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Oral Presentations

101
THERAPEUTIC MANAGEMENT OF ORAL MUCOSAL LESIONS
S. Porter
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As a consequence of increasing longevity of life, improved health care strategies, the emergence and re-emergence of infectious disease and changing migration patterns the spectrum of disorders that can affect the oral mucosa continues to widen Changes in the oral mucosa can reflect local and systemic congenital and acquired disease, can give rise to local symptoms that may compromise quality of life, and, albeit rarely, cause significant morbidity and mortality. The course will provide an overview of the contemporary management of both common and uncommon oral mucosal disease. It will highlight controversies as to the diagnosis and treatment of oral mucosal disease, review possible future strategies for complex relevant disease and detail disease that has proven difficult to manage.

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NON-NEOPLASTIC LESIONS OF THE SALIVARY GLANDS
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The histopathological diagnosis of salivary gland tumours can be challenging. There are nearly 40 named epithelial neoplasms in the latest World Health Organisation classification, and some of these show a wide range of variants. In addition, there are many non-neoplastic diseases of salivary glands which present as 'tumours' and some also fall into the histological differential diagnostic spectrum of neoplastic lesions. Such conditions include cheilitis glandularis, sclerosing polycystic adenosis, necrotising sialometaplasia, salivary gland hyperplasias and others. The non-neoplastic lesions, however, have tended to be the Cinderella of salivary disease and are not commonly covered in international continuing education courses. The object of the present course, therefore, is to review a wide range of non-neoplastic salivary gland diseases and, where appropriate, their differential diagnosis and pathogenesis. The diseases selected have been broadly divided into: 1. Developmental defects 2. Cysts 3. Infiltrations 4. Sialadenitis 5. Granulomatous lesions 6. Tumour-like lesions 7. Lymphoepithelial lesion 8. Sjögren's syndrome

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MAXILLOFACIAL IMAGING: TECHNIQUES AND INDICATIONS
P. A. Monsour
Queensland Diagnostic Imaging, Australia

This series of lectures will cover the theory of rotational panoramic radiography, including radiographic anatomy on rotational panoramic radiographs, ghost images, effect of positioning errors on the image and how to interpret rotational panoramic radiographs. The various imaging techniques available for assessment of odontogenic pathology; non-odontogenic pathology of the jaws; TM joint pathology; pathology involving the salivary glands and pathology of the maxillary sinuses will be covered. The imaging techniques covered will include: conventional radiography; tomography; computed tomography; MRI; Nuclear Medicine and ultrasound. Finally a series of interesting cases will be presented to illustrate the various types of pathology found in the jaws and the value of radiology.

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MOLECULAR TECHNIQUES IN ORAL PATHOLOGY
R. Jordan
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Alterations and abnormalities in genes, transcribed RNA and translated proteins underpin the pathological basis of many human diseases. Analysis of these molecules has led to a new understanding of the biological basis and classification of many diseases including cancer. Much of this work has been done on pathological specimens and is being advanced by the discovery of new techniques to analyze DNA, RNA and proteins in diagnostic material. This course will cover modern methods of genetic analysis in pathology specimens examining methods study DNA, RNA and proteins and how these techniques have provide new insights into the pathological basis of human disease. This seminar will provide an overview of specific techniques of relevance to the working pathologist including blotting methods, in situ hybridization, quantitative RT-PCR, microsatellite analysis, ploidy analysis, immunohistochemistry, flow cytometry and proteomic discovery tools. Specific applications will be emphasized to illustrate how their application to the study of disease is providing new knowledge of human disease and their relevance and use in diagnostic surgical pathology.

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ORAL PATHOLOGY AT THE MOLECULAR LEADING EDGE
R. Williamson
University of Melbourne, Australia

The Human Genome Project has put one man's DNA sequence on the web, available to all. The HapMap Project has added the relationships of DNA sequence variation to different populations. Virtually every single gene mutation that causes an inherited dental or orofacial disorder (however rare) has been

mapped and defined. In spite of this, the obvious contributions of genetics and its interaction with the environment to common dental problems, such as caries or tooth crowding, are virtually unexplored. The Human Genome Project has great potential to contribute to public health outcomes. The most important prerequisite for useful applications of genetics to clinical practice is excellent definition of the clinical features of the problem, in individuals and in a population. Alongside this, research is required to empower both the community and professionals to act on new knowledge. Because so much of dentistry is carried out in private practice, dependent on personal funding and in a sporadic and patient-initiated way, it is hard to achieve ideal data bases. In spite of these problems, it is important to find ways to examine some of the remaining clinical problems facing the dental profession, where genetics and/or epigenetics could play a role. May I, a non-dentist, mention just three? First, to what extent can risk for orthodontic and developmental dental problems be predicted genetically on the basis of HapMap data? Second, what (if any) genetic features are shared by those children who continue to develop caries even in places where the water is fluoridated? Finally, are there genetic factors that contribute to the poor state of Aboriginal dental health, in addition to the obvious relationship to deprivation and lack of facilities for care?

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CLINICAL RELEVANCE OF ANEUPLOIDY TO ORAL CANCER

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The aneuploidy-cancer theory proposes that cancer is caused by the abnormal dosage of thousands of normal genes. This is generated by the gain or loss of specific chromosomes or segments of chromosomes; alias aneuploidy. The theory predicts that chromosomal and genetic instability is proportional to the degree of aneuploidy (Duesberg et al., 2004). Therefore the DNA content of abnormal epithelial cells was determined using slide based DNA-Image-Cytometry (DNA-ICM). The aims of our prospective studies were to investigate the diagnostic accuracy of DNA-ICM in combination with minimal-invasive brush biopsies taken from suspicious oral lesions. **Material & Methods:** Cytological diagnoses obtained from 4674 exfoliative smears of 1074 different lesions were compared with histology and/or clinical follow-ups of the respective patients. Additionally nuclear DNA contents were measured after Feulgen re-staining using a TV image analysis system. **Results:** Sensitivity of our conventional cytological diagnosis on oral smears for the detection of cancer cells was 91,98%, specificity 97,56%, positive predictive value 90,28% and negative predictive value was 98,1%. DNA-aneuploidy was assumed if abnormal DNA-stemlines or cells with DNA-content greater 9c were observed. Sensitivity of DNA-aneuploidy in oral smears for the detection of cancer cells was 98,4%, specificity 99,34%, positive predictive value 98,92% and negative 99,0%. **Conclusion:** The application of DNA-Image-Cytometry with DNA-aneuploidy as a marker for neoplastic transformation in oral smears secures cytologic diagnosis of carcinomas. Smears from brushings of all visible oral lesions are an easily practicable and safe screening method for detection of oral precancerous lesions and squamous cell carcinoma in all stages. We conclude that DNA-ICD is a very sensitive and highly specific, objective and reproducible adjuvant tool for identification of neoplastic cells in oral smears.

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INVASION MECHANISMS OF CANCER CELLS

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Invasion is a critical step of the progression of cancers. To acquire invasiveness, neoplastic cells have to fulfill the necessary bioactivities including enhanced cell growth, loss of adhesion molecules, increased motility and degradation of basement membrane. Here, we would like to present our recent studies on the invasion of oral squamous cell carcinoma (OSCC). 1) Squamous cells are characterized by constitutive expression of CD44s and its variants. To correlate CD44v9 expression and invasiveness in OSCC, we first treated OSCC cells with an anti-CD44v9 antibody. The antibody treatment enhanced invasiveness of CD44v9 expressing OSCC cells. Next, we transfected CD44v9 gene into OSCC cells with low CD44v9 expression and examined their invasive potential. Overexpression of CD44v9 resulted in suppressed invasiveness. These findings suggest that CD44v9 expression relates with invasion of OSCC. 2) E-cadherin is another important cell adhesion molecule, serving also as an oncosupressor gene. We isolated highly invasive clones from an OSCC cell line and compared abnormalities of E-cadherin in these cells. The highly invasive clones showed reduction of E-cadherin in comparison with parent cells. We showed that reduced expression of E-cadherin was due to methylation of its promoter region. In fact, most invasive area of OSCCs showed reduced expression of E-cadherin and methylation of E-cadherin. These findings suggest that invasion of OSCC cells requires methylation of E-cadherin. 3) We compared the transcriptional profiles between a highly invasive clone and parent cell by microarray analysis and identified periostin, a fasciclin I-like secreted protein, as the gene demonstrating the highest fold change expression in the invasive clone. Periostin overexpression promoted invasiveness of OSCC cells in vitro and in vivo. Interestingly, Periostin expression level was well correlated with the invasiveness of OSCC cases. These findings suggest that periostin plays an important role for invasion of OSCC. We need further studies to bring to light the full extent of the mechanism of cancer invasion. Analyses of the mechanism provide novel therapies targeting invasion related molecules.

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ORAL CANCER RISK ASSESSMENT

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Prognostication of upper aerodigestive tract squamous cell carcinoma (UADT-SCC) is a complex, multifactorial issue. Treatment choices are made based on tumor overall stage, site, patient status, and patient preferences. Yet across each stage and site, all UADT-SCC are treated the same. Single

histological variables, such as tumor grade, or degree of keratinization have not withstood statistical scrutiny as independent prognosticators, and the rational basis for treatment choices. The concept of histological pattern of tumor invasion, as a single variable and as part of a multivariable scoring system, has been investigated in Europe, but received little attention in the US. We have previously investigated the predictive value of pattern of invasion (POI) at the tumor interface and expanded on the traditional Bryne POI. We found that a very simple scoring system based on three variables (POI, perineural invasion, and lymphocytic host response) was highly predictive of local tumor recurrence and overall survival, independent of overall tumor stage, treatment and margin status. In this practical, interactive lecture, participants will learn the historical and statistical basis for this scoring system. They will learn to recognize the basic histological variables used in scoring. They will learn to apply the various ''rules'' of the scoring system, and how to incorporate risk scoring into surgical pathology reporting. Finally participants will learn the updated results of the follow-up validation study of this risk-scoring schema.

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PLOIDY: FRIEND OR FOE?

E. W. Odell, M. Sperandio, A. L. Brown
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Purpose: To share experiences in establishing a routine ploidy analysis service in the UK and discuss advantages and disadvantages of the technique. High predictive values for transformation of oral lesions have been published using image based ploidy analysis, but from a limited number of centres. The technique has features attractive in a routine diagnostic setting: use of paraffin material, simple preparation and staining procedure and short turnaround time. The primary consideration in implementing the technique must be confirmation of the predictive values of the results in the particular population to be tested and their comparison with conventional dysplasia grading. This is a relatively time consuming phase but is essential to design valid selection criteria for the test. There is, to date, insufficient information to define the circumstances under which ploidy analysis performs best. Given that dysplasia grading is prone to variation, the quality of dysplasia grading may determine the added value of ploidy. In our centre we have found that the technique, though simple, is prone to failure for unidentifiable reasons, requiring a proportion of assays to be repeated. Histogram classification uses continuous variables, for which threshold levels have been defined by only one centre. The predictive value of the test will depend on these diagnostic thresholds as well as the study population. Though we have found ploidy to predict transformation relatively well, our diverse population harbours many apparently innocuous aneuploid lesions. Changes in practice may be required to produce biopsy specimens large enough for levels, special stains and ploidy. Even if predictive, it remains to be established that ploidy can be integrated into care pathways with a positive cost benefit. Only if clinicians can exclude diploid lesions from follow-up will the technique be economic, even though it may be significant in reducing morbidity and mortality.

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CONTACT INDUCED APOPTOSIS OF STROMAL CELLS BY MALIGNANT TUMOUR CELLS: A PREVIOUSLY UNRECOGNISED MECHANISM FOR TUMOUR INVASION

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Purpose: We recently described a contact dependent pro-apoptotic activity in malignant tumour cells for vascular endothelium, indicating a possible role for this in metastasis (J Pathol 2003, 201:395–403). This study was to investigate the further possibility that a similar contact dependent activity may also contribute to tumour invasion separate to metastasis by induction of apoptosis in fibroblasts and smooth muscle cells. **Results:** Human gingival fibroblasts (HGF), human tenons fibroblasts (HTF) and human umbilical artery smooth muscle cells (SMC) were co-cultured with SAOS-2 osteosarcoma cells and the survival of stromal cells monitored over time. Similar to earlier observations in endothelium, all stromal cell types reduced significantly in number during co-culture with SAOS-2 ($p < 0.05$). DNA gel electrophoresis indicates reduced stromal cell number was due to apoptosis. Apoptosis was not due to soluble factors, as tumour cell conditioned medium did not affect stromal cell number. Preliminary data with human colon carcinoma cells (SW480) indicate a similar activity. FACS analysis revealed Fas and Fas ligand are present on stromal and tumour cells, respectively. SMC Fas was functional as demonstrated by agonistic antibody CH11, however, blocking Fas with antagonistic antibody ZB4 did not inhibit stromal cell death. A non-caspase dependent apoptotic pathway, perhaps involving calpains or cathepsins may be involved because inhibition of caspase by Z-VAD-FMK had no effect. Experiments continue characterizing the activity, and also SAOS-2 transfected with green-fluorescent protein to investigate events in-vivo. **Conclusions:** Contact dependent induction of stromal cell apoptosis by malignant tumour cells may contribute significantly to tumour invasion, and this may be by non-caspase dependent mechanisms for induction of apoptosis. This raises the possibility for development of novel strategies for the management of invasive tumours.

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PLOIDY ANALYSIS PREDICTION OF TRANSFORMATION IN POTENTIALLY MALIGNANT ORAL DISEASES

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Aims: To investigate the predictive ability of image-based ploidy analysis in a UK patient population including potentially malignant oral diseases as well as low risk cases. **Methods:** Formalin-fixed paraffin embedded tissue blocks from 1171 biopsy specimens taken from 621 patients with potentially malignant diseases were selected as consecutive eligible cases accessioned between 1990 to 1999. Nuclei were extracted from sections 50 microns thick by enzyme

digestion, cytospin monolayers prepared and stained with Feulgen stain and subjected to image-based ploidy analysis. DNA content was determined in a minimum of 300 cells on a Fairfield ploidy analyser, compared to internal controls and the histograms classified into diploid, tetraploid and aneuploid on the basis of previously published criteria (Sudbo et al. N Engl J Med, 2001. 344:1270). Malignant transformation was determined from pathology department, hospital records, Thames Cancer Registry and the Office of National Statistics. **Results:** Lesions from 63 patients (10.1%) progressed to oral OSCC, of which all lesions were diploid in 13 cases (20.6%), at least one was non-diploid in 33 cases (52.4%). Lesions from 17 (27%) yielded inconclusive ploidy results for a variety of reasons including small specimen size. Of the 558 (89.9%), patients that did not develop carcinoma, all lesions in 211 (37.8%) were diploid, at least one was non-diploid in 122 (21.8%) and in 225 (40.4%) were inconclusive. **Conclusions:** Ploidy analysis predicted malignant transformation in the majority of patients but this lower risk lesion population includes more apparently innocuous aneuploid lesions that previously published series. If applied to routine pathology service without changing procedures, many specimens would be too small for analysis.

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TISSUE PHENOTYPE OF ORAL PREMALIGNANT LESIONS (OPLs): ASSOCIATION WITH MOLECULAR MARKERS AND CANCER DEVELOPMENT

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Prediction of outcome for OPLs is challenging. Although histology is a good predictor for high-grade lesions [severe dysplasia and CIS], it is less effective for lesions with minimal or no dysplasia, which represent the bulk of lesions seen in the community. Molecular markers may play a major role in such assessments. **Objective:** The aim of this study was to assess the potential of the Tissue Phenotype to identify high-risk OPLs by studying its correlation with conventional histopathology, molecular markers (LOH) and cancer development. **Methods:** A total of 131 oral mucosa lesions were analyzed. The distribution of the pathology grades was as follows: normal- 30, hyperplasia -25, mild dysplasia -13, moderate dysplasia-10, severe dysplasia- 7 and invasive squamous cell cancer (SCC) -29 Feulgen stained sections were analyzed by High-resolution Image cytometry. A Morphometric Index measuring the degree of abnormality of the nuclei was calculated for each specimen. Each of the dysplastic cases were analyzed for 19 microsatellite loci on seven chromosome arms (3p, 4p, 8p, 11q, 13q, and 17p). The time course data for these patients has been stratified into those which develop cancer and those which have not developed cancer within 10 years. **Results:** The Morphometric Index correctly identifies 94% of the high-grade OPLs while maintaining a specificity of 74%. MI was significantly higher in dysplasia with LOH than in dysplasia with no LOH for 4 chromosomes arms (3p, 9p, 4q,17p. The MI identified patients which progressed to cancer for 77% of the time while correctly identifying the patient which do not progress 78% of the time. Individuals with a high MI (higher than 4.5) showed a 13.1 fold increase in relative cancer risk than individuals with a low MI. **Conclusions:** These data support the potential utility of Tissue Phenotype as a marker for molecular damages and progressive potential of Oral Premalignant Lesions. (Supported by grant R01DE13124, NIDCR).

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DIFFERENTIATION OF ORAL EPITHELIUM IS REGULATED BY GM-CSF AND KGF AT EARLY BUT NOT TERMINAL STAGES

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Previous studies have shown that fibroblasts have a crucial role on in vitro oral epithelial differentiation, but the responsible factors have not yet been identified. In this study a number of fibroblast-derived factors were tested with respect to their role on oral epithelial differentiation. Organotypic cultures of normal human oral mucosa were constructed from primary normal human oral keratinocytes grown on top of type I collagen gels with or without fibroblasts. The cultured tissues were assessed by histomorphometry, immunohistochemistry, and the TUNEL method. Oral epithelium grown on simple collagen gels in absence of fibroblasts had an undifferentiated phenotype with (1) weak, scattered expression of cytokeratin (CK) 13, (2) expression of EGF-R and integrins throughout all cell layers, (3) no deposition of collagen IV, and (4) TUNEL positive cells randomly distributed within the epithelium. Addition of KGF (10ng/ml) did not change the undifferentiated phenotype of the oral epithelium grown on simple collagen gels. Addition of GM-CSF (10ng/ml) induced the expression of CK 13 in all suprabasal cell layers only. The admixture of GM-CSF and KGF induced, in addition, polarization of EGF-R and integrins to the basal cell layer, and deposition of collagen IV. There was no polarization of the TUNEL positive cells to the superficial layer, suggesting that cells did not complete their terminal differentiation in these cultures. Polarization of TUNEL positive cells to the superficial cell layer (terminally differentiated cells) occurred, in addition to all the others markers of differentiation tested, only in the presence of fibroblasts in the collagen gels either in direct contact or at distance from keratinocytes (sandwich models). These data indicate that major aspects of oral epithelial differentiation are regulated by the synergic combination of GM-CSF and KGF, but its terminal stage is controlled by another yet unidentified fibroblast-derived diffusible factor.

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GENE EXPRESSION PROFILING OF TWO ORAL SQUAMOUS CELL CARCINOMA (OSCC) CELL LINES COMPARED WITH NORMAL ORAL MUCOSAL EPITHELIUM USING cDNA MICROARRAY

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Purpose: Oral squamous cell carcinoma (OSCC) represents the most frequent malignancy of the oral cavity. The overall 5 year survival rate of oral cancer patients has not improved significantly over the past two decades, despite the significant advances with multimodality treatment. The identification of genetic alterations associated with OSCC has been the basis of understanding of how normal cells become malignant. cDNA microarray analysis is a useful technique that allows the comparison of a large number of previously identified genes simultaneously, showing the relative over- or under-expression of genes in malignant cells compared with normal cells. The aim of this study is to identify genes associated with oral carcinogenesis by comparing the relative gene expression of OSCC with normal oral epithelium by cDNA microarray. **Methods:** Two OSCC cell lines were grown in culture, and a normal oral keratinocyte cell line was established from a primary explant of normal human gingiva. Total RNA was isolated, and converted to cDNA by reverse transcription. Samples were labelled with fluorescent dyes, and hybridised onto an 8K human genome array (AGRF). Arrays were scanned and the data analysed. **Results:** Several genes were identified to be over expressed in the OSCC cell lines compared with the normal oral keratinocytes. These genes were associated with cell growth and proliferation, as well as angiogenesis. **Conclusion:** Gene profiling by microarray shows promise for imrpoved prognostication in patients with OSCC, and to identify genes that could serve as biomarkers and as potential targets for biological therapy.

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TRANSFORMING GROWTH FACTOR-BETA (TGFβ) SIGNALING PROMOTES EPITHELIAL MESENCHYMAL TRANSFORMATION (EMT) DURING ORAL SQUAMOUS CELL CARCINOMA PROGRESSION

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Epithelial-Mesenchymal transformation (EMT), a fundamental mechanism of embryogenesis and tumor progression, is most commonly characterized by loss of the cell adhesion molecule, E-cadherin. During EMT, loss of E-cadherin expression correlates with a transition to front end-back end polarity of invasive metastatic cells. The transformation of Oral Epithelial Squamous Cell Carcinoma Cells (UMSCC) into metastatic phenotype has been well documented. However, signaling mechanisms that promote EMT of UMSCC have not been investigated in detail. Here, we show that Transforming Growth Factor-β (TGFβ) transforms UMSCC cell lines into mesenchymal phenotype. By culturing human UMSCC, we have demonstrated that TGFβ signaling induces EMT by forming activated transcription complexes that directly inhibit E-cadherin gene activity. Our data shows that TGFβ signals via PI3K and ERK to activate Snail transcription factor, which binds with the promoter of the E-cadherin gene. Such DNA-protein interactions repress E-cadherin transcription and gene activity. Subsequently, loss of E-cadherin and cell-cell adhesion allow oral cancer cells to become motile and invasive. Comparing current results with that of our previous data, we speculate that TGFβ signals differently to promote EMT during tumor progression, such as Oral Squamous Cell Carcinoma (when EMT is aggressive and uncontrolled) with that of embryonic EMT (subtle and controlled) as shown by us – J Cell Biol.22;163(6):pp1291-130,2003 and Dev Dyn. 234(1):132-42 2005. These results suggest that TGFβ mediated signaling activates epithelial transformation into migratory metastatic cells by repressing E-cadherin gene activity and it is a potent inducer of oral cancer progression. Supported by CoBRE, NIH.

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ORAL SUB-MUCOUS FIBROSIS (OSMF) IN AUSTRALIA?

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Purpose: OSMF is an established pre-malignant condition. OSMF is related to the habitual chewing, for protracted periods of Betel ''quid or ''paan'', which contains a mixture of areca nut and/or betel leaves, various flavourings, including spices, to which tobacco is often added. OSMF contributes to the high incidence of oral squamous cell carcinoma (OSCC), throughout the Indian Sub-continent, Southeast Asia, and locations in the western Pacific. Migrants from these countries to Australia continue to practice this habit. Use of quid/paan has increased with its export from India, as a commercially prepared food product, for sale worldwide, including in Australia. The consequences is an expected rise in the incidence of OSCC. **Method:** Case series, with literature reivew. **Results:** Three cases of OSMF are reviewed, in particular addressing the concern about access to Betel quid/paan products in Australia. **Conclusions:** Habitual Betel quid/paan chewing is an identified risk factor for the development of OSCC. OSMF is a known premalignant condition, with recognisable oral mucosal features. Action is required to prevent this potential increase in the incidence of OSCC. Education of health providers is required to question their patients about Betel nut use and identify SMF. This seems particularly important for those practitioners who cater to immigrants from countries where this habit is entrenched. A preventive program to target this population and limit their acceptance and use of Betel nut products is also needed.

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MICROGENOMICS APPROACH IN FORMALIN-FIXED, DECALCIFIED, PARAFFIN-EMBEDDED AMELOBLASTOMA TISSUE

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Analysis of cell-specific gene expression patterns using microarrays can reveal genes that are differentially expressed in diseased and normal tissue, representing an invaluable resource for the elucidation of pathogenesis and validation of differentially expressed genes as novel therapeutic targets or prognostic indicators. However, the cellular heterogeneity

of the tissues precludes the identification of cell-type specific gene expression profiles. Microgenomics implies the precise molecular analysis of very small, pure cell populations that have been microdissected from biopsies. Laser capture microdissection (LCM) enables the targeting and isolation of defined cells under direct microscopic visualization, while preserving biological molecules of interest. RNA was isolated from laser capture microdissected cells from five formalin-fixed, decalcified, paraffin-embedded ameloblastoma specimens, capturing as few as 100 tumor cells. The Veritas platform was used, incorporating a UV laser that accelerates the speed at which pure cell populations can be collected. Due to the limited quantity of RNA isolated from these specimens, it is necessary to perform an RNA amplification step prior to microarray analysis. The quantity and purity of the resulting total RNA, as well as amplified RNA, were determined using the ND-1000 spectrophotometer and a 2100 bioanalyzer. Further, we performed qRT-PCR on B-Actin, measuring 3'/5' ratios to determine the level of degradation in our samples. The ratio of the PCR product for the 3'/5' was close to 1. Our results demonstrate that microgenomic technologies involving Laser Capture Microdissection can be successfully applied on formalin-fixed, paraffin-embedded tissue to obtain purified cell populations and generate cRNA of sufficient quality for high-density oligonucleotide microarray analysis. Furthermore, RNA isolation was accomplished from decalcified tissue which is unprecedented in the literature to date.

