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HPV infection in women: psychosexual impact of genital warts and intraepithelial lesions

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Introduction

Genital Human Papillomavirus (HPV) infection is the most commonly occurring sexually transmitted viral infection in humans (Capra G. et al, 2008). HPV is a wide family of DNA viruses which may cause benign skin and mucosal tumors (genital, anal or oral warts), or malignant cancers in different organs. Women are more susceptible to the oncogenic effect of HPVs, mostly at the genital site and, specifically, on the uterine cervix (Paavonen J, 2007).

The literature on HPVs is substantial and increasing. The main areas of research include the virological characteristics of HPVs, epidemiology, medical and oncological impact of the infection and related diseases, prevention strategies through appropriate barrier contraception, pap-smear screening and the potential role of vaccines (Moscicki AB, 2008; Barr E et al, 2008; see related chapters, this book).

However, research investigating the relationship between HPV infections and sexual dysfunctions in women is limited. It is only in recent years that research in this area has increased. This has occurred in parallel with the growing rate of infections and consequent psychosocial burden.

HPV infection may have a significant impact on women's sexuality because:

a) it is a sexually transmitted disease, which affects particularly the vulva and the uterine cervix, two key organs for women's eroticism, for biological, emotional and symbolic reasons. HPV infection may: i) threaten the personal and genital health; ii) convey the sense of something degrading, and/or a connotation of stigma, which may induce the woman to feel ashamed, "dirty", inadequate (Conaglen HM et al, 2001; McCaffery K et al 2004; Maggino T et al, 2007; Waller J et al, 2007a, 2007b; Kitchener HC et al, 2007; Clarke P et al, 1996; Scrivener LD et al, 2008; Harper DM, 2004; Anhang R et al, 2004) ; iii) question the health of the partner and his loyalty and commitment to the couple thus potentially affecting sexual function and

raising critical issues for the relationship (Waller J et al, 2007);

b) it may contribute to vulvodynia and sexual pain disorders, namely dyspareunia, associated with and/or consequent to vulvar laser treatment (Morin C et al, 2000);

c) it is a potentially oncogenic disease, which may convey a more serious threat for the woman's genital and general health, specifically increasing fear and anxiety (Conaglen HM et al, 2001; McCaffery K et al 2004; Maggino T et al, 2007; Waller J et al, 2007a, 2007b; Kitchener HC et al, 2007; Clarke P et al, 1996; Harper DM, 2004; Anhang R et al, 2004). Worry associated with repeated exams and consultations, and invasive and painful treatments, which increase in case of recurrences, adds further vulnerability to the woman's emotional and sexual wellbeing (Waller J et al, 2007).

The chapter will analyze the impact of HPVs infections on women's psychosexual health. A concise summary of key medical steps (epidemiology, gender-related issues, diagnosis and treatment) will be included to (re)set the pertinent medical scenario, while referring to specific chapters for a detailed discussion. Medical consequences such as urogenital and proctologic comorbidity will be included when they interfere with the sexuality of the woman and the couple.

Epidemiology

It is estimated that 20 million individuals in the United States are infected with HPV. Age-standardized HPV prevalence has been shown to vary nearly 20 times between populations, from 1.4% in Spain to 25.6% in Nigeria (Clifford GM et al, 2005).

Some studies suggest that 80% of women will have acquired genital HPV by age 50 years, which makes HPV infection the norm rather than the exception (Koutsky LA et al, 1988; Myers ER et al, 2000; Gravitt PE and Jamshidi R, 2005; see chapter 1, Epidemiologic data on cervical cancer, *Vesna Zadnik, Maja Primic Žakel*, this book.)

The majority of sexually active adults will be infected with HPV at least once in their lives. However, it is sexually active women less than 25 years of age who consistently have the highest rates of infection (Ault KA et al, 2006). Besides youth and gender, common risk factors for HPV infection and clinical sequelae of infection include a high number of sexual partners and inconsistent use of barrier protection during sex. These hazardous health behaviors cause an increased risk of co-infections in Sexually Transmitted Diseases (STDs) carriers. This is the reason

why co-infection with HPV and Chlamydia trachomatis or Herpes simplex virus is very common. (TAB. 1).

Clinical consequences

Clinical sequelae in cases of low-risk HPV infection consist of genital warts, which can cause significant physical and psychosocial distress. Clinical manifestations of high-risk HPV infection include abnormal Pap test results, low-grade squamous intraepithelial lesions (LSIL), high-grade squamous intraepithelial lesions (HSIL), and cervical cancer.

The progression of the disease has an impact on sexual health. The sense of health threat can be very different according to the grade of the lesions: Cervical Intraepithelial Neoplasia (CIN) 1 vs CIN III or cancer in situ, as they require a different aggressiveness of treatment and follow up. Currently, there are neither totally effective means of preventing HPV *transmission* nor cures for *clinical manifestations*: infection can only be totally prevented via complete sexual abstinence. Good protection is maintained when there is consistent condom use during every type of intimacy (oral, vaginal, anal) and the condom is applied prior to any contact. This is difficult to achieve but very important for the global health of men and women. This is why early sexual education, focusing on self-protecting sexual behaviours, and anti-HPV vaccination is key for primary prevention. Moreover, a consistent research, carried out on 17622 women treated for CIN I or CIN II, who subsequently underwent quadrivalent vaccination against HPV, indicates a 40% reduction in the recurrences rate, suggesting that vaccines may be of help in secondary prevention at least in a consistent subset of women (Warner Huh et Al, paper presented at the International Congress of Gynecological Oncology, Chicago, on march 17th, 2010). More research is needed to confirm this early finding and possibly identify the "identikit" of women who are more likely to benefit from the quadrivalent vaccine to prevent recurrences of HPV-related intraepithelial cervical lesions (Box 1).

Treatment for clinical sequelae such as genital warts and CIN II or III consists of removing the problematic cells and watching for recurrence. This method consumes significant health care resources and is costly (Fleurence RL et al, 2007). Some costs are difficult to estimate (personal distress, psychological comorbidities, negative sexual outcomes. (see chapter 3, Primary cervical cancer prevention, Wiebren and Tjalma, chapter 4, Screening programs of cervical cancer, Pekka,

and chapter 21, Long term consequences of cervical cancer treatment, Lukanovic, this book).

Diagnosis

The diagnosis of the infection can be made either on:

a) symptomatic women: presenting with vulvar, anal or oral warts; atypical vaginal blood losses, smelly vaginal discharge, introital dyspareunia, urinary or anorectal symptoms, weight loss for malignant proliferation and cancer.

b) asymptomatic women: following an abnormal smear test or HPV testing.

Therapy

Treatments include a wide range of interventions, according to the type and site of lesions, extension and severity.

