Report of the Fifth Brazilian Symposium on HIV/AIDS Research
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In 2003, the Fifth Brazilian Symposium on HIV/AIDS Research was held in Rio de Janeiro, RJ, with 264 participants and comprising lectures delivered by 33 invited speakers, 48 short-presentations, and 137 posters. The main subjects were immunology, epidemiology, therapy, molecular biology, and co-infections.

HIV-1 epidemiology in Brazil

The most recent data collected by the National Program of Sexually Transmitted Diseases and AIDS (PN-DST/AIDS) of the Brazilian Ministry of Health were presented by Cristina Possas, scientific advisor. The actions of the Brazilian Government in response to the HIV/AIDS pandemic have to be fast, to include the broad society, must be multi-sectorial, balancing and integrating prevention and care, respecting and promoting human rights in all aspects, and, most of all, fostering scientific and technological development. The latest estimates indicate that 0.65% of the Brazilian population is infected with HIV-1, with 10,000 yearly deaths, totaling 120,000 deaths since 1980, with a resulting decrease in the Brazilians life expectancy of 3 months, overall. Current tendencies of the Brazilian epidemic indicate increases of infection by heterosexual transmission (85% of new infections in recent years), of women, of people living further from major urban centers and of the poorest part of the population. The PN-DST/AIDS hopes to increase access to condoms, increase and speed up HIV infection diagnosis to include a greater proportion of the sexually active population, and to continue with the universal antiretroviral therapy policy. This policy has decreased HIV-related mortality, morbidity, seems to have contributed to the sustained decrease of the number of new AIDS cases and, importantly, has had a major impact on hospitalizations costs, which have significantly lowered since the introduction of highly active antiretroviral treatment of infected individuals.

As the PN-DST/AIDS closely monitor people living with HIV/AIDS, by maintaining networks for CD4+/CD8+ cell counting, for viral load determination and, more recently, for HIV genotyping, one of the results observed is a relatively high therapy adherence (75%), and the low primary ARV resistance observed in Brazil (6.6% vs Argentina 15.4%; US 15-26%, UK 14%, Spain 23-26%).

Present and future strategies of the PN-DST/AIDS include strengthening of clinical research, bio-informatics, vaccine and drug development, and, importantly, inter-institutional links, collaboration within Latin America and with other countries, to stimulate technological transference.

Anti-HIV/AIDS vaccines

A review of the anti-HIV/AIDS vaccine world situation was presented by Saladin Osmanov, of the WHO-UNAIDS HIV vaccine initiative, discussing the just concluded phase III vaccine trials and the trials planned for the new future. Giuseppe Pantaleo presented aims and activities of the Eurovacc Foundation. The vaccine initiative of the ANRS, presented by Michel Kazatchkine in the opening session of the Vth Symposium, was further detailed by Jean-Gerard Guillet, who presented preliminary data on the lipopeptide HIV vaccine trials already concluded (4-12) and being planned (Vac15-19), with emphasis on the significant cytotoxic cell induction observed using the lipidic tail on the peptides chosen in accordance with HIV variability and human lymphocyte antigen variability. Choice and development of a new HIV vaccine vector, a simian adenovirus (AdC5, 6 or 68 gag37), was presented by Aguinaldo R Pinto, with highly encouraging results in mice and macaques.

The need and rational for therapeutic vaccines was discussed by Saladin Osmanov and Brigitte Autran, who presented data on the restoration of cellular immune responses to HIV during highly active antiretroviral therapy (HAART) and during structured therapy interruptions, discussing the difficulties and identifying the most important factors to be considered for therapeutic vaccination, as well as the importance of defining end-points to be reached. A discussion of a phase I therapeutic vaccine trial - ALVAC (Canarypox) vCP1433, trial ANRS 094 – indicates encouraging results for this kind of therapy.

