## **HPV IN RIO 2015**

### **EQUITY – HEALTH PROMOTION**

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#### WINDSOR FLORIDA HOTEL

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#### ABSTRACTS OF PRESENTED PAPERS

#### INTRATYPE GENETIC DIVERSITY OF HPV35, HPV45, and HPV58 IN THE STATES OF RIO DE JANEIRO AND PARÁ

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Introduction: Cervical cancer is the fourth most common cancer in women worldwide (528,000 new cases/year and 266,000 deaths), and the human papillomavirus (HPV) plays a fundamental role being present in more than 95% of the cases. More than 200 types of HPV were described, and 15 types are considered a high carcinogenic risk. Studies suggest that the intratype variants may differ biologically in development and behavior of the tumor, but the majority of the studies examines strains of most prevalent types: HPV16 and 18. Data on other high-risk types, not 16 and 18, are rare and inconsistent. Objective: To analyze the intratype genetic diversity of HPV types 35, 45, and 58 in cervical cancers and the prevalence of variants in patients in the states of Rio de Janeiro and Pará. Methodology: The study included biopsies from 73 women with cervical cancer enrolled in the Instituto Nacional do Câncer (n = 49, in the state of Rio de Janeiro) and the Ophir Loyola Hospital (n = 24, in the state of Pará) which had HPV35 (n = 21). HPV45 (n = 40), and HPV58 (n = 12). The samples were submitted to the Polymerase Chain Reaction and sequencing of the long control region (LCR) and E6 and E7 genes of the viral DNA. For the identification of the variants, a maximum likelihood tree was constructed using the software PhyML using as reference sequences described in the literature for the strains of each type. The analysis of median-joining networks were made using the software Network and for the population analysis, the software Arlequin. Results: For HPV35, 11 haplotypes were identified, 17 patients with the A1 strain and 4 patients with A2, being that the A1 strain was the most frequent in both states. For HPV45, 27 haplotypes were identified, 11 patients with the A1 strain, 3 with A2, 1 with A3, 4 with

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B1, and 21 with B2. For HPV45, the most common strain was B2 in both regions studied. For HPV58, nine haplotypes were found, eight patients identified with strain A2, two with A3, and two with C, A2 being the most common in both regions studied. The population of HPV35 in Rio de Janeiro has a higher gene and nucleotide diversity compared to the population of Pará. HPV35, on the other hand, has a smaller gene and nucleotide diversity compared to the other types of HPV. In the population studied, the presence of haplotypes unique to each region was observed, but there was not a geographical structure in any of the HPV types studied. **Conclusion:** The results show that, for each HPV type, there is a strain which is frequent in both states studied, which indicates that the prevalence of some strains are more recurrent than others. The intratype gene diversity between both populations was virtually the same for all types with exception of HPV35 that showed different gene diversity between the two populations.

 $\textbf{Keywords:} \ \text{Human Papillomavirus; HPV35; HPV45; HPV58; strains; haplotypes.}$ 

#### CONDILOMATOSIS IN CHILDHOOD

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Introduction: The human papillomavirus (HPV) is usually identified by means of its form of clinical manifestation, the condylomata acuminata. Its location can be on the entire lower genital tract, in addition to the urethra, perianal, and anal regions. In pediatric patients, a possible history of sexual abuse should always be investigated if the history of the current disease does not evidence the origin of the condyloma. However, other means of viral transmission may be responsible for the majority of pediatric cases. Potential means for acquisition of HPV in children are described as: heteroinolucação defined by HPV transmission during nonsexual contact with a caregiver while showering or changing diapers; for example, the autoinoculation in which children acquire anogenital injuries from other mucocutaneous sites of themselves and HPV infection in newborns during vaginal birth by contact with the infected maternal genital tract. In addition, HPV DNA was detected in amniotic fluid, in the blood of the umbilical cord, suggesting that the appearance of infection in the uterus and hematogenous dissemination of the virus can be ways of prenatal transmission of HPV. Estimates of the proportion of children with condyloma acuminatum which were sexually abused vary widely from <10 to 90%. Once diagnosed, imiquimod may be chosen as a form of treatment. Objective: The objective of this study was to demonstrate the efficacy and safety of the use of imiquimod in childhood. Case **Description:** B. I. S. J., 1 year and 8 months, white, born by cesarean section was referred to the Vulvar Pathology Service of the Hospital Universitário Antônio Pedro (HUAP) in March 2015 due to verrucous lesions in genitalia noticed by her grandmother, with