Early and late recurrences of the infection and related pathologies are frequent. They may have a very different impact from the psychosexual point of view, according to the severity of lesions, aggressiveness of related treatments and their side effects, frequency of recurrences and their severity, and quality of psychosexual support from relatives and healthcare providers (see chapter 17, Surgical treatment of cervical cancer, *Heinz Scholz, chapter 18,* Laparoscopic surgery in cervical cancer, *Borut Kobal, chapter 19,* Irradiation and chemotherapy for patients with cervical cancer, *Albert Peter Fras, chapter 20,* Histopathology of invasive cancer of the cervix uteri, *Sigurd Lax, chapter 21,* Long term consequences of cervical cancer treatment, *Adolf Lukanovič, this book).*

Knowledge of HPV and cervical cancer in women

Even though HPV is so prevalent among the population, the general public lacks knowledge and awareness of HPV infection (Anhang R, et al 2003). Little research had explored women's questions and concerns about HPV or their attitudes towards HPV testing. Breitkopkf, Pearson, and Breitkopkf (Breitkopkf CR, et al, 2005) found that women undergoing cervical cancer screening stated that they were aware that they should be screened; however, they often lacked basic understanding of the process, limitations, and results of the Pap test.

Although women usually undergo screening for cervical cancer, most have a poor understanding

of HPV and its association to cervical cancer. Studies of women experiencing an abnormal Pap test found that they had insufficient knowledge about abnormal results and follow-up procedures (Breitkopkf CR, et al, 2005). The women felt that it was the physicians' responsibility to explain their diagnosis and make appropriate recommendations (McCaffery K and Irwig L, 2005). However, Linnehan and Groce (Linnehan MJ and Groce NE. 1999) reported that in a large study of patients with HPV, a majority noted their provider's failure to offer advice on emotional issues, to ask questions about sexual practices, to supply written information and to provide a referral for more support.

To determine the HPV knowledge level of women undergoing PAP smear, Cermak et al submitted a survey containing 33 questions to 109 primarily professional women. Based on the data collected it seemed that physicians were not routinely providing information about HPV to their female patients (Box. 2). Overall women in this study did not feel that their physicians educated them well related to testing for HPV and cervical cancer, risk factors associated with contracting HPV, and preventive measures associated with HPV (Cermak M et al, 2010).

Multilevel educational interventions have been tested to inform preteens, teenagers, and college students about sexually transmitted infections, specifically HPV and its relation to cervical cancer. Middle-aged and older women are overlooked in research studies, despite the fact that 80% of women will be infected with HPV by the age of 50 and 35% of cervical cancer deaths occur in women over the age of 65 (Centers for Disease Control and Prevention [CDC], 2008). Studies have demonstrated limited HPV knowledge and unrealistic health beliefs in both the adolescent and college age populations, but there are few published studies that examine similar knowledge and health beliefs in women over the age of 40. Anecdotal observations in clinical practice suggest women over the age of 40 are unaware of either HPV as a sexually transmitted infection or its relationship to cervical cancer (Graziottin, unpublished data). Hence, middle-aged and older women may not believe themselves at risk and may not practice preventive measures that can potentially save their lives. Compounding this may be their shock when their Papanicolau (Pap) smear reveals a diagnosis of HPV and they're informed this is a sexually transmitted infection.

Because survival rates for cervical cancer are over 90% if detected early and managed properly, it is crucial that women of all ages be armed with a strong knowledge base of HPV, including its acquisition, its potentially serious consequences, and prevention strategies in order to make

informed decisions for their own health and wellness (Friedman & Shepeard, 2007).

According to data from the National Health and Nutrition Examination Study (NHANES) 2003–2004, the prevalence of HPV among U.S. females (N = 2026) aged 14–59 years was 26.8%, with the highest prevalence (33.8%) among adolescent and college age women (ages 14–24) and the lowest prevalence in middle-aged (40–49 years) and older women (50–59 years) at 25.2% and 19.9%, respectively (Dunne et al., 2007). Although this study demonstrates a drop in HPV prevalence as women age, it is not eradicated and HPV continues to threaten the lives of many women in this age group.

According to NHANES, one out of every four women over the age of 40 has already been exposed to HPV. Studies performed utilizing worldwide populations at high risk for cervical cancer suggest a bimodal HPV prevalence distribution showing a first peak around the age of 20 years and a second peak around the age of 40–50 years. Despite recent attempts by health agencies, pharmaceutical companies, news media, special interest groups, and the Internet to provide education specifically targeted to the adolescent and college age populations about HPV, the information is often conflicting, inaccurate, outdated, biased, incomplete, or written at inappropriately high literacy levels for general audiences, contributing to public confusion about HPV. In addition, although HPV also affects women over the age of 40, there are no current HPV educational campaigns or prevention vaccinations targeting middle age and older adult female populations (American Cancer Society [ACS], 2007; Montgomery K and Bloch JR, 2010).

Psychosexual impact of HPV infections

Despite HPV infection being amongst the most common STDs seen in clinical practice, attention has only begun to focus on the psychological or psychosexual impact of this diagnosis on the individual. The few studies that exist suggest adverse psychological and psychosexual sequelae may be common (Linnehan MJ and Groce NE, 2000; Voog E and Löwhagen GB, 1992).

The evidence emerging from the literature and from our clinical experience suggests the existence of several peaks of vulnerability due to HPV infection. The available studies are focused on genital – i.e. vulvar/vaginal/cervical – lesions. However, oral and anal infections are increasing and should be considered also from the point of view of their potential psychosexual impact (**see Box 3 and Box 4**).

Genital lesions

Different stages in the diagnosis and treatment of HPV infection may have a different impact on women and couples. The "timing" effect can overlap with a number of variables, causing psychosexual impairment or leading to overt sexual dysfunctions.

Psychosexual impact of the diagnosis

HPV testing may offer a number of advantages to conventional cervical screening, such as increased sensitivity for high grade precancerous disease, the potential to increase screening intervals for HPV negative women and the reduction of unnecessary colposcopies among women with borderline smears. However, HPV testing has been criticized for its lack of specificity and the potential for large numbers of women to test positive in the absence of clinically significant cytological abnormality (Woodman CB et al, 2001; Miller AB, 2001).

Fear and anxiety at first HPV diagnosis

Conaglen et Al (2001), in their individual case control study on 101 consecutive clients attending an STD clinic, evaluated with 4 validated questionnaires, found that those diagnosed with first episode of HPV had considerable psychological difficulties (25% of the HPV positive group complained suffering for social dysfunction vs 7,9% of the HPV negative group; 17,9% reported severe depression vs 10,5%); 29% of men and 10% of women with a first episode of genital warts could be classified as having sexual concerns at their first visit. However, the diagnosis of HPV was not associated with a greater psychological or psychosexual impact than that reported for other sexually transmitted infections (Conaglen HM et al, 2001) .

Similar results were reported in a study by McCaffery et al (2004). A postal questionnaire survey was sent to 428 women aged 20–64 years to measure psychosocial and psychosexual consequences of HPV infection. Anxiety, distress and feelings about current, past and future sexual relationships were also investigated. Women with normal cytology who tested positive for HPV (HPV+) were significantly more anxious and distressed than HPV negative women using both a state anxiety measure [$F(1,267) = 29$, $P < 0.0001$] and a screening specific measure of psychological distress [$F(1,267) = 69$, $P < 0.0001$]. Women with an abnormal or unsatisfactory

smear result, who tested HPV+:

- were significantly more distressed than HPV negative women with the same smear result [F (1,267) = 8.8, P 1⁄4 0.002], but there was no significant difference in state anxiety.
- felt significantly worse about their sexual relationships. Approximately one-third of women who tested positive reported feeling worse about past and future sexual relationships compared with less than 2% of HPV negative women.

