

PL6**Sub-epithelial vesiculobullous disorders: treatment now and on the horizon**

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Sub-epithelial vesiculobullous disorders are mainly chronic autoimmune disorders arising from reactions against components of hemidesmosomes or basement membranes of the basement membrane zone of stratified squamous epithelia. Non-immune disorders involving these components typically have a genetic basis: the prime example is epidermolysis bullosa. The term immune-mediated sub-epithelial blistering diseases (IMSEBD) have been used for the acquired forms. Mucous membrane pemphigoid (MMP) is the most common IMSEBD but a number of variants exist. All sub-epithelial vesiculobullous disorders produce clinical pictures of blistering and erosions. Therefore the diagnosis must be confirmed by perilesional biopsy with immunostaining, sometimes with other investigations. No single treatment regimen reliably controls all disorders. The main treatments available are anti-inflammatory and/or immunosuppressive. There is only a weak evidence base: clinical trials of treatments are few, most include patients with heterogeneous entities, few include more than a limited number of patients, and thus reliable data from randomized controlled trials are unavailable. Currently, apart from improving oral hygiene, immunomodulatory therapy is typically used to control the oral lesions of MMP. The immunological differences within the disorders might account for significant differences in responses to therapy. It is not known if the specific subsets of MMP respond to different agents.

PL7**Oral viral infections that could be transmitted oro-genitally**

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Orogenital transmission has been suggested for several viruses, e.g. herpes simplex virus-1 and -2 (HS-1 and HSV-2), Epstein-Barr virus (EBV), cytomegalovirus (CMV), human herpesvirus-8 (HHV-8), human papillomavirus (HPV) and HIV. Most studies have focused on HIV, HSV and HPV. Unprotected orogenital contact, especially receptive oral intercourse, is associated with greater risk of HIV transmission than previously thought. Factors potentially associated with increased risk of HIV transmission through oral sex include poor oral health, the salivary anti-HIV properties such as peroxidases and thrombospondin-1, the local and systemic immunological responses, concomitant sexually transmitted infections, ejaculation in the mouth, local mucosal integrity, and the level of infectious HIV present at the oral mucosa. The probability of per act transmission in oral intercourse with ejaculation is 0.04%. HSV-2 has been regarded as a sexually transmitted virus while HSV-1 is causing primary herpetic gingivo-stomatitis, muco-cutaneous oro-facial disease and ocular disease. Also HSV-2 might be detected occasionally in oro-facial area. Recent data on young women with a primary genital infection indicate that HSV-1 is much more frequent than HSV-2. Oro-genital route of transmission is more common than expected in genital HSV-1 infections. EBV is a tumorigenic herpes virus that is carried as a persistent infection by more than 90% of adults. Most persistently infected people produce EBV in their saliva, and transmission is through close contact. There is a significant association between sexual intercourse and EBV seropositivity, increasing with numbers of sex partners. Because EBV has been found in genital secretions from healthy seropositive men and women, direct spread of virus during sexual intercourse is possible. Today, 106 HPV types have been sequenced of which almost 40 have been detected also in oral mucosa, causing benign epithelial lesions (papillomas, condylomas, warts and focal epithelial hyperplasia, or FEH). Recent meta-analyses of the case-control studies have confirmed HPV as an independent risk factor for oral SCC with odds ratios (OR) 3.7 to 5.4. HPV16 is the overwhelmingly most frequent type. HPV has been regarded as a sexually transmitted disease but this view is challenged by frequent detection of HPV in children. Unlike in genital tract, natural history of oral HPV infection is poorly studied. As part of the Finnish HPV Family Study we evaluated natural history of oral HPV in within family members. The detection rate of HR HPVs varied from 15% to 27%. Our results indicate that natural history of HPV infection in oral mucosa mimics that of genital HPV infections. Oral sex had no association to oral HPV infection, but a persistent oral HPV infection of the spouse increased the risk of persistent oral HPV infection in the other spouse 10-fold.

