PL6

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

C Scully CBE

Eastman Dental Institute, University College London, UK

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

S Syrjänen

Department of Oral Radiology and Pathology, Institute of Dentistry, Research Laboratory, Faculty of Medicine, University of Turku, Turku, Finland

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

K Syrjänen

Department of Oncology and Radiotherapy, Turku University Hospital, Turku, Finland

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 Skerlev[1], L Žele-Starčević[2], S Ljubojević[1]

[1]*Department of Dermatology and Venereology, 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 Venereology 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, podophyllotoxin, 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

G Laskaris

A. Sygros' Hospital, Medical School of University of Athens, Greece

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.

Many of these bacterial infections present predominantly with characteristic oral signs and symptoms. As a result, it is imperative for the oral physician (stomatologist) to keep abreast of the latest updates in the behavior and to be aware of the whole spectrum of clinical manifestations of these diseases. Orogenital bacterial infections may be divided into two major categories: (i) Common including syphilis and gonorrhoea and (ii) Rare, including chlamydia trachomatis infection and tropical sexually transmitted infections (chancroid, donovanosis, lymphogranuloma venereum). Syphilis is the leader of sexually transmitted diseases and has been of great interest in the past and today and has played a central role in medicine for several decades. The oral lesions of syphilis (primary secondary and tertiary stages) have a broad spectrum of manifestations, which mimic a lot of other oral lesions. The recent incidence data, the oral manifestations, the laboratory tests and treatment of both categories of these diseases will be discussed, as the increased practice of oral sex has become a more important potential route of transmission for oral and genital bacterial pathogens. Stomatologists and Dentists, frequently evaluate oral mucosal manifestations and thus play an important role in the diagnosis and treatment of many of highly infectious sexually transmitted infections.

PL11
Infections – past, present and future

PD Welsby
Western General Hospital, Edinburgh, UK

The reasons that some past infections, including smallpox and diphtheria, have been conquered or controlled will be explored, as will the reasons that some other infections such as tuberculosis and leprosy remain a problem. At present HIV remains a major problem. All antiretroviral drugs are viristatic and thus, even in combination, not curative. Killing HIV will require a 'guided missile' drug that will penetrate every infected cell to remove the HIV-directed DNA within the host genome and this will not be possible, I predict, for decades. Even if a vaccination were available there will be numerous practical problems. The reasons why Edinburgh (incorrectly) received the accolade 'The AIDS Capital of Europe' will be explored and dismissed as a media creation. In the future influenza will cause a world pandemic (the question is not if, but when). Drug resistant infections will continually develop in, and be spread from, hospitals. Most bacteria divide rapidly and it is surprising that drug resistance takes so long to develop. Jet travel will allow infections to spread to anywhere on the globe within 36 h. The fact that HIV and similar retroviruses insert themselves into host cell genomes, and that these sequences can thereafter function genetically, raises the possibility that some genetic disorders were originally infections and also that such inheritance of acquired characteristics opens the door for genetic manipulation which has implications for manipulation of Darwinian evolution in humans and their pathogens.

Update Sessions

US1
HIV – changing patterns in HAART era, patients' quality of life and occupational risks

PA Reichart
Department of Oral Surgery and Oral Radiology, Center for Dental Medicine, Charité Hospital, Berlin, Germany

Oral manifestations are early and important indicators of HIV-infection. Several lesions with strong association to HIV infection have been described: oral candidiasis (OC), oral hairy leukoplakia (OHL), Kaposi's sarcoma (KS), Non-Hodgkin-Lymphoma (NHL), necrotising ulcerative gingivitis and periodontitis. These lesions may be present in up to 50% of patients with HIV-infection and up to 80% of those with AIDS. *Changing patterns in HAART era*: With the advent of highly active antiretroviral therapy (HAART) the prevalence of OC, OHL and HIV – associated periodontal disease has decreased in adults. The prevalence of KS has not changed. However, there has been an increase in HPV-associated oral lesions (papillomas, condylomas and focal epithelial hyperplasia) and HIV-related salivary gland disease. In children receiving HAART no change in the prevalence of HIV-related oral lesions has been found. *Quality of life*: The presence of oral lesions has a marked impact on health related quality of life. HIV-associated orofacial lesions may lead to facial disfigurement (KS, NHL) or may impair speech and swallowing. Consequently, weight loss and pain may be result. Studies have shown that patients with OC, angular cheilitis and OHL have a high score of decayed teeth (DMFT). Xerostomia and taste disturbances may also be factors with impact on quality of life. *Occupational risks*: Occupational exposure to HIV has resulted in 57 documented cases of HIV sero-conversion among healthcare workers in the US (December 2001). Exposure to HBV and HCV carries a much higher risk of occupational infection than that for HIV-exposure.

