of the divergent findings. Tenofovir-emtricitabine taken orally for PrEP has been approved by regulators in the US and Africa, and is being considered for approval in several African and European countries. New approaches to chemoprophylaxis are under study, including the use of vaginal and rectal gels, vaginal rings, and injectable agents. Because antiretroviral PrEP does not protect against other sexually transmitted infections (STI), it must be given as part of a comprehensive sexual health package, which includes counseling and screening for treatable STI. Other interventions that can decrease HIV transmission include adult male circumcision of HIV-uninfected men, recreational drug treatment, including access to clean syringes and other drug paraphernalia, and opiate substitution therapy. The advent of new biomedically-based prevention interventions does not obviate the need for behavioral interventions, but suggests that counseling interventions should incorporate reinforcement of medication adherence, as well as risk reduction counseling.

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Time: 10:15-12:15
Room: Hall 5

The good, the bad and the beautiful: Anti-retroviral therapy considerations in children and adolescents

A. Shet

St. John's Medical College, Bangalore, India

Abstract: HIV care for infants, children and adolescents has improved by leaps and bounds. Whereas the landscape two decades ago was bleak for children born with HIV who faced inevitable death, it is now filled with hope with the ever-increasing access to anti-retroviral therapy (ART) and care. Coupled with this progress is the success of prevention of mother-to-child transmission of HIV interventions, again with ART, resulting in fewer new infections in children. Yet, there is a long pathway to be traversed before we can achieve complete control of pediatric HIV.

Challenges: Being born with HIV or acquiring HIV in childhood can be devastating, even in the era of ART. Taking ART is a lifelong practice; the risk of long-term adverse effects is real and lasting, and children generally have to take ART for an average of 20 years longer than an adult. This could mean constant monitoring, and in many cases, life-threatening long-term consequences. Adolescence is a time when adherence to any treatment or norms established earlier is questioned, and HIV care suffers the same fate. Rebellion and poor adherence to ART results in risk of drug resistance and treatment failure. Perinatally infected children may face mental challenges, including learning disabilities and behavioral disorders. Integrated with the social support offered for these challenges, one also needs to maintain an honest and respectful discussion with children about growing up with HIV, including their sexual and reproductive health.

A hopeful future: The ambitious "90-90-90" goal launched by UNAIDS in 2014 focuses not just on the 90% of the HIV-infected population that they aim to diagnose and treat, but also on the 90% of all treated who will be virologically suppressed. This shift in our focus from mere volume of care, to actual quality of care in terms of retention and suppression, are key to optimal HIV outcomes. Nelson Mandela once said, "*There can be no keener revelation of a society's soul than the way it treats its children*." The know-how and tools that are available in today's world offer the global community the very real and beautiful possibility of controlling pediatric HIV.

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Manifestations and management of IRIS

G. Meintjes

University of Cape Town, Cape Town, South Africa

Abstract: In many resource-limited settings a substantial proportion of HIV-infected patients still commence antiretroviral therapy (ART) with advanced HIV-related immunosuppression with low CD4+ T-lymphocyte counts and active opportunistic infections. Such patients are at high risk for developing the immune reconstitution inflammatory syndrome (IRIS) in the first weeks to months of ART as immune responses to opportunistic infection antigens are rapidly restored resulting in inflammatory reactions directed at antigens of the opportunistic infection. This may result in hyper-inflammatory new presentations of opportunistic infections or paradoxical deterioration in patients already on treatment for the opportunistic infection. IRIS is most commonly described in association with mycobacterial, fungal and viral infections.

