stable on the level of 30,000 new cases per year for the last 5 years. The number of infected women is consistently increasing throughout the epidemic as man to women ratio is down to 1.5:1 from 3.2:1 10 years ago. There is an increasing geographic spread of the cases. In lower economic regions the incidence is still increasing while decreasing in the most developed areas of Brazil. Free drug therapy is a government policy and more than 150,000 individuals are under HAART therapy. As a consequence the number of opportunistic diseases decreased enormously and patient's median survival under treatment multiplied by 4 since 1996. The main AIDS-malignancy Kaposi's sarcoma (KS), in Bahia peaked 10 years ago and it is showing a tendency to decrease slowly (from up 40 cases [Incidence: 5.6%] in 1993-1994 to 24 [Incidence: 2.4%] in 2001-02) in the same direction Brain lymphoma seems to be decreasing. On the other hand the invasive cervical cancer associated to the HIV infections seems to be increasing peaking in the last 2 years with 13 cases. Non Hodgkin's Lymphoma (NHL) presentation seems to be stable as 5-8 cases are found biannually and male and females seems to have the same incidence (8.5/1,000 patients). Differently from KS and Burkitt Lymphoma that male stands for twice the incidence. Implemented 3 years ago the databank for AIDS related malignancies at University Hospital (HUPES) has already catalogued 2150 cases of the most important malignancies related to infectious diseases mostly to AIDS. Annually more than 500 cancer cases are tested. The median age of individuals enrolled is 50 years, with the NHL patients in the upper bound of the bell shaped age distribution curve. Most of our patients come from the main reference hospital for cancer patients in the State – Hospital Aristides Maltez, seconded by the CICAN, and State Reference Outpatient Cancer Center.

Cervical Cancer and HIV: The Bahia/Brazil Situation

Conceição Queiroz

There are epidemiological evidences that persistent infection, with a high viral load of oncogenic types of human papiloma virus (HPV) plays a pivotal role in the development of uterine cervix cancer. Association of other co-factors seems to be necessary for oncogenesis, such as infection with human immunodeficiency virus (HIV). HIV related cervical intraepithelial neoplasias (CIN) show higher rates of progression and persistence, are more refractary to treatment and often recurrent than in HIV negative women. This is the reason why seropositive patients need more aggressive approach. HPV induced-lesions can be routinely diagnosed using tests such as colposcopy, cytology and histopathology. These tests do not allow identification of the viral type or its oncogenic potential, as molecular hybridization tests do. However, in Brazil, they are very restricted because they are very expensive, nevertheless, colposcopy is low cost and has high technical quality.

CIN prevalence in HIV patients in Brazil is quite variable. In São Paulo, Auge et al. (2000) found 15.2% (n=99) using colposcopy and cytology, much lower than the percentage of 72.1% (n=115) detected by Coelho et al. (2004) based on cytology only. In Rio de Janeiro, Fialho (2002) found 30% (n=130) using cytology and histopathology, similar to the 35.5% (n=354) detected by Oliveira and Silva (2003) using colposcopy and cytology. At the AIDS State Reference Center (CREAIDS), Bahia, we found 12.9% (n=833) of cytological atypia between 2002 and 2004, a much lower rate than the 37% detected between 1998 and 2000 at the same service. A possible explanation for this variation is the fact that some patients are being followed since 1998 and treated as soon as the lesion is diagnosed. Other possibility could be the very high prevalence of antiretroviral therapy.

Although there are no definitive results, some consensus about the co-infection HIV-HPV is under way: (1) The prevalence of HPV infection is higher among HIV patients than in other patient groups. Matos et al. (2003) found a prevalence of 42.9% *versus* 8.2% in HIV positive and negative patients, respectively and Auge et al. (2000) showed similarly 15.2% versus 3.8%. (2) There is a high rate of HPV-DNA in the cervical mucosa of

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-