THE
HIV/AIDS NEWSLETTER

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From the Director's Desk

Around the globe HIV research continues apace with newer ideas, perspectives, drug discoveries, diagnostic development and technological innovations. In this issue, a repertoire of interesting reviews by our experts on anti-viral drug resistance and challenges on our way forward, chances of development of therapeutic innovations with biological options, newer diagnostic tools and recent updates from around the globe on HIV science is described. While HIV-1 and HIV-2 Group O infections are predominant in Africa, these days, it is not uncommon to detect these strains in other parts of the world. We welcome the announcement by FDA that it has approved the first nucleic acid test to screen for the presence of 2 divergent HIV types: HIV-2 and HIV-1 group O that would assure safer blood supply through enhanced screening of blood and tissue. Other highlights of this issue include articles on TB, syphilis, TLR7 polymorphism and disease progression and much more updates on anti-retrovirals.

We have also included a report on CART 2009 (HIV disease and antiretroviral treatment update) and TYBS 2009 (Bioethics update) hosted by YRGCARE in January 2009. In continuation, I welcome readers of this newsletter to register for our Second HIV Science Symposium to be held in August 2009.

I hope that you enjoy reading this issue and will nourish us with your suggestions and feed back.

Sincerely,

Prof. Suniti Solomon, MD.
Editor-in-Chief

MINIREVIEW
Drug Resistance

Antiretroviral Drug Resistance Evolution in the Context of HIV Diversity

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At the end of 2007, an estimated 33 million people were living with the Human Immunodeficiency Virus (HIV), and more than 25 million have died of AIDS (http://www.unaids.org). International involvement in global HIV/AIDS care and access to life-saving combination antiretroviral therapy (cART) are progressively increasing. Failure to respond to therapy can result from lack of adherence, pharmacological factors, or pre-existing or acquired HIV drug resistance [Shafer *et al.*, 2008]. The understanding of the principles of drug resistance evolution in the context of the vast HIV diversity is important, as more viral recombination is identified and human immigration and migration are intensified.

HIV Drug Resistance.

Pre-existing, or transmitted, drug resistance occurs when a patient is infected with an HIV variant that is already resistant to one or more antiretrovirals [Geretti, 2007]. Acquired drug resistance occurs when a specific viral population within an infected individual gains selective advantage over other populations by antagonizing specific medications, and replicates despite the presence of those drugs [Shafer *et al.*, 2002]. This selective advantage occurs through evolution of mutations in viral proteins that serve as drug targets, which prevent effective drug binding and action and permit viral replication. To complete the circle, viruses that acquired drug resistance mutations can in turn be transmitted to HIV non-infected or even infected individuals.

Evolution of drug resistance is concerning because it can limit treatment options, reduce probability of complete viral suppression and lead to current or future regimen failure. Moreover, drugs from one drug class have a similar mode of action, and resistance to one drug can result in cross resistance to other drugs from the same class. To further complicate things, some resistant viral populations exist as minority variants, as small hard-to-recognize proportions of the entire viral population, and others integrate their viral nucleic acids into human genetic material. Both of these scenarios result in preservation of potentially resistance viral variants that can replicate in convenient circumstances like suitable drug pressure and eventually lead to treatment failure. In settings where cART has been around for a significant period of time, drug resistance is prevalent. Reported rates are as high as 20% for transmitted resistance in untreated individuals [Little *et al.*, 2002], and 70% for acquired resistance in patients on cART [Richman *et al.*, 2004]. As a result, the use of resistance testing in clinical care is incorporated into treatment guidelines, mostly for examination of drug resistance upon infection, prior to treatment initiation, upon treatment failure and in pregnancy [Hirch *et al.*, 2008]. In India, as in many resource-limited settings, the use of drug resistance testing in clinical care is still uncommon. However, local expertise is being developed at YRG CARE [Balakrishnan *et al.*, 2005], as well as other locations [Sen *et al.*, 2007; Arora *et al.*, 2008], to adequately assess the inevitable and expected rise in drug resistance prevalence.

HIV Diversity.

HIV is characterized by a wide range of viral genetic diversity among distinct types, groups and clades, or subtypes [McCutchan, 2006]. The viruses that

cause AIDS are the only known members of the lentivirus family of retroviruses, which infect humans, after undergoing cross species transmission events from non-human primates. There are two distinct types of human retroviruses, HIV-1 and HIV-2. These viruses are distinguished by their genome organizations and phylogenetic relationships. HIV-1 is the major pathogen responsible for the AIDS pandemic. Further analyses of different strains of HIV-1 from diverse geographical origins, show that isolates can be subdivided into groups, subtypes, sub-subtypes and circulating recombinant forms (CRFs). Groups refer to distinctive HIV-1 lineages M (for Major), O (for Outlier), and N (for New, or Non-M, Non-O). HIV-1 is the most common HIV type globally. It has developed an extraordinary degree of genetic diversity, and can be further divided into different groups subtypes, sub-subtypes and recombinant forms. There are nine pure subtypes within group M HIV-1: A, B, C, D, F, G, H J and K; 43 circulating recombinant forms; and multiple additional recombinant forms.

Subtype B is the predominant subtype in North America, Europe and Australia, where most drug resistance research and drug design have been conducted. Thus although it only comprises 12% of the global HIV pandemic, the vast majority of resistance knowledge is derived from patients infected with this subtype. The most common global HIV variant is subtype C, responsible for more than 50% of the global HIV-infected population [Hemelaar *et al.*, 2006]. This is the most common subtype in Southern Africa, as well as in India. As treatment access increases globally, the number of non-B viruses that are exposed to antiretroviral therapy will dramatically increase and reveal its consequences with regard to evolution of drug resistance.

Implications of HIV Diversity on Drug Resistance.

HIV-1 subtypes differ from one another by 10%–12% of their nucleotides, corresponding to 5%–6% of their amino acids in protease and RT. These differences, which basically define the different subtypes and recombinant forms, occur throughout the genome, at times in or close to, functionally important positions, and/or loci that are related to drug resistance. This diversity can affect baseline (pre-treatment) susceptibility to cART, as well as the position, rate and magnitude of drug resistance acquisition once drug pressure is present. These changes can result in new mutations at known resistance positions, new resistance positions, new rates of resistance accumulation and diverse co-variability of mutations. Those, in-turn, can impact interpretation of drug resistance patterns and its implication on patient care [Kantor, 2006]. There are many observational studies that suggest that currently available cART is as active against non-B viruses as it is against subtype B viruses. Additional data show that drug resistance mutations that occur in subtype-B infected persons also occur in non-B subtypes [Kantor *et al.*, 2005]. However, increasing data on the genetic mechanisms of drug resistance in non-subtype B viruses suggest that some differences in drug resistance evolution among HIV subtypes occur. New mutations at known and at new positions are emerging and novel patterns of resistance are accumulating [Kantor *et al.*, 2005; Abecasis *et al.*, 2005; Arioshi *et al.*, 2003; Grossman *et al.*, 2002; Brenner *et al.*, 2003; Brenner *et al.*, 2006].

