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Invited Speakers - Plenary Sessions

1
Genetics of diseases of the mouth

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Of the more than 7 000 human diseases identified, 30–40% manifests some dental/oral/craniofacial findings. This lecture overviews how developments in genetic research are being applied to identify the genetic basis of diseases of the oral cavity. Examples of how specific gene mutations that cause diseases affecting enamel, dentin and the gingiva will be presented. Diseases reviewed will include amelogenesis imperfecta, dentinogenesis imperfecta, hereditary gingival fibromatosis, Papillon–Lefèvre syndrome and tricho-dento-osseous syndrome. Methods to evaluate how mutant genes cause each disease will be reviewed. Clinical implications and applications of these discoveries will be discussed.

2
Genotype–phenotype analysis of the face

P Hammond
Molecular Medicine Unit, Institute of Child Health UCL, London, UK

Over 700 genetic conditions involve facial dysmorphology and the recognition of an associated facial gestalt is important in the early stages of their diagnosis. 3D dense surface models of face shape are proving highly accurate at discriminating between the faces of controls and individuals affected by conditions such as Cornelia de Lange, Noonan, Smith–Magenis, Williams and 22q11 deletion syndromes. Multi-disciplinary combinations of face shape, molecular and behavioural analyses of affected humans and associated animal models are identifying the effects of individual genes on craniofacial development in genotype–phenotype studies in Bardet–Biedl, Cardio-facio-cutaneous, Costello, Noonan, Williams and Wolf–Hirschhorn syndromes. The detection of unusual facial asymmetry is also proving useful in delineating endophenotypes and potential differences in parental contribution in the polygenic condition autism spectrum disorder.

3
Genetic aspects of Sjøgren's syndrome

AI Bolstad
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Molecular dissection of complex traits is widely seen as the next frontier in medical genetics, and during the last decades, autoimmune diseases such as Sjögren's syndrome have become the target of genetic investigation. Thus far, most genetic studies on Sjögreńs syndrome have been designed with the candidate gene approach, with focus on genes encoding molecules involved in inflammation. A limitation of the studies has been the small study populations. To avoid the problem of small cohorts and genetic heterogeneity, research on inbred strains of disease susceptible animal models has been initiated. Collecting patient material as a joint effort in a collaborative international network, as has been done with systemic lupus erythematosus (SLE), will probably give the best outcome in identifying susceptibility genes of Sjögren's syndrome.

Burning Mouth Syndrome

1
Aetiology and pathophysiology of burning mouth: its connection with taste

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Disturbed neuronal balance between taste mechanisms and sensory function was suggested as a possible etiologic factor for Burning Mouth Syndrome (BMS). It has been shown that sweet taste detection threshold is higher in BMS patients demonstrating altered taste sensation. Application of Dyclonin (a local anesthetic solution) to the tongue of BMS patients reduced phantom dysgusia but did not reduce the burning sensation. Moreover in 40% of the cases the pain was aggravated. Data suggests that in healthy state the chorda tympani and the lingual nerves exert mutual inhibitory mechanisms. Consequently, altered chorda tympani function can disrupt equilibrium with the lingual nerve employing a putative lingual nerve hyper-function being perceived by the patient as burning sensation. Individuals who suffer from BMS are likely to be 'supertasters' (can taste the bitter compound phenylthiocarbamide) and have large numbers of fungiform papillae. These are innervated mostly (75%) by the trigeminal and partly (25%) by the chorda tympani nerve. Hyperactivity of the sensory component of the trigeminal nerve following loss of central inhibition as a result of taste damage in the chorda tympani may induce a burning sensation. Damage to the chorda tympani nerve that has been demonstrated in a group of BMS patients suggests an involvement in the pathogenesis of BMS.

