HIV/AIDS Prevention and Care Newsletter

Moving Towards Universal Access

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HIV, organ impairment and cancer

Introduction

As people live longer and remain in good health, thanks to antiretroviral therapy, the pattern of illness associated with HIV is changing. There is increasing recognition of the direct pathogenic effect of HIV on many organs, including kidneys, heart and liver and a rise in non-AIDS cancers.

Opportunistic infections (OIs), typically related to immunosuppression, are becoming less common. Tuberculosis is an exception and continues to be the most common OI in people living with HIV. The new concept of serious non-AIDS events (SNAs) has emerged following data from the Strategies for Management of Antiretroviral Therapy (SMART) trial and other studies.[1–4]

SNAs (end-stage liver and kidney disease, cardiovascular disease, and non-AIDS cancers) are becoming more common in treatment programmes, especially in developed and middle-income countries. They have so far been less well characterized in resource-limited settings.

1. HIV and the Kidney

HIV-associated nephropathy (HIVAN) is common and directly related to infection of the renal cells with HIV. Previously called AIDS-related nephropathy, HIVAN is the most frequent cause of renal failure in persons living with HIV infection. As people survive longer on antiretroviral therapy (ART), renal disease has become an important contributing factor to morbidity and mortality.[5]

The cellular targets are the renal glomeruli and tubular epithelium.[6] The mechanism by which HIV affects the kidney is by direct viral infection within renal cells causing glomerular collapse and consequent loss of renal function.[7–8] While ART reduces the incidence and severity of HIVAN, some antiretrovirals such as tenofovir and indinavir have been reported to be associated with renal impairment in some patients.[9]

In the United States of America, HIVAN accounts for approximately 1% of new cases of end-stage renal failure with one third of cases among African Americans. Males outweigh females by 10 to 1.[10] The epidemiology of the disease is not well defined in resource-limited settings.[11] In a study from South Africa, HIVAN histology was present in 43% of (99) renal biopsies performed in HIV-positive patients.[12] There are limited data on HIVAN in the Asia Pacific region,

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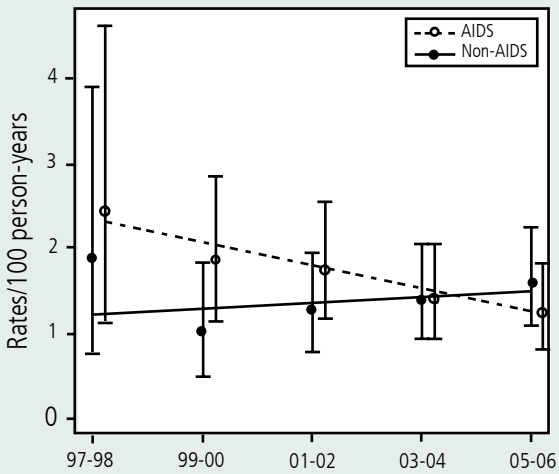
Figure 1: Changes in causes of death over time in Brazil



Source: Temporal Changes in Causes of Death Among HIV-Infected Patients in the HAART Era in Rio de Janeiro, Brazil. Antonio G. Pacheco, *et al.*, *Journal of Acquired Immune Deficiency Syndrome*, 2009; 51:624–630

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where awareness of chronic kidney disease is generally low among patients and physicians.[13] In a single case report from Hong Kong (China), a 52-year-old man infected with HIV for six years and on ART presented with acute renal failure and nephrotic syndrome. Renal biopsy was consistent with HIVAN. The authors said that HIVAN is rare in Asian populations.[14]

While HIVAN is not specific to the route of HIV transmission, 50% occurs in people who inject drugs.[15] SMART trial compared intermittent versus continuous ART in diverse ethnic populations. Intermittent therapy was associated with inferior outcomes not only in terms of opportunistic disease and death but also an increased risk of fatal or non-fatal renal disease.[12–13]

The clinical presentation of HIVAN is progressive renal failure, with enlarged kidneys on ultrasound and nephrotic syndrome (proteinuria, hypoalbuminemia and edema).[16]

ART is effective in preventing and treating HIVAN.[17] Adjunctive therapy includes angiotensin-converting enzyme (ACE) inhibitors and corticosteroids in selected patients with significant interstitial inflammation or rapid progression.[16]

2. HIV and the Heart

People living with HIV are at risk of cardiovascular disease from the same factors posing risk in the general population: smoking, dyslipidemia, hypertension, obesity and diabetes. However, HIV infection itself, opportunistic infections and ART are additional risk factors. The most common cardiac manifestations of HIV are dilated cardiomyopathy, myocarditis, pulmonary hypertension, pericardial effusion, endocarditis, malignancy and drug-related cardiotoxicity.[18]

HIV causes cardiovascular adverse events through direct and indirect pathways. These include direct HIV infection of endothelium and vascular smooth muscle cells, and cytokine-mediated inflammation. Indirectly, HIV causes dyslipidaemia, enhanced atheroma formation, insulin resistance, glucose intolerance and a prothrombotic state.[19]

The incidence of pericarditis, with or without pericardial effusion, in patients with severe immunosuppression (CD4 count<200 cells/mm^3) not receiving ART has been reported as 11% per year.[20] While there are some case reports of identified pathogens, the effusion is mostly linked to inflammation associated with advanced HIV infection. In contrast, endocarditis typically has an infectious origin and is rare except in injecting drug users.[21]

3. HIV and the Liver

Liver disease is an increasing problem in people living with HIV. In those who are able to take antiretroviral therapy, the forms of liver disease have changed and their relative importance has increased.[22] Liver disease is caused by HIV itself and co-infection with hepatitis B (HBV) and hepatitis C (HCV). It tends to occur more commonly in people with HIV infection due to the shared transmission routes of hepatitis B and C and opportunistic infections unique to immunosuppression, such as tuberculosis and HIV-related cholangitis. Morbidity and mortality due to liver disease have increased, coinciding with the impact of ART in reducing HIV-related mortality. The pattern of liver disease has changed from the pre-ART era when opportunistic infections and cancers predominated, to chronic viral hepatitis, HIV-related fibrosis and non-alcoholic fatty liver. End-stage liver disease has become a major cause of death in HIV and hepatitis co-infected patients.[23–24] High viral loads, low CD4 cell counts and incomplete suppression of HIV Ribonucleic acid on ART are all associated with an increased risk of liver-related death.[23] HIV causes liver fibrosis and fatty liver by directly infecting hepatocytes (causing cell death) and liver stellate cells (the major cell type involved in liver fibrosis).[25]

The impact of HIV on the liver is inextricably linked to HBV and HCV infection. HIV infection increases the HCV viral load and the risk of cirrhosis and reduces the chance of spontaneous clearance of HCV infection.[26] HIV infection reduces spontaneous HBV surface antigen clearance and accelerates progression of chronic hepatitis B.[27] Both HBV and HCV can complicate the initiation of ART by causing hepatic Immune Reconstitution Inflammatory Syndrome (IRIS) soon after ART is started.

In the Multicentre AIDS Cohort study (MACS) cohort, there was a fourteen-fold increase in liver mortality rate among those with HIV/hepatitis B co-infection.[28]

Liver disease	Effect of HIV
HIV infection	Fibrosis and fatty liver
HCV infection	Increased prevalence
	Decreased spontaneous clearance
	Increased HCV RNA level
	Increased mother–infant transmission of HCV
	Increased incidence of cirrhosis and liver failure
HBV infection	Increased prevalence of chronic hepatitis B
	Increased incidence of cirrhosis and liver failure
Drug induced	Increased antiretroviral drug toxicity

4. Antiretroviral-associated liver disease

Approximately one of every eight persons taking a new antiretroviral regimen develops hepatotoxicity, ranging from elevations of hepatic enzymes and hyperbilirubinaemia to acute liver failure and death.[29] Hepatotoxicity is more common in patients with coexisting HBV or HCV infection and may be part of generalized hypersensitivity reaction, such as that caused by Abacavir. However, the short-and long-term hepatic toxicity of ART is outweighed by its positive impact on reduction of HIV replication, restoration of immune responses and prolongation of life.[22]

5. Non-AIDS malignancies

Invasive cervical cancer, Kaposi's sarcoma and non-Hodgkin's lymphoma are well known AIDS-defining cancers. However, people living with HIV (PLHIV) are at increased risk of developing non-AIDS cancers. In a recently published meta-analysis (4797 cases), PLHIV were twice as likely to develop non-AIDS defining cancers compared to HIV uninfected individuals.[30] The most frequently observed were lung cancer (847 cases), Hodgkin's lymphoma (643 cases) and anal cancer (254 cases). Malignancies linked to viral infections (human papillomavirus, hepatitis B and C and Epstein Barr virus) also are more common among PLHIV. Other risk factors such as smoking may play a role in the development of these malignancies.

PROGRAMME MANAGER'S VIEWPOINT: Hong Kong (China) Experience in Combating the HIV Epidemic Among Men Who Have Sex With Men

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With a local population of around 7 million people, Hong Kong (China) has remained a low HIV prevalence area since the first HIV case was diagnosed in 1984. As at end of June 2009, the accumulated total number of HIV and AIDS reported cases reached 4249 and 1071 respectively.[31] Sexual transmission accounts for almost three quarters of the reported cases, while 17% were of undetermined transmission route due to inadequate information. Injecting drug users only accounted for 6% of the reported cases. The HIV prevalence among drugs users as reflected in the methadone clinic attendees is kept low at about 0.4% due to the high coverage and low threshold for access of methadone treatment services provided by the 20 methadone clinics since the

early 1970s. Since the turn of the 21st century, the main challenges come from a resurging HIV epidemic among men who have sex with men (MSM), which has become apparent since 2005 in multiple sources of data.

Prior to 2005, there were only two nongovernmental organizations which ran condom distribution and outreach testing programmes for MSM in saunas and bars. One of these nongovernmental organizations documented a rise in HIV prevalence among MSM in bars and saunas from their voluntary counselling and testing service statistics, from less than 1% in 2002 to around 2.5% in 2005. In the Department of Health's voluntary case reporting system, the number of MSM case reports also increased steeply from 28 cases in 2000 to 96 cases in 2005. Molecular studies have identified several major clusters of transmission among MSM.