The increasing global use of genotypic drug resistance testing in non-subtype B infected persons will surely augment our understanding of the mechanisms that lead to drug resistance and potential differences in drug resistance evolution among different HIV variants. The potential implications of such understanding are immense, with more that 90% of the global HIV infected population harboring these variants. Whether subtype is a clinically important factor in the evolution of drug resistance still remains to be determined.

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MINIREVIEW
Pathogenesis

GB Virus Co-infection in HIV Disease: Setting Stage to do a Good Turn or yet another Wild Goose Chase?

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Disease vs Disease: A Different Outcome.

HIV infection is characterized by an acute stage followed by the chronic phase that culminates in the development of a plethora of opportunistic infections and neoplasms. Myriad host and viral factors are believed to be associated with HIV disease progression, notably host HLA factors and genetic polymorphisms of genes that encode the HIV co-receptor CCR5 or co-receptor ligands [Rowland-Jones, 1999]. It is widely known that accelerated HIV disease progression and mortality are associated with some opportunistic coinfections [Stiehm, 2006]. Could some coinfections possibly have the opposite effect and delay HIV-related mortality?

Scientific observations such as the existence of a systemic disease or disorder, preventing or ameliorating the severity of another disease have led to important therapeutic advances, exemplified by Edward Jenner's use of cowpox to prevent smallpox in the late 1770's. This is followed by the observation that certain erythrocytic disorders namely ß-thalassemia and sickle cell anaemia effectively alleviates the extent of malaria pathology. The concept is further exemplified by the fact that subjects that are carriers of cystic fibrosis may confer genetic resistance to tuberculosis and/or secretory diarrhoea. Likewise, the salubrious effects of malnutrition have led to therapeutic diets for seizures, coeliac disease, type 2 diabetes, and inflammatory bowel disease. Rh immunoglobulin for Rh haemolytic disease prevention followed the observation that ABO incompatibility prevented Rh sensitization. The natural immunosuppression of measles may cause remission of nephrosis, and that of leprosy prevents psoriasis. Patients with X-linked agammaglobulinemia are resistant to Epstein-Barr virus infection. Recent Uganda study has shown that active TB does not always increase HIV viral load, which further raises the possibility that more such diseases influencing other coexisting conditions otherwise could exist [Srikantiah *et al.,* 2008]. While it is known that HIV/AIDS is prevented or modified by co-receptor mutations (notably the CCRΔ32 chemokine mutation) and HIV-2 infection, recent investigations from independent research groups provide provocative data supporting previous observations that coinfection with GBV virus C (hepatitis G virus) is associated with a more favourable prognosis in HIV-positive patients. Recent evidence suggest that HIV-positive subjects that are co-infected with a non-pathogenic human flavivirus, the GB virus type C (GBV-C), survive significantly longer than HIV-positive individuals without GBV-C infection [Stapleton, 2003]. Numerous studies have demonstrated a surprising survival benefit among subjects who are coinfected compared with those who are infected with only HIV. Intriguingly, it is to be noted that infection with GBV-C can persist for decades with no apparent clinical signs of any illness or death [Kennedy *et al.*, 1998]. Numerous attempts were made to link GBV with other disease pathologies, namely hepatocellular carcinoma, lichen planus, cryoglobulinaemia and some haematological illnesses. However, these failed to correlate with any specific disease. In view of the overwhelming lack of association with any disease pathology, the USFDA advised not to screen blood supplies for the GBV in blood transfusion units.

GBV: Sailing in the Same Boat to Cramp HIV's Style?

GBV-C is a positive-sense, single-stranded RNA virus. The genome is ~9400 nucleotides long, with a long open-reading frame that encodes a polyprotein of ~3000 amino acids [Leary *et al.*, 1996]. Being a flavivirus, GBV-C is the most closely related HCV and also to dengue, yellow fever, Japanese B encephalitis and West Nile viruses. Similar to HIV, GBV is also transmitted parenterally, as demonstrated by the high viraemia in subjects that received multiple transfusions of blood products and in high-risk groups such as injecting drug users (IDUs) [Bjorkman *et al.*, 2001]. Mother-to-child transmission [Moaven *et al.*, 1996] and sexual contacts (similar to HIV) [Bjorkman *et al.*, 2001] have been reported. Interestingly, higher rates of GBV infection have been reported in subjects with

HIV-1 infection, regardless of intravenous drug usage [Dawson *et al.*, 1996]. Studies have reported higher rates of HIV-GBV coinfection among homosexual men and IDUs [Puig-Basagoiti *et al.*, 2000]. The beneficial effects of GBV and HIV coinfection have been reviewed recently [Shankar, 2008].

"Benign GBV Controls HIV Disease Progression" – Is it a Sacred Cow Notion, or Simply a Hammer and Tongs Argument?

GBV-C has been shown commonly to co-infect patients with HIV infection. Conceptually, although it is not yet clear to describe whether or not HIV and GBV replicate in the same CD4+ T-cells [Xiang *et al.*, 2001], recent evidence suggest that GBV-C efficiently replicate in human PBMCs *in vitro*. Ability of HIV and GBV-C to infect and replicate within PBMCs suggests that GBV-C and HIV have similar cell tropism. Numerous researchers have observed that GBV infection in HIV-1- positive subjects prolonged HIV disease progression [Bjorkman *et al.*, 2003; Nattermann *et al.*, 2003; Tillmann *et al.*, 2001, 2002; Xiang *et al.*, 2004, 2006a, 2006b; Yeo *et al.,* 2000]. cell/mm^3 and TLC <1700 cells/mm^3 with CD4 <350 cells/mm.

Williams *et al.* (2004) suggest that men who were viraemic with GBV-C were 2.8 times less likely to die 5 to 6 years after HIV seroconversion than those with persistent GBV-C viraemia. However, protection by GBV-C wanes when viraemia disappears, thus excluding it as a vaccine candidate. In a series of experiments to determine if GBV-C altered HIV replication *in vitro*, researchers tested the production of p24 antigen, a marker of HIV growth, in cell cultures infected with HIV alone, GBV-C alone, and both HIV and HGV-C. Cells infected with both viruses produced 30 - 40% less HIV than those infected with HIV only.

The Mechanism: How GBV Crack the Whip at HIV!