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DETECTION OF PTCH MUTATIONS IN CHINESE PATIENTS WITH ODONTOGENIC KERATOCYSTS

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Purpose: Odontogenic keratocysts (OKCs) are common cystic lesions of the jaws that could occur sporadically or in association with nevoid basal cell carcinoma syndrome (NBCCS). The gene responsible for NBCCS is PTCH gene, the homologue of the Drosophila segment polarity gene patched. The aim of this study was to investigate the frequency, type and distribution of PTCH mutations in sporadic and NBCCS related OKCs in Chinese patients. **Methods:** Genomic DNA was extracted from fresh cyst fragments and peripheral blood samples of 20 patients with OKCs (14 sporadic and 6 associated with NBCCS). PTCH gene mutations were detected by direct sequencing. **Results:** Ten novel and one known PTCH mutations were identified in 5 sporadic and 6 NBCCS related OKC patients. Of the 11 mutations identified, five were somatic mutations (3913G > T, missense; 3074_3075insGAGGCCG, frameshift; 1361_1364delTGTC, framshift; 3300_3301insCACGTT; 3124_3125insGTGTGC) in 5 sporadic OKCs and 6 were germline mutations (1939 A > T, missense; 3913G > T, missense; 2619C > A, nonsense; 331delG, frameshift; 361_362insGAGC, frameshift; 1338_1339insGCG) in 6 cysts associated with NBCCS. One nonsense and 4 frameshift mutations identified were predicted to cause premature truncation of the PTCH protein. In addition, ten previously reported polymorphisms in PTCH were also detected in 17 patients. **Conclusion:** Germline mutation of PTCH frequently occurs in Chinese patients with NBCCS and somatic mutation of PTCH is also detectable in some sporadic OKCs. This is the first to describe PTCH mutations in both sporadic and NBCCS related OKCs in Chinese patients. The results provide further evidence for the possible role of PTCH mutation in the pathogenesis of OKCs.

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A CLINICOPATHOLOGIC STUDY OF ADENOMATOID ODONTOGENIC TUMOURS IN MALAYSIANS (1985–2004)

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Objective: To review the profile of adenomatoid odontogenic tumours in Malaysians over a 20 year period. **Methods:** A retrospective analysis of 85 cases of new adenomatoid odontogenic tumours diagnosed at the Stomatology Unit, Institute for Medical Research, Kuala Lumpur, Malaysia was carried out. Clinical data was retrieved from biopsy request forms for analysis of onset age, sex, race, site of recurrence, clinical signs and symptoms, radiographic presentation and clinical diagnosis. **Results:** There were 30 males and 55 females (M:F 1:1.83). The ages of presentation ranged from 10 to 51 years (mean = 19.94 years, median = 17 years). Preponderance were of Malay ethnicity (65.8%). The complaint of a swelling (84.75%) was the most common clinical presentation, with complaint of a missing tooth being the next most common (12.94%). The most common site was the anterior maxilla (52.94%). Radiographs were typically described as a well defined radiolucent lesion with 14% of the cases being a radiolucent lesion with speckled radioopacities. The most common pre-operative diagnosis was a dentigerous cyst (57.64%). Treatment was generally curative with enucleation. **Conclusions:** Adenomatoid odontogenic tumour in Malaysians in common with other published data occurs predominantly in females and occurs in the anterior maxilla.

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VARIATIONS IN THE MICROSCOPIC MORPHOLOGY OF ODONTOGENIC KERATOCYSTS

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Introduction: Although the classic, diagnostic microscopic features of the odontogenic keratocyst are well-described, the varied morphology often seen in these lesions has not been clearly documented. These morphologic variations may, on occasion, cause diagnostic confusion if one is not familiar with such. **Purpose:** To describe the varied morphologic patterns encountered in odontogenic keratocysts. **Methods:** Archival material (250 cases) with the diagnosis of odontogenic keratocysts from the University of Nebraska Medical center College of Dentistry biopsy service 1979 through 2005 were examined with H&E and Mayer's mucicarmine stains. **Results:** 22% contain significant areas of non diagnostic epithelium. (To be illustrated). 21% contained hyperplastic epithelium while 10% exhibited epithelial atrophy.

5% exhibited mucinous metaplasia. 1.3% showed ciliated cell metaplasia. The cyst wall stroma showed cartilaginous metaplasia in 4%; myxoid change in 5% and ossification/calcification in 7%. Incidental data regarding gender, age, recurrence and location will be presented. Theories as to the pathogenesis of these morphologic variations will be discussed.

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PERIPHERAL ODONTOGENIC TUMORS

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Background: Peripheral (extraosseous) odontogenic tumors are rare, and most of the reports in the literature have been single case reports or a small series of cases. The aim of this study is to determine the relative frequency of POT in an oral pathology biopsy service and to compare these data with information that is available in the literature. **Methods:** The files of the Pacific Oral and Maxillofacial Pathology Laboratory of the University of the Pacific. Files were systematically searched for all cases of peripheral odontogenic tumors during a 20-year-period. **Results:** Of the 91,178 cases accessed, 1133 (1.24%) were identified as central and peripheral odontogenic tumors. 1088 (1.2%) were identified as central tumors and 45 (0.05%) as POT. Of the total 1133 central and peripheral odontogenic tumors, peripheral tumors account for 4%. Of the 45 peripheral odontogenic tumors, peripheral odontogenic fibroma was the most common tumor accounting for 51.1% (23 cases) followed by peripheral ameloblastoma 28.9% (13 cases) and peripheral calcifying odontogenic cyst 13.3% (6 cases). Three additional POT that were identified include the peripheral calcifying odontogenic tumor, peripheral ameloblastic fibroma and peripheral ameloblastic carcinoma – each comprised 2.2% (one case each). **Conclusion:** There is only scarce information in the literature on the relative frequency of POT. In order to determine the true relative frequency, more studies should be performed.

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EXPRESSION OF NOTCH1 AND JAGGED1 IN AMELOBLASTOMAS

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Objectives: Odontogenesis is a complex biological process, and this process directly reflects the development of odontogenic neoplasms, especially ameloblastomas. In general, Notch signaling plays cytological regulation in morphogenesis. In this presentation, therefore, we have examined Notch1 and Jagged1 and their genes (mRNA) in collected ameloblastoma cases. **Materials and Methods:** Ameloblastoma materials examined in this study were obtained from operation materials, whose diagnoses were carried out in the Department of Oral Pathology, Faculty of Dentistry, University of Malaya, Kuala Lumpur, Malaysia. After histopathological examination (HE), we examined the distribution of transcription factors and their mRNA (NICD and Jagged) in ameloblastoma by means of immunohistochemical (IHC) and in situ hybridization (ISH) techniques. **Results and Discussion:** Histopathologically, follicular nests of ameloblastoma were proliferated in the fibrous stromal tissue. Some nests had a cyst formation in the follicular nests. NICD positive products were observed in most proliferating nests of ameloblastomas by IHC. Strong reactions were seen in the cells at the peripheral layer of the nests. Jagged1 positive reactions were also observed in the same type of cells of the nests. The strength pattern was also the same as that of NICD. Both of these gene expressions were detected in the cytoplasms of these IHC positive cells by ISH. Previously, we have reported the examination results of immunohistochemical expression of Notch1, Runx2, Delta in collected series osteosarcoma cases in Japan. The results showed these morphogenesis regulation factors are closely related to cytological differentiation in neoplastic cells. Therefore, in this examination, the IHC and ISH examination results also suggest that Notch1 signaling plays some role in cytological differentiation or acquisition of tissue specific characteristics in these neoplastic cells of ameloblastomas.

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THE EXTRACELLULAR MATRIX PROTEINS OF ODONTOGENIC TUMOURS

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Extracellular matrix (ECM) regulates cellular behaviours such as proliferation, migration and differentiation. Dynamic expression of ECM in the cells of tooth germ is observed. Dysregulation of these proteins may lead to an uncontrolled proliferation of the cells of tooth germ, resulting in odontogenic tumours. **Purpose:** To investigate the expression of ECM proteins including laminins 1 and 5, collagen type IV and fibronectin in 3 types of odontogenic tumours namely ameloblastoma (14 cases), calcifying odontogenic cyst (COC; 7 cases) and adenomatoid odontogenic tumour (AOT; 7 cases). **Methods:** Immunohistochemical study was performed. The primary antibodies against laminins 1 and 5, collagen type IV and fibronectin were used. Negative controls were omission of the relevant primary antibody. **Results:** Linear deposits of all proteins were found at the epithelial-mesenchymal junction in all tumours, but with different intensity. LM1 was expressed in the cytoplasm of tumour cells, regardless of cell types in ameloblastoma (14/14), COC (7/7) and AOT (6/7). In ameloblastoma, laminin 5 (14/14) and fibronectin (13/14) was seen in the cytoplasm of central cells, but only laminin 5 was occasionally present in the ameloblast-like cells (9/14). In COC, weak cytoplasmic expression of fibronectin was seen in basal (6/7), suprabasal (7/7) and ghost cells (7/7). Laminin 5 was found as weak intensity in the stellate and squamous cells (5/7) and very strong intensity in ghost cells (7/7). In AOT, strong expression of laminin 5 (6/7) and weak expression of fibronectin (6/7) was noted focally in a group of stellate cells. **Conclusions:** The expression of ECM proteins in amelo-

blastoma, COC and AOT were characterized. The profiles of these proteins among these tumours were different, suggesting that the origin of these 3 tumours derives from either different cell sources or similar cell types but different stages of tooth development.

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EXPRESSION OF ADAM 12 (A DISINTEGRIN AND METALOPROTAESE) IN KERATOCYSTIC ODONTOGENIC TUMOUR

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Introduction: ADAM 12 is a cell membrane glycoprotein that is involved in intercellular adhesion and has metalloprotease and sheddase activities. There is recent evidence showing ADAM 12 upregulated in breast, liver, gastric and oral carcinomas. **Aim:** We explored the expression of ADAM 12 in keratocystic odontogenic tumours aiming at explaining the neoplastic nature and the high recurrence rate of this tumour. **Materials and Methods:** This was a retrospective study of formalin-fixed, paraffin-embedded archival material which included radicular cysts, dentigerous cysts, odontogenic keratocysts/keratocystic odontogenic tumours and normal oral squamous epithelium. Immunohistochemical staining was performed and visualized by DAB chromogen mediated by Streptavidin biotin complex. Each slide was then reviewed and the degree of staining of the epithelium graded both mathematically using ImageScope software package and in a blinded fashion independently by two experienced oral pathologists. **Results and conclusion:** Preliminary results show over expression of ADAM 12 in keratocystic odontogenic tumour as compared to radicular and dentigerous cysts in a manner which can explain the aggressive and recurrent nature of this tumour.

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RELEVANCE OF Ki-67 AND p53 IN DISCRIMINATING BENIGN, LOW GRADE AND HIGH GRADE NEOPLASMS OF SALIVARY GLANDS

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Objective: To investigate whether Ki-67 and p53 proteins can be used to differentiate between benign, low grade and high grade neoplasms of salivary glands. **Study design:** Formalin fixed and paraffin embedded specimens from 106 cases of salivary gland tumors were histologically diagnosed and classified according to 1991 WHO classification criteria and then were categorized into benign tumors, low grade and high grade malignancies. Ki-67 and p53 immunostaining was performed using standard strepto-avidin-biotin peroxidase method. Ki-67 immunoreactivity was assessed by identifying an area with most intense staining "hot spot" where a percentage of positive cells were calculated in 500 nuclei using Weidener et al. method. Nuclear p53 immunostaining was evaluated by a semi-quantative and grading system that considered both intensity of staining(0 to 3) and the proportion of tumor cell nuclei ($<10\%$ to $>50\%$). Staining index was calculated as a product of staining intensity and positive area. SPSS statistical package was applied for analysis. **Results:** The difference in mean and median Ki-67 values in benign tumors versus all malignant tumors was statistically significant ($p<0.001$ Mann-Whitney U test), but was neither between benign and low-grade tumors ($p=0.158$) nor between low-grade and high-grade tumors ($p=0.0227$). Among the benign tumors, only 6.3% of cases had strong p53 positivity, while 78.6% of high grade malignancies had high staining index. With intermediate malignancy group, there was equal distribution between those with low and those with high index. The difference between benign and all malignant tumors was highly significant ($p<0.001$), and substantial difference was observed between p53 positivity of low grade malignancy and benign tumors ($p=0.041$, Pearson's chi square test). **Conclusion:** The expression of Ki-67 and p53 proteins can discriminate benign salivary tumors from malignant ones, but have limited value in differentiating low grade and histologically-well differentiated high grade salivary malignancies.

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MASPIN EXPRESSION IN NORMAL, INFLAMMATORY AND BENIGN TUMORS OF MINOR SALIVARY GLANDS

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Purpose: Maspin is involved in inhibition of cell motility, invasion and metastasis. Reduction in maspin expression has been associated with malignant progression in epithelial tumors. The purpose of this study was to investigate maspin expression in normal and inflamed minor salivary glands (MSG) and to compare it to benign salivary gland tumors. **Methods:** Cases of normal MSG, sialadenitis and benign tumors (pleomorphic adenoma) (10 cases for each category) were immunohistochemically evaluated for maspin expression by "point-counting" morphometry. Positive cytoplasmic or nuclear staining was evaluated on 10 HPF separately for epithelial acinar cells or tumoral solid areas and ductal structures. Results are presented as the mean percentage of positively stained cells from the total number of cells of each type. **Results:** The highest mean percentage of positive cells was found in the epithelial cells of solid areas of pleomorphic adenoma ($68.6+22.4$) and this was significantly different from acinar cells in normal MSG ($32.14+24$) and sialadenitis ($27.8+29.1$) ($p<0.001$). No significant differences in maspin expression were found in all examined cases in regard to the ductal structures ($p>0.05$). **Conclusion:** Maspin expression is present both the acinar and ductal structures of normal MSG. Its expression is upregulated in pleomorphic adenomas, especially in the solid areas, in contrast to what has been previously reported in epithelial malignant tumors. Maspin expression is not influenced by inflammatory changes. This study was supported by the Lepco Fund for Medical Research, School of Dental Medicine, Tel Aviv University.

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RARE CASES OF MULTIPLE RETENTION CYSTS OF MINOR SALIVARY GLANDS

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Purpose: We present two rare cases of multiple retention cysts of minor salivary glands. **Methods: Case 1:** A 59-year-old man was referred for a slightly painful swelling of the left cheek. Examination revealed a 2cm large erythematous submucosal nodule under the left commissure, and multiple bilateral 0.5–2cm firm bluish nodules in upper and lower lips and adjacent cheek, covered by a smooth mucosa with an occasional excretory duct. They had been present for at least 20 years. **Case 2:** a 74-year-old woman treated for depression was referred for a traumatic gingival lesion. Examination revealed also multiple bilateral painless, freely movable submucosal nodules in the upper and lower lip and under the right commissure. Two biopsies were performed in Case 1 and one in Case 2. **Results:** Histological features were similar in both cases. The sections showed multiple cysts of different size in the parenchyma of minor salivary glands or in the nearby connective tissue. They were lined by a columnar or cubical epithelium of variable thickness with occasional mucous cells and large areas of oncocytic cells. The cysts contained saliva mixed with some inflammatory cells. In Case 2 one cyst contained an inspisssated mucous plug. Pericystic connective tissue was more or less fibrotic and contained areas of chronic lymphocytic infiltrate of variable density, with occasional germinal centres in Case 1. The adjacent glandular parenchyma was normal, or contained a mild lymphoplasmocytic inflammatory infiltrate, with some dilated ducts and dedifferentiated acini. **Conclusion:** Multiple retention oral cysts are very rare, or published with other names: we found only one article about two cases. Differential histological diagnosis includes glandular cheilitis, cystadenoma, and intraoral Warthin tumour. They could be related to an abnormally viscous saliva causing blockage, or to an anomaly of the ducts. Diagnosis is important to avoid multiple unnecessary surgical operations.

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RESEARCH IN SALIVA – A SIMATS ENDEAVOUR

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Saliva is a unique fluid and interest in it as a diagnostic medium has advanced exponentially in the last five years. The ability to measure and monitor a wide range of molecular components has made it feasible to study microbes, chemicals and immunological markers. As a consequence, these advances in technology have helped to move saliva beyond measuring oral health characteristics to where it now may be used to measure essential features of overall health. **Aim:** The aim of this presentation is to bring to forefront the various research of saliva as a Predictive, primary diagnostic and prognostic tool among Indian population in Pre cancer, OSCC, Systemic diseases and Infections **Materials and Methods:** 1. Predisposition to pre-cancer and cancer by nitrites estimation in smokers: 10 with more than 10 years habit, 10 with less than 5 years habit, 10 negative controls, 10 positive controls: oral squamous cell carcinoma patients 2. Antioxidant status in oral cancers studying LPO, GSH and Uric acid Group A – 40 OSCC patients, Group B – 40 healthy controls 3. Diagnosing and monitoring in Nephrotic syndrome and Diabetes mellitus in pediatric subjects by assessing pH, Urea, total protein, albumin, cholesterol and glucose. Group I - 20 pediatric patients with established Nephrotic syndrome aged between 5–8 yrs from CTH.(15boys and 5 girls), Group II - 10 controls who are free from the disease aged between 5–8 yrs from our institution. Study group - 16 pediatric children with established type I diabetes, between 5–12 yrs of age. Control group – 16 apparently healthy children between 5–12 yrs of age. 4. Assesment of Candidal carriage, species variation and Nystatin sensitivity in 4 study groups - 10 controls, 10 hospitalized, 10 transplants, 7 HIV infected patients. **Conclusion:** Results were found to be highly significant. Thus, saliva based testing proves to be more than being a mere adjunct, is an innovative, emerging and a very promising diagnostic trend.

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LOW-GRADE MYOFIBROBLASTIC SARCOMA OF THE TONGUE

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Purpose: To describe the clinico-pathological features of a low-grade myofibroblastic sarcoma of the tongue, a rare mesenchymal tumour with myofibroblastic differentiation. **Methods:** A 49-year-old woman was referred for a tender submucosal nodule of two months duration of the left lateral border of the tongue. The tongue surface presented a pyogenic granuloma related to a previous but inconclusive biopsy. The lesion was removed en bloc along with the overlying mucosa. **Results:** Gross examination revealed a $1.6 \times 1.4 \times 1.1$cm fragment with a deeply seated firm unencapsulated greyish nodule of $1.0 \times 0.4 \times 0.3$ cm. Microscopic examination revealed a spindle-shaped cell proliferation, with mild enlarged nuclei and slight nuclear pleomorphism, arranged in fascicles, infiltrating the muscle and adipose tissue. The excision was incomplete. Immunohistochemical staining showed that the cells were positive for vimentin, desmin, and fibronectin, but negative for alpha smooth muscle actin, pankeratin, laminin and S100 protein. Three months later a complete excision was performed. One year later a suture granuloma was excised. Five years later a desmoid tumour of the fascia of the left biceps was removed. Follow-up at 8 years showed neither recurrence nor metastasis of the tongue. **Conclusion:** Low-grade myofibroblastic sarcoma is a recently described entity arising mainly in adult patients. Local recurrences are common but distant metastases are infrequent. They occcur in deep soft tissues, limbs, trunk, abdominal/pelvic cavities and parotid gland. Five cases have been reported to occur in the mouth and four in the tongue. The clinical aspect is not specific and not evocative of sarcoma. Histological and immunohistochemical examinations are necessary for the diagnosis and to exclude other lesions such as leiomyosarcoma, fibrosarcoma, fibromatosis, myofibromatosis, and solitary fibrous tumour. In our case simple

local excision with negative margins seemed to be the effective treatment.

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PREVALENCE OF ANODONTIA OF PERMANENT TEETH IN PATIENTS WITH OCULOAURICULO-VERTEBRAL SPECTRUM
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This study evaluated the prevalence of anodontia of permanent teeth in patients with oculoauriculovertebral spectrum (OAVS), by investigation of 52 panoramic radiographs of patients with OAVS, regardless of race, of both genders, aged 7 to 17 years, registered at HRAC/USP. Considering the possibility of previous tooh extraction, the patients' records were assessed in addition to radiographic examination to verify the dental procedures previously performed. All teeth were considered except for the third molars because of their extreme variability, and both right and left sides were analyzed. This group was compared to a control group of 52 panoramic radiographs from the files of normal patients of an orthodontic clinic, matched to gender, age and race. Fifty-two percent (n = 27) of patients with OAVS presented anodontia of at least one tooth, being 40.7% (n = 11) were at the side affected by hemiatrophy. The control group did not present anodontia. It was concluded that the sample of patients with OAVS exhibited a high prevalence of anodontia, especially at the affected side, revealing a possible association with the anomaly.

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CONJOINED TWINS WITH MIRROR-IMAGE CLEFT LIP AND PALATE: CASE REPORT IN BRAZIL
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A few cases of conjoined twins with mirror-image cleft lip and palate have been reported so far. Investigation on the occurrence of such cases may be helpful for a better understanding on the mechanism underlying the formation of conjoined twins as well as of cleft lip and palate. A pair of male thoracopagus twins was born to a 20-year-old woman in Brazil. The twins were stillborn; twin A exhibited intensive cyanosis. Examination of the head and neck revealed the presence of complete unilateral cleft lip and palate in both twins, with mirror-image configuration, affecting the left side for twin A and the right side for twin B. The twins also shared some organs. The observation of mirror-image clefts in conjoined twins may suggest an influence from environmental factors, e.g. poor blood supply, on the appearance of clefts. The present case will be discussed with similar information found in the literature, with reference to possibly related etiologic factors. Report on the occurrence of such cases throughout the world is important to shed some light on the aspects underlying the formation of clefts.

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WHITE SPONGE NEVUS: CLINICAL RESPONSE TO TOPICAL TREATMENT
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White Sponge Nevus (WSN) is a rare,benign,predominantly inherited disorder of the mucous membranes with high penetrance,affecting mainly the oral mucosa. Cases with no genetic background have also been reported. The condition is painless, nevertheless patients are often symptomatic, complaining of a disturbed texture of the mucosa or that lesions are anaesthetic. No standard treatment has been established although several therapeutic methods have been attempted. This study reports treatment in 5 cases of WSN, 3 in women(aged 23, 27 and 46 years) and 2 in men (aged 11 and 24 years). Two of these patients were siblings and the other three had no relatives affected by WSN. Diagnosis was confirmed by histologic examination in all cases. Patients were treated with 0,25% aqueous tetracycline mouth rinse used daily for 12 weeks and tested for Candida; if positive,they were given anti-fungal agents concomitantly to the tetracycline regime. Patients were followed up for 6 months after treatment. Results showed that 3 patients with no other familiar member affected became completely free of lesions, and only minor recurrences were seen during the follow-up period. The siblings were partially benefited, with improvement on the size, thickness and roughness of the lesions. In conclusion, topical tetracycline seems to be very effective for WSN cases with no genetic background, while the inherited types have some benefits, with partial resolution of the lesions.

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TRIGEMINAL SMALL-FIBER SENSORY NEUROPATHY CAUSES BURNING MOUTH SYNDROME
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Burning mouth syndrome affects women in the 5th-7th decade. It is characterized by persisting painful symptoms involving the tongue, mainly tip and anterior two-thirds, hard palate, lips, and alveolar ridges. Systemic and local diseases and psychological causes were claimed to play a causal role. Recently, primary neuropathic dysfunction was suggested, but the site of pathology in BMS was not identified and no diagnostic test was available. We examined 12 patients with BMS for at least 6 months. Patients with oral infections, contact sensitivity, systemic disorders or peripheral neuropathies were excluded All patients and 9 healthy subjects underwent a 3-mm punch biopsy at the anterolateral aspect of the tongue close to the tip. Sections were immunostained with anti-protein-gene-product 9.5 (PGP 9.5) antibodies. Two trained observers, blinded to the diagnosis, quantified the linear density of epithelial nerve fibers (ENF/mm). Densities were compared between groups by analysis of variance. Immunohistochemistry and confocal microscope double staining with anti-unique β-tubulin antibodies for cytoskeleton, and anti-myelin basic protein and anti-peripheral myelin protein 22 antibodies for

myelin sheath and Schwann cell was performed. Patients complained of burning pain in the anterior two-thirds of the tongue for 12 ± 2 months (range 6–18). Mean VAS score was 6 ± 1.8 (SD). Hard palate and/or lips were involved in 5 of them. Five patients had dysgeusia but noneloss of taste or thermal sensation. BMS patients showed a lower ($p = 0.0004$) density of ENF (10.29/mm; 95% CI 15.89-5.01) than controls (27.73/mm; 95% CI 37.71-20.35). Similarly, the epithelial innervation density per papilla was lower ($p = 0.03$) in patients than in controls. There was a trend toward correlation between loss of ENF and duration of symptoms. Nerve fibers showed diffuse axonal degeneration. Confocal double staining studies revealed that ENF are naked axons with no Schwann cell ensheathment and that fungiform papillae are innervated also by myelinated fibers. The loss of tongue ENF definitely demonstrated that BMS is associated with a small fiber neuropathy and that biopsy can be used to assess the diagnosis and to target treatment strategies.

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ASSESSMENT OF PATIENTS WITH ORAL LICHEN PLANUS IN THE INDIAN SUB-POPULATION

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Background: Erasmus Wilson in 1869 first described Lichen Planus as a relatively common chronic dermatologic disease with a wide range of clinical manifestations. The oral mucosa is commonly involved and may be the only site of involvement. The prevalence of oral lichen planus(OLP) is uncertain since very few population studies have been conducted. OLP characteristics have been studied in different countries like Hungary, Australia, Spain and Israel. To our best knowledge, no such study has been conducted in the Indian sub-population(NW region). **Purpose:** This study aimed at evaluation of the clinical characteristics of OLP in a group of patients from Indian sub-population. Methods: A retrospective descriptive study using information from patient records in the Department of Oral Pathology between Nov 2000 and Nov 2005. The diagnosis of OLP was based on accepted clinical and histopathologic criterion. Information regarding the age at first onset of oral signs and symptoms, sex, sights of involvement, clinical forms, skin involvement, general health conditions, habits, symptoms and treatment responses were reviewed and analyzed. **Results:** A total number of 207 patients diagnosed with OLP were studied. The mean age of onset was 53 yrs. 59% i.e. 122 were females. Symptoms generally coincided directly with severity of OLP forms. We found no evidence suggesting a connection between OLP and diabetes, cardiovascular disease, smoking, hepatitis-c.105 i.e. 51% of the patients reported experience of stressful event at the time of OLP onset. Skin involvement was found in 1/5th of the patients. **Conclusion:** Our profile of patients with OLP was generally similar to that found in other studies. OLP was more prevalent in middle aged women and buccal mucosa was the most common site. Though there was no positive correlation between OLP and diseased state, stress emerged as a significant factor. However reliability of this approach needs further evaluation using larger sample size.