progressive evolution of their size in the past 4 months. There were reports of treatment for maternal vulvar warts during pregnancy. Physical examination revealed condylomatous lesion, of approximately 4 cm, covering the bottom of the mons Venus, extending to the labia majora in its upper thirds. Imiquimod was prescribed for a month, in alternate days. In the third-day follow-up, regression was observed in 90% of the lesion in mons Venus and labia majora, still remaining a lesion of approximately 0.5 cm in the anterior commissure of the labia majora and reactional erythema at the application site. **Results:** There was improvement, with remission of the lesions only by use of imiquimod. It is assessed, therefore, that this method is a great option for pediatric patients for being safe, noninvasive, and painless. **Conclusion:** The use of imiquimod for the treatment of genital and perianal warts has shown to be efficient. Its administration in childhood is safe and guided by several studies in the medical literature, but there is still a limitation in the data on its safety and efficacy in children under 12 years. The indicated treatment is of application three times a week, from 1 to 4 months. It is usually well tolerated by children. Its most common side effect is skin irritation at the application site.

**Keywords:** Human Papillomavirus; condyloma acuminatum; vulva; child; therapy.

### SEXUALLY TRANSMITTED INFECTIONS AND DEAFNESS: THE PRODUCTION OF DIDACTIC MATERIAL TO APPROACH IMPORTANT ISSUES FOR WOMEN'S HEALTH

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Introduction: Currently, sexuality is presented heterogeneously in the literature; and experienced since childhood, it is a search for pleasure and may or may not be related with the sexual organs. Sexuality is directly linked to cultural aspects and is a component of personal relations. In this context, the deaf community is directly affected by its bilingual characteristic established by law, in which their first language, the Brazilian Sign Language (LIBRAS), is not guaranteed by the government bodies for dissemination of important issues for women's health. Objective: To develop informative and communicative materials in Portuguese and LIBRAS addressing female sexuality, its characteristics and relation with sexually transmitted infections (STIs), focusing on human immunodeficiency virus, human papilloma virus (HPV), and syphilis for being STIs belonging to the group of higher incidence, according to the Ministry of Health. Methods: The signs on the topic of choice in LIBRAS were found in the Accessibility Brazil Dictionary in multimedia format and the Illustrated Trilingual Encyclopedic Dictionary of the Brazilian Sign Language (LIBRAS), edited by Fernando César Capovilla and Walkiria Duarte Raphael. Results: We performed a search on the three signs: Acquired Immunodeficiency Syndrome (AIDS), condylomata acuminata (HPV), and syphilis. In this work, we identified two signs, AIDS present in both sources and syphilis present only in the Illustrated Trilingual Encyclopedic Dictionary of the Brazilian Sign Language (LIBRAS), edited by Fernando César Capovilla and Walkiria Duarte Raphael. Conclusion: The final product will be the development of the website Sexually Transmitted Infections and Deafness at the Universidade Federal Fluminense (UFF) in partnership with the Santa Casa de Misericordia of Rio de Janeiro (SCMRJ). The technological progress for society and individuals in general plays an important role in the life of Brazilian citizens, because with the use of Internet, information is transmitted and received in real time and worldwide in several languages, including in sign language. To promote access to information is to provide education, culture, and experience, which are essential bases for the development of a full citizen in society.

Keywords: Sexually transmitted diseases; teaching; women's health; deafness.