The mechanism of protective effects of GBV can be explained in detail as numerous possibilities exist. One is presumed to be due to alterations ensued in the cytokine profile in patients that are dually infected with GBV and HIV-1. It is to be remembered that changes in Th responses play a key role in the progression to terminal AIDS stage. Interestingly, findings suggest that the levels of type 1 helper T (Th1) cytokines, notably IL-2 are reportedly elevated in co-infected subjects, whereas those that are chronically infected with HIV alone, generate increased levels of type 2 helper T (Th2) cytokines (e.g., IL-4 & IL-10) and decreased levels of Th1 cytokines; suggestive of immune activation, often seen in systemic parasitic infections . Therefore, it is clear that GBV could effectively prevent the onset of immune activation, a feature of terminal HIV disease. Furthermore, it is noteworthy to remember that intact Th1 profile is one of the immune mechanisms responsible for protective effect in the host. Also the ability of the both the viruses to effectively infect PBMCs raises the possibility that the two viruses could interact either directly or indirectly, to effect the cell cycle, and that at one point or the other, GBV interferes with the life cycle of HIV inside the host cell. Therefore, the mechanisms for the protective effect of GBV-C may involve modulation of co-receptor expression, enhanced cytotoxicity, or activation of innate immune components.

GBV: Potential Candidates of Entry Inhibitors?

GBV reportedly blocks the entry of HIV into important cellular targets, such as CD4+ T lymphocytes & macrophages. In cell cultures, the GBV-C envelope protein E2 reportedly decreases the entry of HIV by down-regulating a major chemokine coreceptor of HIV, CCR5. This down-regulation appears to result from the direct binding of GBV-C E2 to CD81 on CCR5+ cells, which, in turn, alters the quantity of CCR5 on the cell surface. In addition, certain ß-chemokines, especially regulated on activation, normal T-cell expressed and secreted (RANTES), may be up-regulated in patients with dual infection. E2 reportedly induces up-regulation of RANTES *in vitro*. Subsequently RANTES binds to CCR5 and thus may block viral entry directly or may act through the down-regulation of CCR5. Recent studies have shown that GBV-C may also increase the levels or augment the activity of intracellular inhibitors of HIV internalization.

Conclusion.

With majority of studies showing significant survival beneficial among HIV-positive patients, not all studies have confirmed the findings and there is still a bone of contention among research groups over the hypothesis. The existence of different HIV inhibitory phenotypes *in vitro* may explain the controversial epidemiological data on the influence of GBV-C infection for HIV disease progression. In addition, it would be crucial to look at long-term nonprogressors or slow progressors to evaluate the presence and impact of GBV-C on their disease, in much the same way that researchers examine presence of the CCR5Δ32 mutation that confers resistance to HIV infection and replication. It must also be noted that HLA Complex P5 (HCP5) and the zinc ribbon domain–containing 1 (ZNRD1) genes conferring HIV control (associated with HLA-B*5701), could lead to therapeutic applications and must be investigated to reveal any possible association with GBV. In addition, the implication of HLA-C in HIV-1 control could present important avenues, given that the HIV-1 accessory protein *nef* selectively down-regulates the expression of HLA-A and -B but not that of HLA-C on the surface of infected cells. Any possible association of HLA-C with HIV control via *nef*-down regulation to GBV-HIV coinfection also can never be ruled out. Additional exploration of genetic, infectious, and metabolic influences on HIV disease progression may provide new therapeutic approaches to HIV prevention.

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RESEARCH COMMENTARY

TB Diagnostics

Now Mobile Phones could Change the Tune in Modern TB Diagnostic Labs!

Original article: Zimic *et al.* Can the power of mobile phones be used to improve tuberculosis diagnosis in developing countries? *Trans R Soc Trop Med Hyg.* 2008 Nov 24. [Epub ahead of print].

Summary. Recent studies from Peru have brought the implementation of microscopic-observation drug susceptibility (MODS) assay. This novel assay is cost-effective (2 - 3US$), rapid liquid culture detection system and has been validated in resource-limited settings. The challenge with this assay is to read the culture plate by a trained personnel. This study evaluated the efficacy of mobile phone in TB diagnosis by transmitting the electronic image of the culture morphology (captured by an inverted light microscope) to a remote site for expert analysis and then receiving the results of analysis.

Commentary. TB-HIV co-infections in developing countries have been a disaster and TB is known to be one of the leading causes of death among HIV infected persons. Alarmingly fewer than half of TB cases in HIV infected patients are diagnosed before death. Although the MODS assay represents a major potential advance in reducing delay to diagnosis and detection of multi-drug resistance strains, extensive use of this assay in developing countries may be limited because reading of the growth pattern of mycobacteria requires trained personnel. The study by Zimic and coworkers has shown high concordance rate (98.7%) between direct observation on the microscope and the mobile phone transmitted image. Therefore, use of mobile phone could maximize the use of MODS assay in resource-limited settings particularly India, where mobile phone service coverage is well established.

P. Balakrishnan, PhD.

Arizona Scientists Optimistic about an Outbreak of HIV between 1884 and 1924 in Africa

New research indicates that HIV began spreading among humans between 1884 and 1924, suggesting that growing urbanization in colonial Africa set the stage for the HIV/AIDS pandemic. It was once believed that HIV could have originated in the 1930s. Worobey and colleagues at the University of Arizona in Tucson screened a number of tissue samples and uncovered the world's second-oldest genetic sequence of HIV-1 group M, which dates to 1960. These sequences along with other previously known HIV-1 genetic sequences were used to construct a range of plausible family trees. The lengths of the tree branches represent the periods of time when the virus genetically diverged from its ancestors. The timing and number of these genetic mutations enabled the scientists to calibrate the probable range of rates of evolution of HIV-1 group M. Based on this range of rates, the scientists projected back in time to the period when the trees most likely took root around the turn of the 20th century. This marks the probable time of origin of HIV-1 group M, according to Worobey and the others. [Worobey M, *et al.* Nature 2008; **455**(7213):661-4 © 2008 Nature Publishers, USA].

Blockade of PD-1 could Improve Immunity to SIV and Survival of Macaques

PD-1 (programmed death-1) is an immune receptor molecule that is known to inhibit immune responses against chronic viral infections in addition to increasing plasma viral load. By discovering ways to block PD-1, scientists at the Yerkes National Primate Research Centre of Emory University in association with other research laboratories have explored possible novel ways of reducing plasma viral loads (PVL) and prolonging survival of rhesus macaque monkeys severely infected with SIV (the nonhuman primate version of HIV). The scientists injected nine SIV-infected monkeys with an antibody to human PD-1 four times over 10 days. Of the nine animals, five were infected for three months and four were infected for about 21 months at the time of antibody treatment. Another five SIV-infected monkeys received a control antibody at the same dose and schedule. The researchers then tested the function of the anti-SIV killer cells, antibody responses to the virus and PVL. Results showed that the improved anti-viral immune responses were associated with a reduction in PVL and prolonged the survival of the infected animals. The PD-1 antibody treatment also increased the proliferation of memory B cells and the anti-SIV antibodies, a finding that has never been reported before elsewhere. [Velu V, *et al.* Nature 2008; **458**(7235):206-10 © 2008 Nature Publishers, USA].