Anti-HIV immune response

The importance of a sustained cellular immune response against HIV-1 was emphasized by Giuseppe Pantaleo, who presented the most recent data on cellular identification and function of the different lymphocyte subtypes. Brigitte Autran discussed the need for an effective cytotoxic T lymphocyte (CTL) response in HIV infection, the needed perforin levels and of IFNg secretion, the importance of "antigenic sin" in CTL induction of a specific CTL response, and the need for a sustained CD4 cell response. Studies carried out by Esper Kallas

amplified these issues. Studies analyzing the influence of dendritic cells on immune activation and CTL response and of the influence of T-CD8 cells on suppression and stimulation of HIV-1 replication permitted a comprehensive discussion of anti-HIV immune response. Studies on differences in HIV-1 and HIV-2 pathogenicity were presented by Rui Victorino, calling attention to the many similarities between anti-HIV-1 and HIV-2 immune response, with strong indications that disease might not be simply a result of "destruction-replacement", but that a strong case can be made for alternative immune activation-centered hypotheses.

Results of studies on mother-to-child HIV-1 transmission were presented by Gabriella Scarlatti, who found that a decrease in sensitivity to the R5 virus inhibitor RANTES can be detected ahead of a switch to X4 HIV-1 prevalence. A comparison of mother-to-child HIV-1 transmission between different geographical regions of Brazil was presented by Mariza Morgado.

A review on HIV-1 infection in women was presented by Beatriz Grinsztejn, with special emphasis on chemotherapy sensitivity in women.

HIV-1 molecular biology

Details on the regulatory roles of *tat* and *nef* on HIV-1 replication and latency were presented by Matija Peterlin, together with the latest data on efforts to develop therapies based on recent findings. Studies on variations in the *nef* gene during progression to AIDS and the finding that an isogenic HIV-1 strain carrying late *nef* alleles showed infectivity and replication properties significantly enhanced when compared with their early versions were presented by Enrique Arganaz. Studies on the mechanism of HIV-1 budding from host cells revealed details on reverse transcriptase activation (Aguiar et al.).

Studies on HIV-1 types prevalent in Brazil, such as the differences of HIV-1 subtype distribution in the Southern and Southeastern regions of Brazil, the increase of genotype C HIV-1 in Southern Brazil (Morgado et al.), and the increasing frequency of genotype recombinations were presented by several researchers.

Diagnosis of HIV-1 infection

The applicability of STARHS (serological testing algorithm for recent HIV seroconversion) was discussed by Haynes Sheppard and Ricardo Diaz, both concluding that STARHS is useful for incidence estimation but error-prone in attempts of timing individual HIV-1 infection. The application of this approach to evaluate incidence of HIV-1 infection in distinct settings, such as blood banks, pregnant women, injection drug users was heavily discussed by several speakers. The usefulness of real time PCR for viral load determination was shown by Rodrigo Brindeiro.

Chemotherapy/resistance

One of the major points discussed in the Vth Brazilian Symposium was the use of chemotherapy for the control of HIV-1 infection, highlighting the development of new drugs, as well as different aspects of resistance to chemotherapy and of side-effects of current therapeutic regimens.

A review of the targets for HIV-1 replication inhibition, and of development of protease inhibitors in Brazil was presented by Octávio Antunes. David Katzenstein reviewed the importance and implications of HIV-1 drug resistance, of the methodology currently available and of the importance of guided antiretroviral therapy (GART), as well as of the implications of drug resistance on HIV-1 transmission and of the limitations of drug resistance assays.

The metabolic complications resultant from antiretroviral therapies (ART) were discussed by Judith Currier, who showed differences in male and female ART toxicity, possible treatment options, and the conclusion that no treatment is advisable based on trials run up to now, but that early recognition and management of lipid disorders and abnormal glucose metabolism is of key importance.