# $Immuno histochemical \ analysis \ of \ CD45RA^+ \ and \ CD45RO^+ \ cells \ in \ high-grade \ cervical \ intraepithelial \ neoplasia$

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Introduction: The viral infection by human papillomavirus (HPV) is the most prevalent sexually transmitted disease in the young female population. The primary factor for the development of cervical intraepithelial neoplasia (CIN) is the infection by HPV types considered of high risk for malignant progression. The majority of these infections occurs in a transient mode and are generally asymptomatic. Viral persistence is required for the development and progression of precursor lesions of cervical cancer. The immune response is actively involved in the control of HPV infection and progression to malignancy. Intratumoral lymphocytes are clearly identified in cervical lesions and play an important role in carcinogenesis. Objective: This research had as main objective the evaluation of the activation of T lymphocytes in cervical lesions diagnosed with high-grade carcinogenic evolution (Highgrade Squamous Intraepithelial Lesion - HSIL). Methods: Twelve women with HSIL were included, and cervical samples were obtained after diagnostic confirmation by histopathology. Immunohistochemical reactions using anti-CD45RA antibodies (naïve cells) and anti-CD45RO (activated cells) were performed. The positive cells were detected in epithelial, subepithelial, chorion, and perivascular layers. Results: At the epithelial layer, the focus of viral replication. it was found an increased frequency of activated T cells (CD45RO +  $1.62 \pm 7.7$  cells/mm<sup>2</sup>) than naïve cells (CD45RA  $\pm$  3.38  $\pm$  3.36 cells/mm<sup>2</sup>), demonstrating an active inflammatory profile in the lesions. The same profile was observed in the subepithelium ( $2.06 \pm 2.04$  and  $4.2 \pm 2.61 \text{ cells/mm}^2$ ), chorion  $(7.43 \pm 9.28 \text{ and } 19.07 \pm 15.13 \text{ cells/mm}^2)$ , and perivascular regions (2.86  $\pm$  4.00 and 10.39  $\pm$  15.79 cells/mm<sup>2</sup>), showing the recent migration of these cells. Conclusions: The migration of lymphocytes to sites of infection by HPV is important to induce an inflammatory environment and eliminate cells infected by HPV. Other studies are necessary to evaluate the involvement of these cells in the control of precursor lesions of cervical cancer and the evolution of the carcinogenesis.

Keywords: HPV; immunohistochemistry; CD45RA; CD45RO.

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## Immune regulatory profile "in situ" in anal lesions of patients coinfected with HPV/HIV-1

AWARDED BEST POSTER

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The human papillomavirus (HPV) is the main etiologic agent of anogenital tract cancer. Higher prevalence and incidence of development of carcinoma and diseases associated with HPV have been observed in HIV-infected individuals. The natural history of HPV infection is not yet fully elucidated, as well as the immune response in HIV/HPV coinfection, especially in Anal Intraepithelial Neoplasia (AIN). **Objective:** To analyze the immune response "in situ" of biopsies of HIV-infected individuals monitored at the Instituto Nacional de Infectologia da Fundação Oswaldo Cruz (IOC/Fiocruz). **Materials and Methods:** In all, 114 biopsies were analyzed using the Tissue Microarray format, being 15 of individuals not

infected by HIV, all without lesion, and 99 of HIV-infected individuals: 21 without lesion. 39 with AIN1, and 39 with AIN2/3. Polymerase Chain Reaction and sequencing for genotyping of HPV and immunohistochemical analysis of immune markers CD4, CD8, Foxp3, T-bet, IL-10 and SLPI were performed. The statistical analysis was performed using the software SPSS, version 15.0 by applying the tests: Kruskal-Wallis, χ²-test and Fisher's Exact Test. Results: HIV-infected patients with AIN2/3 presented CD4+ nadir <50 cells/ mm<sup>3</sup> compared to normal patients (p = 0.01). As for the immune markers, HIV-infected individuals showed higher expression of FoxP3 and IL-10 according to the severity of the lesion (p = 0.002). A positive correlation coefficient was observed between FoxP3 and IL-10 (r = 0.34; p = 0.027). In all, 93.4% (101/107) of the samples presented HPV DNA, being the most prevalent types: HPV 16 (26,9%), HPV 6 (15,7%), HPV 59 (13%), and HPV 18 (10.2%). Samples of individuals with high-oncogenic risk HPV were negative for SLPI, as well as there was lower expression in samples with AIN2/3 compared to the group without lesion of HIV-infected individuals, showing an inverse correlation with the HPV type and degree of lesion. Conclusion: The results of this study suggest that individuals infected with HIV present a greater risk to develop the anal cancer, due to the high prevalence of HPV 16 and the increase of IL-10 (Th2) and FoxP3 (T-Reg), which show an immune response regulatory profile, emphasized by the decrease of T-bet cells (Th1), in these high-grade lesions. The majority of HIV-infected individuals have been exposed to the four types of HPV of the quadrivalent vaccine, suggesting that HPV vaccination should be regarded as a prophylactic measure to reduce the risk of anal intraepithelial lesions in HIV-infected individuals. Our study seems to be the first to describe the SLPI protein as possible biomarker in samples of anal lesions and to describe the T-bet transcription factor in anal lesions.