HIV Could Deceive a Woman: Study Shows Virus can Penetrate Healthy Genital Skin

U.S. researchers have identified a new route of male-to-female transmission of HIV in which the virus can traverse healthy genital skin to reach immune cells, in what could be thought as unlikely otherwise, in just four hours! Women account for 26% of all new HIV cases in the US, according to CDC reports. Based on its most recent analysis of 2005 data, the CDC estimated that there were 56,300 new HIV infections that year, and 31% were due to high-risk heterosexual contact. Scientists under the head of Prof. Thomas Hope of the Northwestern University Feinberg School of Medicine have found that HIV can penetrate normal, healthy genital tissue to a depth where it can get to immune cells and infect them. The researchers labelled HIV viruses with photo-activated fluorescent tags and were able to track the viruses as they penetrated the outer squamous epithelial layer of the female human genital tissue. With more than half of the new cases of HIV infection worldwide are women, the present finding is expected to have a huge impact on the development of newer microbicides and vaccines to protect women from HIV. [Hope T, *et al.* ASCB 48th Annual Meeting, 2008, San Francisco, USA]

Infection with ID Viruses: Why Some Primates Feel like a Million Dollars whilst Humans Kick the Bucket?

Ever since HIV was found to be a cause of AIDS 25 years ago, extensive research has been put forward to identify the source of the virus. These studies have led to the discovery that chimpanzees and sooty mangabeys (SM) could be infected in the wild with SIV, and whose transmission to humans and macaques could have lead to AIDS. However, it still remains a million dollar question as to how, despite infection with immunodeficiency (ID) viruses these primates are still healthy. A team of scientists from the Yerkes National Primate Research Centre and the Emory Vaccine Centre have discovered that during both HIV infection in humans and SIV infection in macaques, the host immune system becomes highly activated, experiences increased destruction and decreased production of key immune effector cells and progressively fail as a result. In contrast, natural hosts for SIV infection, like SMs, do not exhibit aberrant immune activation and do not develop AIDS despite high levels of ongoing SIV replication. The reasons could be attributed to significant differences in immune signaling with a specific type of dendritic cells (DCs) in AIDS-susceptible or resistant host species. The observation that DCs of SMs are less susceptible to activation by SIV may explain why SMs do not exhibit aberrant immune activation and do not develop AIDS. Understanding the particular details of TLR signaling pathways in the SMs may help guide the development of specific therapeutic approaches that could beneficially limit chronic immune activation in HIV-infected humans. [Mandl JN,*et al.* Nat Med 2008; **14**(10):1077-87© 2008 Nature Publishers, USA].

Ocular Syphilis could be a Marker of Previously Unknown HIV Status?

German researchers have proposed that ocular syphilis could be an indicator of past unknown HIV status and therefore cases with ocular syphilis must always be screened for HIV co-infection. Jan Kunkel and others from the Charité-University Medicine, Berlin, retrospectively compared the prevalence of ocular syphilis and other co-infections in HIV-positive and -negative patients between 1998 and 2006. The investigators studied the patients' characteristics, laboratory results, major ophthalmologic finding, treatment and course from amongst 24 consecutive patients treated for ocular syphilis of which, 11 were co-infected with HIV. Interestingly, the HIV-status had previously been unknown in 7 of the HIV-positive subjects and notably, 6 of these were in an early HIV disease stage (CDC category A). Except for the significantly elevated levels of C-reactive protein (CRP) the clinical and laboratory findings did not differ between HIV-positive and -negative. The study shows that ocular syphilis led to new diagnosis of HIV-infection in an unexpectedly high number of patients, which emphasises that patients with ocular syphilis need to be screened for HIV-co-infection. [Kunkel J, *et al. Journal of Infection* 2009; **58**(1): 32-6 © 2008 Elsevier].

TB doesn't always Increase Viral Load: Ugandan Findings Add Newer Dimensions to HIV Pathogenesis

While it is widely believed that TB is usually associated with an increase in HIV viral load, recent investigations by Srikantiah and colleagues from two different clinical trials have shown low level HIV viraemia in 25% of Ugandan patients. The investigators could not find any obvious patient characteristics associated with a lower viral load during active TB infection. Furthermore, the study has shown that patients with viral load below 1000 copies/ml when they started treatment with

anti-TB drugs were more likely to have an increase in viral load than those with a higher baseline viral load. The researchers believe that further studies investigating the host and viral factors may give clues on the potential causes of reduced HIV viral loads in the active TB setting and may provide additional insights into HIV and TB pathogenesis. [Srikantiah P, *et al. Journal of Acquired Immune Deficiency Syndromes* 2008; **49**: 458–60 © 2008 Lippincott & Wilkins]

Toll-like Receptor 7 Polymorphism, *TLR7 Gln 11Leu* Linked to Rapid HIV Disease Progression

Toll-like receptors (TLRs) are implicated in the innate immune response to infectious organisms especially, TLR7 recognizes RNA of various viruses including HIV. However, recent studies have shown that the presence of certain polymorphisms in TLR7 could be associated with higher viral loads and accelerated progression in HIV patients. Djin-Ye and others from the Charité University Medical Center, Germany, genotyped a population of 734 HIV-positive adults and 545 healthy controls for three TLR7 single nucleotide polymorphisms. They subsequently assessed the frequency of TLR7 genetic variations and related to HIV disease progression. The results showed that the presence of the most frequent TLR7 polymorphism, TLR7 Gln11Leu, was associated with higher viral loads and accelerated HIV disease progression. This is the first report of a functional TLR7 variant to be associated with susceptibility to and a more severe clinical course of HIV-1 disease. These results may have implications for the risk assessment of individual patients as well as for HIV-1 therapy and vaccination strategies in the future. [Djin-Ye O *et al. AIDS.*2009; **23**:297-307 © 2009 Lippincott & Wilkins].

Two-Drug Treatment: A Breakthrough Option Likely against XDR-TB

The currently available treatment options for multi-drug-resistant TB are relatively lengthy, toxic and often could result in confinement for the patient. In cases of extensively drug resistant TB (XDR-TB) the situation is even worse. Scientists from the Albert Einstein College of Medicine, New York, have found that a combination of two antibiotics already in use to treat other bacterial infections could potentially treat XDR-TB. The study was aimed to determine whether it was possible to make *M. tuberculosis* (MTB) susceptible to an antibiotic from the β-lactam class, which includes penicillin that has not been proved active against *M. tuberculosis* owing to the presence of the enzyme β-lactamase that blocks the activity of β-lactam antibiotics. However clavulanic acid, the only FDA-approved β-lactamase inhibitor, irreversibly inhibits the enzyme, so the researchers looked at the activity of the β-lactam antibiotic meropenem in combination with clavulanic acid against 13 strains of XDR-TB and laboratory strains without drug resistance. A sterilising cure - complete eradication of MTB was achieved within 9-13 days, and the combination was equally effective in drug-susceptible and drug-resistant strains. The US-NIAID, the co-sponsor of the study, is now talking to manufacturers to provide clavanulate in a suitable formulation. [Hugonnet JM, *et al.* Science 2009; **323**:1215-18 © 2009 Science].