In 2005 and 2006, Dr Tim Brown, senior fellow at the East West Center in Hawaii (United States of America) and also an external consultant of Hong Kong Department of Health, analyzed the epidemiological data to prepare estimates and projections for the local epidemic. He also shared the latest regional findings of rapid HIV growth among MSM around Asia, with some places having severe MSM epidemics, e.g., Bangkok. If Hong Kong (China) does not step up its HIV preventive responses among MSM, it was projected that about 30% of local MSM would be HIV-positive by 2020.[32] This would translate into millions of dollars worth of antiretroviral treatment. Dr Brown also pointed out that the consistent condom use was dangerously low among MSM at around 40% for regular partners and 70% for non-regular partners. In order to turn around the rising epidemic, consistent condom use must reach 80% among MSM.

Hong Kong (China) adopted a pragmatic approach in tackling the HIV epidemic among MSM. Firstly, the Advisory Council on AIDS (ACA) identified HIV prevention among MSM as the pressing priority for action in its five-year AIDS Strategies from 2007 to 2011.[33] ACA also advocated for consistent condom use to reach 80% among at-risk community groups including MSM. Testing coverage was to be scaled up with community mobilization for preventive programmes among MSM.

The Council for the AIDS Trust Fund (ATF), the biggest funding source of community projects in Hong Kong (China), also launched a Special Project Fund on 1 December 2006 to invite applications for HIV preventive projects for MSM in the community. Based on the findings of a community needs assessment, ATF laid down pre-defined areas of public health interventions such as improving condom and lubricant accessibility, promoting HIV testing, promoting sexual health services, reducing HIV risk in the context of recreational drug abuse and internet use, and empowering MSM who had recently come out, etc. This provided the MSM community the resources it needed for active engagement in the response and greatly expanded community-based efforts. Between 2006 and 2008, ATF disbursed around HK$ 13.6 million to support 42 community-based HIV prevention and research projects targeting MSM. In 2009, there are 10 nongovernmental organizations which provide HIV preventive and support services for MSM.

The Red Ribbon Centre (RRC), the HIV health promotion and technical unit of the Department of Health, appointed two liaison officers to improve collaboration and communication with the MSM community and the nongovernmental organizations engaged in MSM targeted work. A Working Group on HIV Prevention in MSM was set up in early 2006. The membership of the Working Group includes MSM service providers, MSM business and media owners, opinion leaders and academics who contributed their views to the preventive strategies, strategic information, risk communication and health promotion campaigns. RRC launched three HIV awareness and health promotion campaigns, namely "Do It Safely" (2006), "Zero Heroes" (2007) and "Syphilis Prevention Campaign in MSM" (2009). An informational website (www.21171069.com) was set up as well as an MSM hotline (2117 1069) to provide information, counselling and HIV testing.

Technical assistance was provided to ATF applicants when they made their applications on MSM projects. Capacity-building workshops were organized with assistance from overseas experts, including Dr Tim Brown of East West Center (Hawaii, United States of America), Dr Susan Kegeles of University of California, San Francisco (San Francisco, United States of America), the

Albion Street Centre (Sydney, Australia) and the AIDS Council of New South Wales (Sydney, Australia). Furthermore, WHO, UNAIDS, UNDP and the Department of Health in Hong Kong (China) held a technical consultation on the health sector response to HIV among MSM from 18 to 20 February 2009. It was an excellent opportunity for local AIDS workers and MSM community members to learn from the international delegates on best practices in the region.[34]

A community-based surveillance programme named PRISM was conducted in 2006 and 2008 to track the HIV epidemic in MSM. PRISM consists of both seroprevalence and behavioural surveys. A mapping exercise was performed to determine the number of MSM bars and saunas, which could subsequently be included in the survey. In both PRISMs, over 800 urine samples were collected to estimate the HIV prevalence which has increased slightly from 4.05% in 2006 to 4.31% in 2008. The proportion of MSM who had a HIV test in the past year and knew their results rose from 24% in 2006 to 36% in 2008. The level of consistent condom use among MSM with regular partners was 41% in 2006 and only rose to 45% in 2008. The level of consistent condom use among non-regular partners was 73% in 2006 and rose to 75% in 2008.

With the introduction of antiretroviral treatment, AIDS is managed as a chronic disease. In Hong Kong (China), as a general principle no person is denied of access to health care because of lack of means. The government provides affordable and accessible HIV treatment services. This is a very important public health initiative as those patients who are receiving quality treatment, care and support services will also reduce their onward HIV transmission.

In terms of creating an enabling environment, the government passed the Disability and Discrimination Ordinance to offer protection for persons living with HIV against discrimination in education and employment. It also prescribes that services and facilities are to be made available to them. Since 1996, the law has been in force and also helps to induce acceptance and achieve inclusion.

The cornerstone of success in scaling up the HIV prevention response in MSM is to develop an open and trusting partnership between the government, nongovernmental organizations, the MSM community and other related sectors. It is important to know our own epidemic and make evidence-based decisions in terms of setting AIDS policies and allocation of resources. The right proportion of resources must be channeled to scale up preventive responses such as condom accessibility and testing programmes. Communities must remain central to the response, making the provision of resources, capacity building, training and technical assistance critical elements for expanding effective HIV preventive programmes in the community. After the initial scaling up of the HIV responses, the programmes must be monitored, evaluated and refined in terms of coverage and quality. The government has responsibility for the overall coordination of the AIDS response including setting evidence-based policies, providing an enabled environment, gathering strategic information, tracking the HIV epidemic and communicating HIV risks to both affected communities and the larger public in an open and transparent manner. Best practices identified both locally and elsewhere must be shared and disseminated. And most importantly, the MSM community must buy in, take ownership of the AIDS response for its members, and become active and engaged partners in that response. Otherwise preventive efforts will be unsustainable in the long term and the epidemic will continue to grow.

Acknowledgement

We wish to thank all those AIDS stakeholders who have contributed to combat the HIV epidemic in Hong Kong (China). A special note of thanks to Dr Tim Brown, Senior Fellow of the East West Center in Hawaii, and Dr Jaime Sin of the Secretariat of the Council of the AIDS Trust Fund for their invaluable comments on this article.

9th International Congress on AIDS in Asia and the Pacific (ICAAP) Conference Highlights 9–13 August 2009, Nusa Dua, Bali, Indonesia

More than 4000 delegates took part in ICAAP at the Bali Convention Centre in Indonesia from 9 to 13 August 2009. The theme was Empowering People, Strengthening Network, which calls for strengthening commitment to achieving universal access and providing prevention, care, support and treatment for those who need it most. The conference also urged nations to work towards implementing the Declaration of Commitment adopted at the United Nations General Assembly Special Session on AIDS in 2001 and the Political Declaration of 2006, despite the pressures of the global economic crisis.

It is evident from the conference that some countries in the Asia Pacific region are beginning to see success in their efforts to reverse the spread of HIV, but not enough to break the trajectory of the epidemic. There is still recognition of the need to protect and enhance involvement of marginalized populations including sex workers, MSM, transgender people, injecting drug users and their intimate partners. The need to update guidelines on antiretroviral therapy was highlighted at ICAAP, including second-line therapy in resource-limited settings, the management of treatment-experienced patients, cost-effective initiation of ART, the public health approach to the management of first-line regimen failure and the need to have equitable guidelines for high-income and middle- and low-income countries. There were also calls to scale up structural interventions, including policies on decriminalization of sex workers and MSM, as well as reducing stigma and discrimination.

WHO in Action

The World Health Organization (WHO) technical leadership has also been highlighted in various symposia and satellite sessions. The majority of the sessions were well attended and participants appreciated the technical content. The WHO aims to ensure effective responses through the dissemination of technical guidance in the health sector response and to contribute to strengthening networks and empowering communities towards universal access to prevention, care, support and treatment. WHO Regional Offices in New Delhi and Manila contributed to the following sessions in collaboration with partners including UNICEF, Family Health International (FHI), Asia Pacific Coalition on Male Sexual Health (APCOM), UNODC, UNFPA and the Asia Pacific Network of Sex Workers (APNSW).

Symposia included:

- Recent advances in ART – Implications for programme scale up and implementation in the Asia Pacific region (WHO South East Asia and Western Pacific Regional Offices)
- Scaling up harm reduction services towards universal access in Asia: Models of good practice (UN Task Force on HIV on IDU and WHO Western Pacific Regional Office)
- Falling through the cracks: Addressing the reproductive health needs of female sex workers (APNSW, FHI, UNFPA, UNICEF and WHO South East Asia and Western Pacific Regional Offices)

Satellite sessions included:

- MSM and HIV in Asia and the Pacific: Cross-cutting issues (APCOM, FHI and WHO Western Pacific Regional Office)
- Where's the Care? – Palliative Care as cornerstone of comprehensive HIV services in the era of ART (FHI and WHO South East Asia and Western Pacific Regional Offices)
- Linking HIV/STI Services and Reproductive, Adolescent, Maternal, Newborn and Child Health Services: Opportunities for Universal Access (UNICEF and WHO South East Asia and Western Pacific Regional Offices)
- Data sources, data uses: identify gaps in HIV data for decision-making in the Asia-Pacific region (UNICEF, UNAIDS, WHO)

The following satellite sessions were organized by WHO Headquarters:

- Addressing TB/HIV: The critical role of people living with HIV (PLHIV) and HIV service providers (UNAIDS and WHO HQ)
- Entry points for integrating gender into HIV/AIDS programmes in the health sector (WHO HQ)

WHO has disseminated numerous publications and technical resources. Two new publications were launched during the conference as follows:

- HIV Counselling Resource Package for the Asia- Pacific (UNICEF, FHI and WHO)
- Integrating gender into HIV/AIDS programmes in the heath sector: Tool to improve responsiveness to women's needs (WHO HQ)

From Mekong to Bali: scale up of HIV/TB collaborative activities in Asia Pacific

Prior to ICAAP, a meeting "From Mekong to Bali: scale up of HIV/TB collaborative activities in Asia Pacific" was organized by WHO in collaboration with the HIV/TB Working Group of the Stop TB Partnership from 8 to 9 August 2009. WHO staff from the Stop TB and HIV/STI units attended in the TB-HIV meeting along with 127 participants from 18 countries with high TB and HIV burdens. The meeting aimed to catalyze the implementation of collaborative HIV/TB activities in the Asia Pacific region which has more than half of the global burden of TB and 12% of the global burden of HIV. Participants shared experiences and best practices to inform plans to accelerate the implementation of nationwide collaborative HIV/TB initiatives. The meeting followed on from the first regional HIV/TB meeting held in the Mekong subregion in Ho Chi Minh City, Viet Nam, in October 2004. National TB and HIV programme managers were joined by a broad range of AIDS and TB stakeholders active in the Asia Pacific region, members of the HIV/TB Working Group, and representatives of bilateral and multilateral organizations, nongovernmental organizations, and faith-based organizations. The meeting came up with various recommendations to scale up HIV/TB initiatives. Some of the recommendations include the following:

(1) Scale up provider-initiated HIV testing and counselling (PITC) to all TB patients and suspect cases and promote early and maximum uptake of co-trimoxazole preventive therapy and ART for HIV-positive TB patients to reduce mortality rates. Decentralize HIV testing and counselling and HIV care and treatment services to facilitate access to integrated HIV/TB prevention, treatment and care.