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THE CLINICAL UTILITY OF THE CARBON-DIOXIDE (CO_2) LASER IN ORAL MEDICINE PRACTICE

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Purpose: A prospective clinical review of the utility of the carbon-dioxide (CO_2) laser in oral medicine practice. **Results:** 22 patients, of which 14 had leukoplakia with varying grades of dysplasia (mild to severe) underwent CO_2 laser ablation of their oral mucosal lesions. Results were favourable in terms of acute morbidity, with improved healing, and less scarring, in comparison to scalpel biopsy. The complication rate was low. **Conclusion:** The CO_2 laser shows excellent promise as another useful modality for the management of oral mucosal lesions. Further, ongoing, long-term studies are required to determine its utility in the definitive management of oral mucosal dysplasia and leukoplakia.

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A PROPOSED CLINICAL SCORING SYSTEM FOR MONITORING ORAL LICHEN PLANUS (OLP): A PRELIMINARY STUDY

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Methods: A scoring system for OLP was developed, based on a previously published system (Piboonniyom S, et al. 2005). Our modified clinical scoring system aimed to record the site of involvement, the clinical features, and clinical severity relative to the size of the lesions. Weighted scores were given to erythematous and ulcerative lesions, with these areas scaled by 1.5x and 2.0x respectively. A 10-point visual analogue scale (VAS) was used to record the patients' own assessment of their oral discomfort as related to the OLP. A second 10-point VAS was used to record the clinician's assessment of the severity of the patient's oral discomfort. Scores for lesions from each site were totalled to give an overall weighted score for each patient. The oral cavity was divided into 16 sites. Lesions were graded as reticular (R) scoring 0 or 1 (0 = no lesion, 1 = presence of a lesion); erythematous (E) scoring from 0 to 3 (0 = no lesion, 1 = less than 1cm2 , 2 = 1-2 cm2 , 3 = 2-3cm2); and ulcerative (U) areas scoring from 0 to 3 (0 = no lesion, 1 = less than 1cm2 , 2 = 1-2 cm2 , 3 = 2-3cm2). Total scores were calculated using $\Sigma R + \Sigma (E \times 1.5) + \Sigma (U \times 2.0)$. To date, four independent observers examined 20 patients with OLP. Each observer had a different level of clinical experience, ranging from that of a final year dental student to an Oral Medicine specialist. **Results:** This scoring system appears to be a potentially useful clinical tool. **Conclusions:** Further modifications may be needed to improve intra and inter-observer reliability. This scoring system allows for monitoring the progress of OLP and response to therapy, and appears to by

reproducible, reliable and user-friendly. It could potentially be adapted to record oral lesions in chronic graft versus host disease as well as other ulcerative and vesiculo-bullous conditions.

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MAXILLARY ANTRAL SQUAMOUS CELL CARCINOMA PRESENTING TO A DENTAL CLINIC IN RURAL AUSTRALIA

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Malignant tumours of the maxillary sinus is rare comprising less than one percent of all human malignancies1. Although most paranasal sinus cancers originate from the maxillary sinus as they present at an advanced stage, it is difficult to determine the primary site of the tumour. We present a case of a seventy four year old male referred to the Orange Community Dental Clinic in January 2005 by his general practitioner, complaining of difficulty in eating, due to food trapping under his upper denture. The patient was noted to have a scar over his right cheek attributed to a skin cancer removed a year ago. Intra-oral examination revealed on the right maxillary tuberosity area a 1 cm diameter lesion with jagged margins resembling an exit lesion into the oral cavity. Despite the biopsy of the oral swelling, reported as ''no evidence of squamous cell carcinoma'' examination of the maxillary antrum with multiple biopsies carried out under general anaesthesia, confirmed squamous cell carcinoma. The investigation, treatment and final outcome with a review of the literature will be presented.

Reference: Malignant Tumours of the Maxillary Sinus. A ten year experience. Popovic. D and Milisavljevic. D. Medicine and biology vol 11. No 1, 2004. pp 31–34.

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DETECTION OF THE EPSTEIN-BARR VIRUS IN THE LESIONS OF ORAL LICHEN PLANUS

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The aim of this study was detect the epstein-barr virus (EBV) by polymerase chain reaction (PCR)in patients diagnosed as oral lichen planus (OLP), and to establish the relationship between the tobacco use and the presence of the EBV. 20 patients with OLP diagnosed histopathologically and confirmed by direct immunofluorescence and 10 patients as control were selected. The tissue samples were frozen at −70°C for PCR test. Each OLP case were tested for the presence of EBV genome. 10/20 (50%)of the patients cases were positive to the presence of the virus. In the control group only one patient (10%) was positive for the viral genome. a statistically significant difference was observe between the two groups. Of the 10 positive cases for EBV 4/10 (40%) were tobacco user while the positive EBV positive case in the control group was a non smoker.We may conlude that greater incidence of the genome of EBV was detected in the samples coming from the patients with OLP when compared with the control group, that could suggest a possible association between this virus and the etiology of the desease.We observed a considerable number of smokers in the EBV positive group.although, we cannot conclude in the present study a definitive association between smoking and the presence OLP.

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COMPARISON OF THE DIAGNOSTIC POWER OF H&E STAINING METHOD IN EVALUATION OF SOFT TISSUE UNDIFFERENTIATED SARCOMAS OF HEAD & NECK REGION

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Sarcomas are the cancers derived from mesenchymal tissues which involve the soft tissues and bones throughout the body and are seen in different forms and kinds. These tumours greatly vary with respect to tumour site, degree of malignancy, response to treatment and prognosis. A major problem in histopathological diagnosis of sarcomas by H & E staining method is the identification and classification of tumours based on morphological characteristics.In this study twenty-four paraffin embedded samples of head and neck tumours, previously labelled as 'undifferentiated' were selected and stained with Immunohistochemistry (IHC) antigens (DAKO) using the standard Avidin-Biotin Complex (ABC) method. The diagnostic powers of H & E staining and IHC method (gold-standard) were compared in distinguishing the undifferentiated sarcomas and carcinomas of head and neck region. IHC confirmed H & E diagnoses of sarcoma in 88 percent of the cases but only 50 percent of H & E diagnoses of carcinoma were confirmed by IHC. We conclude that the IHC should be utilized as a mandatory diagnostic tool in the assessment of undifferentiated tumours.

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AMELOBLASTOMA AND ITS PREVALENCE AMONG PATIENTS REFERED TO FIVE MAJOR IRANIAN DENTAL SCHOOLS IN A PERIOD OF TEN YEARS

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Purpose: Ameloblastoma is the most common clinically significant odontogenic tumor. This lesion is usually unicentric, non functional, intermittent in growth, anatomically benign and clinically persistent. The aim of this study was to investigate age, sex, anatomic distribution and histopathologic type of the ameloblastoma patients refered to iranian dental schools. **Methods:** An existing data analysis was performed using patient's case notes from oral pathology deparments of five dental schools in IRAN. Cases where evaluated from those refered to these departments between 1988 to 1998. A check list was provided to record all proposed data which were later analysed. **Results and conclusion:** This study indicated that ameloblastoma was in 1% of all patients. The mean age of the whole population of this study was 30.34 years. Male to female ratio was 1.27/1. Mandible and posterior segment were predominantly affected. Plexiform type lesions were more common, histopathologically unicistic and conventional type of ameloblastoma was found to have been presented with a similar frequency.

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STUDY OF MYOEPITHELIAL CELL MARKERS IN HISTOGENESIS OF PLEOMORPHIC ADENOMA AND MUCOEPIDERMOID CARCINOMA

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Introduction: The applicaion of immunohistochemistry methods has been resulted in marked improvement of the microscopic diagnosis of neoplasms in combined with H&E staining. Although unique cellular antigen has not been found in salivary gland neoplasms,multiple less specific immunomarkers have been used and may be helpfull in elucidating the role of myoepithelial differentiation in those neoplasms. The aim of this study was to evaluate immunohistochemical myoepithelial markers (GFAP Actin, Vimentin and S100) in mucoepidermoid carcinoma and pleomorohic adenoma of salivary gland. **Materials and methods:** Formalin-fixed and parafin embedded tissue sections of 25 pleomorphic adenoma and 25 mucoepidermoid carcinoma were immunohistochemically analyzed for the presence of actin, vimentin, GFAP and S100 protein. A standard biotin-streptavidin procedure after antigen retrieval was used. Immunoreactivity of myoepithelial cells and chondromyxoid areas in pleomorphic adenoma, mucus cells,epidermoid cells and intermediate cells in mucoepidermoid carcinoma were evaluated and immunoreactivity was scored on a scale of 0 to 4+ (Regezi method) with 0 as negative, 1+ as scattered staining, 2+ indicate 25% to 50% of positive tumor cells and 4+ indicate more than 50% positive cells. The datas were analyzed with chi-square test. **Results:** In 25 pleomorphic adenoma all nonluminal cells and chondromyxoid areas were 4+ for GFAP and vimentin, 0 to 3+ for muscle-specific actin (12:0, 12:1+,1:3+) and 1+ to 4+ for S100 protein (3:1+, 3:2+, 18:3+, 1:4+). But all mucoepidermoid carcinomas regardless of their grades were negative for all mentioned markers ($p < 0.001$) and there were no immunohistochemical difference in major and minor salivary glands neoplasms. **Conclusion:** Expression of myoepithelial cell associated markers in pleomorphic adenoma confirmed role of myoepithelial cells in histogenesis of this tumor and lack or limited exprtssion of these antigens in mucoepidermoid carcinoma indicated the minimal myoepithelial differentiation in this tumor. Therefore evaluation of myoepithelial cell markers can be helpful in differential diagnosis of salivary gland neoplasms with myoepithelial cell differentiation.

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KEPIVANCE® (RECOMBINANT KERATINOCYTE GROWTH FACTOR (rHuKGF)) IN THE MANAGEMENT OF ORAL MUCOSITIS IN PATIENTS UNDERGOING CONDITIONING THERAPY FOR HAEMATOPOIETIC STEM CELL TRANSPLANTION: A CASE REPORT

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Purpose: To review the use of Kepivance in the prevention of oral mucositis. Kepivance has shown excellent early results to decrease the incidence, severity and duration of severe oral mucositis (OM) in patients with hematologic malignancies receiving myelotoxic chemotherapy and hematopoietic stem cell support. It appears to be well tolerated. The use of Kepivance in such patients could potentially decrease the use of opioid analgesics and expensive total parenteral nutritional support, avoid complications such as catastrophic airway embarrassment, and possibly limit life-threatening septicaemia. **Method:** Case report with literature review. **Conclusions:** This case together with laboratory-based experiments and early clinical trials, to date, with admittedly small numbers of patients, does suggest that Kepivance may limit mucositis in patients receiving intensive chemotherapy or even radiotherapy to the head and neck region. The aetio-pathogenesis of oral mucositis and the mechanisms by which Kepivance is thought to act to limit the development of mucositis will be reviewed.

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ORAL LEISHMANIASIS IN AN HIV POSITIVE PATIENT – REPORT OF A CASE INVOLVING LIP AND PALATE

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Leishmaniasis is a parasitic endemic infection with different clinical types that may involve skin and oral mucosa. Recently, an association on HIV positive patients has been reported. We present a case in a 40 year old male HIV positive patient with multiple papular lesions affecting skin of the face that precede the oral mucosal, mainly located on lower lips and palate. Incisional biopsy was made on these locations for histopathological diagnosis. Confirmation of the Leishmaniasis was made by Giemsa and Faracco stainings. Mucocutaneous Leishmaniasis may be related to HIV infection and could be related to immune depression state.

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INVESTIGATION OF A SOFT TISSUE SWELLING IN THE LABIAL MANDIBULAR VESTIUBULE

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A 60-year-old female was referred to the Kuwait University Dental School Clinic for assessment of a painless swelling in the labial vestibule of the anterior mandible. The lesion was first noticed by the patient 12 months ago and she was increasingly concerned over a gradual size increase. The mass was firm and mobile with no cervical lymphadenopathy. A panoramic radiograph showed erosion of the adjacent bone cortex. The lesion was excised and reported as an odontogenic tumour. The aim of this paper is to detail the subsequent investigations required to determine a final diagnosis in cases of an uncertain provisional diagnosis of odontogenic tumour.

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INVESTIGATION OF RECURRENT LIP SWELLING IN A 21-YEAR-OLD KUWAITI FEMALE

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A 21-year-old female presented to the Kuwait University Dental Clinic with a 4 year history of recurrent swelling, pain and fissuring of the upper lip. Treatment elsewhere with topical nystatin and multivitamins gave no clinical improvement. A previous biopsy was reported as non-specific inflammation. Examination showed a swollen and firm upper lip with deep transverse fissures but without the intraoral findings typically associated with inflammatory bowel disease. There was no history of weight loss or abdominal symptoms and a full blood examination was normal. A further biopsy was again reported as non-specific inflammation. The aim of this paper is to detail the sequential investigations needed in this type of complex case and subsequent patient management based on the underlying disease mechanisms.

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EXPRESSION OF HUMAN TELOMERASE REVERSE TRANSCRIPTASE (hTERT) PROTEIN IS SIGNIFICANTLY ASSOCIATED WITH THE PROGRESSION, RECURRENCE AND PROGNOSIS OF ORAL SQUAMOUS CELL CARCINOMA IN TAIWAN

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The purpose of this study was to assess whether expression of human telomerase reverse transcriptase (hTERT) protein is associated with the progression, recurrence and prognosis of oral squamous cell carcinoma (OSCC) in Taiwan. This study used an immunohistochemical technique to examine the expression of hTERT protein in 82 specimens of OSCC, 116 specimens of oral epithelial dysplasia (OED), and 21 specimens of normal oral mucosa (NOM). The cytoplasmic and nuclear hTERT staining intensity (SI), labeling indices (LIs, defined as the percentage of positive cells in total cells), and labeling scores (LSs, defined as SI $\times$ LI) in OSCC, OED, and NOM samples were calculated and compared among groups. The correlation between the cytoplasmic or nuclear hTERT LS in OSCCs and clinicopathological parameters or survival of OSCC patients was analyzed statistically. The mean cytoplasmic hTERT LSs increased significantly from NOM (87% $\pm$ 17%) through OED (95% $\pm$ 18%) to OSCC samples (114% $\pm$ 33%, $P = 0.000$). The mean nuclear hTERT LSs also increased from NOM (80% $\pm$ 14%) to OED (91% $\pm$ 20%) and then decreased to OSCC samples (86% $\pm$ 35%) with no statistically significant difference among the 3 groups. A significant correlation was found between the higher mean cytoplasmic hTERT LSs and OSCCs occurring in male patients ($P = 0.023$), with larger tumor sizes (T3 and T4, $P = 0.048$), with more advanced clinical stages (stages 3 and 4, $P = 0.033$), or from patients with areca quid chewing ($P = 0.029$), cigarette smoking ($P = 0.027$), or alcohol drinking habits ($P = 0.025$). In addition, OSCC patients with nuclear hTERT LSs greater than 100% were prone to have cancer recurrence ($P = 0.044$) and a lower 5-year survival rate ($P = 0.011$). Our results suggest that the increased expression of hTERT is an early event in oral carcinogenesis and hTERT may be a biomarker for OSCCs. Measuring the amount of cytoplasmic or nuclear expression of hTERT in OSCC samples may predict the oral cancer progression, recurrence, and prognosis.

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A NOVEL MUTATION IN THE DENTIN SIALOPHOSPHOPROTEIN (DSPP) GENE CAUSES DENTINOGENESIS IMPERFECTA TYPE III (SHELL TEETH)

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Hereditary dentin defects consists of dentin dysplasia (DD) and dentinogenesis imperfecta (DI). The DI associated with osteogenesis imperfecta has been classified as DI type I, whereas isolated inherited defects have been categorized as DI types II and III. However, whether DI type III should be considered a distinct phenotype or a variation of DI type II is debatable. Recent genetic findings have focused attention on the role of the dentin sialophosphoprotein (DSPP) gene in the etiology of inherited defects of tooth dentin. We have identified novel mutation (c.727G- > A, p.D243N) at the 243th codon of exon 4 of the DSPP gene in a Korean patient with DI type III. The radiographic and histologic features of the patient revealed the classic phenotype of shell teeth. These findings suggest that DI type II and III are not separate diseases but rather the phenotypic variation of a single disease.

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THE ASSESSMENT OF ORAL CYTOLOGY UTILIZING PLOIDY ANALYSIS AND VIRTUAL MICROSCOPY FOR THE EARLY DETECTION OF EPITHELIAL DYSPLASIA AND NEOPLASIA IN ORAL MUCOSAL LESIONS

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Oral squamous cell carcinoma (OSCC) is associated with high morbidity and mortality which is due, at least in part, to late detection. Precancerous and cancerous oral lesions may mimic any number of benign oral lesions, and as such may be left without investigation and treatment until they are well advanced. Over the past several years there has been renewed interest in oral cytology as an adjuvant clinical tool in the investigation of oral mucosal lesions. The purpose of the present study was to compare the usefulness of ploidy analysis after Feulgen stained cytological thin-prep specimens with traditional incisional biopsy and routine histopathological examination for the assessment of the pre-malignant potential of oral mucosal lesions. An analysis of the cytological specimens was undertaken with virtual microscopy which allowed for rapid and thorough analysis of the complete cytological specimen. 100 healthy individuals between 30 and 70 years of age, who were non-smokers, non-drinkers and not taking any medication, had cytological specimens collected from both the buccal mucosa and lateral margin of tongue to establish normal cytology parameters within a control population. Patients with a presumptive clinical diagnosis of lichen planus, leukoplakia or OSCC had lesional cytological samples taken prior to their diagnostic biopsy. Standardised thin preparations were prepared and each specimen stained by both Feuglen and Papanicolau methods. High speed scanning of the complete slide at 40X magnification was undertaken using the Aperio Scanscope^{TM} and the green channel of the resultant image was analysed after threshold segmentation to isolate only nuclei and

the integrated optical density of each nucleus taken as a gross measure of the DNA content (ploidy). Preliminary results reveal that ploidy assessment of oral cytology holds great promise as an adjunctive prognostic factor in the analysis of the malignant potential of oral mucosal lesions.

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BLOCKADE OF THE ERK PATHWAY DOWN-REGULATION MMPS IN ADENOID CYSTIC CARCINOMA

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Objectives: Adenoid cystic carcinoma (ACC) is a familiar malignant tumor of salivary gland, it shows frequent recurrence and metastasis. Matrix metalloproteinase (MMPs) plays an important role in the growth, invasion, and metastasis of tumors. In present study, we investigated whether the PD98059 (PD, a specific mitogen-activated protein kinase/extracellular signal-related kinase inhibitor) is involved in extracellular signal-regulated kinase (ERK) pathway mediated expression of MMPs in ACC cells. **Methods:** 30 cases of adenoid cystic carcinomas were collected. Immunohistochemical staining by S-P to detect MMPs (MMP-2, -3, -9, -14) and ERK protein were performed. Protein and mRNA expression of MMPs and ERK in ACC cells with different invasive potential was measured by semi-quantitative PT-PCR and flow cytometric analysis. ACC cells were stimulated with and without PD98059, Protein and mRNA were extracted after 1, 6, 12 and 24 h of treatment by PD98059. The expression of MMPs protein was evaluated by western blotting. The expression of ERK and MMPs mRNA was evaluated semiquantitatively by real-time reverse transcription polymerase chain reaction (RT–PCR). **Results:** This study declared that the tissue of ACC were strongly positive for ERK and MMP-2, -3, -9, -14 protein expression with proliferative activity. MMPs and ERK mRNA and protein was detected in all ACC cells, the expression level was higher in ACC-M cells with more invasive potential than in ACC-2 cells ($p < 0.05$). There were no significant difference of the positive cell population in the tissue between ERK and MMPs. In ACC cells, ERK and MMPs decreased significantly by PD98059 after 6h of treatment compared with controls. **Conclusions:** The expression of MMPs was regulated by the extracellular signal-regulated kinase (ERK) pathway. Specific blockade of the ERK pathway is expected to result in anti-metastatic effects in ACC tumor cells. ERK inhibitor may be an effective measure for therapy in anti-ACC treatment.

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SIGNIFICANCE OF BCL-2, BCL-XL, MCL-1, BAX, AND BAK PROTEIN EXPRESSION IN ARECA QUID CHEWING AND SMOKING-RELATED ORAL SQUAMOUS CELL CARCINOMAS IN TAIWAN

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This study tried to examine the significance of Bcl-2, Bcl-XL, Mcl-1, Bax, and Bak protein expression in areca quid chewing and smoking-related oral squamous cell carcinomas (OSCCs) in Taiwan. An immunohistochemical technique was used to assess the expression of these apoptosis-associated proteins in 69 specimens of OSCC. Their labeling indices (LIs, defined as the percentage of positive cells in total cells) in OSCC samples were calculated and correlated with clinicopathological parameters or survival of OSCC patients. The positive staining (LI > 10%) rate was 4.4% for Bcl-2, 21.7% for Bcl-XL, 68.1% for Mcl-1, 87% for Bax, and 97.1% for Bak. The expression of Bcl-2 in OSCCs was significantly correlated with the patients' daily consumption of alcohol ($P < 0.05$). The expression of Bcl-XL in OSCCs was significantly correlated with the clinical staging of the cancer ($P < 0.01$) and the patients' daily consumption of cigarettes ($P < 0.05$). The expression of the Mcl-1 in OSCCs was significantly correlated with the T status, N status, and the patients' duration of chewing areca quids ($P < 0.05$). However, there was no statistically significant correlation between the expression of Bax or Bak in OSCCs and the clinicopathological variables of the patients. The Kaplan-Meier analysis showed that OSCC patients with Mcl-1-positive cancers had a lower survival rate than those with Mcl-1-negative cancers ($P < 0.05$). Multivariate analysis revealed that Mcl-1 expression was an independent prognostic factor. This study showed a relatively high expression rate of Mcl-1 (68.1%) and Bcl-XL (21.7%) and a low expression rate of Bcl-2 (4.4%) in OSCCs. These results suggest that in our OSCC cases cancer cells express Mcl-1 and Bcl-XL , but not Bcl-2, to counteract the Bax- and Bak-induced apoptosis and to prolong their survival time. Mcl-1 expression can predict the progression of OSCCs in Taiwan and is also an independent prognostic factor.

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SERUM INTERLEUKIN-8 LEVEL IS A MORE SENSITIVE MARKER THAN SERUM INTERLEUKIN-6 OR TUMOR NECROSIS FACTOR-α LEVEL IN MONITORING THE DISEASE ACTIVITY OF MUCOCUTANEOUS TYPE OF BEHCET'S DISEASE

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The purposes of this study were to investigate whether the serum interleukin (IL)-6, IL-8 or tumor necrosis factor (TNF)-α level was a sensitive marker in monitoring the disease activity of mucocutaneous type of Behcet's disease (MCBD) and to assess whether IL-6, IL-8 or TNF-α was a useful serum marker in evaluating the therapeutic effects of levamisole plus colchicine on MCBD patients. We used a solid phase, two-site sequential chemiluminescent immunometric assay to determine the baseline serum levels of IL-6, IL-8 and TNF-α in 64 patients with MCBD, 9 patients with traumatic oral ulcers (TOU), and 54 normal control subjects. All MCBD patients with serum IL-6, IL-8 or TNF-α levels higher than the upper normal limits were treated with levamisole plus colchicine and their serum IL-6, IL-8 and TNF-α levels were measured after treatment. We found that 67% (43/64), 83% (53/64) or 67% (43/64) of MCBD patients had a serum IL-6, IL-8 or TNF-α level greater than the upper normal limit of 4.7, 8.7 or 7.4 pg/ml, respectively. The mean serum level of IL-6 (9.9 ± 2.4 pg/ml, $P < 0.005$), IL-8

(107.5 ± 21.4 pg/ml, P < 0.001) or TNF-α (22.5 ± 4.1 pg/ml, P < 0.001) in 64 MCBD patients was significantly higher than that (2.1 ± 0.2, 5.7 ± 0.2 or 3.8 ± 0.2 pg/ml for IL-6, IL-8 or TNF-α level, respectively) in normal control subjects. In 46 MCBD patients with the serum IL-6, IL-8 or TNF-α level higher than the upper normal limit, treatment with levamisole plus colchicine for a period of 0.5–11.5 months could significantly reduce the mean serum IL-6, IL-8 and TNF-α levels from 9.0 ± 1.7 to 1.6 ± 0.2 pg/ml (P < 0.001), from 134.6 ± 28.2 to 6.0 ± 0.4 pg/ml (P < 0.001), and from 25.7 ± 5.6 to 3.5 ± 0.4 pg/ml (P < 0.001), respectively. We conclude that serum IL-8 level is a more sensitive marker than serum IL-6 or TNF-α level in monitoring the disease activity of MCBD. Either IL-6, IL-8 or TNF-α is a useful serum marker in evaluating the therapeutic effects of levamisole plus colchicine on MCBD patients.