CLINICAL TRIALS

IL-2 Immunotherapy for HIV-Infected Individuals already on ART

Interleukin-2 (IL-2) is a signaling molecule produced naturally in the body implicated in regulating CD4+ T cell production and survival. As their CD4+ T cell levels drop, people infected with HIV become more vulnerable to develop AIDS-related OIs and death. Earlier research showed that administration of synthetic IL-2 along with ART could boost the CD4+ T-cell counts in HIV positive subjects more than does ART alone, but it was unknown whether this boost translated into better health. It has now been proved that IL-12 fails to reduce their risk of HIV-associated OIs or death compared with combination ART alone. The Phase III trials of two large international clinical trials, the ESPRIT and SILCAAT presented at the recently concluded Conference on Retroviruses and Opportunistic Infections (CROI) in Montreal were originally designed to test whether giving IL-2 to HIV-infected individuals already on ART would keep them healthier longer than HIV-infected individuals taking only ARVs. The studies involved more than 5,800 HIV-infected volunteers in 25 countries. Participants of the study were assigned at random to receive combination ART alone or combination antiretrovirals plus injections of Proleukin (Novartis Pharma, Basel, Switzerland), a synthetic form of IL-2, over several five-day cycles. Though volunteers who received IL-2 and ARV experienced notable, sustained increases in CD4+ T cell counts, these increases did not translate into reduced risks of HIV-associated OIs or death when compared with the risks in volunteers who were taking only ARVs. Although further analyses might help better understand these findings, the two studies clearly demonstrated that the use of IL-2 did not improve health outcomes for HIV-infected people. Therefore, it is believed that the types of CD4+ T cells induced by IL-2 play no role in protecting the HIV-infected patient, and therefore the administration of IL-2 has no benefit. [http://www3.niaid.nih.gov/news/newsreleases/2009/IL_2_therapy.htm]

Vaginal Microbicide Gel Shows Promise in a Large-scale Trial

In a recently completed clinical trial known as HPTN 035 conducted in Africa and United States, funded by the National Institute of Allergy and Infectious Diseases (NIAID), an investigational vaginal gel intended to prevent HIV infection in women has demonstrated encouraging signs of success in Africa and the United States. The study assessed two candidate microbicide gels for safety and their ability to prevent HIV infection in the enrolled 3099 women in study sites of Africa and the US. Investigators of the study have found the microbicide gel—known as PRO 2000 (Indevus Pharma, Inc., Lexington, Mass.)— to be safe and approximately 30 percent effective (33 percent effectiveness would have been considered statistically significant). This is the first human clinical study with encouraging results to suggest that a microbicide—a chemical incorporated into a gel, foam or cream and intended to prevent the sexual transmission of HIV and other sexually transmitted infections when applied topically inside the vagina—may prevent male-to-female sexual transmission of HIV infection. [Karim SA, *et al.* 16th Conference on Retroviruses & Opportunistic Infections, Montreal, abstract 48LB, 2009.]

Efficacy Assessment of Cell-Mediated Immunity HIV-1 Vaccine

With previous observational studies and non-human primate challenge studies suggesting that cell-mediated immune responses might provide control of HIV replication, a double-blind, Phase II, test-of-concept study was undertook at 34 sites in North America, South American and Australia. Three thousand HIV-1 seronegative participants were randomly assigned and 1494 of them were given three injections of MRKAd5 HIV-1 gag/pol/nef vaccine and 1506 were given a placebo, with a primary objective of reduction in HIV-1 acquisition rates or a decrease in HIV-1 viral load setpoint. During the first intermin analysis, since the prespecified futility boundaries were met, the study was prematurely stopped. Results showed that this cell-mediated immunity vaccine did not prevent HIV-1 infection or reduce early viral level and possible mechanisms accounting for insufficient efficacy of the vaccine and increased HIV-1 infection rates in subgroups of vaccine recipients are being investigated. [Buchbinder SP, *et al.* Lancet 2008; **372**(9653):1881-93© 2008 Elsevier].

HIV/STD Guidelines *New*

Antiretroviral Drug Resistance Testing in Adult HIV-1 Infection: 2008 Recommendations of an International AIDS Society – USA Panel.
http://www.journals.uchicago.edu/doi/pdf/10.1086/589297

Antiretroviral Treatment of Adult HIV Infection: 2008 Recommendations of the International AIDS Society - USA Panel. Hammer S, *et al. JAMA.* 2008; **300**: 555 – 70.

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Care of HIV Patients with Chronic Hepatitis B: Updated Recommendations from the HIV/ Hepatitis B Virus International Panel. Soriano V, *et al. AIDS.* 2008; **22**(12): 1399 – 410.

Centers for Disease Control & Prevention; HIV Testing Implementation Guidance for Correctional Settings. – January 2009.
http://www.cdc.gov/hiv/topics/testing/resources/guidelines/correctional-settings/pdf/Correctional_Settings_Guidelines.pdf

Drug-Resistant Tuberculosis: A Survival Guide for Clinicians, 2nd edition – 2008.
http://www.nationaltbcenter.edu/drtb/docs/MDRTB_Web_Mar08.pdf

Enhancing Access to Quality HIV Care for Women of Colour: Final Report - 2008
http://careacttarget.org/library/HIVcare/WOC%20Final%20Report.pdf

Essential Prevention and Care Interventions for Adults & Adolescents Living With HIV in Resource-Limited Settings -2008.
http://www.who.int/hiv/pub/prev_care/OMS_EPP_AFF_en.pdf

European AIDS Clinical Society (EACS) Guidelines for the Clinical Management and Treatment of Chronic Hepatitis B and C Co-infection in HIV Infected Adults. Rockstroh J, *et al. HIV Med.* 2008; **9:** 82 - 8.

European Guideline on HIV Testing, 2008
http://www.iusti.org/regions/Europe/HIV%20Testing%20Guideline%2011.11.08.pdf

Guidelines for the Implementation of Reliable and Efficient Diagnostic HIV Testing, Region of the Americas, Washington D.C.: PAHO, 2008
http://www.paho.org/English/AD/FCH/AI/LAB_GUIDE_ENG.PDF

Guidelines for the Use of Antiretroviral Agents in Paediatric HIV Infection - February 23, 2009.
http://aidsinfo.nih.gov/contentfiles/PediatricGuidelines.pdf

Guidelines for the Use of Antiretroviral Agents in HIV-1-Infected Adults & Adolescents - November 3, 2008.
http://aidsinfo.nih.gov/contentfiles/AdultandAdolescentGL.pdf

Guidelines for Prevention & Treatment of Opportunistic Infections among HIV-Exposed & HIV-Infected Children - June 20, 2008.
http://aidsinfo.nih.gov/contentfiles/Pediatric_OI.pdf

HIV/AIDS Prevention, Treatment and Care in the Health Sector- 2009.
http://www.who.int/hiv/pub/priority_interventions_web.pdf

NACO - Ethical Guidelines for Operational Research on HIV/AIDS -2008.
http://www.nacoonline.org/upload/guidelines/NACO%20Ethical%20Guidelines%20for%20Operational%20Research.doc

Update of the drug resistance mutation in HIV – 1: Johnson V, *et al. Topics HIV Med.* 2008; **16**: 62 – 8.

