive children will die before the age of two, and 80% will die before they turn five years old[7].

In 2004, in keeping with the 3x5 initiative of the W.H.O, Sri Lanka initiated provision of ART free of charge using World Bank funds for those who were eligible for treatment and at present with GFATM support 387 PLHIV are on ART and 95.6% are on the first line regimen with 39% on FDC. It is estimated that the treatment cost is around 800 U$ per patient per year and 4% of the HIV budget is set aside for ART[16].

In 2013, the W.H.O. recommendation for adults was to commence ART when CD4 count reach 500 level and to provide ART to all HIV-positive children aged 5 years or less no matter what their CD4 counts are, as well as all HIV-positive pregnant and breastfeeding

women. Their uninfected partners should also be provided with antiretroviral therapy[17]. Treatment under the 2013 guidelines would help reach 15 million people by 2015 which is the newly set UNAIDS/WHO target and would prevent more than 3 million additional AIDS related deaths and prevent an additional 3.5 million people from acquiring HIV infection through 2025, in comparison with the 2010 guidelines[15].

Although ART helped to achieve undetectable virus levels in the blood it does not bring about a cure. Further, HIV comes roaring back to life almost the moment drugs are stopped. Today's drug therapies are aimed specifically at the current strains of HIV, but the virus is reflexively and rapidly mutating as every virus eventually does and it may appear to haunt us in a new form. The virus is mysteriously persisting in the viral sanctuaries- gut, kidneys, liver, and brain and hiding in the very immune cells that would kill it[12]. Scientists were hopeful that a vaccine would be the most effective weapon to prevent HIV transmission and containing the epidemic. Yet, none have been shown to be sufficiently safe and effective for approval. Although development of an effective vaccine has been slower than most people anticipated, it should be noted that vaccines against other viral infections such as polio, hepatitis A and B, and measles took two to five decades to develop.

Medical researchers are actively pursuing three broad approaches to combat the virus. Genetic resistance to HIV is being explored by the scientists. A HIV positive man from Berlin experienced a 'functional cure' of HIV infection after aggressive chemotherapy, immunosuppressive treatment and a bone marrow transplant from a donor with genetic resistance to HIV. Recently, two people with HIV who received stem cell transplants for the treatment of lymphoma are now controlling HIV replication both have experienced loss of detectable HIV DNA[18].

In the future, for such a cure to be relevant on a wide scale, it would have to be possible to create the genetic resistant component (CCR5-delta 32 mutation) without a donor and without a transplant—preferably in the form of a single injection. At the University of Southern California instead of a donor, a new form of gene editing known as zinc finger nucleases, which are synthetic proteins that act as genetic scissors are being prepared to target and snip a specific part of the genetic blueprint: they can, for instance, cut out the code that produces the genetic resistance yielding a cell with HIV resistance[18].

The second approach involves latency activators, molecules that lure the virus out of its hiding places and into the open, where the body's immune cells and targeted drugs are able to find and destroy it once and for all. Finally, scientists are intensely studying the immune systems of elite suppressors, who remain healthy after HIV infection, controlling the virus for decades on end[18].

In Sri Lanka, the recommendation to reach at least 80% of the most at risk populations and promote consistent condom use in at least 60% of them is an ambitious task in a scenario where it is estimated that there are 41,000 women who sell sex and 250,000 men who buy sex from them and 34,000 are MSM[11]. Three decades of experience in responding to the H.I.V./AIDS epidemic has provided indisputable evidence that depriving those groups most at risk of H.I.V. infection of their human rights drives them underground. Hence they live in fear of reprisals and have no access to basic health services such as condoms to protect themselves from infection. Awareness programmes of the past helped people to understand what HIV/AIDS is all about and create an enabling environment to implement policies and programmes but what is required at present and in the future are more focused programmes of risk reduction and opting for counseling and testing to know the HIV status.

Although HIV testing capacity has increased over time in Sri Lanka, enabling more people to learn their HIV status, and 4th generation antigen-antibody tests are now available which has shortened the window period the majority of people with HIV are still unaware of their status.

Mass media and other channels such as workplaces, antenatal clinics, immunization clinics, family planning clinics should be utilized to spread prevention messages including the risk factors such as buying and selling sex, injecting drug use as even a single exposure with commercial or causal partners runs the risk of developing HIV it is vital to know your HIV status. At the same time in clinical settings it remains essential that healthcare providers are alert

to those at risk of HIV, or who display signs of early infection, to ensure these patients are tested and treatment is put in place before progressing to AIDS.

Stigma and discrimination towards HIV/AIDS is a global phenomenon and Sri Lanka is no exception. Adverse reactions by the society such as burning down houses of HIV positives are a thing in the past. The stigma Index study done in 2010 found that health care settings were responsible for most instances of stigma and discrimination. The time has come for us to re-visit some of the laws and legislation through the lens of human rights guaranteed under the Constitution and ensure it is aligned to enable progress and to move with planned interventions. In India in July 2009 a High Court ruling found India's 150-year-old statute (Section 377 of the Indian Penal Code) prohibiting homosexual acts as discriminatory and therefore a violation of fundamental rights. The striking down of Section 377 is an example that has had a transformative and beneficial impact on the national AIDS response in India and on public perception of HIV[19]. The law must be a shield that protects, not a sword that punishes and increases vulnerability to abuse, harassment and HIV infection therefore getting the legal environment right is essential for addressing the social and structural inequalities which fuel HIV and impede health and development progress.

The future of the HIV epidemic will depend on actions and decisions with respect to prevention and treatment interventions taken today, on scientific evidence, political leadership, money and manpower available, commitment of stakeholders and prejudices and attitudes of people based on heritage, culture, experience, training, education, religious beliefs, and fashions which shape people's perspectives on, and interpretations of, the world. All these factors will be responsible to make or break the future HIV epidemic.

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