Keywords: HPV; HIV-1; anus; neoplasms; immunology.

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# ANALYSIS OF THE NUCLEOTIDE SEQUENCES OF ORF L1 OF PAPILLOMAVIRUS OF ANIMAL SPECIES COMPARED WITH THE SEQUENCES OF HPV DEPOSITED IN GEN BANK

POSTER AWARDED HONORABLE MENTION

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The papillomavirus genome consists of a circular, double-stranded, nonsegmented DNA molecule, with approximately 8 Kbp and infects a broad spectrum of hosts. Several techniques of molecular biology have recently been employed in the detection of human papillomavirus (HPV). The objective of this study was to analyze the homology of the nucleotide sequences of ORF L1 of various animal species compared with the sequences of HPV deposited in Gen Bank. The procedures for sample collection followed the standards of local research units according to each analyzed species. The DNA of the blood samples and biopsies was extracted using the QIAamp DNA blood mini kit (QIAGEN). Samples of the species Bos taurus, Canis familiaris, Felis concolor, Panthera onca, and Struthio camelus presented sequences of the papillomavirus DNA, using the pair of degenerated oligonucleotides FAP59 (sense: 5' - TTACWGTIGGICAYCCWTATT - 3') /FAP64 (antisense: 5'- CCWATATCWVHCATITCICCATC-3') for the amplification of ORF L1 in PCR assays. All samples were tested for  $\beta$ -globin gene (sense: 5` - AACCTCTTTGTTCACAACCAG - 3') / (antisense: 5' - CAGATGCTTAACCCACTGAGC - 3'). For the sequencing reaction, 5 µL were used of the PCR product purified using the GFX PCR DNA Purification Kit (GE Healthcare). Subsequently, 2 μL of the purified PCR product were quantified. The sequences were analyzed by the Sequence Analyser using Base Caller Cimarron 3.12. The quality of the sequences obtained was evaluated by the software Chromas, version 2.33 and/or Biological Sequence Alignment Editor (BioEdit). The identities of the products were searched using the Basic Local Alignment Search Tool (BLAST) for comparison with the sequences deposited in Gen Bank. By the analysis of the nucleotides sequence of the ORF L1, it was possible to demonstrate that the genome of different animal species is strictly related with the genotypes of HPV-5, 7, 8, 12, 14, 28, 36, 40, 47, 74, 82, 84, 97, and 107 in different nucleotide positions. Bos taurus: Through the bovine papilloma sample amplified by PCR analysis (RMA 28), we found 100% similarity with the HPV-97 papillomavirus isolate W15189 (Access: EF202168.1 - nt:215-228 and 6529-6516), with the HPV-97 isolate 624 complete genome (Access: EF436229.1 - nt:215-228 e 6529-6516), and with HPV-97 (Access: DQ080080.1 - nt:215-228 e 6529-6516). The nucleotides sequence of the same sample also revealed 90% genetic similarity with the partial gene E1 of HPV-7 isolate alb