FUNDING OPPORTUNITIES

Directory of Grants and Fellowships in the Global Health Sciences.
http://www.fic.nih.gov/funding/globaldir06.html

Ford Foundation Grants
http://www.fordfound.org/grants/database

Bill & Melinda Gates Foundation Grants
http://www.gatesfoundation.org/grantseeker/Pages/funding-hiv-aids.aspx

DHHS-CDC Funding
www.cdc.gov/hiv/topics/funding

European Commission RESEARCH- Health
http://ec.europa.eu/research/health/infectious-diseases/poverty-diseases/aids_en.html

US-NIH Grants
http://grants.nih.gov/grants/grant_basics.htm

- Centers of Biomedical Research Excellence (COBRE) (P20)
- Children's Environmental Health and Disease Prevention Research Centers (P01)
- Ruth L. Kirschstein National Research Service Award (NRSA) Institutional Research Training Grants (T32)
- Ryan White HIV/AIDS Program Part D: Grants for Coordinated HIV Services & Access to Research for Women, Infants, Children, & Youth (CSWICY)
- Ryan White Part C: Capacity Development: New Competing Grant
- International Research in Infectious Diseases including AIDS (IRIDA) Program (R01)
- NIDA Avant-Garde Award Program for HIV/AIDS Research (DP1)
- Basic HIV Vaccine Discover Research (R01)
- Unique Interactions Between Tobacco Use & HIV/AIDS (R01 & R03)

The Elizabeth Glaser Pediatric AIDS Foundation Grants (HIV Vaccine & Operational Research Awards
http://www.pedaids.org/GrantsandAwards.aspx

Fogarty International Center Grants - AIDS International Training & Research Program (AITRP)
http://www.fic.nih.gov/funding/index.htm

The Royal Society International Research Grants
http://royalsociety.org/funding.asp?id=1120

SPECIAL NEWS

FDA Approves First Ever Nucleic Acid Test for Screening 2 Different HIV Types in Donated Blood and Tissue

The U.S. Food and Drug Administration (FDA) has approved the first nucleic acid test (NAT) that screens for the presence of 2 different types of HIV in donated blood plasma and tissue.

A major concern regarding the transfusion of blood and blood components is the potential for transmission of viral infections, particularly with Human Immunodeficiency Virus Type 1 (HIV-1) and Type 2 (HIV-2), Hepatitis C Virus (HCV) and Hepatitis B Virus (HBV). The new FDA-approved test called, Cobas ® TaqScreen MPX, is a qualitative multiplex test that simultaneously detects HIV-1 Group M and Group O RNA, HIV-2 RNA, HCV RNA and HBV DNA in infected pooled and individual plasma donations. It is to be noted that though HIV-2 infections and HIV-1 Group O infections are predominantly found on the African continent, detection of cases with these infections are not uncommon in other parts of the world.

Hence, it is believed that with the MPX test, blood donor testing laboratories will now be able to use NAT-based technology to screen for additional HIV strains, further assuring that donated blood and tissue are free from infection and providing better protection for patients [US FDA. FDA News. Dec 30, 2008].

Upcoming Events
2009

April '09

4th International Conference on HIV Treatment Adherence, April 5 - 7, 2009, Miami, Florida, USA.
[www.iapac.org]

25th Clinical Virology Symposium (CVS), April 19 - 22, 2009, FL, USA.
[http://www.virology.org/meetings.html]

The 20th International Harm Reduction Conference, April 20 - 23, 2009, Bangkok, Thailand.
[www.ihraconferences.net]

3rd annual Immunodiagnostics & Immunomonitoring Conference, April 23-24, 2009, Chicago, USA.
[http://gtcbio.com/conferenceDetails.aspx?id=147]

5th European Conference on Clinical and Social Research on AIDS and Drug, April 28 – 30, 2009, Vilnius, Lithuania.
[www.aidsvilnius2009.com]

May '09

Molecular Mechanisms of Host-Pathogen Interactions and Virulence in Human Fungal Pathogens, May 2 - 8, 2009, France.
[http://www.fems-microbiology.org/website/nl/default.asp]

22nd International Conference on Antiviral Research (22nd ICAR May 3, 2009, Florida, USA.
[http://www.isar-icar.com]

European Congress of Clinical Microbiology and Infectious Diseases, May 16 - 19, 2009, Helsinki, Finland.
[http://www.congrex.ch/eccmid2009/]

Retroviruses Conference, May 18 - 23, 2009, New York, USA.
[http://meetings.cshl.edu/meetings/retro09.shtml]

MSK 50th Anniversary International Symposium on Microbiology, May 28 - 30, 2009, Korea.
[http://www.msk.or.kr/msk/eng/]

Workshop on Methods in Epidemiologic, Clinical & Operations Research (MECOR), ICMR-TRC, May 31 – June 6, 2009, Chennai
[http://icmr.nic.in/icmrnews/workshop_nie.htm]

June '09

5th Co-infection Workshop June 4-6, 2009, Lisbon, Portugal.
[www. virology-education.com]

27th Annual Meeting of the European Society for Paediatric Infectious Diseases, June 9-13, 2009, Brussels, Belgium.
[http://www2.kenes.com/espid/pages/home.aspx?ref6=db1]

4th International Workshop on Hepatitis C, Resistance & New Compounds, June, 25 – 26, 2009, Boston, USA.
[http://www.virology-education.com]

FEMS 2009 - 3rd Congress of European Microbiologists, June 28 - July 2, 2009, Sweden .
[www.kenes.com]

July '09

5th IAS Conference on HIV Pathogenesis, Treatment and Prevention, July 19 – 22, 2009, Cape Town, South Africa.
[www.ias2009.org]

3rd Ditan International Conference on Infectious Disease (DICID), July 30 - August 2, 2009, Beijing, China.
[http://www.bjditan.org]

August '09

First International Conference on Alcohol and HIV in India, August 3-4, 2009, Mumbai, India.
[http://www.alchivconf2009.in/]

9th International Congress on AIDS in Asia and the Pacific (ICAAP 9), August 9 - 13, 2009, Bali, Indonesia.
[www.icaap9.org]

October '09

AIDS Vaccine Conference, October 19 - 22, 2009, Paris, France.
[www.VaccineEnterprise.org]

November '09

6th Summer School on Immunology and Immunogenetics, November 16 - 19, 2009, New Delhi, India.
[www.aseatta2009.net]

6th World Congress of the World Society for Pediatric Infectious Diseases, November 18 - 22, 2009, Buenos Aires, Argentina.
[www.kenes.com/WSPID]

International Association of Physicians in AIDS Care (IAPAC), November 29 - December 1, 2009, New Orleans, USA.
[www.iapac.org]

December '09

Fourth International Workshop on HIV Persistence, December 8 - 11, 2009, St.Martin, West Indies.
[http://www.hiv-workshop.com]

February '10

5th International Conference on Sexology. February 13 to 14, 2010, Chennai, India.
[Http://internationalconferenceonsexology.com]

September '10

International Conference on Opportunistic Pathogens. Sep. 28 to 30, 2010. New Delhi, India. [http://icopa-india.org]

YRG CARE
Forthcoming Academic Programmes

PhD Degree Course

Applications for PhD degree programme (affiliated to the University of Madras) at YRG CARE are invited from candidates who have completed their Post Graduate degree in Medical Microbiology /Applied Microbiology / Molecular biology / Biotechnology. Applicants should have passed the national entrance tests for independent fellowships under CSIR /ICMR/ DBT.