PL8**The causal role of genital human papillomavirus (hpv) infections in cervical carcinogenesis**

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Well over 150 different human papillomavirus (HPV) types are currently recognised, divided according to their preferential targets into (i) cutaneous and (ii) mucosal HPV types. The latter are further classified as low-risk (HPV 6, 11, 40, 42, 43, 44, 54, 61, 70, 72,

81, and CP6108), intermediate risk (HPV 26, 53, and 66) and high-risk (HPV 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 68, 73, and 82) types, according to their association with malignant lesions at genital- and extra-genital mucosal sites. Since the recognition of their close association with cervical cancer precursor (CIN) lesions in 1976, HPVs have emerged as the most important human tumour viruses. Beyond any doubt, oncogenic HPV types are the single most important etiological agents of cervical cancer (CC) and CIN lesions, whereas low-risk HPV types are associated with benign mucosal squamous cell lesions (papillomas and condylomas). Apart from extensive epidemiological documentation, the link between HPV and CC has been confirmed by molecular biological research and prospective cohort studies disclosing the natural history of HPV infections and the true precancer nature of high-grade CIN lesions. The latter develop as a result of persistent oncogenic HPV infections, known to predispose the women to significantly increased risk of CC. Factors predicting both the disease outcome (persistence, progression, regression) and the viral events (incident infections, HPV persistence, virus clearance) are emerging only recently. In addition to testing the feasibility of various optional screening tools in early detection of CC precursors, as well as to ongoing clinical trials with prophylactic HPV vaccines, another major focus of current HPV research includes the intense screening of new biomarkers as potential predictors of disease progression and outcome of oncogenic HPV infections.

PL9**The HPV-genital (and oral?) infections – how are we standing now?**M Škerlev¹, L Zele-Starčević², S Ljubojević¹¹*Department of Dermatology and Venerology, Zagreb University Hospital and Medical School of Zagreb University, Zagreb, Croatia,* ²*Department of Clinical Microbiology, Zagreb University Hospital and Medical School of Zagreb University, Zagreb, Croatia*

Human papillomavirus (HPV)-associated genital pathology represents one of the major problems among STIs mostly due to the high recurrence rate, difficult eradication and oncogenic potential. Besides, the young, sexually active population in the generative period is mostly affected. Anogenital HPV infections are the most frequently diagnosed STIs of viral origin. However, oral affections caused (or induced?) by the HPV-'genital' types seem to be rather rare and could be very sporadically associated with the genital lesions in the immunocompetent individuals in spite of the clear involvement of the oral mucosa in the (sexual) mode of transmission. HPV genital infections are also one of the most frequent diagnoses in the Sexually Transmitted Diseases (STD) Outpatient Clinic of the Department of Dermatology and Venerology of the Zagreb University Medical School. As the very careful and friendly-orientated manner of taking the medical history and clinical examination is rather important in order to obtain the exact data (especially regarding the oro-genital mode of transmission), the clinical variations are presented ranging from clinically invisible or poorly visible, 'asymptomatic' lesions to the bizarre forms of giant condyloma of Buschke-Löwenstein type. In spite of the fundamental importance of the clinical examination itself, we wanted to identify the HPV DNA type in these lesions. We wanted to evaluate the significance of viral tests (PCR, hybridization) for HPV-induced, clinically visible lesions (condylomata acuminata, condylomata plana, Buschke-Löwenstein) in men. According to our results, HPV 16 and 18 have been isolated from 'benign' HPV-associated genital lesions in 20% of patients, i.e. more than it is usually expected. Therefore, the diagnostic approach to HPV genital infections needs to be complex including HPV DNA typing whenever it seems appropriate. Different methods are presented for the treatment of genital warts, such as cryotherapy, podophylotoxin, curettage, podophyllin, and imiquimod (in the smaller group, as compared to other treatment modalities). It can be concluded that no definite treatment method has been clearly found superior so far. Thus, treatment should be guided by the available resources, the experience of the provider and the preference of the patient. In general, it can be postulated that, over the last decade, the oncogenic properties of HPVs have been intensively studied. Significant progress has been achieved in the investigation of the HPV prevention. More than 35 types of HPV infect the genital tract; types 16 and 18 inducing about 70% of cervical cancer and high-grade cervical (and not only cervical) intraepithelial neoplasia (CIN), and HPV 6 and 11 causing 90% of anogenital warts. A prophylactic vaccine that targets these types should thus substantially reduce the burden of HPV-associated clinical diseases. The results of the most recent studies have clearly shown that a candidate quadrivalent HPV vaccine (6, 11, 16, and 18) was generally well tolerated, induced high-titres of serum antibodies to HPV types, and effectively prevented acquisition of infection and clinical disease caused by common HPV types.

PL10**Oral manifestations of orogenital bacterial infections**

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Orogenital sex in the last decades has become a common sexual practice (fellatio and cunnilingus) between both heterosexual and homosexual individuals. Consequently, several sexually transmitted diseases (STDs) including bacterial infections, are a persistent problem in Europe and throughout the world, despite vigorous efforts in prevention and people education. The last two decades, HIV infection, revived the interest of the medical community and the people for the sexually transmitted diseases.

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