(2) Develop a coherent communication strategy on the Three I's: Intensified case finding (ICF); Isoniazid preventive therapy (IPT); and Infection control. Scale up IPT, develop and integrate infection control guidelines at all level of health care facilities, and advocate to and build the capacity of communities, patients and health care workers to create a safer TB-free living and working environment.

(3) Structural adjustments to maximize collaboration between national AIDS programmes and national TB programmes.

(4) Strengthen monitoring and evaluation, including improving recording and reporting of collaborative activities and HIV/TB cohort data analysis, as an urgent priority and monitor infection control practices.

(5) Strengthen multisectoral responses to HIV/TB addressing de-stigmatization and decriminalization of behaviours associated with increased risk of HIV and TB.

(6) Explore the benefits of integrating TB and HIV services with sexual and reproductive health.

(7) Increase capacity of community groups to address HIV/TB co-infection.

(8) Increase advocacy to adopt and implement the Three I's.

(9) Government commitment to work with communities.

The meeting report can be accessed in WHO webpage at:

http://www.stoptb.org/wg/tb_hiv/meetingsevents.asp

Excerpts from the 9th ICAAP

With over 370 oral and more than 1000 poster presentations, the 9th ICAAP covered many aspects of prevention treatment and care. This review will focus on areas of harm reduction, palliative care, access to antiretrovirals (ARVs) and linked responses.

Harm reduction and prevention targeting most-at-risk populations

The prevalence of HIV infection among injecting drug users (IDUs) reported at the conference is high, ranging from 7% in the 7th round national sero-surveillance data in Bangladesh, 30% in Pakistan[35] to 60% in some regions of Myanmar and China.[36–37] Sexual partners are also at risk. In one survey from Ha Noi, 14% of partners were reported as being HIV-positive, with a majority of those surveyed considering themselves at risk for HIV infection and believing that their partners would become violent if condom use was requested.[38]

Harm reduction interventions for IDUs included opioid substitution therapy (OST), needle and syringe programmes, and compulsory drug treatment centres. The WHO Collaborative Study on Substitution Therapy for Opioid Dependence[39] examined the effectiveness of OST in East Asia (China, Indonesia, Thailand), Eastern Europe (Lithuania, Poland, Ukraine), and the Middle East (Iran). The HIV sero-prevalence rate was highest in Thailand (52%), followed by Indonesia (28%) and Iran (26%), and lowest in Australia (2.6%). Treatment retention at six months was uniformly high, averaging approximately 70%. The study concluded that OST can achieve significant reduction in heroin and other opioid use, exposure risk behaviours and criminal activity across diverse countries and cultures. In Hong Kong (China), methadone clinics also were used to increase coverage of HIV testing. Twenty methadone clinics with a daily attendance over 6000 implemented a universal HIV testing programme in 2004 achieving coverage of over 80%.[40] One abstract from Indonesia reported the costs of OST to be Rupiah 69 206 (US$ 7.57) per client visit.[41] Other successful large-scale needle and syringe programmes integrated with OST programmes were reported from China, Indonesia and India.[42–44]

Compulsory drug rehabilitation centres are a component of national anti-narcotic strategies in many countries in the Asia Pacific region and the number of centres is increasing.[45]

A report from Thailand noted that large numbers of people were detained for extended periods of time, that HIV risk behaviours were common while in detention, there was little reliable evaluation of their effectiveness in reducing rates of drug use and that this was a neglected area of research into health and human rights.[46]

Men who buy sex constitute an important bridge for transmission of HIV to the general population. Seafarers, a highly mobile population, remain a risk group due to continuing and new risk factors.[47] In Indonesia, a collaboration between port authorities, employers and local communities targeted seafarers, dock workers and truckers. Surveillance data indicate that 43% of high-risk men in East Java used a condom during their last commercial sex encounter and prevalence of any STIs was only 2%, representing some of the best such rates in Indonesia.[48]

Among mobile populations (truck/bus drivers and fishermen) in northern coastal Java and north Sumatra, a non-marital partner (frequently a commercial sex worker) was reported by 45% of drivers and 34% of fishermen, with only 7% condom use.[49] In a small cross-sectional survey of fishermen at a commercial fishing jetty in Malaysia, 40.6% reported injecting drug use.[50] A programme of non-institutional, mobile HIV testing among truckers tested 2094 men over an 8-month period in India, with 1.86% testing positive.[51]

Access to ARV

The impact of generic production on HIV medicine prices since 2001 has played a central role in the scale up of government treatment programmes worldwide.[52] In Thailand, the National Access to Antiretroviral Programme for People living with HIV/AIDS (NAPHA) programme was launched in 2003, with GPOVIR (generic fixed-dose combination of stavudine, lamivudine and nevirapine) as the main first-line regimen. Survival data from Lampang Hospital in north-west Thailand demonstrated a reduction in mortality from 50/100 person years of follow up (PYO) in 1996 to 5.3/100 PYO in 2006.[53] Barriers to

ART scale up remain in many countries. These include limited infrastructure, human resources and leadership capacity, financial constraints, geographical barriers and low uptake of counselling and testing.

However, the same access may not apply to second-line ART with a study from India reporting second-line regimens to be inaccessible, expensive and unaffordable for majority of PLHAs, and that government supply of these drugs is limited and available only in selected centres.[54] A separate abstract from India described plans to rollout second-line ART, commencing in April 2008, to 3000 PLHAs in need.[55] In a centre in Jakarta, Indonesia, where second-line ART was available, 86.7% of patients had viral load <500 copy/ml after 8 months (IQR 3-16 months).[56]

Home-based and palliative care

Often neglected at large conferences, models of home-based care from many countries were reported. In Cambodia, the Khmer HIV/AIDS NGO Alliance (KHANA), working with 60 implementing partners, provides a coordinated response to scale up prevention and care, including palliative care, through 120 home- based care teams. Papua New Guinea is classified as having a generalized AIDS epidemic, with more than 64 000 people living with HIV and AIDS. The Real Involvement of People Living with HIV and AIDS (RIPA) in Madang on the northeastern coast of Papua New Guinea supports people in these communities to care for families affected by HIV through community and home-based palliative care programmes and strengthening referral services that enable PLHA to access treatment, care and support.[57] Cambodia may be characterized as a country emerging from a generalized HIV epidemic but still with a significant impact of HIV on society. Food security and income are critical for individuals, households and communities affected by HIV and AIDS. World Vision Cambodia, in partnership with the United Nations World Food Program (WFP), provides food aid to 2558 HIV/AIDS infected and affected households, with the monthly ration of 30kg of rice, 1kg of vegetable oil and 0.50kg of salt to supplement their own capacity. As one measure of the impact of the programme, the proportion of households which had sold rice land in the last two years fell from 23% in 2003 to 12% in 2008.[58]

In Bangkok slums, another programme run by PLWHA enables people to be cared for while living in the communities as an alternative to being admitted into hospice care. In addition to medical and psychosocial care, the programme supports quality of life essentials such as home repairs and micro-loans.[59]

Linked responses

In response to the parallel epidemics of HIV and tuberculosis, the National AIDS and Tuberculosis Programmes, in collaboration with International Union Against Tuberculosis and Lung Disease in Myanmar, provided same-day provider-initiated HIV counselling, testing and results to all adult TB patients and the spouses/children of TB/HIV patients residing in eight pilot township health centres. Among 3544 adult TB patients in 2008, 95% were offered a HIV test, 81% were tested and 29% were found to be HIV-infected. Of the spouses/children tested, 49% were HIV-infected.[60]

Many people in Pacific island countries (PICs) do not access HIV or sexually transmitted infection (STI) services because of perceived stigma, embarrassment and other cultural barriers. While HIV rates are mostly low, high rates of STIs and unplanned pregnancies exist. Link are being developed between reproductive health and HIV/STI services in several PICs. A comprehensive approach is being applied at policy, systems and service delivery levels, including youth/adolescent-friendly sexual and reproductive health services and "one-stop shops" including reproductive health, VCT, HIV/STI care and outreach to vulnerable populations. In 2007, the International Labour Organization (ILO) collaborated with UNAIDS and the Pacific Island chiefs of police to assist 13 police organizations in the Pacific to develop HIV/AIDS workplace policies. Workshops explored police HIV vulnerabilities and examined negative perceptions of police, injecting drug users, sex workers and men who have sex with men to improve understanding of the human impact of HIV-related discrimination and to reduce the negative images of PLHIV.[61]

In a programme which crosses borders, Medicins Sans Frontieres (Belgium) provides comprehensive care to Laotian and Myanmar

minority people, including ART, information and educational material in Thai, Lao and Myanmar languages, psycho-social support and reduction of stigma and discrimination among these vulnerable groups.[62] In Myanmar, the Private Partnership for Public Health (PPPH) has established a network of private practitioners, community-based care organizations, public hospitals, laboratories and an independent management. This model seeks to increase accountability and trust amongst partners, reinforce third party management, assure quality and empower community groups.[63]