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EXPRESSION OF METASTASIS-ASSOCIATED PROTEIN 1 (MTA1) IS SIGNIFICANTLY ASSOCIATED WITH THE PROGRESSION OF ORAL SQUAMOUS CELL CARCINOMA IN TAIWAN

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Overexpression of metastasis-associated protein 1 (MTA1) has been found to be significantly associated with the progression or prognosis of some human cancers. The purpose of this study was to assess whether expression of MTA1 protein is associated with the progression, recurrence, and prognosis of oral squamous cell carcinoma (OSCC) in Taiwan. We used an immunohistochemical technique to examine the expression of MTA1 protein in 74 specimens of OSCC, 100 specimens of oral epithelial dysplasia (OED; 33 mild, 44 moderate, and 23 severe OED cases), and 21 specimens of normal oral mucosa (NOM). The cytoplasmic and nuclear MTA1 labeling indices (LIs) in OSCC, OED, and NOM samples were calculated and compared between groups. The correlation between the cytoplasmic or nuclear MTA1 LI in OSCCs and clinicopathological parameters or survival of OSCC patients was analyzed statistically. The mean cytoplasmic MTA1 LIs were all over 95% for NOM, OED and OSCC samples. There was no significant association of the cytoplasmic MTA1 LI with any of the clinicopathological parameters of OSCC patients. The mean nuclear MTA1 LIs decreased significantly from NOM (73 ± 13%) through mild OED (71 ± 16%), moderate OED (60 ± 22%), and severe OED (46 ± 25%) to OSCC samples (30 ± 30%, P = 0.000). A significant correlation was found between the lower mean nuclear MTA1 LIs and OSCCs located at the buccal mucosa and tongue (P = 0.001), with larger tumor sizes (T3 and T4, P = 0.020), with regional lymph node metastases (N1, N2 and N3, P = 0.024), or with more advanced clinical stages (stages 3 and 4, P = 0.045). Our results suggest that the MTA1 is universally expressed in the cytoplasm of normal, dysplastic and malignant oral epithelial cells. The nuclear expression of MTA1 significantly reduced from NOM through OED to OSCC samples, and is inversely related to T status, N status, and clinical staging of OSCCs. Therefore, the nuclear MTA1 LI can be used to predict the progression of OSCCs in Taiwan.

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MMP-8 EXPRESSION IN FEMALES CORRELATES WITH THE IMPROVED SURVIVAL OF TONGUE CANCER

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Squamous cell carcinoma (SCC) of the tongue is the most common cancer in the oral cavity and has a high mortality rate. Identification of the most aggressive tumours would be helpful for treatment planning. Some potential markers have previously been shown to correlate with the prognosis of the oral cancer patients. **Methods:** A total of 90 tongue SCC samples collected from all patients from the Northern Finland that were treated in the Oulu University Hospital during the years 1981–2001 were analyzed. Malignancy scores were determined for the SCCs by using the method by Bryne et al. (1992), and thickness of the SCC was determined by measuring the thickest area of each tongue resection slide. Using immunohistochemistry, we analyzed the expression of different potential prognostic markers, such as factor VIII, CD-31, COX-2, αvβ6 integrin, laminin-5γ2, and several matrix metalloproteinases (MMP-2, -7, -8, -9, -20, -26 and -28). Staining intensities and patterns of these markers and patient characteristics were statistically evaluated by using Kaplan-Meier method and Cox's regression model. **Results:** Expression of MMP-8 correlated significantly with improved survival in females (p = 0.0477) but not in males (p = 0.2155). Other markers had no significant correlation with the patient survival. Increased expression of MMP-9 correlated with a higher Bryne category malignancy score and with reduced expression of laminin-5γ2 within cancer cells. Increased expression of laminin-5γ2 within cancer cells correlated with increased expression of αvβ6-integrin. **Conclusions:** Surprisingly, MMP-8 expression in females correlated with the improved survival and may thus potentially be of use as a marker for tumor aggressiveness.

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POTENTIAL ROLES OF LIGHT-EMITTING DIODES IRRADIATION IN CYCLOOXYGENASE, NITRIC OXIDE, PROSTAGLANDINS E2 AND REACTIVE OXYGEN SPECIES PRODUCTION IN ARACHIDONIC ACID-TREATED HUMAN GINGIVAL FIBROBLASTS

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It has been reported that arachidonic acid-derived lipid mediators are intimately involved in inflammation process and cancer. The inflammatory processes are made up of a multitude of complex cascades including COX, PGE2, NO and several ROS. And, there are many reports that the physiological effects of LEDs irradiation are pain reducing and anti-inflammation. The purpose of the present study was to investigate anti-inflammatory effects of LEDs irradiation in arachidonic acid treated inflammatory model. Primary human gingival fibroblasts were used in present study. LEDs used in

present study was manufacutred at a wavelength of 635 nm with energy density of 5 mW/cm2. The expression of the COX mRNA was analyzed by Real-Time PCR. The COX protein level was analyzed by western blot analysis. NO concentration in the supernatant media were measured by the Griess reagent. The amount of PGE2 production was measured by ELISA. Intracellular oxidative stress induced by the arachidonic acid was measured by DCF-DA and DHR 123. Hydogen peroxide (200 uM) was treated to recognize COX protein expression of inflammatory processes. mRNA and protein expression of COX was decreased in the LEDs irradiation after arachidonic acid group than in the only arachidonic acid treated group at 24 hours. The immunofluorescence against COX-2 showed the same result as the mRNA and protein of COX were expressed. ELISA for PGE2 showed that its release was decreaed in the LEDs irradiation after arachidonic acid treated group at 24 hours although increase of PGE2 showed in only arachidonic acid treated group. Also, the quantities of ROS production was decreased in the LEDs irradiation after arachidonic acid group comparing with that of in the only arachidonic acid treated group at 24 hours. These results suggest that LEDs irradiation may play a role in anti-inflammation in arachidonic acid treated inflammatory model of human gingival fibroblasts.

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INTERRELATIONSHIP OF THE MAJOR INFLAMMATORY REACTION PATTERNS OF THE SKIN AND ORAL MUCOSA
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The major epidermal histological reaction patterns in the skin are spongiotic, psoriasiform and lichenoid but in the oral mucosa lichenoid patterns dominate. The differential diagnosis of oral lichenoid reactions from a histological standpoint can be challenging and clinical and cutaneous findings offer the main clues to correct diagnosis. Infections, drugs and cutaneous epidermotropic T-cell lymphomas or parapsoriasis may induce mixed epithelial patterns In contrast dermal reaction patterns such as granulomatous diseases, urticaria or vasculitis are co-expressed in the mouth. The basis for the restricted epithelial reaction patterns may reflect basic differences in lymphocyte homing and fundamental differences in the makeup of the oral mucosa particularly in respect of innate and acquired immunological pathways as well as the oral mucosal physiological properties. The study of differences in these major reaction patterns in the skin and oral mucosa may provide insight into understanding the differences between these sites.

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BENIGN AND MALIGNANT NEOPLASMS OF PERIORAL SKIN
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Histologically, the skin is composed of several distinct layers (epidermis, dermis, adnexal structures and subcutis) each comprising different cellular components, all of which may give rise to benign and malignant neoplastic conditions. It is beyond the scope of this lecture to detail all of these conditions. Rather, the lecture will provide a practical histologic insight into several common or important neoplasms that may arise in perioral skin. Some of these tumours have a predilection for the lip, face or head and neck, while others are common skin tumours that may also affect the perioral region. The clinical and histological features, and the significance of each lesion will be discussed briefly.

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MOLECULAR ASPECTS OF MELANOMA
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Much of the resistance of melanoma to immunotherapy, radiotherapy and cytotoxic treatment is due to an impressive array of molecular defences that derive ultimately from the essential molecular structure of the melanocyte and its biological requirement for defence against apoptosis. The exploration of melanoma susceptibility genes like CDKN2A (inherited in mutated form in 30–40% of families with multiple melanoma-affected members), CDK4 and MC1R has highlighted a number of key pathways in melanomagenesis. Others have been revealed by a systematic exploration of somatic chromosomal and genetic abnormalities in naevi and melanomas. Constitutive activating mutations in Nras and BRAF are the most common somatic oncogene mutation in melanoma, indicating the importance of this pathway in the deregulation of melanocyte growth. Downstream targets of this signalling pathway include the cell cycle regulator cyclin D1 and the melanocyte-specific transcription factor, MITF. BRAF mutations are also seen in 60–80% of benign melanocytic naevi. This suggests that the complex molecular machinery of checks and balances in the cell normally protects against the unrestrained growth stimuli propagated through such abnormalities in the Ras/RAF signalling pathway. The CDKN2A product, p16INK4A is induced by activation of the BRAF pathway and under normal circumstances induces cellular senescence. Escape from this senescence is probably fundamental to melanomagenesis. Melanoma-associated NRas and BRAF mutations do not carry the UV-induced fingerprint, and BRAF mutations appear to be more common in melanomas arising in non-chronically sun-damaged skin and in those with multiple naevi. They are rare in mucosal melanomas and in cutaneous melanoma arising in chronic sun-damaged skin (Curtin, JA et al. N Engl J Med, 353: 2005). The alternate protein product of the CDKN2A gene, p14ARF binds hdm2 leading to stabilisation of the central apoptosis regulator, p53. Inhibitors of apoptosis, like Bcl-2 and Mcl-1 are frequently over-expressed in established melanomas, accounting in part for the observed resistance of melanoma to cytotoxic attack.

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E2F IN SQUAMOUS CELL CARCINOMA DEVELOPMENT AND THE PROPOSED USE OF E2F INHIBITORS AS AN ANTICANCER STRATEGY
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The E2F transcription factor complex comprises an E2F family member (E2F1-8) bound, alone or in a complex, with a DP protein. This complex can then bind to a consensus E2F response element in the promoters of a variety of genes to regulate transcription. Early studies demonstrated that E2F was an essential factor that controlled passage through S phase of the cell cycle. It was no surprise then to find E2F is deregulated in many forms of cancer. In this regard, we have previously shown that E2F1 is overexpressed in squamous cell carcinomas and that E2F activity is deregulated in head and neck squamous cell carcinoma (HNSCC) cell lines (Oncogene, 19:2887–2894, 2000). We have examined whether the deregulation of E2F activity, observed in HNSCC, could also have effects on keratinocyte differentiation. E2Fs1-5 were potent suppressors of differentiation markers in normal keratinocytes (J. Biol. Chem., 278:28516–28522, 2003) which indicated that the effect of deregulated E2F activity is both pro-proliferative as well as differentiation-suppressive. These findings would suggest that the inhibition of E2F activity in HNSCC cells may serve to inhibit proliferation and promote differentiation. This was formally tested using a dominant/negative form of E2F1. These experiments demonstrated that E2F inhibition in squamous cell carcinoma cells could inhibit growth but could not induce differentiation. However, if an E2F inhibitor was used in combination with a differentiation stimulus (eg: phorbol ester) then we could induce differentiation in the squamous cell carcinoma cell lines (J. Biol. Chem., 278:28516–28522, 2003; Oncogene, 24:3525–3534, 2005). These data indicate that the delivery of an E2F inhibitor and a differentiation stimulus may form the basis for a novel differentiation therapy for the treatment of HNSCC. In addition. these data suggest that in normal keratinocytes, the inhibition of E2F is a prerequisite for subsequent differentiation.

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EPITHELIAL STEM CELLS: HOW FAR HAVE WE COME?

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The immense regenerative capacity of the epidermis for cell renewal observed both in vivo and in vitro, has to date been attributed to the epidermal stem cell population. There are still many assumptions on the expected behaviour of epithelial stem cells both in vivo and in vitro, despite mounting evidence to support the notion that vast proliferative potential resides both within the stem cell compartment and outside it in their immediate progeny. Notably, although in vivo stem cells are indeed the longest-lived residents of epithelial tissues, and ultimately responsible for tissue regeneration over the lifetime of an organism, their removal from the in vivo microenvironment unleashes the vast proliferative potential of all cells within the proliferative compartment. For instance, all basal cells in the epidermal and oesophageal epithelium can exhibit ''stem cell activity'' when assayed in vitro or in transplantation settings. The insights gained from studies performed worldwide, including those in our laboratory will be discussed to illustrate this point specifically. The implications from the existing literature strongly indicates the need to re-assess the need for stem cell purification for clinical applications.

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BRUSH BIOPSY FOR THE ASSESSMENT OF ORAL MUCOSAL LESION - EXPERIENCE IN GERMANY

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For early detection of oral cancer it is of utmost importance to discriminate between true precancerous or early malignant lesions and common benigne changes of the oral mucosa. This has not been accomplished satisfactory until now. Clinical inspection is not a great help and excisional biopsy, which can differentiate the two states rather reliable, is an invasive procedure and an improportionate effort in view of the numbers of presumably harmless lesions. A new method of gaining cells from all epithelial layers down to the basement membrane by a ''brush biopsy'' and a computer-assisted evaluation of the samples (OralCDx) has proven to overcome this problem. By this test 3 Categories – negative, positive and atypical can be discriminated. In positive cases a histological evaluation is mandatory. In Germany the oral brush biopsy has been performed since 2003 Since them a total of 5.390 brush biopsies were evaluated. The most common locations were buccal mucosa, gingiva, palate, tongue and floor of the mouth. 82 % were negative, 11 % atypical, 2 % positive and 5 % inadequate. In 31 % there was an important additional diagnosis-most common candidal invasions (4.8%). In 103 cases the result of the brush biopsy could be compared with the histological diagnosis. The sensitivity for dysplasia and carcinoma was 92.3 %, the specificity was 94,3 %. The implications for diagnostic procedure will be discussed.

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ESTABLISHMENT OF COLLAGEN GEL-BASED CO-CULTURE MODELS FOR INVASIVE STUDY WITH RESPECT TO CANCER CELLS AND FIBROBLASTS INTERACTION

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This study was aimed to design in vitro model for investigating the effects of stromal fibroblasts in the invasive growth of squamous cell carcinoma. This study used two oral squamous cell carcinoma cell lines. To establish in vitro system akin to in vivo, we designed collagen gel-based cancer cell culture models; that is, collagen gel-based direct co-culture model (C-Dr) that was designed for direct contact between carcinoma cells and fibroblasts, and collagen gel-based indirect co-culture model (C-In) with intervening collagen layer between cancer cells and fibroblasts. C-Dr and C-In model were compared with other co-culture models devoid of collagen gels; that is, mixed co-culture and separate co-culture using transmembrane system. First, three-dimensional culture with and without fibroblasts embedded in dermal equivalents was performed and was histologically examined. The expression and gelatinolytic activity of matrix metalloproteinase (MMP) 2 and 9 were examined among the different culture models by gelatin

zymography and RT-RCR. Immunohistochemical staining was applied against the culture tissue and the surgical sections from the patients. Western blot was performed for the expression of cathepsin D. As results, gelatin zymography showed that the active form of MMP-2 was induced only by C-Dr model, and thus mixed co-culture showed the same results with C-Dr model, suggesting that MMP-2 activity can be induced by direct contact between cancer cells and stromal fibroblast. Similarly, the immunohistochemical staining showed MMP-2 expression strongly at the interface with the invasive front of cancer cells and stromal tissue. The results suggest that collagen gel-based co-culture models might be appropriate for invasive study with respect to cancer cells and fibroblasts interaction. This study was supported by the Korea Science and Engineering Foundation (R01-2002-000-00454-0).

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HISTOPATHOLOGIC FINDINGS AND ASSESSMENT OF CERVICAL LYMPH NODE METASTASIS IN ORAL SQUAMOUS CELL CARCINOMA OF MALAYSIAN PATIENTS

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Purpose: To evaluate some histopathologic parameters and relate with the occurrence of cervical lymph node metastasis in oral squamous cell carcinoma (OSCC) in Malaysian patients. **Methods:** A total of 44 cases of OSCC resected were included. The resected specimens were examined for the OSCC type, degree of differentiation, pattern of invasion (at the tumour invasive front), greatest dimension and the depth of stromal invasion. Where there is no neck resection, the clinical nodal status was obtained from the Oral Cancer database maintained at the University of Malaya Oral Cancer Research and Coordinating Centre (UM-OCRCC) while the histopathologic data were obtained from examination of the resected specimens of patients whose records were extracted from the UM-OCRCC. **Results:** Among 38 cases of conventional OSCC, 11 cases showed nodal metastasis (28.9 %); two out of 4 cases of basaloid SCC showed nodal metastasis (50%) and none of the papillary SCC (2 cases) showed nodal metastasis (0%). The occurrence of lymph nodes metastasis in well-differentiated, moderately-differentiated and poorly-differentiated OSCC are 17.6% (17 cases), 36.0% (25 cases) and 50.0% (2 cases) respectively. None of the cases with pattern of invasion Type 1 and 2 (cohesive) showed nodal metastasis. The occurrence of lymph node metastasis in tumours with Type 3 and 4 pattern of invasion (non-cohesive) are 34.5% and 42.9% respectively. Ten out of 23 cases (43.5%) with depth of stromal invasion of ≥1.0cm showed nodal metastasis while three out of 21 cases (14.3%) of those with < 1.0 cm depth showed nodal metastasis. Eleven out of 29 cases (37.9%) with tumour greatest dimension of ≥2.0 cm showed nodal metastasis and two out of 15 cases (13.3%) with nodal metastasis was observed among those patients with < 2.0 cm greatest dimension. **Conclusion:** The pattern of invasion, depth of stromal invasion and tumour's greatest dimension appear to be important parameters in the occurrence of cervical lymph node metastasis for the Malaysian OSCC patients.

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PERIOSTIN PROMOTES INVASION AND ANCHORAGE-INDEPENDENT GROWTH IN THE METASTATIC PROCESS OF HEAD AND NECK CANCER

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Head and neck squamous cell carcinoma (HNSCC) is one of the most common types of human cancer. Typically HNSCC cells show persistent invasion that frequently leads to local recurrence and distant lymphatic metastasis. However, molecular mechanisms associated with invasion and metastasis of HNSCC remain poorly understood. Here we identified Periostin as an invasion promoting factor in HNSCC by comparing the gene expression profiles between parent HNSCC cells and a highly invasive clone. Indeed, Periostin overexpression promoted the invasion and anchorage independent growth both in vitro and in vivo in HNSCC cells. Moreover, Periostin overexpressing cells spontaneously metastasized to cervical lymph nodes and to the lung through their aggressive invasiveness in an orthotopic mouse model of HNSCC. Interestingly, Periostin was highly expressed in HNSCCs in comparison with normal tissues, and the level of Periostin expression was well correlated with the invasiveness of HNSCC cases. In summary, these findings suggest that Periostin plays an important role for invasion and anchorage independent growth in the metastatic process of HNSCC.

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EXPRESSION OF HUMAN B-DEFENSIN-3 IN ORAL SQUAMOUS CELL CARCINOMA USING TISSUE MICROARRAY – A PRELIMINARY STUDY

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Purpose: Human b-Defensin (hBDs) is an epithelial origin, cationic antimicrobial peptides. Their expression is reported in oral mucosa, gingiva and salivary glands. However, their protective role is not well understood. It has been suggested that bacterial and viral infection are an important factors in the process of carcinogenesis. This study investigated the expression of hBD-3 in oral squamous cells carcinoma (OSCC). **Methods:** 29 OSCC and 23 samples of normal and dysplastic tissues were obtained from Oral Pathology diagnostic laboratory, faculty of Dentistry, UKM and UM. The tissues were arrayed and the expression of hBD-3 was analysed using immunohistochemistry technique. **Results:** Higher levels of hBD-3 expression were found in stage II and II of OSCC compared to stage I and IV. Expression of hBD-3 was also seen higher in the tumour front arrays. Healthy and dysplastic tissues also seen to expressed hBD-3 but most are moderately stained. **Conclusion:** High levels of hBD-3 expression is seen

especially in stage II and III as well as in tumour front suggest a potential tumour marker, correlation between level of expression and probable infective cancer causes need to be investigate further.

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BETEL QUID, SUPARI AND GUTKA – IS ARECA NUT USED IN AUSTRALIA?

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Purpose: Oral submucous fibrosis is increasingly diagnosed at specialist clinics in Australia. This condition is a chronic, insidious disease, involving the mucosa of oral cavity, as well as the pharynx and oesophagus, and is also known to be premalignant. The condition is associated with the habit of chewing areca nut. It has recently been shown that subjects who use the areca nut are 9.9 times more likely to develop oral carcinoma than non-users. A study was undertaken to determine the use of areca nut in a large city in Australia. **Method:** At two local community festivals celebrating Indian/Asian culture, subjects were randomly selected to participate in an interview in which they were surveyed as to their habitual use of areca nut products. **Results:** 336 Australian residents (Female: 148; Male: 188), median age of 37 yrs, (range 14–90 yrs, SD 14.65) were surveyed. While approximately 20% of the surveyed population chewed the areca nut, 8.6% of the subjects surveyed commenced their habit before 10 yrs of age (43.3% of regular chewers -multiple times per month), this ratio was not significantly different whether the subject was born in Australia or overseas. It was noted that subjects born in Australia, who used the nut multiple times a day indicated that they commenced the habit during their teenage years. The 16 different Asian communities represented in the survey used different words for the areca nut and these will be presented. **Conclusions:** 8.6% of the Indian/Asian community surveyed have experienced long term exposure to the areca nut and are therefore at increased risk of developing oral mucosal pathology. Almost 50% of regular users of the areca nut commenced the habit in early childhood and have exposure to components of the areca nut the alkaloids are at increased risk of developing oral carcinoma.

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FRAGILE HISTIDINE TRIAD (FHIT) EXPRESSION IN NORMAL MUCOSA, POTENTIALLY PREMALIGNANT ORAL LESIONS AND SQUAMOUS CELL CARCINOMA OF ORAL CAVITY

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Inactivation of the Fragile Histidine Triad(FHIT)gene appears to be a frequent event in head and neck cancer, though mutation is uncommon. We sought to extend previous work by studying FHIT expression in potentially premalignant oral lesions (PPOLs) and oral squamous cell carcinomas (OSCCs), addressing the following questions: (i) what is the frequency of loss of FHIT expression in these lesions from UK patients? (ii) does loss of FHIT expression correlate with degree of dysplasia in PPOLs?(iii) can FHIT loss predict high-risk PPOLs that are more likely to progress to malignancy? (iv) does loss of FHIT expression in OSCCs correlate with survival? FHIT expression is generally considered cytoplasmic, but by optimising our immunohistochemical staining protocol, we found that FHIT is expressed in a distinctive strong nuclear and weak cytoplasmic pattern in normal oral tissues. This pattern was confirmed in FHIT-transfected squamous carcinoma cell lines. A series of 94 PPOLs and 86 OSCCs with known outcomes were then studied. Loss of FHIT expression was found in 42/94 (45%) of PPOLs and in 66/86 (77%) of OSCCs. We observed a statistically significant positive correlation between frequency of loss of FHIT expression with increasing grade of dysplasia (chi square $=13.8$, df $=4$, p $=0.008$). Loss of FHIT expression in PPOLs that progressed to malignancy was more frequent than in those that did not (17/25 (68%) vs. 12/29 (41.4%) respectively). This difference was statistically significant (chi square $=3.8$, df $=1$, p $=0.046$). In OSCCs, loss of FHIT staining indicated a worse prognosis (survival rate: 36.2%) than when positive FHIT staining was observed (survival rate: 50%), but the difference was not statistically significant (Kaplan-Meier, log-rank p $=0.546$). FHIT localises to both nuclear and cytoplasmic cellular domains. FHIT inactivation occurs early in oral carcinogenesis and may be useful molecular marker for progressive dysplastic oral lesions.

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MOLECULAR PATHOLOGY OF FIBRO-OSSEOUS JAW LESIONS

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Purpose: Fibro-osseous lesions of the jaw, which are characterized by replacement of bone by a fibrous connective tissue and mineralized materials, including cemento-ossifying fibroma (COF), fibrous dysplasia (FD) and cemento-osseous dysplasia (COD). Pathogenesis of fibro-osseous lesions has never been defined in more stringent studies although the lesions may be derived from osteoprogenitor cells. Moreover, the lesions usually present a diagnostic dilemma for both clinicians and pathologists because of uncertainties concerning the diagnostic significance of clinical, radiological, and histological features. Recently it was demonstrated that Runx2 determined the lineage of osteoblastic cells from mesenchymal cells. Hence, Runx2 expression is thought to be a marker of osteoblastic lineage. In turn, Gs alpha mutation at the Arg^{201} codon is thought to underlie the development of FD. In this study, we investigated the Runx2 expression and the occurrence of Gs alpha mutation in the lesions with a view of the pathological diagnoses. **Methods:** Formalin-fixed, paraffin-embedded tissue blocks of five COF, seven FD and three COD cases, were used for this study. Tissue sections were used for immunohistochemical studies to identify the Runx2-expressing cells using a monoclonal antibody against recombinant Runx2. DNA was extracted from paraffin-embedded tissue sections. We used the PCR-Restriction Fragment Length Polymorphism (RFLP)

procedure to detect Gs alpha mutation as previously reported. **Results:** Runx2-positive cells were present in the fibrous connective tissue of all cases of COF, FD and COD. The Gs alpha mutation at Arg^{201} codon occurred in all seven cases of FD while no mutation at Arg^{201} codon was seen in all five cases of COF and three cases of COD. **Conclusions:** Fibro-osseous lesions of the jaw were characterized by fibrous connective tissue composed of osteoblastic lineage. The detection of Gs alpha mutation is useful to differentiate FD from COF and COD.