(Access: AF322243.1 - nt:151-170 e 32-12) Canis familiaris: It was found a 91% similarity by alignment of the nucleotides sequence of ORF L1 of the RMA 75 sample of canine with the L1 gene of HPV-14 (Access: AF054874.1 - nt:224-245 and 23-45). It was possible to detect by the alignment of the sequences of the nucleotides of sample RMA 78, 100% similarity in nucleotide positions (nt:639-655 and 394-410) of the L1 parcial gene of HPV clone vs75-3 (Access: X79945.1), as well as 100% alignment of the nucleotide positions (nt: 642-656 and 133-147) of the L1 gene of HPV viral capsid clone vs203-2 (Access: X89880.1). By the analysis of the nucleotide sequence of the sample of canine RMA 95, it was possible to verify 100% homology with the complete genome of HPV-5 (Access: M17463.1); HPV-8 (Access: M12737.1); HPV12 (Access: X74466.1); HPV-36 (Access: U31785.1); and HPV-47 (Access: M32305.1). Through the RMA 96 sample, a 94% similarity was found with the genomic DNA of HPV-40 (X74478.1). The analyzed sample also presented a close relationship with the complete genome of HPV-82 (Access: AB027021.1), showing 100% of alignment (NT:161-175 and 971-985). The RMA 97 sample showed a 94% similarity with the HPV-28 complete genome (Access: U31783.1) and 85% with the complete genome of HPV-74, subtype AE10 (Access: AF436130.1). By the alignments of the nucleotides from the adenocarcinomatous lesion (RMA98 sample), 90% homology was identified with the complete genome of HPV-8 (Access: M12737.1), 88% with HPV-40 (Access: X74478.1), and 86% with HPV-31 (Access: EF422120.1) Felis concolor: Were found in the nucleotide positions (nt: 346-365 and 346-363) of RMA 47 sample of feline wild puma, 90% and 94% of similarity with the sequence of the complete genome of HPV-84 (Access: AF293960.1); and HPV-87 (Access: AJ400628.2), respectively. Panthera onca: Through the RMA 46 sample of the jaguar, it was possible to identify a 100% similarity with HPV-7 (Access: X74476.1 - nt: 848-863 and nt: 2319-2274), a viral type of a tropical common skin wart. Struthio camelus: The sample RMA 42 of the ostrich showed a 100% similarity at nucleotide position (nt: 64-81 and 3623-3640), with the complete genome of HPV-74, subtype AE10 (Access: AF436130.1). Through the alignment of the nucleotides sequence of sample RMA 43, 81%of homology was found with the HPV-34 genomic DNA (Access: X74476.1) and 94% with HPV-107 (Access: EF422221.1). Thus, given such diversity in the Papillomaviridae family, it was possible to demonstrate through the similarity between the sequences that share the same ancestry the phylogenetic proximity between the investigated hosts, strictly related with the different genotypes of HPV in different nucleotide positions.

**Keywords:** Sequence alignment; homology of genes; Papillomarividae; polymerase chain reaction.

## DIVERSITY OF METHYLATION PATTERNS IN 3'LCR OF HPV16, HPV18, HPV35, AND HPV45 IN CERVICAL CANCER BIOPSIES

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**Introduction:** In cervical cancer (CC) has been suggested that viral integration is an essential event during malignant transformation due to the loss of E2 repressive functions over E6 and E7 oncogenes. However, in up to 40% of cases showed presence of HPV DNA in an episomal form. On these cases, HPV DNA methylation would play a fundamental role by deregulating E6/E7 during oncogenesis. The characterizing and understanding of these mechanisms will allow answering questions such as why only few HPV infections can lead to cancer. **Objective:** To describe the methylation pattern of CpG sites of promoter regions, 3'LCR, of HPV16, HPV18, HPV35, HPV45, and HPV16 coinfected with others HPV types, associating with tumor characteristics, HPV genetic diversity, and the viral DNA physical state. Methodology: Samples analyzed were obtained from biopsies of patients attended at INCA ambulatory and diagnosed with invasive CC. By means of bisulfite treatment followed by PCR and pyrosequencing, CpGs of 3'LCR were analyzed for methylation presence in 103 samples infected with HPV16 (n = 35), HPV18 (n = 37), HPV35 (n = 06), HPV45 (n = 14), and coinfections (N = 11). CASKI and HeLa lineage were used as methylation control. PCR combining 21 pairs of primers was performed to assess disruption status of E1 and E2 genes for HPV16 and HPV18. Results: The 3'LCR segment of HPV16 showed increased level of average methylation (12%), mainly in coinfections (17%) when compared to the other HPV types (6% for HPV18, 5% for HPV35, and 5% for HPV45). Adenocarcinoma tumors infected with HPV16 were more methylated (24%) than squamous cell carcinoma ones (6%); however, this difference was not significant (p = 0.126). In the same way, European variants of HPV16 were more methylated (27%) when comparing with non-European ones (8%), but