Faith-based organizations play an important role in the response to HIV in the region. In Indonesian Papua, three Christian denominations formed a group of 48 pastor-leaders to provide HIV knowledge within the context of the church. In a rural district of Sri Lanka, the construction of a new harbour was reported to coincide with an increase in STDs in the local and construction communities. In response, Project Vidusetha involved Buddhist and Muslim religious leaders in reproductive health education and HIV prevention methods through 38 Buddhist Sunday schools and 17 Muslim equivalents. Religious leaders combined HIV knowledge with religious concepts regarding sexuality in their teaching activities. Open discussions regarding religion and sexuality helped to spread culturally sensitive messages.[64]

References

1. Lundgren JD, *et al.* Inferior clinical outcome of the CD4+ cell count-guided antiretroviral treatment interruption strategy in the SMART study: role of CD4+ Cell counts and HIV RNA levels during follow-up. *Journal of Infectious Diseases*, 2008, 197(8):1145–1155.
2. Emery S, *et al.* Major clinical outcomes in antiretroviral therapy (ART)-naive participants and in those not receiving ART at baseline in the SMART study. *Journal of Infectious Diseases*, 2008, 197(8):1133–1144.
3. Friis-Moller N, Worm SW. Can the risk of cardiovascular disease in HIV-infected patients be estimated from conventional risk prediction tools? *Clinical Infectious Diseases*, 2007, 45(8):1082–1084.
4. Friis-Moller N, *et al.* Class of antiretroviral drugs and the risk of myocardial infarction. *New England Journal of Medicine*, 2007, 356(17):1723-1735.
5. Gupta SK, *et al.* Guidelines for the management of chronic kidney disease in HIV-infected patients: recommendations of the HIV Medicine Association of the Infectious Diseases Society of America. *Clinical Infectious Diseases*, 2005, 40(11):1559–1585.
6. Leventhal JS, Ross MJ. Pathogenesis of HIV-associated nephropathy. *Seminars in Nephrology*, 2008, 28(6):523–534.
7. Bruggeman LA, *et al.* Nephropathy in human immunodeficiency virus-1 transgenic mice is due to renal transgene expression. *Journal of Clinical Investigation*, 1997, 100(1):84–92.
8. Wyatt CM, *et al.* The spectrum of kidney disease in patients with AIDS in the era of antiretroviral therapy. *Kidney International*, 2009, 75(4):428–434.
9. Lucas GM, *et al.* Highly active antiretroviral therapy and the incidence of HIV-1-associated nephropathy: a 12-year cohort study. *AIDS*, 2004, 18(3):541–546.
10. Schwartz EJ, Klotman PE. Pathogenesis of human immunodeficiency virus (HIV)-associated nephropathy. *Seminars in Nephrology*, 1998, 18(4):436–445.
11. Atta MG, Lucas GM, Fine DM. HIV-associated nephropathy: epidemiology, pathogenesis, diagnosis and management. *Expert Review of Anti-Infective Therapy*, 2008, 6(3):365–371.
12. Gerntholtz TE, Goetsch SJ, Katz I. HIV-related nephropathy: a South African perspective. *Kidney International*, 2006, 69(10):1885–1891.
13. Imai E, Matsuo S. Chronic kidney disease in Asia. *Lancet*, 2008, 371(9631):2147–2148.
14. Wong KM, *et al.* Corticosteroid therapy in a Chinese patient with nephropathy associated with human immunodeficiency virus infection. *Hong Kong Medical Journal*, 2004, 10(3):201–205.
15. Carbone L, *et al.* Course and prognosis of human immunodeficiency virus-associated nephropathy. *American Journal of Medicine*, 1989, 87(4):389–395.
16. Wyatt CM, Klotman PE, D'Agati VD. HIV-associated nephropathy: clinical presentation, pathology, and epidemiology in the era of antiretroviral therapy. *Seminars in Nephrology*, 2008, 28(6):513–322.
17. Lu TC, Ross M. HIV-associated nephropathy: a brief review. *Mount Sinai Journal of Medicine*, 2005, 72(3):193–199.

18. Barbaro G, *et al.* Cardiac involvement in the acquired immunodeficiency syndrome: a multicenter clinical-pathological study. Gruppo Italiano per lo Studio Cardiologico dei pazienti affetti da AIDS Investigators. *AIDS Research and Human Retroviruses*, 1998, 14(12):1071–1077.

19. Grundy SM, *et al.* Definition of metabolic syndrome: Report of the National Heart, Lung, and Blood Institute/American Heart Association conference on scientific issues related to definition. *Circulation*, 2004, 109(3):433–438.

20. Heidenreich PA, *et al.* Pericardial effusion in AIDS. Incidence and survival. *Circulation*, 1995, 92(11):3229–3234.

21. Currie PF, *et al.* A review of endocarditis in acquired immunodeficiency syndrome and human immunodeficiency virus infection. *European Heart Journal*, 1995, 16 Suppl B:15–18.

22. Thomas DL. Growing importance of liver disease in HIV-infected persons. *Hepatology*, 2006, 43(2 Suppl 1):S221–S229.

23. Vogel M, Rockstroh JK. Hepatotoxicity and liver disease in the context of HIV therapy. *Current Opinion in HIV and AIDS*, 2007, 2(4):306–313.

24. Rosenthal E, *et al.* Liver-related deaths in HIV-infected patients between 1995 and 2005 in the French GERMIVIC Joint Study Group Network (Mortavic 2005 study in collaboration with the Mortalite 2005 survey, ANRS EN19). *HIV Medicine*, 2009, 10(5):282–289.

25. S Galastri RB, P Sacchi, editor. The Chemokine Receptor CCR5 Mediates the Profibrogenic Actions of the HIV Envelope Protein Gp120 in Human Hepatic Stellate Cells. 44th Annual Meeting of the European Association for the Study of the Liver (EASL 2009); 2009 22-26 April; Copenhagen.

26. Thomas DL, *et al.* The natural history of hepatitis C virus infection: host, viral, and environmental factors. *Journal of American Medical Association*, 2000, 26;284(4):450–456.

27. Di Martino V, *et al.* Influence of HIV infection on the response to interferon therapy and the long-term outcome of chronic hepatitis B. *Gastroenterology*, 2002, 123(6):1812–1822.

28. Thio CL, *et al.* HIV-1, hepatitis B virus, and risk of liver-related mortality in the Multicenter Cohort Study (MACS). *Lancet*, 2002,360(9349):1921–1926.

29. Sulkowski MS, *et al.* Hepatotoxicity associated with antiretroviral therapy in adults infected with human immunodeficiency virus and the role of hepatitis C or B virus infection. *Journal of American Medical Association*, 2000, 283(1):74–80.

30. Shiels MS, *et al.* A meta-analysis of the incidence of non-AIDS cancers in HIV-infected individuals. *Journal of Acquired Immune Deficiency Syndrome*, 2009, 52(5):611–622.

31. *Hong Kong STD/AIDS Quarterly surveillance report,* Volume 15 No. 2. Centre for Health Protection, Department of Health, Hong Kong SAR, 2009.

32. HIV/AIDS in Hong Kong Living on the Edge, 2006. A Consultancy Report by Dr Tim Brown.

33. Recommended HIV/AIDS Strategies for Hong Kong 2007–2011. Hong Kong Advisory Council on AIDS.

34. WHO Western Pacific Regional Office. *Health Sector Response to HIV/AIDS among Men Having Sex with Men Consultation Report*, 2009.

35. Amjad Khan. Prevention of HIV/AIDS among Injecting Drug Users. 9th International Congress on AIDS in Asia and the Pacific, Bali, Indonesia, 2009.

36. Aye MS, *et al.* Wide Variation in Risk Behaviours among Injection Drug Users. 9th International Congress on AIDS in Asia and the Pacific, Bali, Indonesia, 2009.

37. Nizam UA, *et al.* Sexual act with multiple sex partners is an upcoming threat for rapid transmission of HIV among injecting drug users in Bangladesh. 9th International Congress on AIDS in Asia and the Pacific, Bali, Indonesia, 2009.

38. Nghiem THV, *et al.* Sexual Partners of IDUs in Viet Nam – baseline findings on a neglected risk group for HIV. 9th International Congress on AIDS in Asia and the Pacific, Bali, Indonesia, 2009.

39. Robert A, *et al.* WHO collaborative study on substitution therapy for opioid dependence and HIV/AIDS. 9th International Congress on AIDS in Asia and the Pacific, Bali, Indonesia, 2009.

40. Mak WL, *et al.* Universal HIV testing for drug users in methadone clinics by urine antibody test 4-year experience. 9th International Congress on AIDS in Asia and the Pacific, Bali, Indonesia, 2009.

41. Adiatma YM, *et al.* Costs of Methadone Maintenance Treatment in HIV/AIDS Control among Injecting Drug Users in Indonesia. 9th International Congress on AIDS in Asia and the Pacific, Bali, Indonesia, 2009.

42. He S, Wang L, Zhang G. Analysis of progress in MMT in Seven Programme Province of China Global Fund R4/China-UK AIDS Program. 9th International Congress on AIDS in Asia and the Pacific, Bali, Indonesia, 2009.

43. Shalini S, Luke S. Harm reduction the most effective strategy for management of OST service delivery. 9th International Congress on AIDS in Asia and the Pacific, Bali, Indonesia, 2009.

44. Sabina BB, *et al.* Securing a Comprehensive National IDU treatment package: a Public-Private-Public Initiative in India. 9th International Congress on AIDS in Asia and the Pacific, Bali, Indonesia, 2009.

45. Sonia B, Gimo V. Compulsory Drug Treatment Centres in Southeast Asia: Rights and Effectiveness. 9th International Congress on AIDS in Asia and the Pacific, Bali, Indonesia, 2009.