Even in this investigation, the findings suggest that testing positive for HPV may have an adverse psychosocial impact, with increased anxiety, distress and concern about sexual relationships (McCaffery K et al, 2004).

Maggino et al. (2007) evaluated the impact of the communication of an HPV diagnosis on the cognitive-behavioral aspect, emotional experiences, psychic-physical well-being, and psychosexual sphere in young women between the ages of 20 and 45. Three self-evaluating questionnaires (the CBA-20, the SAT-P, and the BISF-W) were administered to 36 women who had been diagnosed with an HPV infection and 36 women who had never been diagnosed with HPV. 36% of the experimental group reacted to the diagnosis with fear, 29% reacted with anxiety, while only 3% of women did react with anger. Significant differences emerged in two samples regarding state anxiety and obsessive and compulsive aspects, while there were no significant differences between the two groups regarding the subjective satisfaction with life quality and sexual function. A significant positive correlation was found between the sum of anxiety and fear expressed at the time of the diagnosis and the trait anxiety reported in the Cognitive Behavioral Assessment 2.0. The results indicate that the prevalent emotions felt at the time of the diagnosis are fear and anxiety. The persons who were diagnosed with an HPV infection resulted as having higher levels of trait anxiety, obsessions, compulsions, and behaviors and worries related to hygiene (Maggino T et al, 2007).

In a recent study Pirotta et al (2009) assessed the psychosocial burden of testing for human papillomavirus (HPV) related genital disease or of a HPV-related diagnosis and compared an instrument specifically designed to measure HPV-related psychosocial burden (HIP) with other generic quality of life (QoL) instruments.

Researchers recruited 331 women, 18–45 years, who had experienced a normal cervical Papanicolaou (Pap) result, an abnormal Pap result, biopsy confirmed cervical intraepithelial

neoplasia (CIN) or external genital warts (EGW). The HIP is a validated 29-item self-administered questionnaire designed to measure the psychosocial impact of HPV-related health conditions in women. It was developed using literature reviews and interviews with women with HPV. A psychometric evaluation of the HIP (n = 583 US women) found it had favourable reliability, construct validity and good ability to discriminate disease severity. HIP items are scored individually and then combined into a scale or total burden score, and can be grouped to examine seven specific psychosocial domains. Higher scores indicate more negative impact.

They found significant psychosocial impacts on women of screening for, or having a diagnosis of, HPV-related genital disease, including normal Pap tests. HPV-related psychosocial impact was detected best with the HIP, which was more sensitive and comprehensive than either the EuroQol VAS or the SDS. Analysis of the HIP psychosocial domains provided insight in to how different HPV-related diagnoses affect various aspects of women's lives.

Significant psychosocial impacts were found for women screened for, or having a diagnosis of, HPV-related genital disease. The largest impact was in women with CIN 2/3 and EGW. This HPV-related psychosocial impact was most sensitively detected with the HIP. Relative to generic measures of QoL, the HIP provided insight into the full range of psychosocial impacts of HPV testing and diagnoses.

Clinicians need to be aware of the potential psychosocial impact of testing for or diagnosing HPV-related genital disease, in particular CIN 2/3 and EGW.

The HIP survey is a more sensitive measure of the psychosocial impact of HPV-related genital disease than generic QoL surveys (Pirotta M et al, 2009).

Fear and anxiety at repeated HPV testing

To evaluate the psychosocial impact of taking part in repeated testing for HPV, Waller used in-depth interviews that were carried out with 30 women who were HPV positive with normal cytology at trial baseline, and attended for a repeat HPV test 12 months later (Waller J et al, 2007). This excellent qualitative study indicates that feelings of shock, confusion and distress about testing HPV positive were common. These feelings are frequently related to the sexually transmitted nature of HPV and concerns. They were articulated about: a) where the virus had come from; b) anxiety about the health implications of HPV. Anxiety was triggered by lack of

knowledge about HPV and followed by seeking further information about HPV from the Internet. Once some of the confusion had been resolved, women seemed able to put the result to the back of their mind until the next test. Particularly reassuring was the knowledge that the virus could lie dormant for a long time, so exposure was not necessarily recent and its presence did not mean that a partner had been unfaithful (Waller J et al, 2007).

"I mean if he'd had an affair with somebody then I would have been angry and upset. As it is . . . it's something that I think he's had before our relationship, I trust him a hundred per cent." Women were also reassured by the fact that HPV does not cause symptoms, is highly prevalent and can clear spontaneously without treatment. The pattern of initial anxiety is modulated by the attitude of the physician: reassuring vs neglecting to clarify the most critical questions and/or referring the woman to the net.

Quality questions include: "The only thing that I do go back on is like what is it? If I keep carrying on, how long will I have it? What will they do for it? What will the long term effects be for me? They're the questions that go over a lot. The other things are just fleeting thoughts like now I sit and think about it. Could it be that? Could it be this? . . . Every now and again I'll think about it for whatever the reason and they're my thoughts that I always have." (Waller J et al, 2007)

Not surprisingly, emotional responses following the *second* HPV test varied greatly by whether or not that test was positive... "The first one you don't know what it's about whereas with the second one it's important to you. When you find out you're positive again . . . you're like ahh!" Negative feelings included fear and anxiety about cancer and becoming ill, concerns about fertility, feelings of being unclean because of the sexually transmitted nature of HPV, concerns about transmission and sexual relationships, a negative impact on feelings about sex, and relationship issues including blaming a partner for the infection… Overall, women appeared to be more distressed by a second HPV positive result than a single one, and expressed a clear preference for immediate colposcopy over continued surveillance. (Waller J et al, 2007).

Psychosocial impact of HPV testing associated with pap-smear

To assess the psychosocial impact of HPV testing as an adjunct to cytology in routine primary cervical screening a controlled study of the psychosocial impact of HPV testing within a randomized trial of HPV testing to assess its efficacy in cervical screening was carried out. The trial

provides a randomized setting of revealed HPV results versus concealed results permitting valid comparisons for assessing true psychosocial impact. The intervention was a revealed high-risk HPV test result in addition to cervical cytology. The main outcome was measured using General Health Questionnaire (GHQ-28), Spielberger State-Trait Anxiety Inventory, and Sexual Rating Scale (SRS). Among women with either mildly abnormal or normal cytology, receiving an HPV(+ve) result did not impact significantly on GHQ caseness and mean scores or on Spielberger State and Trait scores when compared with women in whom the HPV(+ve) test result was concealed. Among women with normal cytology, receiving an HPV(+ve) result was associated with a reduction in the Sexual Rating Scale compared with similar women whose HPV(+ve) result was concealed. We can conclude that HPV testing does not add significant psychological distress when combined with cytology in routine primary cervical screening (Kitchener HC et al, 2007).

