HIV positive women. Levi et al. (2002) found 66% of positivity using hybridization (Digene) and 98% using PCR (LiPA). Souza et al. (2001) and Queiroz et al. (2004) detected 85.7% and 100% of HPV-DNA by PCR respectively. (3) CD_4 counts under 350 cells/mL and high viral load counts are associated with higher CIN progression.

Highly active antiretroviral therapy has significantly modified the natural history of AIDS, but its relationship with cervical uterine lesions is not well established. At some Brazilian Centers there are Cervical Pathology outpatient clinics for HIV positive patients with well established protocols, but still there are a few. It is necessary to advise physicians about the importance of early investigation of all seropositive women. This could avoid the development of this invasive malignancy.

HIV-HCV Coinfection and Liver Cancer

Aluisio Segurado

Viral infections are recognized as important factors associated with cancer development worldwide. However, since only a small proportion of infected individuals develop cancer, cofactors related to the host's immune response or to the environment seems crucial in cancer pathogenesis. Viral oncogenesis involves sustained viral oncoprotein synthesis, leading to cell proliferation and eventually to transformation. In this context, disruption of cell cycle control with unrestrained cell division and growth and resistance to apoptosis play important roles. Sequential events in cell cycle control will be reviewed with emphasis on the role of cell cyclins and associated phosphokynases. These include interaction of extracellular growth factors with membrane-associated receptors, phosphokynase activation and signal transduction, translocation of cytoplasmatic transcription factors into the nucleus, activation of immediate early genes, cell division and action of cell cycle control proteins (pRB and p53) inducing cell cycle arrest or apoptosis.

HCV is responsible for the most important blood-borne infection, a relevant cause of chronic liver disease and cancer. In Brazil it is a significant public health concern, as sentinel studies show an overall 1.5% to 2% seroprevalence of HCV infection in the general population. Viral transmission routes are mainly blood-borne (associated to blood transfusions or IDU), though sexual intercourse, domestic non-sexual transmission and organ transplantation may also occur. HIV-HCV coinfection is common, results from shared mechanisms of acquisition and its prevalence is estimated as 30% to 40% in Europe and the USA, whereas Brazilian studies indicate 17.7% in São Paulo and 36.2% in Santos.

Although acute HCV infection is usually asymptomatic, 85% of cases develop persistent infection, ultimately leading to chronic hepatitis, cirrhosis and hepatocarcinoma. Risk factors for liver fibrosis in chronic HCV infection include duration of infection, male sex, older age at viral acquisition, severe alcohol intake, HIV coinfection, lower CD_4^+ cell count, overweight and diabetes. Among cirrhotic patients 1% to 4% develop liver cancer each year. Hepatocarcinoma is the most frequent primary liver cancer, runs 5th in incidence among men and 8th among women, but accounts for the 3rd cause of cancer mortality. Malignant disease is often fulminant, due to late diagnosis, poor response to chemotherapy and high recurrence rates after surgery or liver transplantation. Risk factors for HCV-associated liver cancer include male sex, older age, HBV or HIV coinfections, severe alcohol intake, overweight and diabetes.

HCV replication cycle will be reviewed including cell invasion after interaction with cell surface receptors, internalization of viral RNA, viral replication and protein synthesis, post-transcriptional protein processing, set up of the replicase complex, viral particle assembly and budding from the cell surface. So far the mechanisms of HCV oncogenesis are not well understood: there are no oncogenes in the viral genome, replication is totally intra-

cytoplasmatic and the viral genome is not inserted into the cell DNA. Cancer development is thus believed to depend on interaction of viral proteins with the cell cycle and/or to result from continuous liver cell damage and regeneration (cell turnover). HCV core, NS3A and NS5A proteins have been shown to inhibit $p21^{waf}$ expression and p53 activity. In addition, HCV core protein inhibits cell apoptosis induced by TNF-alpha and Fas and NS5A transactivates cell cyclins and growth factors.

HIV-HCV coinfection induces significant changes in the natural history of HCV liver disease, rendering HCV persistence more likely, with higher levels of HCV viremia and faster progression of liver disease. This may be due to less effective anti-HCV CD_4^+ and CD_8^+ cell immune response, as well as to impaired dendritic cell function.

French studies have recently pointed out for a significant increase in HCV-related morbidity and mortality among people living with HIV/AIDS under HAART. Better knowledge about this infection and its relationship with cancer development is essential for the establishment of effective primary and secondary prophylaxis.

The Descriptive and Molecular Epidemiology of HHV-8 among Population Groups of the Amazon Region of Brazil

R. Ishak, R.N. Martins, L.F.A. Machado, A.C.R. Vallinoto, L. Lobato, T. Sata, M.O.G. Ishak

The present study aimed to describe the epidemiology of *HHV-8* among population groups of the Amazon region of Brazil. Four Indian tribes (Kararao, Arara Laranjal, Tiriyo and Zo'e) and a group of HIV-1 infected and/or with AIDS from the urban population of Belém, Para, were tested for the presence of the virus, using serologic (enzyme immuno assay, ELISA, measuring antibodies to ORF59, early and late protein, lytic cycle, ORF65, late protein of the capsid, lytic cycle, K8.1A and K8.1B, variant forms of the envelope gp, lytic cycle and ORF73, latency maintenance protein) and molecular (gene amplification of the ORF26 and the variable region of VR1, gene K1 segments). The presence of antibodies to *HHV-8* was detected in 66 samples of the 221 tested of the Indian groups, namely, six (25%) in the Kararao, 18 (19.6%) in the Arara Laranjal, 24 (42.9%) in the Tiriyo and 18 (36.7%) in the Zo'e. Out of the 477 HIV-1 group, 74 (15.5%) were seroreactive to *HHV-8*. The ORF26 region was amplified in seven samples, one of the Arara Laranjal, one of the Tiriyo, two of the Zo'e and three of the HIV-1 infected group. Subtyping procedures showed the presence of subtypes C (Zo'e), E (Tiriyo) and B (HIV-1 infected). Serologic results confirm the high prevalence of *HHV-8* and the presence of three subtypes in the Amazon region of Brazil. It also describes, for the first time, the prevalence of *HHV-8* among HIV-1 infected and/or AIDS patients.

New Therapeutic Approaches for HIV and EBV Related Lymphomas

William J. Harrington, Jr.

Worldwide, more than 40 million individuals are infected with Human Immunodeficiency Virus (HIV). In impoverished countries the number of deaths due to AIDS has rapidly increased, however the infectious and malignant complications of HIV have fallen where potent antiretrovirals (ARV) are widely available. Nonetheless, the prolonged survival of many HIV carriers is likely to result in greater numbers of malignancies among these individuals. Nearly half of all cases of non-Hodgkin's lymphoma (NHL) in AIDS patients are associated with the presence of a gamma herpes virus, Epstein Barr Virus (EBV) or Human Herpes Virus Type 8 (HHV-8).

AIDS NHLs may be categorized into several subtypes. Large cell immunoblastic lymphoma (IBL) and diffuse large cell lymphoma (DLCL) generally occur in the setting of moderate to severe immunosuppression (CD_4^+