46. Lee MW, Barry, Li CH. Reaching the hard-to-reach MSM through VCT in collaboration with a TCM practitioner. 9th International Congress on AIDS in Asia and the Pacific, Bali, Indonesia, 2009.

47. Don Eliseo Lucero-Prisno III. Understanding Distorted Knowledge as a Pervasive Determinant of risk Among Asia-Pacific Seafarers. 9th International Congress on AIDS in Asia and the Pacific, Bali, Indonesia, 2009.

48. Henri P, *et al.* Reaching Men at High Risk of HIV Infection via Programs in Ports. 9th International Congress on AIDS in Asia and the Pacific, Bali, Indonesia, 2009.

49. Dadun, Heru S, Sabarinah P. Risk of HIV/AIDS Among Mobile Population in Northern Coastal of Java and North Sumatra, Indonesia. 9th International Congress on AIDS in Asia and the Pacific, Bali, Indonesia, 2009.

50. Martin CKK, *et al.* Injecting and sexual risk behaviour among fishermen in Kuantan, Malaysia. 9th International Congress on AIDS in Asia and the Pacific, Bali, Indonesia, 2009.

51. Mohd Dilshad, *et al.* Non-institutional HIV testing among Truckers. 9th International Congress on AIDS in Asia and the Pacific, Bali, Indonesia, 2009.

52. Kajal B. By hook or by crook: new initiatives to enforce greater IP rights & hamper access to generic medicine. 9th International Congress on AIDS in Asia and the Pacific, Bali, Indonesia, 2009.

53. Tsuchiya N, *et al.* Over 10 years of experience of treating HIV/AIDS patients at a government hospital in Thailand. 9th International Congress on AIDS in Asia and the Pacific, Bali, Indonesia, 2009.

54. Francisco XDM, *et al.* Policies for roll-out of second-line Regimen in India. 9th International Congress on AIDS in Asia and the Pacific, Bali, Indonesia, 2009.

55. Chinkholal T, *et al.* Structural Inequities in Universal Access in India. 9th International Congress on AIDS in Asia and the Pacific, Bali, Indonesia, 2009.

56. Alwiyah M, Retnosari A, Rizka A. Immunological and virological response to second-line ARV whose first-line ARV treatment failure. 9th International Congress on AIDS in Asia and the Pacific, Bali, Indonesia, 2009.

57. Joe E. Real Involvement of People Living with HIV and AIDS (RIPA) Initiative in Madang, Papua New Guinea. 9th International Congress on AIDS in Asia and the Pacific, Bali, Indonesia, 2009.

58. Pen S, Srey M. Food Aid Improves Quality of Life of HIV and AIDS-infected and affected households. 9th International Congress on AIDS in Asia and the Pacific, Bali, Indonesia, 2009.

59. Usanee J, *et al.* A successful homecare programme operated by PLWHIV to help PLWHIV in Bangkok's slum communities. 9th International Congress on AIDS in Asia and the Pacific, Bali, Indonesia, 2009.

60. Philippe C, *et al.* Uptake of Provider-Initiated HIV test for Tuberculosis patients and family members in Myanmar. 9th International Congress on AIDS in Asia and the Pacific, Bali, Indonesia, 2009.

61. Surfaka FK. Building empathy between police and MARPs: HIV/AIDS workplace policies are the key. 9th International Congress on AIDS in Asia and the Pacific, Bali, Indonesia, 2009.

62. Chaitha I, Chaitha W. HIV/AIDS Cross Border Competence, Thailand-Lao PDR-Myanmar: Healthcare Model of Chiang Saen Hospital, Thailand. 9th International Congress on AIDS in Asia and the Pacific, Bali, Indonesia, 2009.

63. Tazeem BT, Chris C, Steven L. A Partnership to Scale up ART Better Care/Support and Strengthen Patient Involvement. 9th International Congress on AIDS in Asia and the Pacific, Bali, Indonesia, 2009.

64. Sefnat JDL. The Pastor role: Ability to eliminate stigma and discrimination in the church and community in Merauke. 9th International Congress on AIDS in Asia and the Pacific, Bali, Indonesia, 2009.

This was formerly known as the Antiretroviral Newsletter. The aim of this biannual newsletter is to provide health workers in the Region with a brief, up-to-date summary of the latest developments in HIV prevention and in the management of HIV infection, including antiretroviral therapies and co-morbidities (or associated conditions).

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HIV/AIDS Prevention and Care Newsletter

Moving Towards Universal Access

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WHO releases four new treatment guidelines

During the XVIII International AIDS Conference held in Vienna, Austria, from 18 to 23 July 2010, WHO released four new treatment guidelines:

- *Antiretroviral Therapy for HIV Infection in Infants and Children (2010 revision)*
- *Antiretroviral Drugs for Treating Pregnant Women and Preventing HI V Infections in Infants (2010 version)*
- *Antiretroviral Therapy for HIV Infection in Adults and Adolescents (2010 revision)*
- *Guidelines on HIV and infant feeding*

These guidelines are intended primarily for use by treatment advisory boards, national AIDS programme managers and other senior policy-makers who are involved in the planning of national and international HIV care strategies. The new guidelines are part of WHO's commitment to achieve universal access to antiretroviral therapy (ART) by 2010.

Overarching principles

1. **Do no harm.** Preserve access for the most ill and most in need when introducing changes.
2. **Ensure access and equity.** All clinically-eligible people should be able to enter treatment services including ART with fair and equitable distribution of treatment services.
3. **Promote quality and efficiency.** Ensure delivery of the highest standards of care within a public health approach so as to achieve the greatest health impact with the optimal use of available human and financial resources.
4. **Be sustainable.** Understand the long-term consequences of change with the vision of providing continued, lifelong access to ART for those in need.

From evidence to recommendation

The process of formulating each set of guidelines began with a comprehensive and coordinated review and synthesis of available evidence focused on the three critical patient outcomes of mortality, HIV disease progression and severe adverse events. However, in creating these guidelines, consideration was given by WHO not only to the evidence and its quality but also to the risks and benefits, acceptability, feasibility and financial implications of the recommendations

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within the framework of a public health approach that seeks to maximize enrolment into quality HIV care and treatment programmes. A risk and benefit analysis was performed for each recommendation, resulting in it being rated either as strong or conditional. The quality of evidence was rated as high, moderate, low or very low based on the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) system for interpreting results from systematic reviews and making recommendations, which now is used by WHO for all guidelines' formulation. Details of the GRADE process are available in the WHO *Handbook for Guideline Development*. Geneva, WHO, 2010 (http://intranet.who.int/homes/rpc/documents/grc_handbook_mar2010-1.pdf)

WHO normative guidelines are meant for a global audience and it is expected that each country will adapt these guidelines to meet their own circumstances.

A major challenge in the implementation of these new recommendations in the context of limited human and financial resources will be the sustainability and maintenance of equity for ART access. The cost-effectiveness of ART is well established. However, providing ART to HIV-infected patients with higher CD4 counts, the use of more user-friendly, but currently more expensive, ART regimens and additional monitoring will increase initial financial demands in countries that already are struggling to provide ART to people in immediate need. Therefore, choices will need to be made and priorities set. Immediate and full adoption of these recommendations may not be practical, feasible or affordable in every setting. However, ART country planning should be directed towards the goal of their eventual implementation.

The difference between recommendations and guiding principles

While specific recommendations are provided wherever possible, some guidance is not amenable to the GRADE system of review because it reflects a set of values and practical considerations that should be applied to providing care within a particular programmatic setting. For the sections on laboratory monitoring and the package of care interventions, recommendations are replaced by guiding principles. Additionally, in the infant feeding *Rapid Advice*, recommendations are complemented by an extensive list of key principles (HIV and infant feeding: Revised Principles and Recommendations. *Rapid Advice*, November 2009 http://www.who.int/hiv/pub/paediatric/advice/en/).

Key messages

For adults and adolescents, the key messages are to start ART earlier (CD4 count ≤350 cells/mm^3), use less toxic and more patient-friendly ARV, including gradually phasing out stavudine (d4T) in first-line regimens. In addition, ART should be initiated in all individuals with TB/HIV coinfection and those with HBV/HIV coinfection who need treatment for their HBV and promote better use of laboratory monitoring.

For pregnant women who need ART for their own health, start ART at any gestational age following the same criteria

as for the general population and continue throughout pregnancy, delivery and thereafter. For pregnant women who are not in need of ART for their own health, antiretroviral (ARV) prophylaxis to reduce transmission to the infant should be started from as early as 14 weeks gestation (second trimester) or as soon as possible when women present late in pregnancy, in labour or at delivery.

There are two recommended options – A and B.

Option A consists of antepartum daily zidovudine (AZT), single dose nevirapine (sd-NVP) at the onset of labour, AZT + lamivudine (3TC) during labour and delivery and for seven days postpartum. Sd-NVP and AZT+3TC intra- and post-partum can be omitted if the mother receives more than four weeks of AZT during pregnancy. In breastfeeding infants, maternal ARV prophylaxis should be coupled with daily administration of NVP to the infant from birth until one week after all exposure to breast milk has ended. In nonbreastfeeding infants, maternal ARV prophylaxis should be coupled with the daily administration of NVP or AZT to the infant from birth until four weeks old to six weeks old.

Option B consists of triple ARV prophylaxis starting from as early as 14 weeks of gestation until one week after all exposure to breast milk has ended. Although triple ARVs do not offer any greater protection against *in utero* and intrapartum transmission compared to AZT alone, HIV-infected mothers who breastfeed need to start the three drugs at least three to four weeks in advance of delivery in order to protect their infants against HIV transmission through breastfeeding in the first few weeks of life.

Neither of these options is preferred over the other. All infants born to mothers on option B should receive NVP or AZT from birth until four to six weeks.

Recommendations on HIV and infant feeding include:

National health authorities should decide whether health services principally will counsel and support mothers known to be HIV-infected to either breastfeed and receive ARV interventions or to avoid all breastfeeding as the strategy that most likely will give infants the best chance of HIV-free survival. This decision[1] should be based on international recommendations and consideration of the socioeconomic and cultural contexts of the populations served by maternal, newborn and child health services, availability and quality of health services, local epidemiology, including HIV prevalence among pregnant women, the main causes of maternal and child under-nutrition and the main causes of infant and child mortality.