Psychosexual impact of diagnosing genital warts

In the clinical setting, women who present with flourishing, massive, disfiguring genital warts may express specific “cosmetic” concerns. Concerns over the risk of persistent modification of the genitals and fears of being rejected by partners as a result may be expressed to the listening physician. However, no mention of this specific issue can be found in the clinical literature published so far. The cosmetic impact of flourishing genital warts deserves to be specifically evaluated; given the increasing focus women have of the cosmetic appearance of their genitals and its impact on their self-image and self-esteem (Goodman MP et al, 2007).

Psychosexual impact of the therapy

HPV lesions’ treatment (physical-chemical therapy, diathermocoagulation and laser therapy or pharmacological therapy with imiquimod) is usually long and painful and can cause sexual impairments (Linnehan MJ and Groce NE 2000; Filiberti A et al, 1993). The higher the number of the interventions, the more painful the technique and the severity of the scarring, the more severe is the potential psychosexual impact (Linnehan MJ and Groce NE 2000; Filiberti A et al, 1993). Unfortunately, whilst the etiology of the psychosexual impact has been discussed in different papers, controlled studies on the impact of different therapies are lacking. Filiberti

assessed the psychological and psychodynamic aspects of patients with widespread genital HPV infection entering into a clinical trial in which they were randomly assigned to three treatment groups: CO2 laser ablation, intramuscular interferon-alpha, CO2 laser ablation plus intramuscular interferon-alpha. Results indicated 57% of the patients experienced sexual impairments after therapy. The main reasons for sexuality change were: the disease itself, fear of infecting the partner, pain during the intercourse, forced use of condom. Sixteen percent of the patients reported a worsening of the relationship with the partner. No difference was found between the different treatment group (Filiberti A et al, 1993).

The American Social Health Association (ASHA) surveyed people with (HPV) about their experiences with the disease and its effect on their lives. 489 patients returned completed surveys, which addressed medical history, health care experiences, personal impact, and demographic information. More than three-quarters of respondents reported feelings of depression and anger, and two-thirds feelings of shame. Sexual enjoyment and activity were also negatively affected by HPV. Additionally, respondents expressed dissatisfaction with the diagnosing health care providers' counseling on emotional and sexual issues (Clarke P et al, 1996).

HPV infection, vulvodynia and dyspareunia

The link between genital warts and vulvodynia is controversial. “Vulvodynia” is a prevalent and highly distressing disorder, with major consequences for interpersonal and psychological well-being (Bachmann G et al, 2006). It is a heterogeneous, multisystemic, and multifactorial disease. It is one of the leading causes of dyspareunia in women in the fertile age. As a multisystemic disease, it involves the mucous structure of the vulvar vestibule and the immune, muscular, vascular, and nervous systems, including pain fibers and centers. As a multifactorial disease, its etiology is complex, involving biological, psychosexual, and relational factors (Bachmann G et al, 2006; Graziottin A and Brotto LA, 2004). Vulvodynia impairs the psychological, physical, and reproductive health of approximately 10% of women at some point in their lives (Bachmann G et al, 2006, Zolnoun D et al, 2006). Two subsets of vulvodynia are recognized: generalized and localized pain subtypes, the latter currently referred to as vestibulodynia or vestibulitis. This condition has been shown to affect 15-20% of women in the United States either currently or previously (Bachmann G et al, 2006).

Two studies do not support the association between vulvar HPV infection and vulvodynia or vulvar vestibulitis: Smith found that a history of genital infections is associated with an increased risk of VVS: bacterial vaginosis (BV) (odds ratio, OR = 9.4), Candida albicans (OR = 5.7), pelvic inflammatory disease (PID) (OR = 11.2), trichomoniasis (OR = 20.6), and vulvar dysplasia (OR = l5.7) but no risk associated with HPV, Atypical Squamous Cells of Undetermined Significance (ASCUS), cervical dysplasia, genital warts, chlamydia, genital herpes or gonorrhea (Smith EM et al, 2002).

Gaunt et al. investigated the prevalence of HPV in patients with VVS by using a polymerase chain reaction (PCR) primer set that detects known HPV types. They retrospectively identified 38 patients with VVS who underwent therapeutic surgical excision of the vestibule. Eleven controls without vestibulitis who underwent vestibular excision for conditions unrelated to HPV infection were identified prospectively. Surgical specimens were examined for the presence of HPV DNA by PCR amplification. DNA sequencing was used to determine HPV type. They found that the prevalence of HPV among patients with VVS was 21% vs. 36% among controls. Group B HPV types accounted for 4 of the 10 (40%) HPV types found in patients with VVS. Overall, in both patient and control samples, a spectrum of HPV types was identified, encompassing many branches of the HPV phylogenetic tree. No etiologic association was apparent. Therefore, their study did not support an association of HPV with VVS. The low rate of observed infection in women with and without VVS and the diversity of HPV types identified suggest incidental virus carriage rather than direct cause and effect. The underlying cause of this debilitating condition remains unknown (Gaunt G et al, 2007).

Morin found that there was little support for the idea that HPV might be related to vulvar vestibulitis (Morin C et al, 2000). The most likely association is between *treatment* for vulvar HPV infection and vulvodynia. This can occur when either pharmacologic (Imiquimod) or physical treatment (either laser or DTC) cause persistent introital/vulvar pain as a persistent side effect of treatment. This negative outcome is common when physical treatment is:

a) extensive, due to the magnitude/extension of the vulvar genital warts;

b) repeated due to warts' recurrence or re-infection;

c) overzealous (with deep lesions and neuropathic pain);

d) associated with a defensive contraction of the levator ani, because of the iatrogenic pain. This, in turn, can contribute to introital dyspareunia, reflex inhibition of lubrication, vaginal

dryness and micro-abrasion of the introital mucosa (during intercourse subsequent to treatment) and chronic introital inflammation leading to vulvar vestibulitis and vulvodynia.

Discussion

Women have a gender-specific vulnerability to the health and sexual consequences of HPV infections. They have almost twice the percentage of genital warts in comparison to men (Dinh TH et al, 2008). Women have a higher vulnerability to oncogenic HPV, mostly at cervical and vulvar site.(The age-standardized incidence of vulvar cancer averages between 1 and 2 per 100,000 women in Western countries. Epidemiological studies have identified sexual factors, particularly HPV infection, as increasing risk, Giles GG and Kneale BL, 1995)

The health and sexual risks linked to HPV infections are currently underestimated by women themselves.

Research on the specific impact of genital warts and intraepithelial neoplasias on sexual function and relationship in women is limited. Research focuses more on general psychological outcomes, such as depression, anxiety, guilt, anger, rage, or sexuality as a general issue rather than focusing on specific dimensions of women's sexuality (Conaglen HM et al, 2001; McCaffery K et al 2004; Maggino T et al, 2007; Waller J et al, 2007a, 2007b; Kitchener HC et al, 2007; Clarke P et al, 1996; Scrivener LD et al, 2008; Harper DM, 2004; Anhang R et al, 2004). In previous studies, couple related psychosexual issues have only been explored as part of a broader analysis, with no follow-up studies specifically examining couple outcomes after treatment for genital warts or intraepithelial neoplasia.