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NASAL SPRAY CALCITONIN FOR TREATMENT OF CENTRAL GIANT CELL GRANULOMA – CLINICAL, RADIOLOGICAL AND HISTOLOGICAL FINDINGS AND IMMUNOHISTOCHEMICAL EXPRESSION OF CALCITONIN AND GLUCOCORTICOID RECEPTORS

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Purpose: To provide clinical, radiological and histopathological analyses of 5 patients with central giant cell granuloma (CGCG) treated with calcitonin nasal spray and to compare these analyses to 12 well-documented cases reported in the literature. In addition, lesions were evaluated for immunohistochemical expression of calcitonin and glucocorticoid receptors (CTR and GCR, respectively). **Methods:** Five patients (2 females, 3 males; mean age 20.6 y, range 7 to 45 y) with aggressive CGCG (4 mandible, 1 maxilla), were treated with calcitonin nasal spray, 200 – 400 IU/day, for a period ranging between 13 and 64 months. Frequency of CTR and GCR was examined in biopsies taken at different time points of the treatment. **Results:** There was no significant clinical and/or radiological improvement in any lesion. All patients ultimately had curettage and continued treatment with calcitonin. Significant radiological improvement was noticed 2 to 4 months postoperatively. Each lesion exhibited a different immunoprofile for CTR and GCR before initial treatment. The disappearance of CTR was associated with long-term calcitonin treatment. GCR exhibited variable changes. **Conclusion:** Long-term treatment with nasal spray calcitonin, 200 – 400 IU/day, is not effective for management of CGCG, in contrast to calcitonin injections (as reported in the literature). It is recommended that evaluation of CTR and GCR be carried out at different time points during treatment, especially in lesions that do not demonstrate a desirable response, to obtain the utmost benefit from calcitonin therapy. This study was supported by the Ed and Herb Chair in Oral Pathology, Tel Aviv University.

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HISTOLOGICAL FEATURES OF CENTRAL GIANT-CELL GRANULOMA OF THE JAW AFTER INTRALESIONAL INJECTIONS OF TRIAMCINOLONE

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Central giant-cell granuloma (CGCG) is a benign giant-cell lesion arising within the jawbones. This lesion involves the mandible more frequently than the maxilla. Histologically, it is characterized by the presence of multinucleated giant cell and mononuclear cells within a fibrous stroma, there is not a histological or immunohistochemical feature predictive of its behavior. The pathogenesis of CGCG is not completely understood. The objective of this study was to analyze in detail the histological changes after treatment of CGCG with injections of the steroid triamcinolone. This patient was a 17 year old woman who presented a well define radiolucid lesion in the anterior mandible, teeth were not involved. The treatment consisted of 22 intralesional injections of 2% lidocaine with epinephrine 1:100,000, in a 1/1 solution. After treatment a surgical curettage of the area was performed and the tissue processed for biopsy. Histology showed an almost total disappearance of the giant cells, fibrous collagenic connective tissue and a markedly reactive osteoid formation. The osteoid reaction, which is a consequence to the steroid treatment, could lead to the erroneous diagnosis of osteosarcoma. Intralesional steroid injections are a good alternative treatment for CGCG accompanied by reduction of possible hemorrhagic episode associated with surgery and reduction in size of the lesion without occasional facial disfigurement as consequence to wide surgical procedures.

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PRACTICAL BENEFIT OF IN VITRO AND IN VIVO MODELS OF PROSTATE CANCER BONE METASTASIS IN HEAD AND NECK CANCER

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Prostate cancer (CaP) is the leading cause of male cancer deaths in Western countries. Understanding mechanisms of metastasis is fundamental to the prevention of cancer spread. As the jaws are often involved, the process is of direct relevance to the practice of oral pathology. Furthermore, knowledge from CaP models of the metastatic process may be used to understand the spread of head and neck squamous cancers. We have used two cell culture systems in our studies. A direct co-culture of CaP cells with osteoblasts and an indirect co-culture of cells treated either with conditioned medium from other cells, or a transwell system in which one type of cells was seeded on the bottom of plates, and the other in cell-inserts allowing cells to communicate via the membrane of the insert. We have also established an in vivo model, based on that of Dr Michael Cher, Detroit, in which human bone chips are implanted in the immunodeficient mouse. The cancellous bone fragments were obtained from femoral heads/proximal tibia of male patients undergoing elective hip/knee replacement. CaP cells were injected via the tail-vein home towards bone and form tumors. Results showed that the expression of PSA and MMP-2 was increased in CaP cells co-cultured with osteoblasts at both mRNA by qPCR and protein levels by Western blots, which was correlated with ALP expression-osteoblast marker. In the animal model, PSA was positively detected in tumor cells, inoculated from human epithelial CaP cells, which were confirmed by Cytokeratin immunostaining. In addition, bone related molecules, Collagen type I, Osteonectin, Osteocalcin and TGF-β1 were also detected in both bone and cancer cells by immunohistochemistry. In conclusion, these in vitro and in vivo models have been used to

study the role of candidate genes in the progression of bone metastasis of prostate cancer. We have now introduced this valuable model into our studies of bone metastasis of Head and Neck Cancer at Griffith University.

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DENTAL EXTRACTIONS/ORAL SURGERY SAFELY UNDERTAKEN IN PATIENTS ON BISPHOSPHONATE THERAPY: A PROSPECTIVE TRIAL

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Purpose: A review of a prospective trial of patients who have undergone oral surgical procedures – dental extraction - whilst being on bisphosphonate therapy. Bisphosphonates have a high affinity for mineralised bone, leading to the inhibition of osteoclastic activity. Therefore, they are now widely used in the prevention and management of metastatic disease to the bone and in the treatment of all forms of osteoporosis. Worldwide, there have been reports of osteonecrosis of the jaw (''bis-phossy jaw'') occurring in patients receiving bisphosphonates, particularly those patients in which bisphosphonates have been part of their cancer therapy. Most have been associated with dental extractions and associated local infection. This has led to recommendations that dental extractions/oral surgery should not be undertaken in those patients taking bisphosphonates. At Westmead, we have developed a protocol, involving the pre- and post surgical administration of antibiotics, atraumatic extraction techniques, with primary closure for those patients who have been on long term bisphosphonate therapy.Results: To date 10 patients, median age of 64 (range 60–69) taking various bisphosphonates, have had teeth extracted, and on follow-up of up to 3 months, have not developed osteonecrosis of the jaw(s). **Conclusions:** There are an increasing number of patients who are likely to need and benefit from the use of bisphosphonate agents, particularly the more potent later generation agents. Prospective surveillance of such patients and removal of teeth with a poor prognosis prior to the commencement of bisphosphonate therapy is considered ideal. Nonetheless, protocols need to be developed for the safe oral surgery on occasions when such treatment is unavoidable. The protocol developed by us and outlined above may satisfy this need.

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THE USE OF CALCIUM SULFATE IN BONE LESIONS

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After removing a bone lesion, specially an extensive one,a cavity is left to repair. Literature presents calcium sulfate as being favorable to solve such situations. We conducted an histological study viewing the analisys of bone reactions to a biological material previously develloped by the authors to which was now added calcium sulfate. The material was inserted into cavities produced on 21 rats' tibias, and compared to a control group without any material. After 7, 14, 21, 30, 45, 60 and 90 days the animals were sacrificed and histological specimen were obtained (H.E.). Inflammation was observed, although it was always slighter and its resolution occured faster when compared to control;osteogenesis also took place earlier. The picture was the same in both groups after 60 days. It is possible to conclude that besides its biocompatibility, the material's use promotes an earlier restoration of the affected area, guaranty of security and effectiveness in a damaged area.

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HRPT2 GENE ALTERATIONS IN OSSIFYING FIBROMA OF THE JAWS

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Ossifying fibroma (OF) is a benign neoplasm primarily found in the mandible, composed of both osseous and fibrous components, being characterized by a progressive enlargement of the affected jaw. Recently, the candidate tumor suppressor gene HRPT2 was identified and alterations in this gene were related with Hyperparathyroidism-jaw tumor syndrome that is characterized by parathyroid adenoma or carcinoma, fibro-osseous lesions (mainly OF) of the jaws and renal lesions. The purpose of the present study was to evaluate the HRPT2 gene in OF. Tumour and blood samples were obtained from 3 patients with OF and one with juvenile ossifying fibroma (JOF). The results demonstrated three novel mutations in two out of three genotyped OF. Interestingly, one of these patients showed a germ-line mutation after blood analysis. RT-PCR amplification was performed to analyze HRPT2 mRNA expression and only wild-type HRPT2 transcript was found in all tumours. Investigation of the parafibromim protein by immunohistochemistry showed a similar pattern of immunolocalization with strong nuclear and cytoplasmic staining in all cases. In conclusion, the present study shows for the first time mutations of HRPT2 gene in OF and suggests that OF may arise due to haploinsuficiency of the HRPT2 gene.

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BISPHOSPHONATE-INDUCED OSTEONECROSIS OF THE JAWS: A REVIEW OF 4 CASES

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First reports of a possible relation between bisphosphonate use and osteonecrosis of the jaws surfaced in late 2003. Since then several case reports have appeared in the medical and dental literature that seem to support such an association. The use of long-term and high dose bisphosphonates was common to all these patients largely for the management of multiple melanomas and to control hypercalcemia of malignancy and bone metastases. **Objective:** A review of 4 patients with osteonecrosis of the maxilla and mandible in relation to bisphosphonate use. **Materials and Methods:** Patients who presented with osteonecrosis of the jaw bones and are on bisphosphonate therapy were seen at our clinic in the Department of Oral &

Maxillofacial Surgery, National University Hospital, Singapore were included in this review and their case records were retrieved and analyzed. **Results:** Our four patients were on IV zolendronate, which is an amino-bisphosphonate and presented first with pain in the affected jaw bones. Some patients developed swelling over the region which was subsequently followed by exposure of necrotic bone. All had a history of dental extractions or ill-fitting removable dentures whilst on bisphosphonate therapy. They were managed by sequestrectomy and alveoloplasty under antibiotics cover and antiseptic mouth rinse with minimal effects. Remarkably, the patients' complaints resolved when they were placed under careful oral hygiene regimes with oral antiseptic mouth wash without further surgical intervention. **Conclusions:** Minimal intervention safe for sequestrectomy appears to be the treatment of choice from a management stand-point with patients recovering from their symptoms spontaneously.

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POSTGRADUATE TRAINING IN AUSTRALIA AND NEW ZEALAND
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Oral pathology, either alone or with oral medicine, is recognised as a dental speciality in Australia and New Zealand, but there is lack of uniformity in registration requirements in the various regions. Training in oral pathology has traditionally been university based, with eligibility for specialist registration after a Masters degree (usually three years full-time study). In 1996, the Faculty of Oral Pathology (FOP) of the Royal College of Pathologists of Australasia (RCPA) was formed. Dental graduates, after undertaking accredited training, could now take examinations to become a Fellow of the FOP. Some State Dental Boards recognise the FFOP as a requirement for registration, but for most the Masters degree remains the requirement. Consultation between the State Boards, the Australian Dental Council, the Dental Council of New Zealand, the RCPA and the Universities is necessary to address these issues. Increased university tuition fees, scarcity of funded training positions and uncertain career opportunities has meant there are few applications for positions in oral pathology postgraduate programmes. Pathology laboratories in Australasia must be formally accredited to receive government funding for the tests they provide. Approved Continuing Professional Development (CPD) is mandatory for all Fellows of the RCPA and Dental Boards are increasingly requiring evidence of CPD before issuing annual practising certificates.

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POSTGRADUATE TRAINING PROGRAMS IN SOUTH AMERICA
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The analysis of the answers to a list of questions sent to heads of Departments of Oral Pathology of 10 Dental School of South America is presented. The aim of the questionnaire was to obtain information about the characteristics of the programs available to train oral pathologists and regulations to practice oral pathology in that part of the world. It was asked about number of postgraduate students per class, duration of the program, number of hours per week the students are requested for training (part of full time), percentage of lectures, seminars, microscopic slide work, experimental pathology, experience in immunopathology, rotations in general pathology and oncology services, clinical pathological sessions, training in clinical diagnosis and treatment of oral lesions, training in taking oral biopsies, interactions with other disciplines such as oral and maxillofacial surgery, oral and maxillofacial radiology, dermatology, internal medicine. Also, it was asked if the program counts on a biopsy sevice, if the oral pathology lab is part of a general pathology department in a hospital or it is a pure oral pathology laboratory located in a dental school. It was included also questions on requirements for enter to the program, official recognition as specialists in each country and requirements to practice oral pathology as specialist. Additional questions were addressed to know background of the staff, training fee, kind of document the trainee gets such as: Certificate, Title of Specialist in Oral Pathology, Master Degree.

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POSTGRADUATE TRAINING IN NORTH AMERICA
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Advanced education programs in oral and maxillofacial pathology in the USA are accredited by the Commission on Dental Education which derives its authority from the US Department of Education. The newest accreditation standards were effective January 1, 2000 and define the minimum standards for program compliance. The presentation will review the six Commission accreditation standards which include: Standard 1 Institutional commitment/ Program effectiveness/ Affiliations Standard 2 Program Director and Teaching Staff Standard 3 Facilities and Resources Standard 4 Curriculum and Program Duration Standard 5 Advanced education students Standard 6 Research The presentation will include an overview of the Commission on Dental Accreditation and the minimum requirements for the accreditation of advanced education programs in oral and maxillofacial pathology. Since all training programs must have access to an accredited independent laboratory, laboratory certification in the US will also be addressed. A complete text of the Commission's standards is available at http://www.ada.org/prof/ed/accred/standards/omp.pdf

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POSTGRADUATE TRAINING IN JAPAN AND ASIA
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It has been 15 years since the Board of Pathology for the Certifying Examination in Oral Pathology was started by the Japanese Society of Pathology. To date, there are 94 certified oral pathology specialists in this country. Most of them are faculty members of the 29 dental schools. They teach dental and

graduate students and practice surgical pathology services in their attached dental hospitals simultaneously. In such a situation, professional training for oral pathologists in this country is not only targeted towards diagnostic pathologists but also towards teachers as well as researchers. After graduates of dental schools are certified as dental practitioners by the national examination, they are obliged to take a one-year program for general dental practice. After this training, they can enter graduate schools for further professional training or obtain a fellow position in hospitals or private offices. Therefore, this is the only way for a dentist who wants to work as an oral pathologist to enter graduate school, although a PhD is not a requirement for qualification as a specialist. In graduate school, students have to spend most of their time on their Ph.D. thesis work, which is usually oriented toward experimental pathology. It is thus difficult for new PhD graduates to take the certifying examination, because the requirement for the board eligibility includes 20 autopsies and 1000 surgical pathology reports during at least a five-year professional training period. These graduates usually need to practice another two years or more in general hospitals to meet the requirement.

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POSTGRADUATE TRAINING IN AFRICA
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Oral Pathology is a registered speciality with the Health Professions Council of South Africa (HPCSA). Training takes place at four Universities with Dental Schools. Vacancies for training (registrar) posts are advertised in the national press and candidates must have a dental qualification registered with the HPCSA with two years post qualification experience. The training programme consists of a four year, full-time course leading to a Masters degree of which two years are spent in Anatomical Pathology. A research report (minor dissertation) is a requirement from all four the Universities. The course content is fairly similar between the different Universities as it has to comply with the minimum standards prescribed by the HPCSA. Internal and external examiners in the primary subjects and in both anatomical and oral pathology monitor the course and the examinations. The specialist training programmes of the different Universities are also inspected every four years by the HPCSA and amendments are made if recommended. A fellowship in Oral Pathology has been initiated by the South African College of Pathologists and discussions are currently underway to move towards a unitary final examination. This will go hand in hand with the development of a national framework for pathology programs under the auspices of the Federation of South African Societies of Pathology which will lead to an outcomes-based programme with unitary assessment of registrars while allowing the Universities their individual training programs.

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ORAL & MAXILLOFACIAL PATHOLOGY TRAINING IN THE UK
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Oral Pathology is a Dental Specialty overseen by the GDC. Entry to specialist training follows a two-year period of general professional training, comprising a year each in primary and secondary care. At present it is necessary to pass the Membership in Dental Surgery from one of the Royal Colleges in the UK or Ireland. Owing to changes authorised by the GDC, entry requirements may change from 2006. Specialist training takes five years in the NHS but may take longer (usually another 3 years) for those appointed to clinical academic posts where it is necessary to undertake a higher academic qualification. Posts and educational job descriptions are jointly approved for training by the Specialist Advisory Committee (SAC) of the Royal Colleges of Surgeons together with the Royal College of Pathologists. The national Lead Postgraduate Dean for the specialty confirms training numbers and funding for the post are available by liaising with the NHS Workforce Review Team. Training numbers are matched to local and national need based on impending retirements, weighted capitation and central or local funding. Appointment to posts is by competitive entry. Trainees are provided with an educational supervisor who does formal appraisal twice each year. There is an annual assessment by a panel led by the local postgraduate dean. This process checks that there is a completed and validated logbook, personal development plan, and CPD log that complies with GDC requirements. All trainers involved complete an SAC assessment form. The trainee also completes an evaluation of training received. Satisfactory completion of each year is required to progress, with funding, to the next year. Completion of all five assessments is required, together with completion of both parts of the MRCPath examination to obtain a Certificate of Completion of Specialist Training awarded by the GDC. Competency in histological diagnosis and report writing is required to various levels in eight diagnostic categories.

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PROGNOSIS IMPLICATION OF CASPASE-3 EXPRESSION IN MUCOEPIDERMOID CARCINOMA
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Purposes: We investigated the expression of caspase-3 in mucoepidermoid carcinoma (MEC) and its value in predicting the tumor behavior of MEC. In addition, correlation of caspas-3 expression with tumor angiogenesis, proliferation, and apoptosis were also examined. **Methods:** Caspase-3, CD34, and Ki-67 immunohistochemical staining and terminal deoxynucleotidyl transferase mediated dUTP nick end labeling (TUNEL) were evaluated. The correlations between these measures and the clinical–pathological features were investigated. **Results:** Peritumoral and intratumoral microvessel density (MVD) were 29.5 ± 10.4 and 19.5 ± 7.1, respectively. Intratumoral MVD was correlated with tumor stage. In cancer tissues, the mean proliferation index (PI) was 11.7% ± 5.9% and the mean apoptotic index (AI) was 4.1% ± 2.3%. The PI was significantly correlated with tumor grade, and the PI/AI ratio was significantly correlated with tumor size and stage.

Positive and negative cytoplasmic caspase-3 immunohistochemical expression was observed in 18 of 41 (44%) and 23 of 41 (56%) tumor samples, respectively. Positive nuclear caspase-3 staining was observed in 18 of 41 (44%) tumor samples in comparing to 23 of 41 (56%) negative cases. Cytoplasmic and nuclear caspase-3 protein expression was significantly correlated with the clinical stage of the tumor ($p = 0.002$ and $p = 0.018$, respective). Survival analysis revealed that nuclear caspase-3 expression significantly correlated with patient's survival. **Conclusions:** Our data suggest that intratumoral MVD, the PI/AI ratio, and caspase-3 expression are potentially useful markers of tumor progression in patients with MEC. In addition cytoplasmic expression of caspase-3 in tumor cells reflects the aggressive biological features. In contrast, high proportion of nuclear caspase-3 may be a benign feature in MEC.

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PRONOSTIC MARKERS IN THE MANAGEMENT OF SPORADIC ODONTOGENIC KERATOCYSTS AND ASSOCIATED BASAL CELL NEVOID SYNDROME

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Few studies have focused in the histological variants of odontogenic keratocysts (OKC) in sporadic and syndromic cases. The aim of this study was to analyze the immunohistochemical expression of PCNA, Ki-67 and p-53 in OKC and their association to nevoid basal cell syndrome (NBCS). Nineteen cases previously diagnosed as OKC at Oral Pathology Laboratory, Faculty of Dentistry, Central University of Venezuela, during 1995 to 2005, were studied. From these, 11 cases corresponded to sporadic parakeratinized OKC, and 7 cases were associated to NBCS and one case was orthokeratinized. 3 μm sections were obtained in each case to perform the immunohistochemical analysis, using primary antibodies (PCNA, Ki-67, p53) from Dako Envision System diluted 1:50; 1:25 and 1:25 respectively. The results showed 13/19 cases were positive to PCNA (68.42%), of the 7 cases associated to NBCS, 4 cases were positive to PCNA (57.14%). From the 11 sporadic cases, 9 cases were positive to PCNA (81.81%). Only one case of OKC not related to NBCS was positive for Ki-67. When analyzing p53 expression, only 5/19 cases were positive representing 26.31% and only one case (5.16%) was related to NBCS. We may conclude that PCNA was the most common expressed marker and frequently associated to sporadic cases, followed by p53. These results could suggest a cellular damage and could be related to a local aggressive behavior.

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IMPLEMENTATION OF VIRTUAL MICROSCOPY AND DIGITAL DELIVERY TECHNOLOGY TO ENHANCE STUDENT LEARNING OF PATHOLOGY

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Microscopy of pathological specimens is the staple of practical classes used to teach pathology. The pre-eminence of the microscope as a teaching device has only recently been challenged. This change has been necessitated by financial restrictions, a reduction in the amount of time allocated to instruction in pathology, a major shift in the design of new curricula, and a reduction in the number of academic staff members. In addition, students generally dislike using light microscopes for the examination of tissue specimens. A student-centred approach and the Seven Principles for Good Practice in Undergraduate Education underpin the strategy developed to solve this problem. This report describes the design and implementation of an educational intervention as part of an action learning project to enhance student learning of pathology in an undergraduate dental curriculum. The main focus is the implementation of virtual microscopy (ImageScope) and digital delivery technology (Blackboard) to enhance student learning of pathology, on a back drop of limitations in time for adequate face to face contact between teacher and student. 73.33% of students preferred using the virtual microscope compared to 25% who preferred the light microscope, with only one student having no preference (1.66%). In addition, 73.33% of students felt that the virtual microscope positively affected how they learnt, and 71.43% felt that it positively enhanced their learning of histopathology, while 59.65% felt that using the virtual microscope positively affected their grade for the course. With regard to the digital delivery technology, 91.07% of students found that having access to the autopsy cases on Blackboard and access to the virtual microscope slides together enhanced their learning of pathology. Overall, the introduction of virtual microscopy and digital delivery resulted in an enhancement of student learning seen in many subjective and objective outcome measures. This study emphasises that the introduction of new technologies to the learning environment only leads to innovation and improvement if the technologies are integrated into the curriculum rather than merely added on and used in a superficial way.

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ANALYSIS OF SIGNALLING PATHWAYS THAT MEDIATE TGF-β1-REGULATED APOPTOSIS IN MALIGNANT ORAL KERATINOCYTES

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Transforming growth factor-beta (TGF-β) is a well-recognised suppressor of epithelial carcinogenesis and this effect is thought to be mediated primarily through Smad4. We have previously shown that TGF-β1 induces the regression of oral carcinoma xenografts by sensitising cells to apoptosis through Smad4-independent mechanisms without altering cell proliferation (Thavaraj et al., 2005). This study examined the role of the mitogen activated protein kinase (MAPK) pathways in TGF-β1-potentiated apoptosis in vitro. The inhibition of JNK and p38, but not MEK, partially attenuated the ability of TGF-β1 to sensitise Smad4-deficient cells to cisplatin-induced apoptosis in vitro. The data indicate that Smad4-independent TGF-β1-induced sensitisation of oral carcinoma cells to apoptosis occurs through the activation of JNK and p38 pathways. In addition, this study also examined the relative contribution of the mitochondrial and death receptor

pathways of apoptosis in TGF-β1-induced tumour regression of Smad4-deficient oral carcinoma cells in vivo. Inhibition of the death receptor pathway by the over-expression of $cFLIP_L$ partially abrogated TGF-β1-mediated apoptosis and tumour regression, suggesting that TGF-β-regulated apoptosis in vivo may occur through death receptor-dependent mechanisms. By contrast, the attenuation of the mitochondrial pathway by the expression of dominant-negative caspase-9 did not alter TGF-β1-mediated tumour regression. The data highlight the ability of TGF-β to utilise MAPK pathways in sensitising oral carcinoma cells to apoptosis in circumstances where Smad4 expression is lost. Furthermore, the results of this study suggests that the local expression TGF-β may be of benefit as an adjunct to death receptor targeted therapeutic agents.

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P63 EXPRESSION IN BASAL CELL ADENOMA OF PAROTID GLAND

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Purpose: The P63 gene is a recently discovered member of the p53 family that is expressed specifically in embryonic ectoderm and in the basal regenerative layers of epithelial tissues in the adult. Recent studies have showed the p63 protein is consistently expressed in myoepithelial cells including those in salivary glands. The purpose of this study is to investigate the expression of p63 protein in basal cell adenoma of parotid gland. **Methods:** Immunohistochemical staining was performed in Formalin-fixed paraffin-embedded sections from 17 basal cell adenomas of parotid gland with a monoclonal antibody 4A4 to *Δ*Np63. The antibodies used as controls were anti-smooth muscle actin, anti–calponin and anti-S100 monoclonal antibodies. **Results:** Strong nuclear p63 reactivity was noted in all 17 cases of basal cell adenoma. The positive cells were situated at periphery of duct-like structure, epithelial stands or solid cellular nests, corresponding the modified myoepithelial cells. Immunostaining with smooth muscle actin and calponin antibodies got the same staining pattern as p63. S-100 immunostaining results indicated that the distribution of positive cell was irregular; they might be duct-lining cells, peripheral cells of duct and more frequently stroma cells. **Conclusion:** p63 is uniformly expressed by myoepithelial cells of parotid basal cell adenoma, p63 antigen may be a useful marker of myoepithelial cells differentiation in basal cell adenoma of salivary glands.