Tuberculosis-associated IRIS (TB-IRIS) is the most significant form of the condition encountered in settings where TB endemic. In a recent meta-analysis, we found that TB-IRIS is reported in 18% (95%CI= 16-21%) of patients starting ART while on TB treatment. Major risk factors for the condition are a low CD4 count, high HIV viral load, disseminated TB and short interval between starting TB treatment and ART. A key determining factor thus appears to be antigen load. Innate and adaptive components of the immune system have been shown to contribute. A gene transcriptional signature characterised by innate immune signaling genes distinguished patients who developed TB-IRIS from those who did not, and was evident within a few days of starting ART and prior to symptoms. TB-IRIS is characterized by high concentrations of cytokines in peripheral blood, with elevated interleukin-6 identified consistently across studies. Common clinical presentations are worsening pulmonary infiltrates, enlarging lymph nodes and abscess formation. Central nervous system involvement (eg. meningeal inflammation, enlarging tuberculomas) may be life-threatening. The average duration of the condition is 2-3 months, but a small proportion of cases may have manifestations lasting > 1 year. We demonstrated in a previous clinical trial that prednisone (starting at 1.5mg/kg/day) reduced hospitalization and improved symptoms in patients with TB-IRIS. We are currently evaluating prednisone for prevention of TB-IRIS in high-risk patients with TB starting ART in a randomized placebo-controlled trial (PredART trial: https://www.predart.org/site/index).

Cryptococcal IRIS typically presents with recurrent meningitis in the first months of ART, often with associated raised intracranial pressure. No clinical trials have been conducted, but management usually involves re-initiation of induction antifungal therapy until

relapse is excluded, therapeutic lumbar punctures and in severe cases corticosteroids.

A priority in IRIS research is identifying key inflammatory pathways that trigger the condition that could be targeted with more specific immunotherapy to prevent and/or treat the condition.

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The long-term impact of antiretroviral therapy in resource-limited settings

N. Kumarasamy

YRGCARE Medical Centre, Chennai, India

Abstract: With the advent of antiretroviral therapy (ART), HIV has shifted to a chronic manageable condition, even in resource-limited settings. Now, the long-term effects of being on ART and living with HIV are emerging. These include the adverse effects of long-term ART and morbidity due to non AIDS complications such as cardiovascular, hepatic, renal, metabolic and neurocognitive disease, cancers and ageing as well as complications due to hepatitis B and C co-infection. Although first and second-line antiretrovirals are available in resource-limited settings, new antiretrovirals are urgently needed in order to sustain HIV as a chronic manageable condition. Several clinical trials are underway to eradicate HIV from reservoirs among patients who are on long-term ART and virologically suppressed, leading to the hope of eventual eradication of this virus.

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Active case finding of kala-azar

P. Das

Rajendra Memorial Research Institute, Patna, India

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Treatment of visceral leishmaniasis

S. Sundar

Banaras Hindu University, Varanasi, India

Abstract: Visceral leishmaniasis is the most severe form of leishmaniasis, and if untreated, it is fatal. Although pentavalent antimony (Sb^v) is most widely used drug for its treatment, but in the state of Bihar in India and in Nepal moderate to severe resistance to Sb^v led to it being abandoned in the Indian subcontinent. Governments of India Nepal and Bangladesh lauched an elimination initiative for visceral leishmaniasis (VL) in 2005 and oral miltefosine was selected for treatment. Prolonged regimen of almost one month, frequent gastrointestinal adverse events and teratogenic potential are major hurdles of the miltefosine treatment leading to poor compliance. Further, long half life of miltefosine makes it vulnerable for drug resistance. Recently two important breakthroughs in the treatment of VL provide new perspective in the control of VL in Indian subcontinent. In a randomized controlled study over 300 parasitologically confirmed patients were treated with single dose of 10 mg/kg of liposomal amphotericin B (AmBisome, L-AmB). The cure rate was 95.7% which was comparable to the comparator conventional amphotericin B (96.3%) . In another phase 3 study which closely followed the single dose study multiple combinations of the three available drug, L-AmB, miltefosine and paromomycin were administered between 8-11 days. In this open labelled, randomized, controlled, non-inferiority trial in Bihar, India, single injection of 5 mg/kg L-AmB and 7-day miltefosine; L-AmB and 10-day paromomycin; miltefosine and paromomycin for 10 days were compared with the conventional treatment. The efficacy rates for all patients enrolled (intent to treat, ITT) were: amphotericin B 93.0%; L-AmB and miltefosine 97.5% ; L-AmB and paromomycin 97.5%; miltefosine and paromomycin 98.7% (95.06-99.78). Combination therapies were well tolerated and had fewer adverse events than standard treatment. These studies provide newer vistas in the treatment of VL. Their early implementation will provide a tremendous boost to the Elimination programme.

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