More data have been produced on the impact of HPV diagnosis on the emotional and psychosexual well-being

Communicating the diagnosis, through correct and exhaustive information on HPV infection and its psychosexual meaning should be consistently offered by the clinician to HPV positive women and their partners (if the couple is willing to be consulted together). Many women are surprised and upset upon learning about HPV (Conaglen HM et al, 2001; McCaffery K et al 2004; Maggino T et al, 2007; Clarke P et al, 1996). Many search for information on the Internet and report being even more scared. Partners may present with a wide range of negative affects, that should be addressed in parallel (Harper DM, 2004). Ensuring that women are aware that HPV is a common

condition and limiting negative potential consequences by appropriate follow-up and medical interventions (when needed) may reduce the negative feelings and anxiety experienced by women with HPV (Waller J et al, 2007a, 2007b).

Clinical experience indicate that women with a satisfying sexuality before the HPV diagnosis are those less vulnerable to the long term negative consequences of genital warts and their treatments: however controlled studies are needed to support this claim. Vulnerability increases in women experiencing dysfunctional sexuality prior to diagnosis, in single women, in women with troubled or conflictual relationships, or when the infection strongly suggests the partner has had unprotected sex outside of the relationship (Waller J et al, 2007a, 2007b). Clinical correlates include loss of sexual desire, more difficult mental and genital arousal, dyspareunia, less frequent intercourse, and a qualitative and quantitative reduction of the repertoire of sexual behaviors. After HPV genital infection, many women refuse further passive oral sex for fear of infecting their partner.

Overall, preliminary data indicate that sexual morbidity is more correlated to frequency of recurrences than to different treatments per se (Filiberti A et al, 1993). Prevention and early diagnosis of recurrences may reduce the long-term sexual consequences of HPV infection in women. Active counseling on potential female sexual dysfunctions worsened or precipitated by HPV infection should be part of the routine medical approach.

Physicians should also actively investigate previous unprotected anal sex in women with genital HPV infection, to avoid the collusion of silence and the risk of undiagnosed highly aggressive AIN (Halperin DT, 1999; Fox PA, 2006; Parés D et al, 2006). Health care providers should actively inform women against the risk of unprotected anal sex.

Women are frequently very disturbed to discover that a partner they loved may have infected them. “What is the role of men who are sexual partners of women with genital HPV infection and/or cancer?”. This is a sensitive question increasingly raised in clinical consultation by both affected women and their partners (Waller J et al, 2007a, 2007b). HPV testing of the partner, with penoscopy looking for acetowhite lesions and HPV DNA test, should be considered part of the diagnostic assessment of partners of HPV infected women (Bleeker MC et al 2002; Giles GG and Kneale BL, 2005). The sexual impact of being an inducer or a carrier or HPV infections should be investigated (see **Box. 4**). Psychosexual and informative counselling to *both* partners is critical to

prevent further negative psychosexual outcomes during diagnosis and treatment of HPV related lesions. Husbands and couples express their relief and gratefulness when these issues and potential difficulties and/or misunderstandings are openly and spontaneously raised by the physician during the consultation and when practical suggestions are given to overcome physical and emotional problems. Guilty feelings may be pervasive, rooted in the past personal sex life. On the other hand, aggressive feelings against the partner considered responsible for the infection (of having "caught" it) and the subsequent precancerous or cancerous lesions may dominate the clinical picture in a minority of cases (Grassi L et al, 1996; Seibel M et al, 1980) (see **Box. 5**). Individual and couple counselling is critical to address these feelings that may affect the motivational-affective roots of desire and couple commitment.

Overall, the published data indicate that many more questions remain unaddressed than answered in this emerging field of STDs. More research is needed on all the aspects that remain neglected in the evaluation of psychosexual outcomes of genital warts and intraepithelial neoplasias.

Conclusions

Women are at increasing risk of HPV infections and related lesions, with a specific and underestimated vulnerability to the risk of anal infections. Psychosexual vulnerability increases with number of recurrences of HPV infections. Fear, anxiety, anger and depression are the emotions most frequently reported (Conaglen HM et al, 2001; McCaffery K et al 2004; Maggino T et al, 2007; Waller J et al, 2007a, 2007b; Kitchener HC et al, 2007; Clarke P et al, 1996; Scrivener LD et al, 2008; Harper DM, 2004; Anhang R et al, 2004). However, to date there is no conclusive evidence of a correlation between HPV infection and a specific female sexual disorder. The relationship between HPV and vulvodynia/vulvar vestibulitis related dyspareunia remains controversial (Smith EM et al, 2002; Gaunt G et al, 2007, Morin C et al, 2000) . Vaccine anti-HPV may reduce the incidence of HPV infection and the related psychosexual consequences (Ault KA, 2006; Rambout L et al, 2007). However, no data have been produced so far on this issue. Recent research suggests that the quadrivalent vaccine anti-HPV may reduce recurrences of HPV intraepithelial lesions by 40%. The potential of a “high-risk partners” should be considered and diagnosed while counselling HPV infected women. Specific research on the sexual impact of

genital warts and intraepithelial HPV related lesion in women is needed, to address in a more comprehensive and effective way their concerns, complaints and sexual dysfunctions potentially related to HPV-related pathologies and treatment.

References

- Anaya-Saavedra G, Ramírez-Amador V, Irigoyen-Camacho ME, García-Cuellar CM, Guido-Jiménez M, Méndez-Martínez R, García-Carrancá A. High association of human papillomavirus infection with oral cancer: a case-control study. Arch Med Res. 2008;39:189-97.
- Anhang R, Wright TC, Smock L, Goldie SJ. Women's desired information about human papillomavirus. Cancer 2003;315–320.
- Anhang R, Goodman A, Goldie SJ. HPV communication: review of existing research and recommendations for patient education. CA Cancer J Clin. 2004;54:248-59.
- Anttila T, Saikku P, Koskela P, Bloigu A, Dillner J, Ikäheimo I, Jellum E, Lehtinen M, Lenner P, Hakulinen T, Närvänen A, Pukkala E, Thoresen S, Youngman L, Paavonen J. Serotypes of Chlamydia trachomatis and risk for development of cervical squamous cell carcinoma. JAMA 2001;285:47–51
- Ault KA. Epidemiology and natural history of human papillomavirus infections in the female genital tract. Infect Dis Obstet Gynecol. 2006;40470.
- Bachmann G, Rosen R, Pinn V, Utian W, Ayers C, Basson R, Binik Y, Brown C, Foster D, Gibbons J, Goldstein I, Graziottin A, Haefner H, Harlow B, Kellogg Spadt S, Leiblum S, Masheb R, Reed B, Sobel J, Veasley C, Wesselmann U, Witkin S. Vulvodynia: a state-of-the-art consensus on definitions, diagnosis and management. J Reprod Med. 2006; 51: 447-456
- Barr E, Gause CK, Bautista OM, Railkar RA, Lupinacci LC, Insinga RP, Sings HL, Haupt RM. Impact of a prophylactic quadrivalent human papillomavirus (types 6, 11, 16, 18) L1 virus-like particle vaccine in a sexually active population of North American women. Am J Obstet Gynecol. 2008;198:261.e1-11.
- Bleeker MC, Hogewoning CJ, Van Den Brule AJ, Voorhorst FJ, Van Andel RE, Risse EK, Starink TM, Meijer CJ. Penile lesions and human papillomavirus in male sexual partners of women with cervical intraepithelial neoplasia. J Am Acad Dermatol. 2002; 47:351-7
- Bleeker MC, Snijders PF, Voorhorst FJ, Meijer CJ. Flat penile lesions: the infectious "invisible" link in the transmission of human papillomavirus. Int J Cancer. 2006;119:2505-12.
- Bosch FX, de Sanjosé S. The epidemiology of human papillomavirus infection and cervical cancer. Dis Markers. 2007;23:213-27.