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IDENTIFICATION OF DIFFERENTIALLY EXPRESSED GENES IN ORAL SQUAMOUS CARCINOMA CELLS TREATED WITH INDIRUBIN DERIVATIVES

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A novel indirubin analog, 5'-nitro-indirubinoxime (011) inhibits cell proliferation and induces apoptosis against various human cancer cells. In this study, we performed the microarray analysis to identify genes differentially expressed in the KB oral squamous carcinoma cells after treatment with 5'-nitro-indirubinoxime (011). Of the 10,800 genes analyzed, 1700 genes (15.7%) showed different expression level in the 5'-nitro-indirubinoxime (011)-treated cells with respect to untreated control cells. Among those, 263 genes (15.5%) were down-regulated and 220 genes (12.9%) were up-regulated more than 2-fold. Functionally related gene clusters include genes associated with signal transduction (18.1%), especially genes related with apoptosis (3.5%) and cell cycle regulation (5.8%). Our application of microarray analysis on 5'-nitro-indirubinoxime (011)-treated oral cancer cells allows the identification of candidate genes for providing novel insights into the 5'-nitro-indirubinoxime (011)-mediated anti-tumor activity. *This work was supported by grant No. RTI04-03-03 from the Regional Technology Innovation Program of the Ministry of Commerce, Industry and Energy (MOCIE).

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ENHANCEMENT OF DNA VACCINE POTENCY AGAINST HAMSTER ORAL PAPILLOMAVIRUS-ASSOCIATED ORAL CANCER BY ELECTROPORATION IN VIVO

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In a previous investigation, we developed a highly reproducible carcinogenesis model by combining DMBA application with physical wounding of the hamster lingual mucosa. Using this animal model, we demonstrated the presence of a novel hamster oral papillomavirus (HOPV). Recently it has become clear that more potent methods for DNA vaccine delivery need to be developed to enhance the efficacy of DNA vaccines. In this study, we used this HOPV hamster model to compare the anti-tumor effectiveness of different procedures of DNA vaccine delivery, intramuscular injection alone or with electroporation (EP). Forty hamsters were divided equally into four groups. These groups were designated as V-E- (no treatment), V + E- (vaccination without EP), V-E + (EP without vaccination), V + E + (vaccination followed by EP). The animals in V-E- were injected intramuscularly with vector only, while those in V + E- were injected with DNA plasmids encoding the L1 gene. The animals of V + E + were injected DNA plasmids followed by EP, while those in V-E + were only injected vector followed by EP. Three weeks after the initial DNA injection, all animals were boosted with the same plasmids they had received initially. The lingual tips of hamsters were painted three times a week with DMBA for 8 weeks. The middle portion of the lingual tip was then excised under anaeathesia. Thereafter, the tips were painted daily with DMBA until the animals were sacrificed. The all hamsters of V-E- and V-E + groups showed lingual carcinoma. Some delays in cancer development in the hamsters of V + E- and V + E + group were observed. In paticular, in V + E + group, 9 hamsters showed no lesions. These results suggested that immunization with L1 DNA vaccines followed by EP in vivo delayed carcinoma development of papillomavirus-associated oral cancer, and it is therefore in vivo EP is a potent method for DNA vaccine delivery.

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CK7 AND CK20 CO-ORDINATE EXPRESSION IN SALIVARY GLAND NEOPLASIA

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The cytokeratin (CK) 7 and 20 immunophenotype can help discriminate between carcinomas of different primary sites and aid in the determination of the primary site of origin of metastatic carcinomas. Studies have confirmed the predominant CK7/CK20 co-ordinate expression in many carcinomas, including colorectal adenocarcinoma, pancreatic carcinoma, bronchoalveolar carcinoma, and prostatic adenocarcinoma. Even though there is great morphologic overlap between primary salivary adenocarcinomas and those metastatic to salivary glands, investigations pertaining to salivary gland neoplasia are lacking. **Aim:** To evaluate CK7 and CK20 co-ordinate expression patterns in salivary gland neoplasms. **Methods:** Formalin-fixed paraffin embedded tissue from 131 salivary gland tumours were evaluated independently by 2 different pathologists for CK7/20 immunoreactivity. The tumours included pleomorphic adenoma (22), myoepithelioma (9), adenoid cystic carcinoma (22), mucoepidermoid carcinoma (19), polymorphous low-grade adenocarcinoma (21), carcinoma-ex pleomorphic adenoma (10), acinic cell carcinoma (16), epimyoepithelial carcinoma (7), hyalinising clear cell carcinoma (1), papillary cystadenocarcinoma (1), salivary duct carcinoma (2), adenocarcinoma (NOS) (1) and squamous carcinomas (3). Recommended immunohistochemical staining procedures were performed on each case using the monoclonal antibodies CK7, OV-TL 12/30, CK20, Ks 20.8, and M515 CK AE1/AE3 in the presence of appropriate positive and negative controls. The results were expressed semiquantitatively, according to the estimated percentage of positive tumour cells: 1+ = 5–25%; 2+ = 26–75% and 3+ = 76–100%. **Results:** 100% of both the benign and malignant salivary gland neoplasms showed a CK7+/CK20- immunoprofile ranging from 5 – 100%. The squamous carcinomas showed negative CK7/20 immunoexpression. **Conclusion:** Whilst the CK7/20 immunoprofile is not useful in distinguishing amongst the various types of salivary gland neoplasms or between benign and malignant salivary gland tumours, it may facilitate in the differential diagnosis of a primary salivary gland neoplasm from certain metastatic tumours and squamous carcinomas, and in metastatic salivary gland tumours.

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INTRAORAL PRESENTATION OF ANAPLASTIC LARGE T CELL LYMPHOMA

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Anaplastic large T cell lymphoma involving oral cavity is initially identified as enlargements of the gingiva. This type of lymphoma occurrence in the oral mucosa is rare and not well documented. Anaplastic large T cell lymphoma is characterized by cellular pleomorphism and sinusoidal growth pattern. It revealed variable immunohistochemical pattern. We report a case of anaplastic large T cell lymphoma that 74 years-old Japanese woman with the enlargement of gingiva in upper and lower jaws. The mass had been present for three months and has not respond to a 1-week course of antibiotics. In palpation, lymph nodes were identified as elastic hard and small red-bean size in both light and left sub-mandibular area. A radiograph showed marked alveolar bone absorptions related to periodontitis in the upper and lower jaw with overlying soft tissue mass. An incisional biopy of the soft tissue enlargements was performed. The surgical specimen revealed an intact epithelial covering with diffuse proliferations of large pleomorphic cells within submucosa. These tumor cells showed ovoid nucleus with dispersed chromatin, prominent irregularly shaped nucleoli and observed a high frequency of mitosis. Immunohistochemical studies were carried out with 10% neutral buffered-formalin fixed, paraffin embedded tissue using CSAII kit according to the manufacture's instructions (DAKO). The majority of tumor cells stained strong positively for CD30, Ki-67, Vimentin, and positively for CD3 and CD45RO. While, tumor cells stained negatively for EMA, CD20, CD56, CD79a, Kappa chain, lambda chain and immunoglobulins. The staining result obtained anaplastic large T cell lymphoma, unless negative stained for EMA. Although involving oral mucosa id extremely rear, anaplastic large T cell lymphoma should be included in the different diagnosis and required immunohistochemical analysis to eliminate other malignant lesions.

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ABNORMALITIES OF E-CADHERIN EXPRESSION RESULTING FROM CPG METHYLATION PROMOTER OCCUR IN METASTATIC AND NON-METASTATIC ORAL SQUAMOUS CELL CARCINOMAS

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Loss of E-cadherin expression resulting from CpG methylation promoter has not been investigated in non-metastatic oral cancers as verrucous carcinoma. To further understand the alterations in the methylation profiles of E-cadherin in oral cancer, especially in tumors with lowest metatastic potential, we analyzed nine cases of verrucous carcinoma (VC), twenty oral well differentiated squamous cell carcinoma without lymph nodes involvement (SCC-pN0) and seventeen with lymph nodes involvement (SCC-pN+) by methylation-specific polymerase chain reaction. Immunohistochemical expression of E-cadherin was also performed. The frequency of E-cadherin gene methylation was 55.5% for VC, 60% for SCC-pN0 and 59% for SCC-pN+ and no statistically significant differences (p= 0,975) were found among the tumor groups. The immunohistochemical expression of E-cadherin in oral VC group was significantly higher (p=0.016) when compared to the others SCC-pN0 and SCC-pN+ groups. E-cadherin gene methylation status was not correlated with its abnormal immunohistochemical expression in oral VC and SCC-pN0 groups. All tumors of the SCC-pN+ group with unmethylated E-cadherin gene showed significant loss of E-cadherin immunoexpression (p=0.044). In conclusion, the alteration in immunohistochemical expression of E-cadherin resulting from

CPG methylation promoter is common and has also been shown to be heterogeneous in metastatic and non-metastatic well-differentiated squamous cell carcinomas. The presence of E-cadherin gene methylation in tumors with lowest invasive and metastatic potential as oral verrucous carcinoma suggests the early involvement of this epigenetic event in the multistep progression of oral carcinogenesis.

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CLINICOPATHOLOGIC SIGNIFICANCE OF HIF-1ALPHA EXPRESSION AND VASCULAR STRUCTURE IN ORAL SQUAMOUS CELL CARCINOMA

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Purpose: To examine the correlation of tumor hypoxia and vascular structure with presence of tumor-line vessel and tumor progression. **Methods:** Tumor hypoxia was evaluated by immunostaining of HIF-1alpha. Vascular structure of tumor tissue was examined by multiple staining of mural cell marker, alpha-smooth muscle actin (alpha-SMA) and basement membrane component, collagen type IV. Tumor-lined vessels were identified by double staining using the squamous cell marker cytokeratin, the endothelial marker CD34, and highlights red blood cells (RBC). Statistical analysis of HIF-1alpha; expression and presence of tumor-lined vessels with tumor size, clinical stage, and histologic differentiation was performed. Also, the correlation of HIF-1alpha; expression with vascular structure was analyzed. **Results:** High proportion of blood vessel in the tumor tissue was structural and functional abnormal and immature. Cases with positive HIF-1alpha;immunoactivity presented more tumor-lined vessel than those negative cases. HIF-1alpha; expression significantly correlated with tumor size, stage, histologic differentiation, and the presence of tumor-lined vessel. **Conclusion:** Tumor hypoxia represented with HIF-1alpha;expression, abnormal vascular structure, and presence of tumor-lined vessel may be the progression marker in oral SCC.

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THE EXPRESSION OF PDI (PROTEIN DISULFIDE ISOMERASE) IN POTENTIALLY MALIGNANT AND MALIGNANT ORAL MUCOSAL CONDITIONS

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Introduction: PDI is the most common reticuloplasmin representing more than 1% of soluble cellular proteins. Its role in early protein synthesis and possible control on cell cycle is well studied. PDI is highly expressed in ameloblastoma and parakeratinized odontogenic keratocyst. Interestingly, recent studies have revealed elevated PDI expression in bowel, lung and breast neoplasia. **Aim:** The aim of the present study was to assess if the expression of PDI can be used as a prognostic marker in premalignant oral mucosal conditions, and to compare its expression to p53 protein in the same sample. **Materials and Methods:** Formalin-fixed, paraffin-embedded archival tissues with histopathological diagnoses of fibroepithelial polyp (n = 14), oral lichen planus (n = 16), mild epithelial dysplasia (n = 15), severe epithelial dysplasia (n = 9) and oral squamous cell carcinoma (n = 15) were retrieved from our Oral Pathology Diagnostic Service archive. PDI rabbit antiserum was used as primary antibody which was visualized by DAB chromogen mediated by Streptavidin biotin complex. The same sections were also stained with p53 antibody. Slides were then scanned using ScanScope and the staining was mathematically graded by ImageScope software package and by two experienced oral pathologists independently in a blinded fashion. **Results:** Results showed no significant variation in the expression of PDI among the different clinical entities studied. The pattern of this staining is thus unsuccessful as an early marker of malignant potential of the oral mucosal lesions. p53 however showed upregulation in oral squamous cell carcinoma, followed by dysplasias, then lichen planus. **Conclusion:** PDI expression does not seem to have a potential role in assessing premalignant and malignant conditions in the oral cavity despite previous reports of over expression in non oral cancers. The use of computer mediated virtual microscopy proved to be a useful objective tool for immunohistochemical grading.

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ORAL PATHOLOGY IN EAST TIMOR, THE WORLD'S NEWEST NATION

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Purpose: East Timor presents an interesting spectrum of surgical pathology, including oral. In spite of being located in a betel-nut chewing cultural area, the oral tumours received from Dili National Hospital so far have not been betel nut associated. We describe two oral tumours, the first reported from this country. **Methods:** Surgical operations in East Timor are performed by local general surgeons and visiting subspecialist teams from the Royal College of Surgeons of Australasia. Histology is performed by volunteer pathologists around Australia. The present cases are: 1. A 35-year old Timorese male presented with a lesion of the left mandible thought clinically to be an ameloblastoma. The gross specimen consisted of grey/brown tissue 45x22x8 mm with a firm, grey cut surface. 2. A 16-year old Timorese girl presented with a tumour of the right mandible. The specimen consisted of 3 pieces of pale tan soft tissue measuring 5 to 10 mm each. **Results:** 1. Microscopy showed a biphasic tumour comprising cords and ducts of flattened and cuboidal epithelium dispersed in a loose fibromyxoid stroma without atypia. The diagnosis was odontogenic fibroma. 2. Microscopy showed fibrous tissue lined by squamous epithelium featuring a plexiform pattern and peripheral palisading of basal cell nuclei. The features were those of a unicystic ameloblastoma, plexiform type. **Conclusion:** Both these benign lesions have a low recurrence rate. Neither has a known environmental aetiology, and are not associated with alcohol, tobacco or betel nut. A possible reason we have not seen oral squamous cell carcinoma in an otherwise endemic part of the world

(Southeast Asia and Melanesia), is the pre-selected nature of the material sent from East Timor for histology. Only tissue of unusual interest is sent, and the majority of surgical specimens where the diagnosis is known grossly is discarded. Much work remains to be done on the epidemiology of oral neoplasia in East Timor.

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LIPOID PROTEINOSIS: REPORT OF FIVE CASES FROM IRAN

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Background: Lipoid Proteinosis or Hyalinosis cutis et mucosa is a rare autosomal recessive syndrome. It is characterized by the deposition of an amorphous hyaline like material (glycoprotein) in the mucous membrane and skin. The cutaneous manifestations are papules, nodules, pustules and acneiform scars. Moniliform blepharosis (small papules along the border of eyelids) and hoarseness are the most diagnostic feature of this syndrome. In the mouth, mucosa is rigid and nodular lesions are presented on the lips. The tongue is rigid with a little movement. **Report of cases:** We report five cases of this rare syndrome from two families. All of the patients are female. They have the typical signs of this rare syndrome. From two of them biopsy were done and examined by a pathologist. It is also reexamined in two other pathology centers. Skull radiography was done for all of them. Suprasellar Calcification was seen in four of the patients. **Discussion:** Lipoid Proteinosis is a rare syndrome. Up to now More than 250 cases have been reported. It seems that this syndrome may be not rare in Iran. In two families only female members are involved. In other reports of this syndrome male members might be also involved.

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A COMPARATIVE STUDY OF FINE NEEDLE ASPIRATION CYTOLOGY (FNAC) AND HISTOPATHOLOGY IN SALIVARY GLAND LESIONS

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Purpose: To evaluate the efficacy of FNAC in the diagnosis of salivary gland lesions and to correlate with histopathological findings. **Methods:** This was a cross- sectional study of salivary gland lesions. FNAC and histological correlation was done in 58 cases. The most frequently involved sites were the parotid and the submandibular glands (46.55% each), followed by minor salivary glands (5.16%) and the sublingual gland (1.72%). **Result:** Cytologically, the lesions were categorized into benign cystic lesions (13.79%), inflammatory lesions (13.79%), benign neoplasms (50%), malignant neoplasms (15.52%) and inconclusive cytological findings (6.9%). Histologically, 47 benign (81.05%) and 11 malignant (18.95%) lesions were diagnosed. Of the benign lesions, inflammatory lesions accounted for 22.40%, benign non-neoplastc lesions-3.45% and benign neoplasms- 55.20%. The most commonly diagnosed lesion was pleomorphic adenoma (41.4%). The overall sensitivity, specificity and diagnostic accuracy of FNA cytology was 81.82%, 100% and 96.5%, respectively. There were 2 false- negative cases and no false - positive cases in this study. **Conclusion:** FNAC has a high diagnostic efficacy in diagnosing salivary gland lesions, although limitations were encountered in predicting specific type of lesions in malignancies and cystic lesions. Therefore, this technique is a safe, quick and reliable technique in early diagnosis and treatment of salivary gland lesions.

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ORAL LICHEN PLANUS IS ASSOCIATED WITH THE USE OF THYROXIN MEDICATION. A STUDY OF A FINNISH POPULATION

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Purpose: The purpose of this study was to compare the prevalence of medical conditions and medications in patients with oral lichen planus (OLP) or oral lichenoid lesions (OLL) and in an age and gender matched control group. Our hypothesis was that thyroid hypofunction and thyroxin medication is more prevalent in patients with oral lichen planus or lichenoid lesions than in the general population. **Methods:** We collected data from 222 OLP and OLL patients (157 females and 65 males) from our patient registers at the Institute of Dentistry, University of Oulu, Finland and at the Dentistry and Oral Diseases Clinic, Oulu University Hospital, Finland. The diagnosis of OLP and OLL was based on accepted histopathological and clinical criteria. The control group consisted of 222 randomly selected age and gender matched patients with no records of OLP or OLL from the registers of Institute of Dentistry, University of Oulu, Finland. Medical history of the study and control groups was studied and analysed with SPSS and SAS statistical software. The level of statistical significance was set at $p \leq 0.05$. **Results:** We found that thyroid disease was present in 31 (14%) of patients with OLP or OLL. and in 18 (8.1 %) of the controls. The most common disease was hypothyreosis, which was present in 21 (9.4 %) of the study group and in 11 (5.0 %) of the control group. 21 (9.5 %) of the OLP/OLL patients had thyroxin medication compared to 11 (5.0 %) of the control group ($p = 0.0487$). **Conclusions:** The association of thyroid gland hypofunction and thyroxin medication to OLP or OLL has not been studied before. In our study a statistically significant correlation between OLP/OLL and thyroid gland hypofunction and thyroxin medication was found.

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5-AZA-DEOXYCYTIDINE AND DNMT1 SIRNA INHIBIT DNA METHYLTRANSFERASE 1 IN SALIVARY ADENOID CYSTIC CARCINOMA CELL LINES

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Purpose: To knockdown the DNMT1 in salivary adenoid cystic carcinoma cell lines and lead to demethylation and reexpression of E-cadherin gene. **Materials and methods:** Salivary adenoid cystic carcinoma cell line Acc-2 was incubated in culture

medium with 2 × 10-3M 5-aza-deoxycytidine for 7 days with medium changes on days 1, 3,5 and 7, and cells were harvested and total DNA and RNA extracted on day 7. The expression of DNMT1 and E-cadherin mRNA was analyzed by reverse transcription-PCR (RT-PCR). Sodium bisulfite-treated genomic DNA was amplified by methylation specific PCR(MSP) to assess the promoter methylation status of E-cadherin gene. 4 siRNAs targeting DNMT1 were designed, prepared and transfected to cells of adenoid cystic carcinoma cell lines, Acc-2, Acc-3 and Acc-M. Total RNAs were extracted and quantified in 24, 48 and 72 hours respectively. cDNA was generated with 2 μg of total RNA. The inhibition of DNMT1 was analyzed by PCR and quantitative real-time RT-PCR. GAPDH labled with Cy3 was used as positve control. **Result:** After treated with 5-aza-deoxycytidine for 7 days, DNMT1 was down regulated in Acc-2 and resulted in decrease of methylation level at the E-Cadherin promoter and reexpression of the gene. 2 of the 4 siRNA can effectively knockdown the mRNA expression of DNMT1 in Acc-2, Acc-3 and Acc-M cells. Reduction of DNMT1 was greatest in 48 hours. DNMT1 level decreased up to 75.85%,85.64% and 81.31% in Acc-2, Acc-3 and Acc-M cells respectively. These gene silencing effects diminished in 72 hours. **Conclusion:** Both 5-aza-deoxycytidine and siRNA can inhibit the expression of DNMT1 in Acc cells. 5-aza-deoxycytidine can lead to demethylation and reexpression of E-cadherin gene in Acc-2. Further investigations to detect how siRNA influences the DNMT1 protein expression and methylation status of tumor suppress genes will be performed.

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EFFECTS OF KHAT (CATHA EDULIS) ON NORMAL HUMAN ORAL CELLS

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Background: Khat (Catha edulis) chewing is widely practised in parts of the Middle East and Eastern Africa, yet the studies on the potential side effects are scarce. Some studies have found an association between khat use and various oral conditions including hyperkeratosis and oral cancer **Aim:** This study sought to determine the cytotoxic potential of an extract of khat and khat specific alkaloids on primary normal oral cells. **Methods:** Normal keratinocytes and fibroblasts were isolated from samples taken from the buccal mucosa of adult volunteers undergoing surgical removal of wisdom teeth. The cells were cultured in their standard media supplemented with the test substances. Morphological changes were used to assess the cytotoxic effects. Viability was evaluated using Trypan dye exclusion while DNA stains (Hoechst 33342, PI and YO-PRO-1); TUNEL and Annexin V assays were used to investigate the mode of cell death. **Results:** Morphological signs of khat cytotoxicity included cell shrinkage, membrane blebbing, detachment and complete disintegration. Nuclear chromatin condensation, formation of apoptotic bodies and results from DNA stains, annexin V and TUNEL assays provided evidence of apoptotic cell death. Khat extract at a concentration of 100 μg/ml induced significant chromatin condensation in fibroblasts (57.0 ± 10.1% $p < 0.00$) after 24 hrs compared to 100 μM of the alkaloids (8.8 ± 2.5%) and the controls (8.5 ± 2.3 %). **Conclusion:** Our results suggest that khat might damage the oral mucosa through induction of cell death and that the khat alkaloids probably play a less important role in this cytotoxicity.

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THE CHARACTERIZED ANALYSIS OF IMMORTALIZED HUMAN EPITHELIAL KERATINOCYTE ESTABLISHED BY TRANSFECTION TECHNIQUE OF E6/E7 GENES

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Cervical carcinoma is the 1st most common malignancy in korean females, and oral squamous cell carcinoma is in oral and maxillofacial area. High risk HPV types have been strongly linked to progression of cervical and oral carcinoma. E6 and E7 as a small DNA virus encoding two major oncoproteins of HPV can act together to produce efficient immortalization of primary human epithelial cells. In order to provide further evidence for the role of HPV in tumorogenesis, it is important to pursue the development of Immortalized human epithelial keratinocyte(IHEK) culture model which could be related to the pathogenesis between cervical and oral carcinoma. IHEK transfected by E6/E7 genes will be accepted as a model system for HPV-linked cervical and oral carcinogenesis. The purpose of this study were to culture primary normal human epithelial keratinocyte(NHEK), and to establish IHEK for studying cervical and oral carcinogenesis in the future. NHEK was primarily cultured under normal culture condition, and transformed into IHEK by transfection of E6/E7 genes. After 50 passages under 0.05mM Ca++ condition, IHEK was confirmed by growth curve, cornified cell envelope measurement, TGase 1activity, mRNA detection, tumorogenecity and anchorage independence assay. Cultured IHEK after 50 passages showed most basal cell and monolayer of polyhedral cells under 0.05mM Ca++, while small area of stratification and flattened epithelial cells with irregular border under 1.2mM Ca++. The cultured IHEK showed relatively resistant growth to high calcium condition and the E6/E7 mRNA in cultured IHEK by RT-PCR was detected. During the terminal differentiation the cultured IHEK showed less CEM and TGase 1 activity than those of cultured NHEK. Cultured IHEK showed non-tumorogenecity in nude mice, but week anchorage independence. It suggested that we had developed a technique to transform NHEK into IHEK by transfection of E6/E7 genes, and cultured IHEK might be established as intermediate stage cell for studying the pathogenesis of human cervical and oral carcinoma.

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LED IRRADIATION DECREASES COCL2-INDUCED APOPTOSIS IN HUMAN SH-SY5Y NEUROBLASTOMA CELLS

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It has been reported that light-emitting diodes(LEDs) can be used in the treatment of oral diseases. Although the

bio-stimulatory effects of LED irradiation have been well known, there are few reports about the molecular mechanism associated with inhibition of apoptosis by LED irradiation. The purpose of the present study was to investigate the effects of LED irradiation in CoCl2-induced apoptosis in human SH-SY5Y neuroblastoma cells. The source of light for irradiation was a continuous-wave LED emitting at wavelengths of 590 nm and 730 nm, and manufactured so that the energy density was 5 mW/cm^2 on the sample surface. After CoCl2 treatment, whether or not apoptosis was caused by CoCl2, apoptosis was monitored by several methods; cell viability assay, Diff-Quik (staining, DNA fragmentation assay and western blot assay. Effects of LED irradiation on cells were monitored using DNA synthesis assay with BrdU, and RNase Protection Assay (RPA) with various apoptosis-related molecules. In the cell viability assay, LED irradiation (at 590 nm for 80 minutes) showed more cell proliferation (about 20 %) than the control group. The RPA assay of SH-SY5Y cells using various apoptosis-related molecules showed that pro-apoptosis molecules such as Bax, Bak, and Bid were upregulated in the CoCl2 treatment group. The results demonstrate that LED irradiation can reduce the CoCl2-induced apoptosis by blocking some internal signaling pathway.