In settings where breastfeeding and ARVs are promoted, mothers known to be HIV-infected (and whose infants are HIV-uninfected or of unknown HIV status) should exclusively breastfeed their infants for the first six months, introducing appropriate complementary foods thereafter and continue breastfeeding for the first year. Breastfeeding should then only stop once a nutritionally-adequate and safe diet without breast milk can be provided.

While ARV interventions are being scaled up, national authorities should not

1 WHO is developing guidance to assist countries in this decision-making process, including guidance on steps to reach these standards of care.

be deterred from recommending that HIV-infected mothers breastfeed as the most appropriate infant feeding practise in their setting. ARV interventions to prevent postnatal transmission of HIV make breastfeeding even more advantageous for child development and survival. However, the absence of ARVs should not be a contraindication for HIV-infected mothers to breastfeed where environmental and social circumstances are not safe or supportive of replacement feeding. It is important to prevent the misconception that HIV-infected mothers only should breastfeed if they have ARVs.

Commercial infant formula milk only should be considered as an alternative to breastfeeding if home and social conditions are such that it is safe and carries a low risk of diarrhoea and malnutrition, it is adequate to support normal growth and development of the infant and is feasible and acceptable in the community. For infants more than six months old, animal milk (boiled for infants under 12 months), is another alternative. All children need complementary foods from six months old. Heat-treated, expressed breast milk may be used as an interim feeding strategy, for example in the case of mastitis. When the infant is known to be HIV-infected, exclusively breastfeed for the first six months of life and continue breastfeeding as per the recommendations for the general population, which is up to two years or beyond.

The recommendations are summarized in Tables 1, 2 and 3.

Table 1: Antiretroviral treatment for HIV infection in adults and adolescents

When to start

1. Start antiretroviral treatment in all patients with HIV who have CD4 count ≤350 cells/ mm^3 regardless of clinical symptoms.
2. CD4 testing is required to identify if patients with WHO clinical stage 1 or 2 disease and need to start ART.
3. Start antiretroviral treatment in all patients at WHO clinical stage 3 or 4 regardless of CD4 count.

What to start

First-line therapy should consist of a nonnucleoside reverse transcriptase inhibitor (NNRTI) + two NRTIs, one of which should be AZT or tenofovir (TDF). Start one of the following regimens in ART-naïve individuals eligible for treatment:

- AZT +3TC + efavirenz (EFV)
- AZT + 3TC + NVP
- TDF + 3TC or emtricitabine (FTC) + EFV
- TDF + 3TC or FTC + NVP

Do not start EFV during the first trimester of pregnancy.

ART for HIV/tuberculosis coinfection

1. Start ART in all HIV-infected individuals with active tuberculosis (TB) regardless of CD4 cell count.
2. Start TB treatment first followed by ART as soon as possible after starting TB treatment.
3. Use efavirenz EFV as the preferred NNRTI in patients starting ART while on TB treatment.

ART for HIV/HBV co-infection

1. Start ART in all HIV/HBV coinfected individuals who require treatment for their HBV infection, regardless of CD4 cell count or WHO clinical stage.
2. Start TDF and 3TC- or FTC-containing antiretroviral regimens.

When to Switch ART

1. Where available, use viral load (VL) to confirm treatment failure.
2. Where routinely available, use VL every six months to detect viral replication.
3. A persistent viral load above 5000 copies/ml confirms treatment failure.
4. Where VL is not available, use immunological criteria to confirm clinical failure.

Second-line ART

1. Use a boosted protease inhibitor (PI/r) plus two nucleoside analogues (NRTIs).
2. ATV/r and LPV/r are the preferred boosted PIs for second-line ART.
3. Simplification of second NRTI options is recommended
   - If d4T or AZT has been used in first-line use TDF+3TC or FTC as the NRTI backbone in second line
   - If TDF has been used in first-line use AZT+3TC as the NRTI backbone in second line

Third-line regimens

1. National programmes should formulate policies for third-line therapy that consider funding, sustainability and providing equitable access to ART.
2. Third-line regimens should include new drugs likely to have anti-HIV activity.
3. Patients failing a second-line regimen with no new ARV options should continue with a tolerated regimen.

Table 2: Use of ARVs for treating women and preventing HIV infection in infants

Start ART in all pregnant women with HIV and CD4 count <350 cells/mm^3, regardless of clinical symptoms. Start ART in all pregnant women with HIV and WHO clinical stage 3 or 4, regardless of CD4 count.
HIV-infected pregnant women in need of ART for their own health should start ART regardless of gestational age and continue throughout pregnancy, delivery and thereafter.
Start one the following regimens in ART-naïve pregnant women eligible for treatment: AZT + 3TC + EFV, AZT + 3TC + NVP, TDF + 3TC or FTC+ EFV, TDF + 3TC or FTC + NVP (Do not use EFV in the first trimester)
Infants born to HIV-infected women receiving ART for their own health should receive: a. for breastfeeding infants: daily NVP from birth until six weeks old b. for nonbreastfeeding infants: daily AZT or NVP from birth until six weeks old
All HIV-infected pregnant women who are not in need of ART for their own health require an effective ARV prophylaxis strategy to prevent HIV transmission to the infant. ARV prophylaxis should be started from as early as 14 weeks gestation (second trimester) or as soon as possible when women present late in pregnancy, in labour or at delivery.
Depending on the prophylactic option chosen, either the mother or the exposed infant should receive ARVs from birth until a week after all exposure to breast milk has ended.

Table 3: Infant feeding

Ensuring mothers receive the care they need
Provide lifelong antiretroviral therapy or antiretroviral prophylaxis interventions to reduce HIV transmission through breastfeeding.

Which breastfeeding practises and for how long
Mothers known to be HIV-infected (and whose infants are HIV uninfected or of unknown HIV status) should exclusively breastfeed their infants for the first six months, introducing appropriate complementary foods thereafter, and continue breastfeeding for the first year. Breastfeeding should then only stop once a nutritionally adequate and safe diet without breast milk can be provided.

When mothers decide to stop breastfeeding
Stop gradually within a month. Mothers or infants who have been receiving ARV prophylaxis should continue prophylaxis for a week after breastfeeding is fully stopped. Stopping breastfeeding abruptly is not advisable.

What to feed infants when mothers stop breastfeeding
Infants should be provided with safe and adequate replacement feeds to enable normal growth and development.
Alternatives to breastfeeding include:
For infants less than six months old:
- Commercial infant formula milk so long as home conditions are fulfilled,
- Expressed, heat-treated breast milk

For children over six months old:
- Commercial infant formula milk so long as home conditions are fulfilled,
- Animal milk (boiled for infants under 12 months) as part of a diet providing adequate micronutrient intake. Meals, including milk-only feeds, other foods and combination of milk feeds and other foods, should be provided four or five times per day.

All children need complementary foods from six months old.

Conditions needed to safely formula feed
Only give commercial infant formula milk as a replacement feed to their HIV-uninfected infants or infants who are of unknown HIV status, when specific conditions are met: (*referred to as AFASS – affordable, feasible, acceptable, sustainable and safe*)

a. safe water and sanitation are assured at the household level and in the community, and,
b. the mother, or other caregiver reliably can provide sufficient infant formula milk to support normal growth and development of the infant, and,
c. the mother or caregiver can prepare it cleanly and frequently enough so that it is safe and carries a low risk of diarrhoea and malnutrition, and,
d. the mother or caregiver can, in the first six months, exclusively give infant formula milk, and,
e. the family is supportive of this practise, and,
f. the mother or caregiver can access health care that offers comprehensive child health services.

Heat-treated, expressed breast milk

Consider expressing and heat-treating breast milk as an interim feeding strategy:

- In special circumstances such as when the infant is born with low birth weight or is otherwise ill in the neonatal period and unable to breastfeed; or
- When the mother is unwell and temporarily unable to breastfeed or has a temporary breast health problem such as mastitis; or
- To assist mothers to stop breastfeeding; or
- If antiretroviral drugs are temporarily not available.

When the infant is HIV-infected

Mothers strongly are encouraged to exclusively breastfeed for the first six months of life and continue breastfeeding as per the recommendations for the general population, which is up to two years or beyond.

Update on nevirapine (NVP)

The efficacy and safety of nevirapine in adults and pregnant women was the subject of much discussion during the preparation and peer review of these guidelines.

On the question of efficacy, six randomized clinical trials (RCTs) which have compared NVP to EFV found no differences in virological outcomes.[1–6] One RCT reported that EFV was less likely than NVP to be associated with development of antiretroviral resistance.[5]

On NVP safety, while WHO continues to recommend caution in the use of NVP in women with CD4 counts >250 cells/mm^3 or in those with unknown CD4 cell counts, the review conducted during the formulation of the guidelines did not confirm an increased risk of serious adverse events in this group. This became an important issue since NVP is recommended for initial ART and the new CD4 cell threshold for initiation is ≤350 cells/mm^3. The United States of America Food and Drug Administration (FDA) has cautioned against the use of NVP in women with CD4 cell counts 250-350 cells/mm^3 and men with CD4 count >400 cells/mm^3. In addition, the manufacturer includes a black boxed warning in the product information.