HIV/AIDS SCIENCE SYMPOSIUM 2009

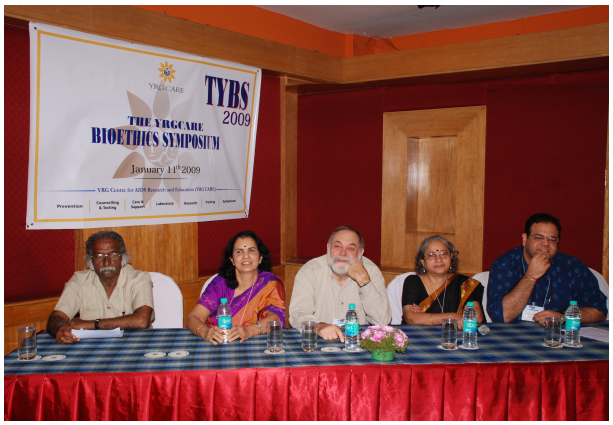
The second annual Science Symposium on HIV/AIDS will be organized by YRG CARE in Chennai on 21-22, August 2009. The annual HIV symposium will bring together leading faculties/experts/scientists to provide updates on HIV/AIDS. This symposium will cover various topics related to HIV epidemiology, pathogenesis, host-HIV interactions, immune responses to infection, disease progression, opportunistic infections, current treatment strategies, natural history of HIV disease in India, vaccines, sexually transmitted diseases, and co-infections with TB and hepatitis viruses. This will provide a forum for young people to address key scientific issues and gaps in knowledge and, will also be an opportunity to identify priorities for future action to fight against HIV/AIDS. The symposium is focused for young professionals including the post-graduate students from medical, para-medical, science colleges /universities /research institutions. For more details please visit www.yrgcare.org or write to HIVsymposium@yrgcare.org.

PGDMLT Course (Infectious Diseases) 2009 – 10

This Post Graduate Diploma in Medical Laboratory Technology (Infectious Diseases) aims to provide a broad understanding of various basic laboratory techniques in serology, microbiology, haematology, clinical chemistry, immunology and clinical pathology. Special emphasis is given on the laboratory diagnostics in HIV/AIDS, sexually transmitted diseases (STDs) and Good Clinical Laboratory Practices (GCLP). This is a full-time one-year vocational course (non-semester). The course is designed to provide technical skills and practical knowledge in infectious diseases, to train on the standards to be followed for GCLP and the requirements of clinical laboratories for conducting clinical trials. For more details regarding admission notifications, please visit www.yrgcare.org or write to PGDMLT@yrgcare.org

TYBS 2009 Bioethics Symposium

YRG CARE conducted "TYBS 2009" a bioethics symposium on January 11th, '09, at Quality Inn Sabari, Chennai. The symposium explored ethical issues in research involving human participants. The programme was attended by participants from YRG CARE, IRB members and staff from research institutions. Besides, several national and international experts in the field of bioethics actively participated in the deliberations of the symposium.



Prof. Suniti Solomon, Director, YRG CARE, welcomed the gathering. Prof. Jayapaul Azariah, Bioethicist & Member, YRG CARE delivered the keynote address and following which, numerous experts delivered talks on interesting ethical issues related to research involving human participants. The main speakers were Dr. Richard Cash, Harvard School of Public Health, Boston, Dr. Anant Bhan, Bioethics & Public Health, Pune, Dr. SV Joga Rao, Solicitors & Healthcare Consultants, Bangalore, Dr Nandini K Kumar, ICMR, New Delhi, Prof. G Ravindran, St. John's Medical College, Bangalore, & Dr. Vasantha Muthuswamy, Traditional Medicine & Bio-Medical Ethics, ICMR, New Delhi. Dr. Swarnalakshmi, the IRB/CAB/Regulatory Coordinator, YRG CARE coordinated the programme.

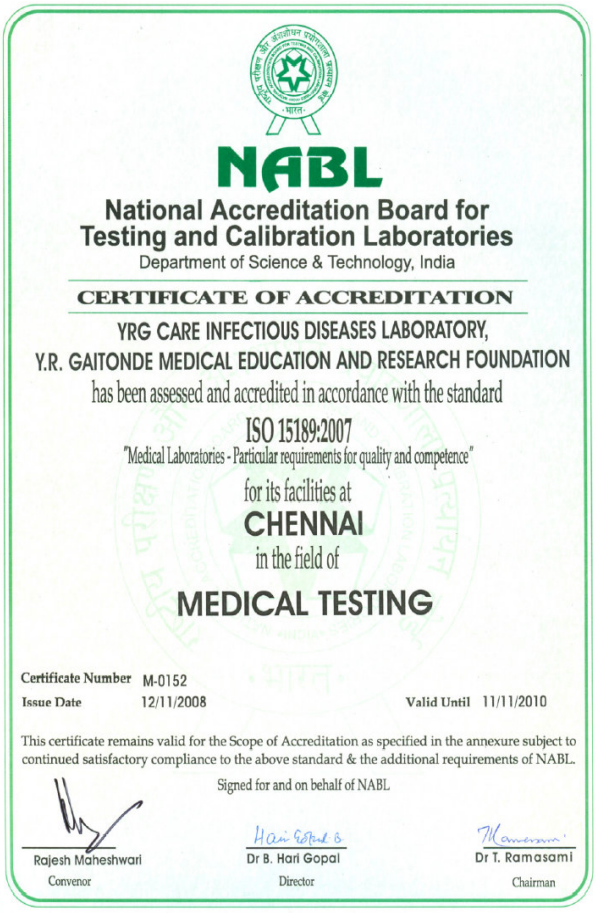
CART 2009: Chennai ART Symposium – Experts Discuss Advancements in HIV Therapeutics

Chennai ART (CART) 2009 Symposium was organised by YRG CARE on January 9th and 10th '09 at GRT Grand Hotel, Chennai. The Symposium was focussed to provide the practising clinicians with latest clinical update on management of HIV infection and updates on the current concepts of antiretroviral therapeutics, newer drugs, resistance and toxicities. The programme was attended by clinicians involved and interested in HIV care and researchers. Prof. Suniti Solomon, Director, YRG CARE welcomed the gathering and Dr. Kumarasamy, Chief Medical Officer, YRG CARE gave an introduction of the symposium.