the difference was not significant (p = 0.245). Moreover, average methylation at 3' LCR of HPV16 was positively associated with patient age (r = 0.437; p = 0.008). Regarding the HPV DNA physical state, disruptions in E1 and/or E2 were more frequent in tumors with HPV18 than in HPV16 positives (p = 0.005). For HPV16 and HPV18, the disruption of E1/E2 was associated to a low level of average methylation (3% vs. 22% for HPV16, p = 0.004; and 4% *versus* 13% for HPV18, p = 0.023). **Conclusion:** It was observed a higher average methylation for HPV16 (in single and coinfections) in comparison with HPV18, HPV35, and HPV45. For HPV16 and HPV18 were found differences in methylation level between viruses with intact and disrupted E1/E2, and between intratype variants of HPV16, a finding not observed for tumors associated to HPV18.

Keywords: Papillomavirus Human; DNA methylation; Cervix Uteri.

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#### INFECTION BY HUMAN PAPILLOMAVIRUS CONCOMITANT TO PSORIASIS

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Introduction: The human papillomavirus (HPV) is a DNA virus of the papovavirus group with tropism for epithelial cells, causing infections of the skin and mucous membranes. HPV replication occurs in the nucleus of squamous cell, and its life cycle is directly related to the differentiation program of the host cell. In addition to being responsible for benign verrucous lesions of the skin and mucous membranes, it is also involved in the development of several tumors in these areas. On the other hand, psoriasis is a chronic inflammatory disease characterized by hyperproliferation of the epidermis, of multifactorial origin with interaction of genetic conditions and immune responses to external factors, which are necessary for both the onset and evolution. It is known that there are several predisposing factors, among them, the infections caused by viruses, including the HPV. It often affects the extensor surface of the limbs, trunk, sacral region, and scalp. The form of inverted psoriasis is characterized by more humid lesions in areas of flexure (such as the axillary, inguinal, inframammary, and perigenital regions), being more common in individuals infected by HIV and melanodermics. In psoriasis, there is an accelerated evolutive cycle of keratinocytes and an inappropriate immune activation. The HPV penetrates the epithelium from the basal and parabasal cells, causing a genetic mutation and predisposing the development of psoriasis. In addition, the involvement of the HPV in psoriasis pathogenesis is still uncertain, being postulated that the virus may act as a superantigen or is activated from a latent state by inflammatory cytokines. There is a hypothesis that replication of HPV in psoriatic keratinocytes can cause the epidermal hyperproliferation, as well as the stimulation by the antigen, which induces the autoimmune phenomena. Objective: To report a case of HPV infection in a site previously affected by psoriasis in an immunocompetent patient. Case Report: A male patient, 38 years old, mullato, coming from Rio de Janeiro, sought the outpatient clinic reporting the presence of hyperchromic verrucous lesions on the bilateral inguinal region, perineum, and testicular region a year ago. He reported discrete local itching, denied previous treatments, and informed having had a previous diagnosis of inverted psoriasis, being treated with acitretin 30 mg/day and phototherapy. The patient had undergone inguinal hernia surgery before. At physical examination, a brownish verrucous lesion was evidenced, with linear arrangement, bilateral, on a basis of erythematous scaling on the perineal area. Presence of erythematous-violaceous plaques as well, with silver desquamation on the trunk, genital region, and limbs. Tests were performed, in which VDRL serology and anti-HIV 1 and 2 were negative. Biopsy was performed of the cutaneous lesion of the perineum, and the findings were of epithelial hyperplasia verrucosa compatible with viral etiology (HPV). The patient began treatment with biweekly application of 90% trichloroacetic acid (TCA) on the HPV lesions, associated subsequently with the use of imiquimod cream (5%) three times a week. The patient evolved with complete improvement of the cutaneous lesion related to HPV. After 3 months, in its follow-up, he