- Breitkopkf CR, Pearson HC, Breitkopkf DM Poor knowledge regarding the pap test among low-income women undergoing routine screening. Perspectives on Sexual and Reproductive Health 2005; 78–84.
- Cameron JE, Hagensee ME. Human papillomavirus infection and disease in the HIV+ individual. Cancer Treat Res. 2007;133:185-213.
- Campisi G, Panzarella V, Giuliani M, Lajolo C, Di Fede O, Falaschini S, Di Liberto C, Scully C, Lo Muzio L. Human papillomavirus: its identity and controversial role in oral oncogenesis, premalignant and malignant lesions (review). Int J Oncol. 2007;30:813-23.
- Capra G, Giovannelli L, Bellavia C, Migliore MC, Caleca MP, Perino A, Ammatuna P. HPV genotype prevalence in cytologically abnormal cervical samples from women living in south Italy. Virus Res. 2008; 133:195-200
- Castellsaguè X, Munoz N. Chapter 3: Cofactors in human papillomavirus carcinogenesis: role of parity, oral contraceptives, and tobacco smoking. J Natl Cancer Inst Monogr. 2003;20–28.
- Cermak M, Cottrell R, Murnan J.Women's Knowledge of HPV and Their Perceptions of Physician Educational Efforts Regarding HPV and Cervical Cancer. J Community Health. 2010 Feb 5.
- Clarke J, Terry RM, Lacey CJ. A study to estimate the prevalence of upper respiratory tract papillomatosis in patients with genital warts. Int J STD AIDS. 1991;2:114-5.
- Clarke P, Ebel C, Catotti DN, Stewart S. The psychosocial impact of human papillomavirus infection: implications for health care providers. Int J STD AIDS 1996;7:197-200.
- Clifford GM, Gallus S, Herrero R, Muñoz N, Snijders PJ, Vaccarella S, Anh PT, Ferreccio C, Hieu NT, Matos E, Molano M, Rajkumar R, Ronco G, de Sanjosé S, Shin HR, Sukvirach S, Thomas JO, Tunsakul S, Meijer CJ, Franceschi S; IARC HPV Prevalence Surveys Study Group. Worldwide distribution of human papillomavirus types in cytologically normal women in the International Agency for Research on Cancer HPV prevalence surveys: a pooled analysis. Lancet 2005;366:991-8.
- Conaglen HM, Hughes R, Conaglen JV, Morgan J. A prospective study of the psychological impact on patients of first diagnosis of human papillomavirus. Int J STD AIDS;2001;12:651-8.
- Dinh TH, Sternberg M, Dunne EF, Markowitz LE. Genital warts among 18- to 59-year-olds in the United States, national health and nutrition examination survey, 1999--2004. Sex Transm Dis. 2008;35:357-60.
- Epstein RJ. Primary prevention of human papillomavirus-dependent neoplasia: no condom, no sex. Eur J Cancer. 2005;41:2595-600.
- Filiberti A, Tamburini M, Stefanon B, Merola M, Bandieramonte G, Ventafridda V, De Palo G. Psychological aspects of genital human papillomavirus infection: a preliminary report. J Psychosom Obstet Gynaecol. 1993; 14:145-52.

- Fleurence RL, Dixon JM, Milanova TF, Beusterien KM. Review of the economic and quality of life burden of cervical Human papillomavirus disease. AJOG. 2007;196:206-12
- Fox PA. Human papillomavirus and anal intraepithelial neoplasia. Curr Opin Infect Dis. 2006;19:62-6.
- Friedman AL, Shepeard H. Exploring the knowledge, attitudes, beliefs, and communication preferences of the general public regarding HPV: findings from CDC focus group research and implications for practice. Health Educ Behav. 2007;34:471-85.
- Gaunt G, Good AE, McGovern RM, Stanhope CR, Gostout BS. Human papillomavirus in vulvar vestibulitis syndrome. J Reprod Med. 2007;52:485-9.
- Giles GG, Kneale BL. Vulvar cancer: the Cinderella of gynaecological oncology. Aust N Z J Obstet Gynaecol. 1995;35:71-5.
- Goodman MP, Bachmann G, Johnson C, Fourcroy JL, Goldstein A, Goldstein G, Sklar S. Is elective vulvar plastic surgery ever warranted, and what screening should be conducted preoperatively? J Sex Med. 2007;4:269-76.
- Grassi L, Indelli M, Marzola M, Maestri A, Santini A, Piva E, Boccalon M. Depressive symptoms and quality of life in home care assisted cancer patients. J Pain & Sympt Management 1996;12:300-307
- Gravitt PE, Jamshidi R. Diagnosis and management of oncogenic cervical human papillomavirus infection. Infect Dis Clin North Am. 2005;19:439-58.
- Graziottin A, Brotto LA. Vulvar vestibulitis syndrome: a clinical approach. J Sex Marital Ther. 2004;30:125-39
- Halperin DT. Heterosexual anal intercourse: prevalence, cultural factors, and HIV infection and other health risks, Part I. AIDS Patient Care STDS.1999;13:717-30.
- Hariri S, Dunne EF, Sternberg M, Unger ER, Meadows KS, Karem KL, Markowitz LE. Seroepidemiology of Human Papillomavirus Type 11 in the United States: Results From the Third National Health and Nutrition Examination Survey, 1991-1994. Sex Transm Dis. 2008;35:298-303.
- Harper DM. Why Am I Scared of HPV? CA Cancer J Clin 2004;54;245-247.
- Kitchener HC, Fletcher I, Roberts C, Wheeler P, Almonte M, Maguire P. The psychosocial impact of human papillomavirus testing in primary cervical screening-a study within a randomized trial. Int J Gynecol Cancer. 2008;18:743-8.
- Koutsky LA, Galloway DA, Holmes KK. Epidemiology of genital human papillomavirus infection. Epidemiol Rev1988;10:122-63.
- Linnehan MJ, Groce NE. Psychosocial and educational services for female college students with genital human papillomavirus. Family Planning Perspectives 1999;137–141.