Chief guest of the event, Dr. S. Vijayakumar IAS, Project Director and Member Secretary, Tamilnadu State AIDS Control Society (TANSACS), inaugurated the symposium by lighting the Kuthuvilakku. Various international and national experts of HIV care and research, delivered informative and enlightening talks. The main speakers were Prof. Kenneth Mayer, Professor of Medicine, Brown University, US, Prof. Constance Benson, PI and Chair of the Executive Committee and Vice-Chair of Scientific Steering Committee of NIH/NIAID ACTG, UCSD, Prof. Robert Schooley, Division of Infectious Diseases, UCSD, Dr. Davey Smith, Division of Infectious Diseases, UCSD, Prof. Christine Wanke, Tufts University School of Medicine, Boston, Dr. Rami Kantor, Brown University, Rhode Island, Dr. Sowmya Swaminathan, Tuberculosis Research Centre, ICMR, Chennai and Dr. Srikanth Tripathy, Scientist F, NARI, ICMR, Pune.

YRG CARE Infectious Diseases Laboratory Accredited with NABL

YRG CARE Infectious Diseases Laboratory added another feather to its cap when it was certified as one amongst the few infectious diseases laboratories across India accredited with the prestigious NABL certification programme conferred to laboratories that satisfy the requirements for quality and competence in medical testing.



NABL

National Accreditation Board for Testing and Calibration Laboratories

Department of Science & Technology, India

CERTIFICATE OF ACCREDITATION

YRG CARE INFECTIOUS DISEASES LABORATORY,
Y.R. GAITONDE MEDICAL EDUCATION AND RESEARCH FOUNDATION
has been assessed and accredited in accordance with the standard
ISO 15189:2007
"Medical Laboratories - Particular requirements for quality and competence"
for its facilities at
CHENNAI
in the field of
MEDICAL TESTING

Certificate Number M-0152
Issue Date 12/11/2008 Valid Until 11/11/2010

This certificate remains valid for the Scope of Accreditation as specified in the annexure subject to continued satisfactory compliance to the above standard & the additional requirements of NABL.

Signed for and on behalf of NABL

Rajesh Maheshwari, Convenor
Dr B. Hari Gopal, Director
Dr T. Ramasami, Chairman

Publications

Can iron depletion inside macrophages serve to prolong HIV disease progression? Shankar EM, Vignesh R, Velu V, Ponmalar E, Murugavel KG, Sundaram M, Balakrishnan P, Solomon S. *Bioscience Hypotheses (In press).*

Challenges of expansion of voluntary counselling and testing in India. Solomon S, Venkatesh KK, Srikrishnan AK, Mayer KH. *Sex Health. 2008; 5(4): 371 - 2.*

Changes in antioxidant profile among HIV- infected individuals on generic HAART in Southern India. Sundaram M, Saghayam S, Priya B, Venkatesh KK, Balakrishnan P, Shankar EM, Murugavel KG, Solomon S, Kumarasamy N. *Int. J. Infect. Dis. 2008; 12(6): e61 – 6.*

Co-factors for abnormal lactate levels among persons with HIV disease at a tertiary HIV care setting in South India. Sundaram M, Srinivas CN, Shankar EM, Deepak M, Murugavel KG, Balakrishnan P, Solomon S, Kumarasamy N. *Food Chem. Toxicol. 2008; 46(8): 2823 – 5.*

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Establishment of T-lymphocyte subset reference intervals in a healthy adult population in Chennai, India. Murugavel KG, Balakrishnan P, Mohanakrishnan J, Solomon SS, Shankar EM, Pulimi S, Sundaram M, Kumarasamy N, Piwowar-Manning E, Livant E, Mayer KH, Thyagarajan SP, Solomon S. *Indian J. Med. Res. (in press).*

Evaluation of two human immunodeficiency virus -1 genotyping systems: ViroSeqTM 2.0 and a home-brew method. Saravanan S, Vidya S, Balakrishnan P, Kumarasamy N, Solomon SS, Kantor R, Katzenstein D, Ramaratnam B, Mayer KH. *J. Virological Meth. (In press)*

Expansion of HIV laboratory diagnostic services in Chennai, India 2001-2006: is the growth commensurate with the need? Srikrishnan AK, Venkatesh KK, Solomon S, Thamburaj E, Anand S, Kosalaraman KG, Balakrishnan P, Mayer KH. *PLoS ONE. 2008; 3(10): e3471.*

Filarial/human immunodeficiency virus coinfection in urban southern India. Talaat KR, Kumarasamy N, Swaminathan S, Gopinath R, Nutman TB. *Am. J. Trop. Med. Hyg. 2008;79(4):558-60.*

GB virus infection: a silent anti-HIV panacea within? Shankar EM, Solomon SS, Murugavel KG, Balakrishnan P, Vignesh R, Sundaram M, Kumarasamy N, Solomon S. *Trans. R. Soc. Trop. Med. Hyg. 2008; 102(12):1176 – 80.*

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Gender-related differences in quality of life domains of persons living with HIV/AIDS in South India in the era prior to greater access to antiretroviral therapy. Solomon S, Venkatesh KK, Brown L, Verma P, Cecelia AJ, Daly C, Mahendra VS, Cheng N, Kumarasamy N, Mayer KH. *AIDS Patient Care STDS. 2008;22(12):999– 1005.*

High prevalence of HIV, HIV/hepatitis C virus coinfection, and risk behaviors among injection drug users in Chennai, India: a cause for concern. Solomon SS, Srikrishnan AK, Mehta SH, Vasudevan CK, Murugavel KG, Thamburaj E, Anand S, Kumar MS, Latkin C, Solomon S, Celentano DD. *J. Acquir. Immune Defic. Syndr. 2008; 49(3): 327 - 32.*

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Safety, Tolerability and Effectiveness of Generic HAART in HIV-Infected Children in South India. Kumarasamy N, Venkatesh KK, Devaleenol B, Poongulali S, Mothi SN, Solomon S. *J. Trop. Pediatr. (in press).*

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The prevalence of hepatitis B virus and hepatitis C virus infection among patients with chronic liver disease in South India. Saravanan S, Velu V, Kumarasamy N, Shankar EM, Nandakumar S, Murugavel KG, Balakrishnan P, Solomon SS, Solomon S, Thyagarajan SP. *Int. J. Infect. Dis. 2008; 12(5): 513 – 8.*

Ask the Experts

Readers are invited to send their queries on HIV/AIDS, which will be answered by experts from YRG CARE.

Invitation for Contributors

We welcome your contribution towards YRG CARE. Donations to YRG CARE are eligible for tax deductions under **Section 80G** of the Income Tax Act. The Foundation is registered with the Ministry of Home Affairs to receive Foreign Contributions under the Foreign Contributions Regulation Act **(FCRA)** vide registration No. 75900630/12 July 1991. Please mail us with the subject head 'Donations' with your contact details.

THE HIV/AIDS NEWSLETTER

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