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EXPRESSION OF ADAM 12 (A DISINTEGRIN AND METALLOPROTEASE) IN POTENTIALLY MALIGNANT AND MALIGNANT ORAL MUCOSAL LESIONS

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Introduction: ADAM 12 belongs to a family of over 30 multifunctional glycoproteins that are bound to cell membrane and involved mainly in cell adhesion and ectodomain protein shedding. ADAM 12 upregulation is thought to accelerate tumour progression and invasion. There is recent evidence linking upregulation of ADAM 12 to breast, liver, gastric and oral carcinomas and to glioblastoma. **Aim:** The aim of this study was to assess ADAM 12 expression in potentially malignant and malignant oral lesions and to compare that to p53 protein expression in the same sample. **Material and methods:** Formalin-fixed, paraffin-embedded archival tissues with histopathological diagnoses of fibroepithelial polyp, oral lichen planus, mild epithelial dysplasia, severe epithelial dysplasia and oral squamous cell carcinoma were retrieved from our Oral Pathology Diagnostic Service archive. Immunohistochemical staining was performed and visualized by DAB chromogen mediated by Streptavidin biotin complex. Each slide was then reviewed and the degree of staining of the epithelium graded both mathematically using ImageScope software package and in a blinded fashion independently by two experienced oral pathologists. **Results:** Early results show overexpression of ADAM 12 in malignant and potentially malignant lesions consistent with the expression of p53. Computer-based assessment of the stain proved to be reliable and reproducible. **Conclusion:** There is good evidence that ADAM 12 expression can be used as a prognostic tool to assess the malignant potential of oral precancerous lesions.

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SOFT TISSUE TUMOURS OF THE HEAD AND NECK IN CHILDREN

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This is not going to be an exhaustive list of paediatric soft tissue tumours in the head and neck but those which have been encountered over the past 10–20 years at The Children's Hospital at Westmead. This presentation will highlight a range of paediatric soft tissue tumours in the head and neck which have been encountered over the past 10–20 years at The Children's Hospital at Westmead. The presentation is not intended to be exhaustive, but will concentrate on the clinical presentation, and macroscopic and microscopic features of myogenic tumours, adipose tumours, vascular lesions, and myofibroblastic lesions.

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ENAMEL AND DENTINE PATHOLOGY

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Developmental anomalies of the teeth may be acquired or inherited. Genetic disorders can be inherited as an X-linked, autosomal dominant or autosomal recessive trait. Sporadic cases are also encountered, some of which might represent new dominant mutations. Several classifications for the most common disorders, amelogenesis imperfecta and dentinogenesis imperfecta, have evolved. These are based primarily on phenotype, with the mode of inheritance being used in some systems as a secondary factor in allocating a case into a particular category. The benefits and shortcomings of these systems are reviewed. As a result of advances in molecular genetic studies in the past decade it has become apparent that there is considerable variability in the manifestations of different mutations in the same gene in both enamel and dentine disorders. Furthermore, mutations in different genes appear able to yield virtually identical clinical phenotypes. As we move further into an era of establishing the molecular basis of dental genetic disorders a robust mechanism for classification and cataloguing of these disorders is proposed which parallels systems used in medical genetics. This system is applicable to individuals and families irrespective of current or future knowledge of the molecular defect involved. This system is of probably of more benefit to these individuals and families than previous classifications.

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INHERITED DISORDERS OF BONE AND CARTILAGE - CLINICAL AND MOLECULAR UPDATE

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The inherited disorders of bone and cartilage (skeletal dysplasias) are a large, heterogeneous group of conditions caused by abnormalities in the development, growth and maintenance of the human skeleton. This talk will discuss the nosology and

classification of these numerous disorders, clinical approach to diagnosis, and the emerging clinical-pathologic-molecular correlations. Recently these rare disorders have provided a basis for understanding the pathogenesis of several common conditions including osteoarthritis, lumbar disc disease and osteoporosis and these insights and their ramifications will be discussed.

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CONTROVERSY OR CONSENSUS? IS ODONTOGENIC KERATOCYST REALLY A TUMOUR?
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There are some controversies regarding odontogenic keratocyst (OKC) nature. The aggressive behavior and high recurrence rate of OKC suggest a true neoplastic potential. Mutations in the tumor suppressor gene Patched (PTCH) were identified as the underlying genetic event in nevoid basal cell carcinoma syndrome (NBCC, Gorlin's syndrome) and sporadic OKCs. It has been proposed that the development of an OKC would follow the 'two-hit' model. According to this, odontogenic keratocysts present in NBCC arise from precursor cells that contain a hereditary 'first hit' and the allelic loss represents loss of the normal allele while sporadic OKC might arise from susceptible cells in which two somatic 'hits' have occurred. Surprisingly, a study performed by our group demonstrated that OKCs with PTCH mutations predicted to result in a truncated protein still have positive immunolabelling in immunohistochemistry reactions using antibody against the carboxy-terminal region of PTCH. This evidence suggests that OKC may arise due to haploinsufficiency of PTCH, which means loss of only 1 allele. Therefore, the cyst may arise through the same mechanism responsible for the developmental abnormalities present in NBCC syndrome. This last theory does not contradict the idea that OKC is a benign neoplasm because haploinsufficiency has been considered to be an important mechanism in the development of some human neoplasias. Finally, the hypothesis that OKC are neoplastic rather than developmental in origin is also supported by loss of heterozygosity of other common tumor suppressor genes in OKC cases.

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CHALLENGING CASES IN ORAL MEDICINE
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An increasingly wide spectrum of disorders can affect the oral mucosa, these sometimes reflecting emerging and re-emerging disease, changing patterns of population, improved care of congenital and acquired systemic disease, and increasing lifespan. Additionally patients have ever-increasing expectations for their oral health careThe lecture will comprise detail patients with oral mucosal disease that is complex and/or challenging to diagnose and manage. The clinical presentation, pathology and therapy of relevant disorders will be reviewed, and the challenges such disease bring to attending clinicians highlighted.

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INVESTIATION OF LYVE-1 POSITIVE LYMPHATIC VESSELS IN TONGUE CANCER
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Identification of lymphatic vessels has some difficulty, because lack of particular lymphatic marker. However, recently developed LYVE-1 and D2-40 were specifically reacted with lymphatic endothelium. We analyzed the distribution of lymphatic vessels in tongue cancer with LYVE-1 and D2-40 antibodies. Moreover, the association of LYVE-1 + lymphatic vessel density (LVD) and lymph node metastasis, tumor extent, invasion depth, histological grade and degree of lymphatic infiltration were studied. The LVD assessed number of lymphatic vessel enumerated under the microscope. Fifty-two cases of 10% buffered formalin fixed and paraffin embedded tongue carcinoma were obtained from the file of our department. Serial sections were made and immunosatined with CSAII Kit (DAKO) followed by manufacture's instructions. Antigen retrieval steps were performed before immunostaining. Polyclonal LYVE-1 and D2-40 preferentially identified lymphatic vessels. High LVD was found in the muscles compared within the submucosa by using LYVE-1, while D2-40 was failed to detect lymphatics in the muscles. Tumor invasion into lymphatic vessels was found in 5 cases, which were identified at the peritumoral fibrous connective tissue (PFT) and peritumoral submucosa (PSm). The LVD of PFT, PSm and intratumoral area (IT) were lower than that of tumor free area. Multivariate analysis demonstrated that LVD in PFT and PSm were not associated with regional lymph node metastasis ($P < 0.05$ and $P < 0.01$ respectively). These results indicate that the LYVE-1 is a stable marker to identify the endothelial cells of lymphatic vessels in normal and pathological conditions. The discrepancy from multivariate analysis and lymph node metastasis frequency lead that the lymphatic vessels may easily degrade by inflammatory condition and proteinase synthesized from the tumor cells. However, tumor growing in size and increased volume of stroma were indicating increased level of LVD in the tumor.

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A PATHOLOGICAL STUDY OF SKIN WOUND HEALING IN TYPE II DIABETES MODEL MOUSE
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The purpose of this study was to elucidate mechanism of wound healing delay. Full thickness skin wounds were created to both normal and type II diabetes mellitus model mice female BKS.Cg- + Leprdb/ + Leprdb/Jcl (db/db mice, mean body weight 40g). Both db/db and normal mice were divided into these groups such as 0, 3 and 7 days after operation. At 0 day, db/db and normal mice skin wounds were created and sacrificed straight away. Histopathologically, hematoxylin-eosin staining showed slightly inflammatory response characterized mainly by neutrophils was recognized, around the edge of the wound of db/db and normal mice. At 3 days after operation, db/db and normal mice were sacrificed. Histopathologically,

necrosis was observed in the wound area. Moderate amount of inflammatory cells, mainly neutrophils were found. Capillary dilatation was also identified in db/db mice. Granulation tissue formation in db/db mice was unremarkable in comparison with normal mice. At 7 days after operation, neutrophils were still the main inflammatory cells observed under the regenerated epidermis of db/db mice. As for the normal mice, the regenerated epidermis almost covered the wound area. Histopathologically, using toluidine blue pH2.5, the mast cells were seen in the wound area. The peak of mast cells number was significantly different between db/db and normal mice on each time after operation, indicating a delay of the wound healing in db/db mice (Welch's t-test). Immunohistochemically, increase of iNOS-positive fibroblasts was observed in wound area of db/db mice compared with that of normal mice. From these results, the delay of the wound healing in db/db mice was closely associated with typeIallergic reaction, by increased mast cells and elongation of the state of purulent inflammation. In addition, the appearance of the mast cells and iNOS-positive fibroblasts might be related to inhibit fibrogenesis during wound healing of the skin in db/db mice.

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CLINICAL AND BIOLOGICAL BEHAVIOR OF ORAL BASALOID AND CONVENTIONAL SQUAMOUS CELL CARCINOMA BASED ON PCNA, E-CADHERIN AND BETA-CATENIN EXPRESSION

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Seventeen cases of basaloid squamous carcinoma (BSC) localized exclusively in mouth, diagnosed and treated from 1970 to 2000 at Department of Head and Neck Surgery and Otorhinolaryngology of Cancer Hospital A. C. Camargo, were compared to 26 cases of squamous cell carcinoma (SCC) poorly differentiated (PDSCC) and 28 cases of well to moderately differentiated SCC (W/MSCC) matched by stage and tumor site. It was evaluated some characteristics like gender, race, tobacco, alcohol abuse, localization of primary tumor, stage by TNM system, treatment, occurrence of local and cervical recurrence, regional lymph node and distant metastasis and second primary tumors. In addition, PCNA, E-cadherin and β-catenin expression in BSC, PDSCC and W/MSCC were evaluated in relation to their clinicopathological features and prognostic values using Kaplan-Meier method and Cox regression models. No statistically significant differences were found among all three groups in regard to clinical features and immunohistochemical reactivity for PCNA. Reduction or absence of E-cadherin staining observed in more than 80.0% of PDSCC and BSC and it was statistically significant when compared to W/MSCC ($p = 0.019$). A strong expression of β-catenin was observed in 26.9% of W/MSCC, 20.8% of PDSCC and 41.2% of BSC. The 5-year and 10-year overall and disease-free survival rates demonstrated no significant differences among BSC, PDSCC and W/MSCC groups and the PCNA, E-cadherin and β-catenin also showed no prognostic value. Metastasis in regional lymph node (N+) was an independent prognosis factor for the oral BSC, PDSCC and W/MSCC patients. These results suggest that the clinical and biological behavior of BSC, W/MSCC and PDSCC of the oral cavity are similar when matched by clinical stage and tumor site. The histological grade in SCC or the microscopic tumor variant (BSC or SCC) is not a determinant parameter to predict the prognosis when these tumors present advanced clinical stage.

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INCREASED EXPRESSION OF GALECTIN-1 IN THE INVASION FRONT AND ADJACENT STROMA AS ADVANCED CLINICAL STAGE AND TUMOR THICKNESS OF ORAL SQUAMOUS CELL CARCINOMA

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Oral squamous cell carcinoma (OSCC) is one of the most common neoplasm worldwide. Metastasis is a final and fatal step in the progression of OSCC and it may occur in a small primary tumor, so early diagnosis for metastasis is important for its management. The molecular mechanisms of metastasis still need to be elucidated. In our preliminary studies, galectin-1 has also been proved to be one of significant up-regulated tumor-associated protein via the proteomics analysis in OSCC tissue. Galectin-1, a prototype of the galectin family, has been shown to play important functions in several aspects of cancer biology, including modulation of apoptosis, cell migration and adhesion, and immune modulation. Aggressive tumor behavior was correlated with the increased galectin-1 in the invasion front and the adjacent stroma of many types of tumors. In this study, a large number of specimens including 5 normal volunteer and 60 well-classified OSCC paraffin embedded tissues were examined the expression of galectin-1 in this specific area by immunohistochemistry staining. Galectin-1 expression was significantly up-regulated among samples of early clinical stage, metastatic phase and larger tumor thickness ($p < 0.05$). The transcripts expression analysis by the quantitative real-time PCR assay also showed the same phenomenon ($p < 0.05$). We also found that galectin-1 expressed higher correlation in these samples when focusing on cancer-associated stroma harvesting from laser-assisted microdissection ($p < 0.01$). This study contributes to elucidate the positive relationship of galectin-1 expression in adjacent stroma and clinical aggressiveness, which may validate a powerful diagnostic marker for oral cancer detection as well as the design of better therapeutic targets. The pathogenetic roles of galectin-1 expression for oral tumorigenesis deserve further investigation.

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THE TRANSCRIPTION AND EXPRESSION OF DRUG METABOLIZING CYTOCHROME P450- ENZYMES IN HUMAN SALIVARY GLANDS

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Cytochrome p450-enzymes (CYP) is a family of liver enzymes conducting a number of processes in the human body. The CYP1-3 subfamilies are the most important enzymes in phase 1 metabolism of drugs, but are also significant in the activation and inactivation of other exogenous substances. CYP expression and activity have been demonstrated in extra-hepatic human tissues. In this study the CYP1A2, 2D6, and 3A4 protein expression and mRNA transcription were examined in labial (LG), submandibular (SG), and parotid salivary glands (PG). **Method:** Sections of histomorphologically normal salivary gland tissue from LG (n:10), SG (n:5), and PG (n:10) were used for immunohistochemistry (IH) and in situ hybridization (ISH). For IH, deparaffinized sections were heated for antigen retrieval and incubated with primary polyclonal antibodies against the enzymes. For ISH, deparaffinized sections were treated with proteinase K and incubated with enzyme specific hybridization probes and a tyramid amplification system (Dako) was used for signal amplification. Absence or presence of IH reactions and/or ISH signal in the tissue components was based on consensus among three investigators. **Results:** In both LG, SG, and PG the cytoplasm of all segments of the ductal system showed positive immune reactions and ISH signal for all enzymes. The serous acinar cells of LG, SG, and PG were IH and ISH positive for CYP1A2, 2D6 and 3A4, however, considerable variations between adjacent cells were observed. In the cell periphery of the mucous acinar cells of the LG positive ISH signal but inconsistent immune reaction was seen, however, the mucous acinar cells of the SG were negative. **Conclusion:** Generally, the ductal system and, in varying degree, the serous acinar cells of the LG, SG, and PG show mRNA activity and CYP-protein expression. There are strong indications that human salivary glands have the potential for metabolism of drugs and other xenobiotics.

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ORAL MUCOSITIS IN FANCONI ANEMIA PATIENTS UNDERGOING ALLOGENEIC BONE MARROW TRANSPLANTATION

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Oral mucositis is frequently studied in samples where distinct types of diseases and conditioning regimens are grouped together. Objectives of this work were to verify the frequency of oral mucositis in patients diagnosed with Fanconi Anemia (FA) and possible risk factors to a higher grade and duration of mouth lesions. Thirty-four clinical charts were reviewed from patients who received allogeneic grafts, in the period between 1991 and 2001, from the BMT Unit/UFPR/Brazil. Maximum grade and duration of mucositis (WHO) were considered dependent variables. Pre and post-transplantation data were selected as independent variables. All non survivors until day +100 post-transplantation were excluded from the sample. Although Fanconi anemia patients were conditioned with ciclophosphamide, which is considered a less stomatotoxic drug, 97,05 % (n = 33) of patients presented grade 3 or grade 4 oral lesions. Mucositis maximum grade was inversely correlated to the methotrexate dose (p.0,048) but positive correlated to the duration of oral lesions (0,023). Number of infused cells was close to the level of statistical significance when compared to mucositis maximum grade (p.0,056). The mean duration of oral mucositis was 16,55 days (S.D. 5,48) and it was positively correlated to hospital length of stay (p.0,023). Samples stratified for type of diagnosis can be suitable for better understanding the underlying mechanisms of oral mucositis' natural history. This can lead to better prevention and treatment strategies. Methotrexate was not a determinant of higher grade or longer duration oral mucositis episodes. Oral mucositis duration was correlated to length of hospital stay and maximum mucositis grade could be influenced by the number of bone marrow cells infused.

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PILOMATRICOMA – AN EXPERIENCE IN EASTERN NEPAL

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Pilomatricoma are calcifying cutaneous tumor of the hair matrix cells. Few studies on clinical and histopathological spectrum of pilomatricomas are available from the western countries with occasional reports from Indian subcontinent. 5 years retrospective analysis from the requisition forms and case records of biopsy samples received in the Department of Pathology, B. P. Koirala Institute of Health Sciences, Dharan, Nepal, during January 2000 – December 2005 was done where pilomatricoma was reported as the final diagnosis to see the prevalence, common site, age of presentation and correlation between clinical and histopathological diagnosis in Eastern Nepal. Total numbers of cases studied were 21. The age of patients ranged from 11–70 years. Duration of lump varied from 5 months to 6 years. There were 6 males (28.5%) and 15 females (71.42%). 90.47% of the patients had solitary lesions. In 14 cases (66.67%) the tumor was located in the head and neck region ,the commonest site being face seen in 9 cases (64.29%). The size of the tumor varied from 0.2 – 3.0 cm. Only in 4 cases (19.04%), clinical diagnosis of Pilomatricoma was considered. 6 cases (28.57%) of Pilomatricoma cases were diagnosed on fine needle aspiration. Of the commonly reported features the presence of basaloid cells and ghost cells in cytology smears associated with a cutaneous location of the lesion was sufficient for a confident cytologic diagnosis of Pilomatricoma. In cytologic literature this lesion is a rarity. The main diagnostic pitfall on cytology is a false positive diagnosis of malignancy. The results of our study show that it is possible to arrive at a conclusive diagnosis of pilomatricoma on FNA smears after a careful analysis of all cytological features, even in cases with an uncommon clinical presentation. It is concluded that in pilomatricoma, FNA cytology is characteristic and will allow a conclusive diagnosis even in cases with an aberrant clinical presentation.

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FINE NEEDLE ASPIRATION CYTOLOGY OF TUMORAL CALCINOSIS: A STUDY OF 18 CASES FROM EASTERN NEPAL

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Calcific deposits in soft tissue are rare and may clinically resemble a tumour.Tumoral calcinosis is not a tumor in the neoplastic sense but is an encapsulated, saccular, multi-loculated calcific deposit . It seems feasible, therefore, to investigate them by the non-invasive technique of fine needle aspiration cytology (FNAC), however such investigations have been only rarely been used in view of few reports in the literature.In our study cases are described in which FNAC was indicative of tumoral calcinosis. The present study was conducted in the department of Pathology, B. P. Koirala Institute of Health Sciences, Dharan, Nepal over a period of five years from July 1999 to June 2005. Fine needle aspiration was performed using a 23 gauge needle and a 10 ml disposable syringe. Smears fixed immediately in 95% alcohol were stained with Papanocolaou stain. Air dried smears were stained with May-Grunwald-Gimesa (MGG). Tissue for histopathology was available in 8 out of 18 cases. Total numbers of cases studied were 18. Male to female ratio was 1:8. 11 cases (61.11%) were less than 20 years of age. In 3 cases (16.67%) history of trauma in the past was present. In 8 cases (44.44%) lesions were found in head and neck area. In 2 cases (11.11%) lesions were located in the hard palate region . The size of lesion varied from 2.5 to 4 cm. In none of the case diagnosis of tumoral calcinosis was considered clinically. All other investigations were normal and no significant family or medical history was present. Cytology in all cases showed only abundant acellular calcium. The patients on follow up were clinically well with no changes. The cases are interesting, since the cytohistological findings in the aspirate sample appeared to be strongly indicative of tumoral calcinosis. FNA along with clinical and radiological findings can help in prompt diagnosis of tumoral calcinosis in comparison to histopathology which is considered to be gold standard.

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PYOGENIC GRANULOMA – AN EXPERIENCE IN EASTERN NEPAL

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Pyogenic granuloma is relatively common benign vascular lesion of the skin and mucosa whose exact cause is unknown. A 5 year retrospective analysis (May 1999 – May 2005) of histopathological record of patients diagnosed as cases of pyogenic granuloma were done to analyze the prevalence, common site, age of presentation and to see correlation between clinical and histopathological diagnosis. Total number of cases studied were 175. The age of the patient ranged from 1.5 to 70 years. There were 89 (50.85 %) males and 86 (49.14%) females. Male to female ratio was 1.03 :1. All patients had solitary lesions. In 105 (60%) patients the tumor was located in head and neck region. The lip was the most common site (38%), followed by the nose (29%), oral mucosa (18%), and tongue (15%). The pregnancy tumor variant of pyogenic granuloma most frequently was found along the maxillary intraoral mucosal surface. 16 cases (9.14%) having oral mass were diagnosed as cases of granuloma pyogenicum in children in the present study illustrating the importance of formulating a more extensive differential diagnosis on discovery of an oral mass in children. Plethora of common clinical diagnosis made were papilloma (12%), sebaceouscyst (6.29%), parasitic lesion (3.43%), squamous cell carcinoma (3.43%),mucous retention cyst (3.43%) and naevus (2.86%). Pyogenic granuloma cases diagnosed clinically as cases of malignant melanoma are also been reported in 3.43% of cases. Pyogenic granuloma is a benign lesion; however, discomfort and bleeding occasionally may be significant. The latter may rarely be severe enough to cause anemia. Lesions that recur despite repeated excisions can be particularly problematic. A number of malignant tumors may clinically mimic pyogenic granuloma, making histopathologic confirmation important if the presentation is atypical.

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FINE NEEDLE ASPIRATION CYTOLOGY IN THE DIAGNOSIS OF CYSTICERCOSIS-AN EXPERIENCE IN EASTERN NEPAL

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Over a period of six years from September 1999 to August 2005, 72 cases of cysicercosis were diagnosed in the Department of Pathology, B. P. Koirala Institute of Health Sciences, Dharan, Nepal. All the patients presented with swellings of different regions of the body. FNA was performed with 22 gauge needle and 10 ml disposable plastic syringe. Aspirated materials were smeared onto the glass slides. Two slides were fixed immediately in 95% ethylalcohol and stained with Papanicolaou stain. Two air dried smears were stained with May-Grunwald-Giemsa stain. Cases which were biopsied were processed for histopathological examination, stained with hematoxylin and eosin. The age ranged from 1.5 to 76 years with peak incidence in 3rd – 4th decade. No sex predilection was noted. In 11 cases (15.28%) lingual cysticercosis was diagnosed which is a rare presentation. Clinically majority of the cases (98.7%) presented with a solitary lesion. Clinical diagnosis of dermatofibroma, neurofibroma and sebaceous cyst were given in 24 cases (33.33%). On cytomorphological examination, parts of cysticercus cellulose were seen in (97.22%) cases. In one case (1.38%) anaphylactic reaction was seen, smears of which showed many eosinophils in an inflammatory background. Cytomorphologic findings seen in the present study was predominantly bluish fibrillary glial like structure were seen. Outer wall layer was seen thrown into rounded wavy folds with tiny ovoid nuclei in a fribrillary stroma comprising of thin reticulin fibrils beneath it. In rest two of the cases (2.77%) diagnosis was suggested on associated other cytomorphologic features and inflammatory reaction comprising of eosinophils, neutrophils, histiocytes, epithelioid cells, lymphocytes and giant cells in varying proportions which were confirmed later on biopsy. Cytomorphologic spectrum of cysticercosis has been analyzed and studied for the first time from Eastern region of Nepal to the best of our knowledge.

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MUTATION AND EXPRESSION ANALYSIS OF AXIN1 GENE IN ORAL SQUAMOUS CELL CARCINOMA

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Purpose: To analyze the genetic alterations and expression levels of Axin1 in oral squamous cell carcinoma (OSCC) and to clarify whether Axin is involved in the pathogenesis of OSCC. **Methods:** Mutation analysis of Axin1 gene were performed by DHPLC and direct sequencing in 44 cases of OSCC patients, meantime, protein and mRNA expressions of Axin1 were detected by immunohistochemistry and in situ hybridization in these OSCC specimens. **Results:** DHPLC screening identified heterozygous elution profiles showing multiple peaks. Aberrantly profiles appeared in 26 oral squamous cell carcinomas. After sequencing analysis, four mutations and five polymorphisms were identified. One case of poor-differentiated oral squamous cell carcinoma with metastasis, contained two mutations, one of which revealed a T > G substitution at nucleotide 324 in exon 1 result in a glycine to stop codon substitution at amino acid residue 108, and the other revealed a A > G heterozygous mutation in the intron 7, locating very near to exon 8. In other two patients with moderate-differentiated oral squamous cell carcinoma and metastasis, a G > T heterozygous mutation at codon 488 in the exon 5 and a C > G substitution at intron 5 + 26 position were detected, respectively. Five frequent polymorphisms were also found in 44 cases of oral aquamous cell carcinoma with frequency of 64% (28/44), 14% (6/44), 9% (4/44), 23% (10/44) and 16% (7/44), locating at positions of codon 254 (GAT → GAC),condon 429(GTC → ATC), condon525 (GAC → GAT), codon609 (GCT → GCC), and intron 4 + 17 (G > A), respectively. Immunoreactivity for Axin was strongly positive in normal stratified squamous epithelium and localized in the cytoplasm and significantly reduced in most of the 44 primary tumours (35/44). **Conclusions:** Mutational inactivation and reduced expression of Axin1 gene may play a pivotal role in OSCC carcinogenesis and metastasis.