- Linnehan MJ, Groce NE. Counseling and educational interventions for women with genital human papillomavirus infection. AIDS Patient Care STDS, 2000;14:439-45.
- Maggino T, Casadei D, Panontin E, Fadda E, Zampieri MC, Donà MA, Soldà M, Altoè G. Impact of an HPV diagnosis on the quality of life in young women. Gynecol Oncol. 2007;107:S175-9.
- McCaffery K, Waller J, Forrest S, Cadman L, Szarewski A, Wardle J. Testing positive for human papillomavirus in routine cervical screening: examination of psychosocial impact. BJOG 2004, 2004;111:1437-43.
- McCaffery K, Irwig L. Australian women's needs and preferences for information about human papillomavirus in cervical screening. Journal of Medical Screening 2005;134–141.
- Miller AB. Natural history of cervical human papillomavirus infections. Lancet 2001;357:1816.
- Montgomery K, Bloch JR. The human papillomavirus in women over 40: Implications for practice and recommendations for screening. J Am Acad Nurse Pract. 2010;22:92-100.
- Morin C, Bouchard C, Brisson J, Fortier M, Blanchette C, Meisels A. Human papillomaviruses and vulvar vestibulitis. Obstet Gynecol. 2000;95:683-7.
- Moscicki AB. HPV infections in adolescents. Dis Markers. 2007;23:229-34
- Moscicki AB. Conservative management of adolescents with abnormal cytology and histology. J Natl Compr Canc Netw. 2008;6:101-6.
- Myers ER, Mc Crory DC, Nanda K, Bastian L, Matchar DB. Mathematical model for the natural history of human papillomavirus infection and cervical carcinogenesis. Am J Epidemiol 2000;151:1158-71.
- Paavonen J. Human papillomavirus infection and the development of cervical cancer and related genital neoplasias. Int J Infect Dis. 2007;11S2:S3-9.
- Parés D, Mullerat J, Pera M. Anal intraepithelial neoplasia. Med Clin (Barc). 2006;127:749-55.
- Pirotta M, Ung L, Stein A, Conway EL, Mast TC, Fairley CK, Garland S. The psychosocial burden of human papillomavirus related disease and screening interventions. Sex Transm Infect. 2009;85:508-13.
- Rambout L, Hopkins L, Hutton B, Fergusson D. Prophylactic vaccination against human papillomavirus infection and disease in women: a systematic review of randomized controlled trials. CMAJ 2007;177:469-79.
- Saleh MM, Seoud AA, Zaklama MS. Study of the demographic criteria and management of adolescents referred with abnormal cervical smears. J Obstet Gynaecol. 2007;27:824-7.
- Scrivener LD, Green J, Hetherton J, Brook G. Disclosure of anogenital warts to sexual partners. Sex Transm Infect. 2008;84:179-82

- Seibel M, Freeman M, Graves WL. Carcinoma of the cervix and sexual function. Obstet Gynecol 1980: 55:484-487.
- Smith JS, Herrero R, Bosetti C, Muñoz N, Bosch FX, Eluf-Neto J, Castellsagué X, Meijer CJ, Van den Brule AJ, Franceschi S, Ashley R; International Agency for Research on Cancer (IARC) Multicentric Cervical Cancer Study Group. Herpes simplex virus-2 as a human papillomavirus cofactor in the etiology of invasive cervical cancer. J Natl Cancer Inst. 2002;94:1604–1613.
- Smith EM, Ritchie JM, Galask R, Pugh EE, Jia J, Ricks-McGillan J. Case-control study of vulvar vestibulitis risk associated with genital infections. Infect Dis Obstet Gynecol. 2002;10:193-202.
- Steben M, Duarte-Franco E. Human papillomavirus infection: epidemiology and pathophysiology. Gynecol Oncol. 2007;107:S2-5.
- Strickler HD, Burk RD, Fazzari M, Anastos K, Minkoff H, Massad LS, Hall C, Bacon M, Levine AM, Watts DH, Silverberg MJ, Xue X, Schlecht NF, Melnick S, Palefsky JM. Natural history and possible reactivation of human papillomavirus in human immunodeficiency virus-positive women. J Natl Cancer Inst. 2005;97:577–586.
- Voog E, Löwhagen GB. Follow-up of men with genital papillomavirus infection: psychosexual aspects. Acta Derm Venereol 1992;72:185-6.
- Waller J, Marlow LA, Wardle J. The association between knowledge of HPV and feelings of stigma, shame and anxiety. Sex Transm Infect. 2007a;83(2):155-9.
- Waller J, McCaffery K, Kitchner H, Nazroo J, Wardle J. Women's experiences of repeated HPV testing in the context of cervical cancer screening: a qualitative study. Psycho oncology 2007b; 16:196-204
- Winer RL, Feng Q, Hughes JP, O'Reilly S, Kiviat NB, Koutsky LA. Risk of female human papillomavirus acquisition associated with first male sex partner. J Infect Dis. 2008;197(2):279-82.
- Woodman CB, Collins S, Winter H, Bailey A, Ellis J, Prior P, Yates M, Rollason TP, Young LS. The natural history of cervical human papillomavirus infection in young women: a longitudinal cohort study. Lancet 2001;357:1831 – 1836.
- Zolnoun D, Hartmann K, Lamvu G, As-Sanie S, Maixner W, Steege J. A conceptual model for the pathophysiology of vulvar vestibulitis syndrome. Obstet Gynecol Surv. 2006;61:395-401.

Box 1. The new HPV vaccines: a hope for the future

New prophylactic HPV vaccines promise to dramatically reduce the incidence of HPV infection, genital warts, and cytologic abnormalities. The tetravalent vaccine currently approved by FDA and EMEA utilizes 4 different "proteins-number-plate", thus enabling the immune system to attack viruses corresponding to genotypes 6,11, 16 and 18. This will reduce 90% of condylomata and 70% of invasive cervical cancers (the remaining being caused by others genotypes, Ault KA, 2006).
Among women aged 15–25 years not previously infected with vaccine-type HPV strains, prophylactic HPV vaccination appears to be highly efficacious in preventing HPV infection and precancerous cervical disease (Rambout L et al, 2007).
However, consistent protection with condoms should be recommended also to vaccinated women to protect them from: a) HPVs infections other than strains 6,11,16 and 18; b) other sexually transmitted diseases.

Box 2. Women perception of physician Education Efforts regarding HPV (Cermak M et al, 2010)

- Seventy-eight (71.6%) of the 109 women responding reported that the topic was not at all mentioned or discussed.
- Only 15 (13.8%) of the women reported that the topic was thoroughly discussed and an opportunity for questions was provided.
- 90 (82.6%) of the women were not instructed about the difference between an HPV and Pap test.
- 94 (86.2%) of their physicians did not mention risk factors associated with HPV infection.
- 94 (86.2%) did not bring up the increased risk associated with smoking and HPV infection.
- 92 (84.4%) did not mention increased risk associated with oral contraceptive use.
- 81 (74.3%) failed to discuss safer sex practices.
- 68 (62.4%) of the physicians took no sexual history and did not mention increased HPV risk associated with multiple sexual partners.
- 77 (70.6%) of the women received no information on how to prevent HPV infections.
- 83 (76.1%) of the women could remember no mention of the new HPV vaccine.
- younger physicians to provide more education regarding HPV and cervical cancer than older physicians.
- married and widowed women did not perceive that they received as much education from their physicians on the topic of HPV and cervical cancer as single, engaged and divorced women.