Amilcar Tanuri presented data from studies evaluating drug resistance of non-B HIV-1 genotypes, with results for genotype F and C. Differences in resistance mutations in the *pol* gene from B, F, and C isolates were made evident, and Brazilian genotype C showed different signatures from those prevalent in African genotype C HIV-1. These differences apparently correlate to higher or lower susceptibility to antiretroviral drugs, but conclusions on overall degree of resistance to individual drugs can not be drawn as yet.

Data from the Brazilian National Network for HIV Genotyping (Renageno), established by the Brazilian Government through the National Program of STD and AIDS to evaluate resistance mutations occurring in patients being treated by the network of Brazilian health units the program for the universal access to antiretroviral drugs were presented by groups from Rio de Janeiro and São Paulo. Both groups reported similar results, concluding that the distribution of HIV-1 resistance mutations was related to the antiretroviral therapy already employed. The accumulation of PI related mutations with subsequent regimens was limited, with a significant number of mutations acquired already at first regimen. A high level of primary ARV resistance was found in a population from Santos, SP, including the presence of multi-drug-resistant strains, probably due to the long term use of antiretrovirals in this area of Brazil

A study of the phenotypic resistance profile, fitness and virus replicative capacity of HIV-1 subtype B and C proteases carrying Nelfinavir-resistance mutations was presented, with the identification of a subtype C specific mutation.

Studies on structured therapy interruptions (STI) observed a trend to the reemergence of "old strains", but V3 genetic diversity was low among a small number of patients suggesting either the absence of variable provirus or recombination (less likely). NSI strains often replaced SI strains suggesting that activation of old provirus could be more efficient than viral adaptation during short STI.

Co-infections

The study of co-infections between HIV-1 and a variety of other infectious agents has been shown to be of high importance. Thus, analyses of cytomegalovirus

(CMV) infection and, importantly, co-infection of HIV-1 and CMV, has been of very high importance for clarifying the lack of immune control observed in HIV-1 but not in CMV infection, as presented by Giuseppe Pantaleo.

The assessment of Hepatitis C infection – a proxi for early parenteral exposure – toward a better understanding of HIV-1 dynamics among injection drug users was discussed by Francisco Bastos.

Co-infection of HTLV and HIV was studied in Salvador, BA, by Bernardo Galvão-Castro, observing that the majority of individuals infected with HTLV-I and HIV-1 were older than 30 years, suggesting that exposure to these viruses has declined in the 16-30 age group over the past 10 years. The importance of drug injection as an important risk factor for HTLV-II transmission, but not for HTLV-I, among the HIV-1 infected population was pointed out, and data confirming the decrease of HIV-1 infection in injection drug users were discussed.

Observations on co-infection of HIV-1 with *Leishmania* spp. were presented by Roberto Badaró, reviewing data that show that HIV-1 infection does exacerbate *Leishmania* infection, and that *Leishmania* spp. may lead to a faster progression of HIV-1 infection toward a full clinical syndrome. This was not the case for HIV-1 and *Trypanosoma cruzi* or HIV-1 and *Mycobacterium leprae* co-infections. Co-infections of HIV-1 with human papiloma virus HPV and human herpes virus HHV-8 were briefly discussed.

The world-wide problem of co-infection of HIV-1 with tuberculosis was reviewed by Valéria Rolla, highlighting the challenges of treating TB and HIV in poor-resource settings, where both diseases are prevalent and a complex structure is necessary to diagnose and treat co-infected patients.

To conclude a meeting that once again allowed a comprehensive scientific discussion of HIV-1 research in Brazil and fostered contacts with expert foreign researchers already collaborating or discussing collaborations with Brazilian research groups, the Peggy and Hélio Pereira award was presented to the best studies presented by students. RS Aguiar, LMF Gonzalez and CC Cirne-Santos were selected by the Scientific Committee.

The Next Symposium will be held in Ouro Preto, MG, Brazil, in 2005, and will be presided by Dr Dirceu Greco (Faculdade de Medicina UFMG, Belo Horizonte, MG, Brazil).

Index of studies presented at the V Brazilian Symposium on HIV/AIDS Research

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