Data are conflicting, with increased rates of hepatotoxicity and hypersensitivity reported in some studies[6–12] and not in others.[13–20] Some studies reported no difference in adverse events between those with low and high CD4 cell counts in virologically suppressed patients switching to NVP.[16, 21, 22] These studies support the concept that a suppressed viral load is a protective factor for NVP-related hypersensitivity when patients need to switch from an EFV- (or PI) based regimen to NVP. Only one study reported an increased risk of hypersensitivity and hepatotoxicity in men with a CD4 count >400 cells/mm^3.[23]

On NVP safety in pregnant women, data from two prospective cohorts report no association between NVP and liver enzyme elevation. However, pregnancy itself was associated with an increased risk of any liver enzyme elevation.[24]

On whether NVP can be used once or twice daily, WHO continues to recommend

that NVP be dosed at 200 mg twice daily. Currently, only the guidelines of the European AIDS Clinical Society (www.europeanaidsclinicalsociety.org/guidelines.asp) recommend that NVP can be dosed at 400 mg once daily. However, this recommendation applies to patients who begin a standard regimen of 200 mg BID (with a two-week lead-in dosing), achieve subsequent virological suppression and then switch to 400 mg OD. The evidence is mixed. Three studies have reported failure to suppress viral replication in patients receiving NVP once daily.[25–27] However, the ARTEN study reported noninferiority among patients taking either NVP once or twice daily or ATZ/r arm, both in combination with two NRTIs.[28] Data from cohort studies (AIDS Therapy Evaluation in the Netherlands [ATHENA] and Swiss HIV Cohort) support that NVP once daily is at least as effective in suppressing VL as NVP twice daily.[29] It should be noted that, in the landmark 2NN study, higher rates of hepatotoxicity were reported NVP in the 400 mg OD arm of the study.[6] For now, NVP 200 mg BID remains the recommendation in resource-limited settings, especially when VL and liver enzyme monitoring is not available.

Update on generic antiretroviral drugs

As of 25 February 2010, the FDA had issued approval or tentative approval of 107 generic ARV drugs, either as single products or dual and triple fixed-dose combinations.[30] Tentative approval means that the product has met all safety, efficacy and manufacturing quality standards for marketing in the United States of America but the product still has marketing protection there. This FDA approval scheme was started in 2004 to support the roll-out of ART under the United States President's Emergency Plan for AIDS Relief (PEPFAR), which can purchase any product that has either a "full" or "tentative" FDA approval.[30] The largest manufacturer of generic ARVs is India, with all WHO-recommended first- and second-line ARVS available from one of the many Indian companies.

The WHO-prequalified list of generic ARVS does not include atazanavir. India's Patent Office (IPO) recently rejected a patent application for darunavir, paving the way for generic versions of this second generation protease inhibitor, which is now recommended by WHO as one of the components of third-line regimens. [31]

The World Health Organization Network for HIV and Health in the Western Pacific Region: An Innovative Approach to Technical Support

By: Ms Charmaine Turton of the Albion Street Centre, Sydney, Australia

Introduction

A comprehensive response to HIV and AIDS requires mobilization and collaboration across many sectors and partners. The health sector plays a central leadership and coordination role in response to the epidemic and provides many critical opportunities for scaling up HIV-related services.

WHO, within the Joint United Nations Programme on HIV/AIDS (UNAIDS), is responsible for providing technical support for the health sector response to HIV/AIDS.[32] With increased availability of funds and resources, there has been unprecedented demand from Member States for assistance in responding to the complexities of global health issues and the interpretation of the technical contents of WHO's programme on HIV/AIDS.

To address this demand, the Western Pacific Regional Office recognized the potential to build a network of WHO Collaborating Centres and other key Technical Partners that are well positioned to provide technical cooperation to Member States. Following a review of the technical expertise of existing WHO Collaborating Centres and partner institutions to contribute towards effective HIV/AIDS interventions, a consultation was held in December 2008 that, among other things, endorsed the establishment of the WHO Network for HIV and Health in the Western Pacific Region.[33]

Since then, work has progressed steadily to establish the Network. In November 2009, a second consultation was held to consolidate achievements to date and identify future steps and strategies for the advancement of the Network.[34]

The Innovative Concept and Establishment of the WHO Network for HIV and Health in the Western Pacific Region

The concept of the WHO Network for HIV and Health in the Western Pacific Region is to implement a multidisciplinary approach to HIV as a public health issue. In contrast to other networks, the aim is to link centres beyond a single topic area, recognizing both HIV-specific centres and those with the potential to work alongside these centres, to provide valuable input to HIV approaches and activities and support the HIV response.

In accordance with the concept of a multidisciplinary network, preliminary research was completed in 2008 to map the capacity and potential of existing collaborating centres and technical partners in the Western Pacific Region to contribute to a regional HIV network. Through a two-stage process of database analysis[35-36] and survey methodology from almost 200 institutions, 25 were selected for invitation to the initial consultation in December 2008.[33] Seventeen of these conducted work with a direct or strong

relationship to the field of HIV and eight had possible potential to contribute to an HIV network. Some had related overlapping interests (communicable disease, harm reduction, nursing, paediatrics, reproductive health, women) and others had broader fields of expertise (health promotion, health systems planning, research).

Overview of the WHO Network for HIV and Health in the Western Pacific Region

Mission

To collaborate in supporting Member States to implement effective multidisciplinary public health approaches to HIV according to WHO strategic directions.

Objectives

(1) Provide Member States with sustainable technical assistance through a multidisciplinary Network.
(2) Ensure quality of technical assistance through consistent and coherent approaches provided by a Network of experts in the field.
(3) Support Member States to build health system capacity in HIV and health.
(4) Contribute to critical review, update of evidence, scientific debate and operational research related to HIV and health.

Functions

- Advocacy
- Capacity-building
- Information dissemination
- Networking
- Operational research
- Technical support
- Tools and guidelines

Membership

Membership has been based on the concept of establishing a network of multidisciplinary organizations which together have the capacity to support the HIV response within a public health approach focused on the strengthening of health systems as a whole.

The Network is composed of 18 core and founding member institutions that attended the first and second consultations and each of which have completed a Declaration of Commitment to the Network. Fifteen of these are WHO Collaborating Centres and three are Technical Partners of WHO*. Overall, they represent nine countries from the Western Pacific Region across a range of disciplines and fields of expertise.

Table 4: Members of the WHO Network for HIV and Health in the Western Pacific Region

INSTITUTION	COLLABORATING CENTRE (CC)	COUNTRY
The Albion Street Centre	WHO Collaborating Centre for Capacity Building and Health Care Worker Training in HIV/AIDS Care, Treatment and Support	Australia
National Serology Reference Laboratory	WHO Collaborating Centre for Diagnostics and Laboratory Support for HIV/AIDS and Other Blood-Borne Infections	Australia
Key Centre for Women's Health in Society, Melbourne School of Population Health	WHO Collaborating Centre for Women's Health	Australia
Programme of International Research and Training, National Drug and Alcohol Research Centre	WHO Collaborating Centre for the Prevention and Control of Alcohol and Drug Abuse	Australia
Department of Microbiology, The Prince of Wales Hospital	WHO Collaborating Centre for Sexually Transmitted Diseases	Australia
Royal Children's Hospital, Melbourne	WHO CC for Research and Training in Child and Neonatal Health	Australia
*Burnet Institute (Macfarlane Burnet Institute for Medical Research and Public Health)** *Centre for International Health* *Centre for Population Health* *Centre for Virology* *Centre for Immunology*		Australia
Shanghai (Red Cross) Blood Centre	WHO Collaborating Centre for Blood Transfusion Services	China
National Center for STD Control, China CDC	WHO Collaborating Centre for Prevention and Control of Sexually Transmitted Infections	China
Clinical Research Center for AIDS/STD, Beijing Ditan Hospital	WHO Collaborating Centre for Comprehensive Management of HIV Treatment and Care	China
The Hong Kong Polytechnic University	WHO Collaborating Centre for Community Health Services	Hong Kong, (China)

INSTITUTION	COLLABORATING CENTRE (CC)	COUNTRY
Research Institute of Tuberculosis	WHO Collaborating Centre for Reference, Research and Training on Tuberculosis	Japan
*University of Malaya** *Centre of Excellence for Research in AIDS (CERIA)*		Malaysia
Pacific Paramedical Training Centre	WHO Collaborating Centre for External Quality Assessment in Health Laboratory Services	New Zealand
College of Nursing, University of the Philippines	WHO Collaborating Centre for Leadership in Nursing Development	The Philippines
Communicable Disease Education Department, Adult Health Division, Singapore Health Promotion Board	WHO Collaborating Centre for Health Promotion and Disease Prevention	Singapore
Occupational Disease Department, National Institute of Occupational & Environmental Health	WHO Collaborating Centre for Occupational Health	Viet Nam
*National Centre in HIV Epidemiology and Clinical Research** *University of New South Wales (NCHECR/UNSW)*		Australia

*Technical Partner

Management

Management of the Network is the responsibility of the Western Pacific Regional Office, mainly through its HIV/AIDS/STI (HSI) team within the Division of Combating Communicable Diseases (DCC). The Albion Street Centre, WHO Collaborating Centre for Capacity Building and Health Care Worker Training in HIV/AIDS Care, Treatment and Support (Sydney, Australia), has supported the Western Pacific Regional Office HSI team by acting as key facilitator to follow up the agreed next steps from consultation meetings.

Next steps in the Western Pacific Region

The WHO Network for HIV and Health in the Western Pacific Region has achieved significant progress since the endorsement of its establishment in December 2008. Members have committed to progression of the Network guided by the agreed mission, objectives and principles of operation. These include quality, synergy, coherence, timeliness, predictability, country ownership, approaches for sustainability and long-term national capacity.

The Network possesses a diverse range of multidisciplinary expertise to support Member States in the continued scale-up of interventions for the health sector response to HIV, health systems strengthening and progress towards universal access and the Millennium Development Goals. In addition to responding to requests for technical assistance from Member States, the Network proactively will pursue initiatives for regional health systems strengthening. Approaches of the Network will be directed by knowledge of the epidemic and national health systems and will ensure monitoring and evaluation measures that can document results and demonstrate success.

Dr Shin Young-soo, WHO Regional Director for the Western Pacific, has stated that his expectations from the Network are for significant increases in the volume and quality of technical support provided to national programmes in the Region. In addition, he hopes that the Network will engage in other functions to make use of its technical competencies, such as promoting and engaging in technical dialogue and exchanges on critical scientific matters and developments and offering a regional audience for analysis and interpretation of emerging issues.

Key goals of the Network in the next phase of its evolution are establishing a viable business plan and building self-sustainability in order to attract donor funds. Promotion of the Network -- through engagement of WHO Country Offices, the establishment of a website and an official launch, including a white paper for public distribution -- will play a major role in this phase.