2
Epidemiology, diagnosis, co-morbidity, prognosis in burning mouth syndrome (BMS)

A Sardella
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The aetiology of burning mouth syndrome (BMS) -a chronic intraoral pain condition that is not accompanied by clinical lesions or systemic diseases- is unknown. Recently, new evidence for a possible neuropathic pathogenesis of BMS is emerging. Although epidemiological data are limited owing to a lack of strict diagnostic criteria, the reported prevalence in general population varies from 0.7% to 15%, even though it is necessary note that many studies relate to the symptoms of burning mouth rather than BMS itself. The prevalence of BMS increases with age in both men and women even though the ratio between women and men varies from 3:1 and 16:1. The evaluation of a patient with oral burning pain/sensations should be extensive. The history should include a review of systemic diseases and medication treatments. A detailed review of the patients' complaint should focus on onset, location, character, course. It is also important to gain information about symptoms as xerostomia. Furthermore, the patients may complain of thirst, headache, temporomandibular joint pain or pain in masticatory muscles. The history should also include information on previous or current psychosocial events possible related to the onset of oral burning symptoms. It is important to note that, usually, pain/burning sensations increase in intensity at the end of each day but very rarely interfere with sleep. The several clinical and laboratory features generally investigated as causative aspects of BMS could be evaluated in order to exclude dental or medical cause of an oral burning sensation. Medical delay in diagnosing, referring and appropriately managing BMS patients occurs frequently. Very few studies on natural course or spontaneous remission in patients suffering from BMS are available and, following the existing data, the spontaneous remission of oral symptoms is rare, occurring in less thazn 4% of the patients.

3
Investigations in BMS quantitative sensory testing (QST) and neurophysiological recordings

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The aetiology of primary burning mouth syndrome (BMS) is unclear, but recent studies have shown increasing evidence of neuropathic mechanisms being involved in its pathogenesis both at the peripheral and the central levels of neuraxis. This lecture will elucidate the clinical utility of thermal quantitative sensory testing (QST) and neurophysiologic recording of the trigeminal brainstem reflexes in patients complaining of BM symptoms. Within the lingual nerve distribution, cool detection thresholds (CDT) and warm detection thresholds (WDT) have been found higher in BMS patients compared to healthy controls subjects, whereas heat pain detection thresholds (HPT) do not differ between these groups. The prepain-range (the arithmetic difference between WDT and HPT), is narrower in BMS patients than in controls. In BMS patients, electrical stimulation thresholds for BR extra-segmentally at the supraorbital nerve distribution are higher than in controls, and additionally, with supraorbital nerve stimulation, latencies of ipsilateral R2-response are longer. However, within the symptomatic distribution, lingual and mental nerve BR latencies do not differ between patients with primary BMS and healthy subjects. On the contrary, in secondary BM due to lingual nerve damage or more central lesion in the trigeminal system, the reflex recordings may demonstrate the correct level of neural pathology. Habituation of the supraorbital nerve BR has been found abnormal in about 30% of the BMS patients which reflects increased excitability of this brainstem reflex that is under striatal dopaminergic inhibitory control in a subgroup of patients. The clear hypofunction of small Aσ and C fibre afferents mediating innocuous cool and warm within the symptomatic distribution in BMS patients is compatible with recent evidence from mucosal biopsies showing decreased density of small fibre nerve endings in the tongue mucosa of BMS patients. Neurophysiologic recordings are of value in the differential diagnosis of BMS, as some patients with clinically typical BM symptoms may suffer from neurophysiologically evident neuropathic pain after peripheral lingual nerve injury or central pain due to brainstem lesions.

4
Importance of communication in management of a pain patient

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Burning mouth syndrome management begins with careful history taking, examinations and selected investigations to rule out other causes of burning. All patients need to be reassured and given a clear explanation for their symptoms and this should be complemented by written information that is free of medical jargon. There have been a number of randomised controlled trials conducted using the following: cognitive behaviour therapy, topical clonazepam, selective serotonin reuptake inhibitors and alphalipoic acid which have been incorporated into a Cochrane systematic review. Although they show some evidence of efficacy this is low and so a wide range of other topical and systemic treatments used in neuropathic pain are utilised. Empathic approach and support are essential.

5
Evidence based approach to management of BMS

A Woda
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The treatment for true burning mouth syndrome (BMS) must be medical with consideration for contribution from psychological factors. Over treatments including surgical modalities may be harmful. A few randomized, placebo-controlled trials have been performed. Only two pharmacological treatments, topical clonazepam and alpha-lipoic acid, an anti-oxidant nutritional supplement have shown to be significantly better than placebo. Another controlled study has shown that cognitive-behavioral therapy one hour per week for four mouths was successful in decreasing pain intensity. Other proposals have arisen from open-label studies and case reports, some echoing therapy used for other neuropathic pain syndromes. For example, systemic clonazepam, tricyclic antidepressants, anticonvulsivants, antipsychotics, anxiolytic, have been proposed with a rather poor outcome. Several topical treatments such as xylocaine gel, capsaicin cream, salivary substitutes and systemic analgesics such as tramadol are frequently used, although there is little literature to support their use for BMS.