US2
Drug related oro-facial disease

I Alajbeg[1], TA Hodgson[2]
[1]*Department of Oral Medicine; School of Dental Medicine; University of Zagreb, Zagreb, Croatia,* [2]*Oral Medicine, Special Care Dentistry and Orofacial Pain, Eastman Dental Hospital, UCL, London, UK*

Drugs may be defined as substances used in the diagnosis, treatment, or prevention of a disease or as a component of a medication or alternatively as chemical substances, such as a narcotic or hallucinogen, affecting the central nervous system, causing changes in behavior and often addiction. Orofacial drug-related adverse reactions may present initially to the dental surgeon or doctor and require specialist opinion. Due to the complexity of clinical presentation including symptoms (pain, dysgeusia, xerostomia and dysaesthesia) and signs (mucosal and bone pathology) diagnostic problems are common and a detailed prescribed and non-prescribed medication history invalid. New therapeutic interventions are continually introduced across Europe and health care practitioners should be vigilant for unreported oro-facial adverse reactions and be able to access the local reporting mechanism. The benefits of the drug prescribed weighed against the risk from the oro-facial adverse reaction will determine if drug cessation is appropriate. This paper aims to update practitioners on the spectrum of drug-related oro-facial disease, review factors to be elicited from the drug history, focus on newly introduced drugs and their, in some cases devastating, oro-facial adverse effects and discuss management options.

US3
Allergy in dental practice

D Biočina-Lukenda[1], PD Diz[2]
[1]*Department of Oral Medicine, School of Dental Medicine, University of Zagreb, Zagreb, Croatia,* [2]*Special Needs Unit, School of Medicine and Dentistry, Santiago de Compostela University, Spain*

Allergy reactions of the oral mucosa comprise an array of clinical manifestations, some of them difficult to differentiate from toxic reactions. Type-I reactions are most frequently seen related to application of polymers in the oral cavity, such as orthodontic bonding and fissure sealant materials. There may also be systemic manifestations such as urticaria. Type-IV reactions may be seen related to most dental materials used, from amalgam and gold to polymers. These reactions appear as chronic reddening and/or ulceration of the oral mucosa. Lichenoid reactions have histopathological characteristics compatible with type-IV allergy reactions and are the most prevalent material-adverse reactions seen in the oral cavity. Recent advances have been made in characterizing the more prevalent allergens on oral mucosa, such as methacrylates, natural rubber latex (NRL) proteins, rubber glove chemicals and disinfectants. This improved understanding has clearly enhanced the success, particularly for type I NRL allergies. Skin patch tests, applying a series of dental materials in non-toxic concentrations on the skin, have been used to identify sensitization. However, the value of those tests can be questioned. Although obvious advances have been made in characterizing dental allergens and understanding potential exposure, improved diagnostic and management techniques are still needed. Corticosteroid therapy is all too often the only treatment. Drug allergy including local anaesthetics, and systemic antibiotics and NSAIDs, may also present in the dental environment, causing life-threatening emergencies specially in 'at risk patients'. The GDP has to know the principles of prevention, diagnosis and management of these situations.

US4
Pharmacotherapy complicating dental surgery

V Vučićević Boras[1], G Lodi[2]
[1]*Department of Oral Medicine, School of Dental Medicine, University of Zagreb, Zagreb, Croatia,* [2]*Oral Medicine Unit, Dental School University of Milan, Italy*

Planning dental treatments for patients taking antithrombotic can be difficult for the general dental practitioner, particularly when surgical interventions are needed. The drugs employed in the long-term treatment of such patients include platelet aggregation inhibitors and oral anticoagulants. Platelet aggregation inhibitors do not represent a contraindication to oral surgery. The activity of oral anticoagulants can be affected by many substances, for this reason it is necessary to monitor by INR the patients taking those drugs. When INR is within therapeutic limits for the more common conditions, most of the oral surgery interventions do not need any special precaution. Evidence indicates that suspending antithrombotic drugs is not indicate, as complications following a thrombotic accident are more frequent and serious than bleedings following oral surgery. It is well known that systemic corticosteroid therapy due to the effect on adrenal suppression can interfere with dental surgical procedures. However, that is largely dependent on the type and dose of corticosteroid that patient is currently taking, or has been taking in the last 12 months and on the type and extent of surgical procedure which is to be performed. Surgical management of dental patients with history of systemic corticosteroid therapy is proposed from the existing literature.