Initiatives in other regions

The innovation of the WHO Network for HIV and Health in the Western Pacific Region has guided the exploration of a new paradigm of response at a broader level within Headquarters. Mirroring the Western Pacific Region's experience, this response involves multidisciplinary collaboration among WHO Collaborating Centres, Knowledge Hubs and other key Technical Partners and Institutions with established expertise in various aspects of the health sector response to HIV/AIDS.

In September 2009, Headquarters convened a consultation which endorsed the establishment and development of WHO HIV/AIDS Regional Technical Support Networks.[37] The consultation built extensively on the initial experiences of establishing this Network in the Western Pacific Region and expanded the lessons learnt to all other WHO regions. An operational framework was generated as a foundation for a common and shared approach across regions, and the Western Pacific Region Network progress is in line with the agreements and overarching framework of the September 2009 global consultation. The Western Pacific Region Network is leading the way with this innovation and future work undertaken will indeed be looked upon by other regions with interest.

For more information

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References

1. Ayala Gaytan JJ, et al. Nevirapine or efavirenz in combination with two nucleoside analogues in HIV infected antiretroviral naïve patients. *Medicine Intern Mexico*, 2004(20:24).

2. Manosuthi, W., et al. A randomized trial comparing plasma drug concentrations and efficacies between two non nucleoside reverse-transcriptase inhibitor-based regimens in HIV-infected patients receiving rifampicin: the N2R Study. *Clinical Infectious Diseases*, 2009. 48(12): 1752–1759.

3. Nunez, M., et al. SENC (Spanish efavirenz vs. nevirapine comparison) trial: a randomized, open-label study in HIV-infected naive individuals. *HIV Clinical Trials*, 2002. 3(3):186–194.

4. Sow PG, et al. Efficacy and safety of lamivudine+zidovudine+efavirenz and lamivudine+zidovudine+névirapine in treatment HIV1 infected patients. A rétrospective cross study analysis. XVI International AIDS Conference. 2006. Toronto, Canada.

5. van den Berg-Wolf, M., et al. Virologic, immunologic, clinical, safety, and resistance outcomes from a long-term comparison of efavirenz-based versus nevirapine-based antiretroviral regimens as initial therapy in HIV-1-infected persons. *HIV Clinical Trials*, 2008. 9(5): 324–336.

6. van Leth, F., et al. Comparison of first-line antiretroviral therapy with regimens including nevirapine, efavirenz, or both drugs, plus stavudine and lamivudine: a randomised open-label trial, the 2NN Study. *Lancet*, 2004. 363(9417): 1253–1263.

7. Hitti, J., et al. Maternal toxicity with continuous nevirapine in pregnancy: results from PACTG 1022. *Journal of Acquired Immune Deficiency Syndrome*, 2004. 36(3): 772–776.

8. Jamisse, L., et al. Antiretroviral-associated toxicity among HIV-1-seropositive pregnant women in Mozambique receiving nevirapine-based regimens. *Journal of Acquired Immune Deficiency Syndrome* , 2007. 44(4):371–376.

9. Mocroft, A., et al. Risk of discontinuation of nevirapine due to toxicities in antiretroviral-naive and -experienced HIV-infected patients with high and low CD4+ T-cell counts. *Antiretroviral Therapy*, 2007. 12(3): 325–333.

10. Lyons, F., et al. Maternal hepatotoxicity with nevirapine as part of combination antiretroviral therapy in pregnancy. *HIV Medicine*, 2006. 7(4):255–260.

11. Kiertiburanakul, S., et al. Risk factors for nevirapine-associated rash among HIV-infected patients with low CD4 cell counts in resource-limited settings. *Current HIV Research*, 2008. 6(1): 65–69.

12. Taiwo, B.O., Nevirapine toxicity. *International Journal of STD & AIDS*, 2006. 17(6): 364–369; quiz 370.

13. Knobel, H., et al. Risk of side effects associated with the use of nevirapine in treatment-naive patients, with respect to gender and CD4 cell count. *HIV Medicine*, 2008. 9(1): 14–18.

14. Kondo, W., et al. Nevirapine-induced side effects in pregnant women: experience of a Brazilian university hospital. Brazil *Journal of Infectious Diseases*, 2007. 11(6): 544–548.

15. Bonjoch, A., et al. Long-term safety and efficacy of nevirapine-based approaches in HIV type 1-infected patients. *AIDS Research and Human Retroviruses*, 2006. 22(4): 321–329.

16. De Lazzari, E., et al. Hepatotoxicity of nevirapine in virologically suppressed patients according to gender and CD4 cell counts. *HIV Medicine*, 2008. 9(4): 221–226.

17. Torti, C., et al. Analysis of severe hepatic events associated with nevirapine-containing regimens: CD4+ T-cell count and gender in hepatitis C seropositive and seronegative patients. *Drug Safety*, 2007. 30(12): 1161–1169.

18. Manfredi, R. and L. Calza, Nevirapine versus efavirenz in 742 patients: no link of liver toxicity with female sex, and a baseline CD4 cell count greater than 250 cells/microl. *AIDS*, 2006. 20(17): 2233–2236.

19. Manfredi, R. and L. Calza, Safety issues about nevirapine administration in HIV-infected pregnant women. *Journal of Acquired Immune Deficiency Syndrome*, 2007. 45(3): 365–368.

20. Phanuphak, N., et al. Nevirapine-associated toxicity in HIV-infected Thai men and women, including pregnant women. *HIV Medicine*, 2007. 8(6): 357–366.

21. Kumarasamy, N., et al. Safety of switching to nevirapine-based highly active antiretroviral therapy at elevated CD4 cell counts in a resource-constrained setting. *Journal of Acquired Immune Deficiency Syndrome*, 2007. 45(5): 598–600.

22. Wit, F.W., et al. Discontinuation of nevirapine because of hypersensitivity reactions in patients with prior treatment experience, compared with treatment-naive patients: the ATHENA cohort study. *Clinical Infectious Diseases*, 2008. 46(6):933–940.

23. Baylor, M.S. and R. Johann-Liang, Hepatotoxicity associated with nevirapine use. *Journal of Acquired Immune Deficiency Syndrome*, 2004. 35(5): 538–539.

24. Ouyang, D.W., et al. Increased risk of hepatotoxicity in HIV-infected pregnant women receiving antiretroviral therapy independent of nevirapine exposure. *AIDS*, 2009. 23(18): 2425–2430.

25. Lapadula, G., et al. Risk of early virological failure of once-daily tenofovir-emtricitabine plus twice-daily nevirapine in antiretroviral therapy-naive HIV-infected patients. *Clinical Infectious Diseases*, 2008. 46(7): p. 1127-9.

26. Towner W, K.H., LaRivie`re M et al. . Efficacy of a once daily regimen of nevirapine (NVP), lamivudine (3TC) and tenofovir (TDF) in treatment-naive HIV infected patients: a pilot study. in Seventh International Congress on Drug Therapy in HIV Infection. 2004.

27. Rey, D., et al., High rate of early virological failure with the once-daily tenofovir/lamivudine/nevirapine combination in naive HIV-1-infected patients. *Journal of Antimicrobial Chemotherapy*, 2009. 63(2): 380–388.

28. Vicente Soriano, S.K., Horacio Migrone, et al. Prospective randomised comparison of Nevirapine and Atazanavir/ritonavir both combined with Tenofovir DF/Emtricitabine in treatment-naïve HIV-1 infected patients: ARTEN Study week 48 results in 5th IAS Conference on HIV Pathogenesis, Treatment and Prevention 2009. Capetown, South Africa.

29. Alexandra Calmy, A.N., et al. and for the Swiss HIV Cohort Study and the Netherlands ATHENA Observational Cohort. Nevirapine Administered Once Daily Is as Efficient as a Twice-daily Dosing. A Collaborative Cohort Study. 15th Conference on Retroviruses and Opportunistic Infections. 2009. Boston.

30. FDA. International Programs President's Emergency Plan for AIDS Relief Approved and Tentatively Approved Antiretrovirals in Association with the President's Emergency Plan. 2010

[cited 22 March 2010]; Available from: http://www.fda.gov/internationalprograms/fdabeyondourbordersforeignoffices/asiaandafrica/ucm119231.htm.

31. Kartik K Venkatesh, N.K.a.K.H.M., Indian manufacture of new generic antiretrovirals: implications for global access to anti-HIV drugs. *HIV Therapy*, 2010.

32. World Health Organization (2007). *Towards universal access by 2010: How WHO is working with countries to scale-up HIV prevention, treatment, care and support*. WHO Press: Geneva, Switzerland. Available from: http://www.who.int/hiv/pub/advocacy/universalaccess/en/

33. Consultation on the Development of a Regional Network of WHO Collaborating Centres and Technical Partners on HIV/AIDS in the Western Pacific Region, WHO Western Pacific Region, Manila, Philippines 3-4 December 2008, Report Series Number RS/2008/GE/52(PHL). http://www.wpro.who.int/internet/resources.ashx/HSI/report/MeetingReport_CollabMtg_Dec2008.pdf

34. Consultation on the Strengthening of the World Health Organization Network for HIV and Health in the Western Pacific Region, WHO Western Pacific Region, Manila, Philippines 24-26 November 2009, ReportSeriesNumberRS/2009/GE/66(PHL). http://www.wpro.who.int/sites/hsi/meetings/whocollabmtg_nov2009.htm

35. WHO Regional Office for the Western Pacific Database http://www.wpro.who.int/information_sources/collaborating_centres/collaborating_centres.htm

36. World Health Organization (WHO) Collaborating Centres Global Database http://www.who.int/collaboratingcentres/database/en/

37. Consultation on the Development of Regional Networks of World Health Organization Collaborating Centres, Knowledge Hubs and Technical Partners on HIV/AIDS, WHO Headquarters, Geneva, Switzerland, 24-25 September 2009 (Draft version, yet to be released).

This was formerly known as the Antiretroviral Newsletter. The aim of this biannual newsletter is to provide health workers in the Region with a brief, up-to-date summary of the latest developments in HIV prevention and in the management of HIV infection, including antiretroviral therapies and co-morbidities (or associated conditions).

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