Key point: Physicians are selective in their education of patients and may be making assumptions about the HPV risk level of women based on their age and/or marital status.

Box 3. Oral HPV infections

Unprotected oral sex is becoming an area of increasing concern for sexually transmitted diseases, including HPV. Therefore, specific questions about oral sex should be made to avoid the "collusion of silence" and the consequent potential diagnostic omissions of STD.
Respiratory tract papillomas are associated with HPV types 6 and 11; these HPV types are also commonly associated with genital warts. The incidence of respiratory tract papillomas in young adults is increasing (Clarke J et al, 1991; Campisi G et al, 2007; Anaya-Saavedra G et al, 2008). It has been postulated that oro-genital contact is the means of transmission in this age group. In view of the high infectivity of genital warts, it is interesting to note the low prevalence of oro-pharyngeal warts in adults indulging in oro-genital contact. Oral HPV is strongly associated with oral squamous cell carcinoma (OSCC), suggesting that HPV-16 and -18 are risk factors for oral cancer. A significant association with tobacco and alcohol has been confirmed. In addition, a family history of cancer is associated with OSCC (Clarke J et al, 1991; Campisi G et al, 2007; Anaya-Saavedra G et al, 2008). Whilst much research has been published on the mode of transmission of HPV-related oral lesions, epidemiology and other oral-disease-related issues, to the author's knowledge, no studies have been published on the psychosexual consequences of oral HPV infections.

Box 4. Anal HPV infections

Anal HPV infections in women are usually underestimated because women do not think or report they had unprotected anal sex and physicians usually do not ask about this sexual practice. The health risks of anal sex appear to be severely underestimated by a substantial proportion of sexually active women and men. Among heterosexuals reported rates of condom use are almost universally lower for anal than for vaginal intercourse (Halperin DT, 1999). A U.S. survey and other data suggest that, in terms of absolute numbers, approximately seven times more women than homosexual men engage in unprotected receptive anal intercourse (Halperin DT, 1999). Anal intraepithelial neoplasia (AIN) is a consequence of chronic HPV infection in the anal canal and appears to be driven by high viral loads of HPV. AIN natural history resembles that of cervical intraepithelial neoplasia. Low-grade lesions frequently resolve, but high-grade lesions are much more stable. HIV-positive men and women who practice receptive anal intercourse are at highest risk of AIN (Fox PA, 2006). The incidence of AIN has increased significantly in the last decades (Parés D et al, 2006).After the diagnosis of perianal or anal HPV related infections, many refuse any further anal intimacy. In the clinical setting, the most frequently reported feeling is a sense of guilt, anal sex still being considered in many countries as inappropriate or even transgressive.
To investigate psychological functioning, relationship factors, perception of stigma, disclosure outcomes and regret about the disclosure decision in people being treated for anogenital warts and to evaluate possible predictors of disclosure and non-disclosure, a self-completion questionnaire was completed by 54 participants recruited from a London genitourinary medicine clinic. There were 36 disclosers and 18 non-disclosers. It resulted that disclosers were significantly less anxious than non-disclosers ($p<0.01$). Compared with non-disclosers, disclosers also rated their relationships as significantly longer-lasting ($p<0.001$) and closer ($p<0.01$). Disclosers were

significantly less likely to express regret about their disclosure decision than non-disclosers ($p<0.001$). There were no significant differences between groups in depression, self-esteem, perceptions of level of stigma associated with STDs or expectations about the likely outcome of disclosure, although there was a trend towards higher stigma perception in disclosers ($p=0.15$). The actual partner response to disclosure was significantly more supportive than had been expected ($p<0.001$). A binary logistic regression model used three variables to predict disclosure status with an accuracy of 83%. Disclosers were predicted by lower anxiety levels, longer relationship duration and higher stigma perception (Scrivener LD et al, 2008).

Box 5. The silent carrier or the high risk man: the he-partner

A specific issue to be dealt with when counselling women which HPV infections relates to "who infected whom".[8] This question becomes more painful when oncogenic HPV strains are etiologically related to precancerous lesions that can progress to cervical or vulvar cancer (Maggino T et al, 2007; Waller J et al, 2007a). Studies assessing the carrier or infected status of partners of HPV infected women indicate that subclinical lesions are far more common that diagnosed by simple visual genital examination (Bleeker MC et al, 2002; 2006)
Penile lesions were seen in 68% of the male sexual partners of women with intraepithelial cervical neoplasia, when examined by visual inspection with the colposcopic instrument after acetic acid application to the penis. More than one lesion type was diagnosed in 15% of cases. Flat lesions, papular lesions, and condylomata acuminata were seen in 83%, 29%, and 4%, of cases respectively. HPV was detected in 59% of the penile scrapings, containing mainly oncogenic HPV types. When penile lesions were present at penoscopy, 67% of penile scrapings were positive for HPV, whereas 37% were HPV-positive when no lesions were visible. Penile lesions are frequently found in sexual partners of women with cervical intraepithelial neoplasia, *when appropriately examined*. Most of these lesions are *subclinical* (ie, only visible after acetowhite staining and/or with HPV DNA test of the partner). They are often associated with the presence of high-risk HPV, indicating that male sexual partners of women with cervical intraepithelial neoplasia might constitute a reservoir for high-risk HPV (Bleeker MC et al, 2002; 2006).

Tab. 1: HPV infection risk factors and gender vulnerability in women

Youth	Moscicki Ab, 2007. Saleh MM, Seoud AA, Zaklama MS, 2007. Winer Rl, Feng Q, Hughes JP et Al, 2008.
Gender (female)	Steben M, Duarte-Franco E, 2007. Hariri S, Dunne EF, Sternberg M, et Al, 1991. Dinh TH, Sternberg M, Dunne EF, 2008.
High number of sexual partners	Moscicki Ab, 2007. Saleh MM, Seoud AA, Zaklama MS, 2007. Winer Rl, Feng Q, Hughes JP et Al, 2008.
Non consistently protected sex	Epstein RJ, 2005.

Co-infection with Chlamydia trachomatis	Anttila T, Saikku P, Koskela P, et al. 2001. Bosch FX, de Sanjosè S., 2007. Ault KA, 2006.
Coinfection with Herpes Simplex virus	Smith JS, Herrero R, Bosetti C, et al, 2002. Bosch FX, de Sanjosè S., 2007.
Smoking	Castellsaguè X, Munoz N. 2003. Bosch FX, de Sanjosè S., 2007.
Immunosuppression (HIV, immunosuppressive therapy)	Strickler HD, Burk RD, Fazzari M, et al. 2005. Cameron JE, 2007.
Pregnancy	Strickler HD, Burk RD, Fazzari M, et al. 2005.