presented new verrucous cutaneous lesions in the genital region, in a different area of the previously affected, but also in the area of inverted psoriasis. The biweekly application of 90% TCA was restarted, and the patient showed significant improvement. **Discussion:** The involvement of the HPV in psoriasis uncertain, and the virus may act as a superantigen or is activated from a latent state by inflammatory cytokines. Furthermore, phototherapy can be an underlying factor that predisposes patients with psoriasis for infectivity by HPV due to induced immunosuppression in these cases. The appearance of new lesions of HPV in a different area previously affected by the virus, but in a topography affected by psoriasis, reinforces this thesis. **Conclusion:** The reported patient presented HPV infection in the area previously affected by psoriasis (inverted form) and evolved with satisfactory therapeutic response combined with application of TCA and use of imiquimod in both moments. The patient remains in treatment for psoriasis with acitretin and phototherapy. The relevance of the case described is by the rarity of the association of a immunoinflammatory diseases, psoriasis with another infectious (viral) disease in a same topography.

Keywords: Condyloma acuminatum; Papillomaviridae; psoriasis.

# EVALUATION OF THE VIRAL LOAD OF HIGH RISK HUMAN PAPILLOMAVIRUS DETECTED BY HYBRID CAPTURE 2 TEST (HC2) IN THE SCREENING OF CERVICAL CANCER PATIENTS TREATED BY THE SISTEMA ÚNICO DE SAÚDE (SUS)

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Introduction: Persistent infection with one or more types of high-risk human papillomavirus (HR HPV) is the main factor for the development of cervical cancer. Currently, biomolecular tests for HR HPV detection are used as an adjunct to Pap smear or as an independent method for screening of cervical-uterine precancerous lesions in developed countries. However, in Brazil, the Ministry of Health recommends only performing a Pap smear. Objective: To evaluate the positivity and the viral load (VL) of the HPV test for its insertion in the screening program of cervical cancer in Brazil by the Sistema Único de Saúde (SUS). Methods: Samples from 509 patients from the Vale do Ribeira (SP) region were analyzed, the cytopathological tests were performed in material collected in Sure Path® liquid medium, and in its remainder the hybrid capture 2 test (CH2) for HR HPV was performed. Histopathological examination was performed in 204 patients and colposcopy in 202. The Kruskal-Wallis test with 5% significance was applied for evaluating VL. The VL values were compared between the cases of cervicitis, CIN 1 (and CIN not graded), and CIN 2+ (CIN 2 and more severe lesions). The cytopathologic evaluation, the HC2, histopathological examination, and statistical analysis of the results were carried out at the Instituto Adolfo Lutz de São Paulo. The project was funded by the Políticas Públicas para o SUS/Fundação de Amparo à Pesquisa do Estado de São Paulo (PPSUS/FAPESP) (n°2012/51738-7). Results: Were positive for HC2, among the cytopathologic findings: 23/270 (9%) negatives; 1/8 (13%) AGC; 40/125 (32%) ASC-US; 18/32 (56%) ASC-H; 32/45 (71%) LSIL; 21/28 (75%) HSIL e 1/1 (100%) CEC. Were positive for HC2, among the histopathological diagnoses: 37/130 (29%) cervicitis; 20/34 (64%) CIN 1 and CIN not graded 16/18 (89%) of CIN 2: 14/17 (82%) CIN 3 and 1/2 (50%) CEC. The sensitivity of the HC2 test was 91% and the Negative Predictive Value (NPV) of 97% for the detection of a CIN 2+ lesion. The Kruskal-Wallis test of the distribution of the results of VL according to the cytopathologic result showed that an elevated VL in lesions cytopathologically classified as Low-Grade Squamous Intraepithelial Lesion (LSIL) and atypical squamous cells of undetermined significance, not excluding high-grade squamous intraepithelial lesion (ASC-H) are associated with the histopathological diagnosis of CIN 2+. Conclusion: The HC2 exhibited sensitivity and NPV desirable values for a technique for the screening of CIN 2+ lesions. The evaluation of VL in patients with cytopathological results of LSIL and ASC-H may assist in the follow-up of patients, and, in this way, the indication of colposcopy in patients with LSIL and high HL for HR HPV may contribute to a better effectiveness of early detection of high-grade lesion or carcinoma.

**Keywords:** Screening programs; uterine cervical neoplasms.