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RISK FACTOR ASSESSMENT IN SINGLE AND MULTIPLE ORAL PREMALIGNANT LESIONS

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Objectives: Oral premalignant lesions (OPLs) are usually associated with identifiable aetiological factors. However, it is still unclear precisely how these factors relate to clinical presentation. The purpose of this study, therefore, was to assess the diagnostic features of multiple OPLs, and to determine whether the severity of risk factors is related to the development of multiple rather than single lesions. **Material and Methods:** 63 consecutive patients presenting with either single or multiple OPLs were asked to complete a detailed-questionnaire covering demographic data, smoking and alcohol consumption, diet, use of medication, and sexual habits. Clinicopathological features of related OPLs were recorded. **Results:** 36 males and 27 females, age range from 31 to 91 years (mean 60.3), were recruited. 49 patients presented with a solitary lesion whereas 14 showed multiple OPLs at initial presentation. Most single lesions presented clinically as leukoplakia (57.1%), and the floor of mouth (46.9%) and lateral tongue (22.6%) were the most common sites. Moderate dysplasia was the predominant histopathological diagnosis. Leukoplakia was also the most common clinical appearance amongst multiple OPLs, but most of these lesions were situated on the buccal mucosa (34%). Mild and moderate dysplasia accounted for the majority of histological diagnoses (90%). No association was found between lesion type (Single/Multiple) and age, gender, smoking behaviour, alcohol consumption, medication status, or sexual behaviour. However, a significant association was found between lesion type and the number of fresh fruit/vegetable portions consumed perday ($p = 0.03$, χ^2). **Conclusion:** Multiple OPLs are more likely to occur in patients with a low level of daily fresh/fruit intake. Further studies with a larger population sample are required to investigate the relationship between single and multiple OPLs.

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INDUCTION OF APOPTOSIS BY INDIRUBIN DERIVATIVES AND ITS APPLICATION TO THE NEWLY DEVELOPED RAT TUMOR MODEL

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Indirubin is the active ingredient of Danggui Longhui Wan, a mixture of herbal medicine that is used to treat chronic myelocytic leukemia in traditional Chinese medicine. Here, we show that new indirubin derivatives, 5'-nitro-indirubinoxime, 5'-fluoro-indirubinoxime and 5'-trimethylacetamino-indirubinoxime, have potent anti-proliferative activity on various human cancer cells and oncogenic RK3E-ras rat kidney cells with IC50 concentration ranging from 1–25 μM. When the RK3E-ras cells were treated with indirubin derivatives for 24 h, the activity of caspase-3 and caspase-7 was induced followed by apoptosis. On the other hand, the activity of SAPK/JNK was inhibited over the same period. Indirubin derivatives also showed strong anti-tumor activity in rat solid and oral tumor models. The inhibition of tumor growth was observed in animals bearing RK3E-ras-induced tumor given subcutaneous dose of 100 mg/kg every other day for 10 days. Histologically, treatment of indirubin derivatives caused significant inhibition of tumor formation associated with increased apoptosis and decreased proliferation of tumor cells. These findings provide the potential value of indirubin derivatives as a novel candidate for anticancer agents. *This work was supported by grant No. RTI04-03-03 from the Regional Technology Innovation Program of the Ministry of Commerce, Industry and Energy (MOCIE).

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EPIDEMIOLOGY OF ORAL MALIGNANCY IN ZIMBABWE 1988–1997

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Population-based studies on oral cancer/malignancy epidemiology in Africa are scarce. This study analyses the pattern of distribution of oral cancer in Zimbabwe during the period 1988–1997, e.g. the frequencies, incidence rates and the cumulative (lifetime) risks in the study population by site, age, gender and race. A total of 873 cases of registered oral malignancy cases were accessed from the Zimbabwe National Cancer Registry (ZNCR) in Harare for the 10-year period. Oral cases contributed 1.8% of the total cancers recorded during the study

period with a high histological verification rate of 77.3%. Blacks were overall affected more than whites and males more than females (M:F ratio = 1.97:1). Whites had more squamous cell carcinoma (SCC) than blacks and lip cancer was 3-fold more common in whites. The palate and tongue were the most commonly affected sites in blacks and whites respectively. Inclusion of lip cancers in oral cancers raised the incidence rates and chances of developing oral cancer. Females irrespective of race had a higher risk of cancer of the lower lip. Kaposi's sarcoma (KS) and SCC constituted respectively 51% and 38.3% of the oral cancers; KS superseded SCC as the most common form of oral cancer after 1994. KS affected mostly the 25–29 female age group and the 30–34 male age group while SCC mainly affected the elderly. High oral cancer frequencies and rates in the young were predominantly due to KS which mostly affected the palate in blacks. Females had a greater burden of other oral malignancies (besides KS and SCC), which affected mostly the cheek mucosa. KS was the predominant HIV-associated malignancy during the study period. Although only 7 cases (0.8%) of non-Hodgkin's lymphoma were recorded in the study period, the Zimbabwean data suggest that the epidemiology of SCC in southern african countries with a heavy burden of HIV/AIDS is changing and that oral KS and oral lymphoma now constitute a largest portion of oral malignancies.

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EXPRESSION OF TGF-β1, MMP-1 AND TIMP-1 IN IRRITATION FIBROMA

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Background: Oral irritation fibroma (IF) is the most common tumor-like lesion. IF is characterized by over-production of collagen and, thus, resembles scar tissue. TGF-β1, MMP and TIMP play an essential role in remodeling extracellular matrix during scar formation. This study investigated the pathogenesis of IF with respect to the coordinated expression of wound healing-related factors. **Methods:** Proliferative activity and expression of TGF-β1, MMP-1 and TIMP-1 were observed using immunohistochemistry in 88 cases of IF and 9 cases of normal oral mucosa (NOM). **Results:** Expression of TGF-β1 and TIMP-1 were increased in IF compared to NOM. The proliferative activity of fibrous portion was increased in IF than that of NOM. MMP-1 expression of IF was not different from that of NOM. **Conclusion:** We propose that IF may be caused by increased expression of TGF-β1 and an imbalance between expression of MMP-1 and TIMP-1. This study was supported by the Foundation of NamSeoul University.

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IMMUNOEXPRESSION OF pRb AND EGFR USING TISSUE MICROARRAY (TMA) TECHNIQUE - A PRELIMINARY STUDY

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Purpose: To assess the expression of pRb and EGFR in oral epithelial lesions using TMA technique. **Methods:** Paraffin embedded specimens were selected from the archives of the Diagnostic Laboratories at the Faculty of Dentistry, University of Malaya and Universiti Kebangsaan Malaysia. Selected epithelial areas were cored and developed into tissue microarray blocks. A total of 32 samples for pRb and 50 samples for EGFR were analysed using immunohistochemical techniques. **Results:** Abnormal pRb staining (1+ or less) was seen in 80% (8/10) OSCC, 38.5% (5/13) dysplastic and 22.2% (2/9) normal/hyperplastic epithelium. Positive EGFR staining was observed in 25/35 (71.4%) OSCC cases with 11 cases (31.4%) showing staining of 2+ or more. Out of 5 epithelial dysplasia and 10 normal/hyperplastic epithelium, positive EGFR staining was noted in 3 (60%) and 8 (80%) cases respectively. Interestingly, only 1(20%) epithelial dysplasia and 1(10%) normal/hyperplastic epithelium showed staining of 2+ or more. **Conclusion:** High frequency of abnormal expression of pRb is observed in OSCC cases as compared to dysplastic and normal/hyperplastic epithelium. EGFR is expressed in OSCC as well as epithelial dysplasia and normal/hyperplastic epithelium. However, higher EGFR positivity is more common in OSCC cases. This study supports the feasibility and ease of using TMA technique for immunohistochemical studies.

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INTRAORAL MINOR SALIVARY GLAND TUMORS: A RETROSPECTIVE STUDY OF 61 CASES

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The purpose of this study was to analyze clinicopathological data of intraoral minor salivary gland tumors from the files of the biopsy services of the Dental School, Prince of Songkla University, Thailand. **Methods:** Retrospective review from archival specimens (1992–2005) encoded as salivary tumors. Microscopic slides of all cases were reviewed and the tumors were classified according to the WHO criteria 1991. **Results:** Sixty-one cases of intraoral minor salivary gland tumor were found. Salivary gland tumors of the lips were also included in this group. The age ranged from 7 to 73 years with a mean of 40 years. The gender distribution consisted of 39 females and 22 males, rendering a ratio of 1.8:1. Most patients had a presenting symptom of a painless swelling/mass for less than 6 months. Twenty-seven cases (44%) were benign (26 pleomorphic adenoma, 1 papillary cystadenoma), 32 cases were malignant, and two tumors were questionably malignant. The most common site was palate (48 cases; 61% malignant) followed by buccal mucosa (6 cases; 50% malignant), retromolar area (3 cases; all malignant), lip mucosa (2 upper, 1 lower; all benign), and posterior floor of the mouth (1 malignant case). The malignant tumors were primarily mucoepidermoid carcinomas, followed by adenoid cystic carcinoma and polymorphous low-grade adenocarcinoma; 78%, 12.5%, and 6.25% respectively. Surgery, either wide excision or partial maxillectomy was the main treatment modality. **Conclusions:** The reported demographics in the present study are in keeping with published reports. One of the main differences between this series and those previously reported relates to the higher incidence of mucoepidermoid carcinomas.

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THE USEFULNESS OF ACETIC ACID WASH AND CHEMILUMINESCENT ILLUMINATION (VIZILITE) IN THE VISUALIZATION OF ORAL MUCOSAL WHITE LESIONS

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A diligent and careful examination of the mouth and oral structures has been historically deficient in revealing pre-malignant and malignant oral lesions. Conventional screening practice for oral neoplastic lesions involves visual scrutiny of the oral tissues with the naked eye under projected incandescent or halogen illumination. Visualization is the principal strategy used to find patients with lesions at risk for malignant transformation; hence, any procedure which highlights neoplastic lesions should aid the clinician. This pilot study examined the usefulness of acetic acid wash and chemiluminescent light (Vizilite) in enhancing visualization of oral mucosal white lesions, and its ability to highlight malignant and potentially malignant lesions. Fifty five patients referred for assessment of a white lesion, were prospectively screened with Vizilite, and an incisional biopsy performed for a definitive diagnosis. The age, sex, and smoking status of all patients were recorded, and all lesions were photographed. The visibility, location, size, border, and presence of satellite lesions, were also recorded. The Vizilite tool enhanced intra-oral visualization of 26 white lesions, but it could not distinguish between epithelial hyperplasia, dysplasia, or carcinoma. Indeed, all lesions appeared ''aceto-white'', regardless of the definitive diagnosis. On one occasion, Vizilite aided in the identification of a satellite lesion that was not observed by routine visual inspection. Vizilite appears to be a useful visualization tool, but it does not aid in the identification of malignant and potentially malignant lesions of the oral mucosa.

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PREVALENCE OF TONGUE LESIONS IN GOLD COAST

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Purpose: While diagnosis of tongue lesions is an essential part of clinical practice, there is no systemic study in these lesions in the Gold Coast region (one of the Australia's fastest growing communities). The aim of the study was to investigate the prevalence of the different tongue lesions in Gold Coast, Australia **Methods:** The demographic and pathological data of tongue lesions in the Department of Pathology, Gold Coast Hospital in the period January 1998 – December 2005 were analysed. **Results:** One hundred and twelve patients (69 men, 43 women; M: F = 1.6:1) with tongue lesions were identified. Their ages ranged from 5 to 91 (median, 60). Four per cent (n = 5) of the tongue lesions were noted in the paediatric population (age < 20). Both benign and malignant tongue lesions were more often noted in the males. Pre-malignant and malignant tongue lesions were found in older patients when compared with benign ones (mean age = 63 versus 53, p = 0.001). Benign tongue lesions were seen in 56% of the patients (n = 63). The benign tongue lesions were often either non-specific inflammation (n = 15) or ulcer (n = 15). The other inflammatory related lesions were Candidiasis (n = 6), squamous hyperplasia (n = 7) and lichen planus (n = 1). The common benign tongue tumours were fibroepithelial polyp (n = 11) and cavernous haemangioma (n = 4). Other than these, there were 2 mucinous extravasation cysts and 1 neuroma found exclusively in the paediatric patients. One lymphoepithelial cyst was also noted. Pre-malignant lesions (squamous dysplasia or carcinoma-in-situ, n = 8) and carcinomas (n = 41) comprised 44% of the tongue lesions. Other than an adenocystic carcinoma, all the malignant tongue lesions were squamous cell carcinomas. **Conclusions:** A variety of benign and malignant lesions can be found in the tongue. Recognition of the prevalence and clinicopathological features of these lesions may provide useful information for improving the management of the tongue lesions.

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POST-KALA-AZAR DERMAL LEISHMANIASIS IN EASTERN NEPAL

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Background: Post-kala-azar dermal leishmaniasis (PKDL) manifests as a skin eruption after healing of visceral leishmaniasis .This study was undertaken to analyze the clinical and pathological features and to see cytological-histopathological correlation in PKDL cases in Nepal. **Methods:** We have studied 50 cases of PKDL from May 1998 to April 2005. The diagnosis was based on clinical presentation, positive slit skin smear and histopathologic studies. **Results:** There were 32 (64%) males and 28 (56%) females. Slit skin smears revealed Leishman Donovan bodies (LDBs) in 39 (78%) cases. Past history of kala-azar was present in 40 (80%) cases. Examination revealed that majority of patients presented with multiple types of lesion comprising of combination of macules, papules, plaques or nodules. The clinical features revealed that most patients showed polymorphic lesions (macules, papules, plaques, and nodules distributed symmetrically and in generalized manner) whereas a few showed extensive or limited facial involvement. In macular lesions, there was a sparse infiltrate of plasma cells, lymphocytes, or histiocytes in the upper dermis. There was a dense chronic inflammatory infiltrate comprising plasma cells, lymphocytes, histiocytes, and epithelioid cells in the entire dermis from papules, plaques, or nodules. Biopsy specimens revealed LDBs in 19 (38%) cases only. Fine needle aspiration from cervical lymph nodes in 3 (6%) cases demonstrated LDBs. **Conclusions:** PKDL in this region seems to be common. High positivity for LDBs were seen on slit smear examination of lesions.This study emphasizes the need to be aware that though the biopsy is gold standard for final diagnosis , LDBs were detected more in the slit smears (78%) as compared to detection of LDBs in 38% cases on histopathology of PKDL cases . Hence slit smear examination may be a useful investigation in PKDL cases as compared to Histopathology.

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FINE NEEDLE ASPIRATION CYTOLOGY (FNAC) DIAGNOSIS OF MYOEPITHELIOMA OF PAROTID GLAND

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Purpose: To avoid misdiagnosis of myoepithelioma from various dermal or subcutaneous tumours. **Methods:** Myoepithelioma is rare but well-characterized tumour, of the salivary gland is the best known. We report 2 cases of myoepithelioma of parotid gland diagnosed on fine needle aspiration cytology and latter confirmed on histopathology. All the 2 cases presented as pre-auricular and intra-auricular subcutaneous mass. The lesions were clinically suspected to be pleomorphic adenoma and benign skin appendageal tumor. The cytology and histopathology revealed that most of the tumour cells showed epithelioid features with oval or spindle eosinophilic cytoplasm. No ductal or syringomatous epithelial structures were observed. The tumour cells showed cytoplasmic immunoexpressions of S-100 protein. Gross specimen of all the 2 cases revealed well-defined mass in superficial lobe of parotid gland, confirming the parotid gland origin. Myoepithelioma of parotid can be presented as a slowly growing tumour of pre- or intra-auricular area. Clinically, it can be misdiagnosed as various dermal or subcutaneous tumours. All the two cases are presented for its rarity and to discuss pitfalls in the diagnosis on fine needle aspiration cytology. **Conclusion:** FNAC is a reliable and accurate method for the diagnosis of myoepthelioma.

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HUMAN PAPILLOMAVIRUS INFECTION IN THE ORAL CAVITIES OF NON-DENTURE WEARERS AND DENTURE WEARERS

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Purpose: Recently, it is reported that HPV infection was related to some factors including sex, age, occupation, smoking habit, alcohol consumption, denture wearing and others. The purpose of this study was to determine the frequency of human papillomavirus (HPV) infections in the oral cavity of dental patients with dentures. **Methods:** In this study, 23 non-denture wearers (11 men and 12 women) and 27 denture wearers (14 men and 13 women), aged from 50 to 81 (Av. 63.7 years old), were randomly selected from the patients in the Department of Prosthodontics, Aichi-Gakuin University Affiliated Dental Hospital. Oral squamous cells were collected from swabs of the buccal mucosa. For this procedure, informed consent was obtained. Extracted DNA was evaluated for HPV infections by PCR methods, using consensus and specific primers, and direct DNA sequencing analysis. **Results:** Twenty-four of 50 specimens (48.0%) were positive for HPV DNA. A statistically significant association was not found in the HPV positivity between men and women. The high rate of infection was recognized from 60 or more years old. A statistically significant association was found in the HPV positivity between non-denture wearers and denture wearers. Frequent HPV types in the specimens of all were HPV11, 4 and 16. In the non-denture wearers, HPV4 and 11 were frequently observed, while frequent HPV types in the denture wearers were HPV11, 16 and 4. **Conclusions:** The results of the present investigation indicated that HPV were present in the oral cavity, especially those of denture wearers. It is suggested, therefore, that the oral cavity of the patients with dentures was a reservoir of HPVs where later HPV-associated diseases, such as oral cancer and other oral lesions, might develop.

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AN ANALYSIS OF ORAL AND MAXILLOFACIAL PATHOLOGY FOUND IN ADULTS OVER A 30-YEAR PERIOD

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Background: The aim of this study was to determine the range of histologically diagnosed lesions in 44,000 oral and maxillofacial pathology specimens, from adults 17 years and older, submitted for diagnosis to our laboratory over a 30 year period (1973 - 2002). **Materials:** All entries for specimens from patients 17 years and older during the 30 year period 1973 - 2002 were retrieved from our computerised Foxpro database. There are fifteen diagnostic categories that contain codes for 627 diagnoses; for this paper the diagnoses were compiled into 12 diagnostic categories. **Results:** During the period, 44,007 specimens came from adults 17 years and older, with a male to female ratio of 0.9: 1. In addition, 4,406 specimens (8.2%) came from children 16 years and under; an analysis of these has been reported elsewhere. The diagnostic category with the largest number of specimens was mucosal pathology (36.0%) followed by odontogenic cysts (13.8%). Malignant tumours accounted for 5.4% of all specimens and benign tumours for 5.6%. **Conclusion:** The range of diagnoses is diverse. This survey has shown that while the majority of diagnoses are benign and often require no further management. However, a large proportion of cases such as dysplasia, lichen planus, mucous membrane pemphigoid and odontogenic keratocysts require long term treatment. Approximately 1 in 19 cases required major head and neck surgery for malignant disease.

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HEAD AND NECK SOFT TISSUE PATHOLOGY

L. Barnes
University of Pittsburgh, USA

This three-hour soft tissue seminar will cover eight benign and malignant soft tissue tumors of the head and neck with emphasis on vascular lesions. A standard didactic approach emphasizing the clinical, gross and microscopic features, immunoprofile, clinically relevant molecular-genetic data, differential diagnosis and treatment and prognosis will be utilized. Each participant will receive a comprehensive syllabus.

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PREVALENCE AND PATTERN OF DENTAL DEVELOPMENTAL ANOMALIES IN KOREAN CHILDREN

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Dental problems cause not only esthetic but dental problems such as functional disorder, dental caries, pulp disease and malocclusions, and in particular, masticatory problem falls on infants or children, which has effect on articulation disorder and emotional development as well as their physical growth. Therefore, it's important to detect dental problems early and to provide comparable indications. The purpose of this study was to find out the prevalence and pattern of dental developmental anomalies in korea. The clinical and radiographic examination was undertaken for 1,032 at age from 1 to 10 years and statistical analysis was done. Among the examined patients, 333 patients (32.3%) showed dental developmental anomalies. The prevalences of individual dental anomalies were as follows; congenital missing teeth 11.6%, supernumerary teeth 6.2%, taurodontism teeth 3.9%, fusion teeth 3.8%, microdontia teeth 3.2%, dens evaginatus teeth 2.3%, dens invaginatus teeth 0.6%, talon cusp teeth 0.2%, macrodontia teeth 0.1%, Dilaceration teeth 0.1%, transposition teeth 0.1%, inverted teeth 0.1%, amelogenesis imperfecta 0.1%. The anomalies of number(53.6%), the anomalies of shape(37.7%,) the anomalies of size(8.3%), the anomalies of position(0.3%) and the anomalies of structure(0.2%.) were examined. Most supernumerary teeth located on middle area showed inverted position and unerupted state. The most frequently missing teeth was the Mn primary lateral incisor(65.6%) and the Mn 2nd. premolar. In the case of deciduous congenital missing teeth, the prevalence of successive permanent congenital missing teeth(65.6%) was highest in Mn lateral incisors. The higher prevalence of microdontia teeth was Mx lateral incisor, dens evaginatus teeth was Mn 2nd premolar, dens invaginatus teeth was Mx lateral incisor, and taurodontism was Mn 1st. molar. Teeth play an important role for mastication, articulation, and aesthetic of adults as well as of children. The health of oral cavity could be kept by controling dental problems of children on the basis of the epidermiologic research of oral pathologic field.

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POLYOSTOTIC FIBROUS DYSPLASIA - A CASE ANALYSIS

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Background: Fibrous dysplasia of bone is a congenital non heritable disorder that was first reliably reported by von Recklinghausen, when he first described patients with pathologic condition of bone characterized by deformity and fibrotic changes that he termed as osteitis fibrosa generalisata. Fibrous dysplasia may involve one bone(monostotic) or multiple bones(polystotic) and occurs throughout the skeleton with predilection for long bones, ribs and cranio-facial bones. 70% of the lesions are monostotic, asymptomatic and identified incidentally. The polyostotic form of disease is often deforming and devastating with multiple skeletal complications like repeated fractures, limb length discrepancies and bone pains. The bone lesion of unknown origin is characterized by slow progressive replacement of normal bone by abnormal proliferative, isomorphic fibrous tissue. **Case Report:** This case report documents a 40 yr old male with severe polyostotic fibrous dysplasia that involved most of the skeleton including long bones of all extremities, pelvis, facial bones and skull base. Initial evaluation consisted of physical examination, plain radiographs which was followed by CT scan, SPECT scan, bio-chemical and hematological investigations and histologic examination. This poster stresses on the clinical implications and management of this rare debilitating disease.

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APERT SYNDROME - A CASE REPORT

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Background: Apert Syndrome /Acrocephalosyndactyly is a rare condition characterized by craniosynostosis. Though this syndrome was mentioned as early as 1842 by Baumgartner, the eponymic credit was given to Apert for presentation of the syndrome in 1906. Acrocephalosyndactyly is a variant of craniosynostosis characterized by acrocephaly and syndactyly of hands and feet often combined with anomalies of other organs. The syndrome has typical clinical features but the relative rarity (1/100,000 to 1/160,000 births) of the condition still poses a diagnostic dilemma. **Case report:** We present a case report of a ten year old male child who reported to the department of Oral Pathology and Medicine for treatment of mal-aligned teeth. Familial medical history revealed increased parental age (<40 yrs). Patients medical history revealed surgery for correction of cleft palate and syndactyly. Clinical and radiological exploration revealed Brachycephaly, Ocular proptosis, Hypertelorism and open mouth appearance. Skull radiographs showed increased digital markings (beaten metal appearance). Characteristic limb defects i.e. syndactyly of hands and feet (1st and 5th digits are joined to the middle digits 2nd, 3rd and 4th). Oral manifestations included cleft of hard and soft palate, maxillary hypoplasia with 'v' shaped arch, class III malocclusion, anterior open bite and anterior and posterior cross bites. **Conclusion:** Because the incidence of the syndrome increases with increased parental age, the importance of pre-natal diagnosis should be emphasized. Interdisciplinary approach using multiple surgical procedures for correction of cosmetic and functional defect. The dentist must be prepared for early diagnosis and treatment.

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ISOLATED NEUROFIBROMAS IN THE HEAD AND NECK: CLINICAL AND HISTOPATHOLOGICAL CONSIDERATIONS

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The neurofibroma occurs, in the head and neck region, as isolated or multiple lesion, frequently associated with neurofibromatosis. The aim of this study was to analyse the clinical and histopathological features of neurofibromas, particularly the plexiform type, located in the skin and in oral mucosa, and to discuss their pathogenesis as well as clinical management of isolated, sporadic lesion, unassociated with neurofibromatosis-1 (NF-1). Sixty six cases of neurofibromas from the files of Stomatology Department – Area of Pathology of the Bauru School of Dentistry and Lauro de Souza Lima Research Institute, were retrospectively reviewed. Clinical data, therapy and follow-up information were obtained from the medical records. Histopathological analysis of the neurofibromas was performed on paraffin sections routinely stained with hematoxilin-eosin. Some features such as cellular morphology, tissue organization, distribution of inflammatory infiltrate, presence of mast cells, and tactile-like bodies were investigated. The results showed a high frequency of cutaneous lesions (81,8%), as compared with those of the oral mucosa (18,2%), occurring mainly in females and patients older than 40 years. Isolated neurofibromas were found in 51.2% of patients and multiple lesions (37,2%) were often associated with the NF-1. Only two plexiform neurofibromas (3,0%), both arising in oral mucosa, were found and one of them, was associated with NF-1. Microscopically, diffused neurofibromas occured more frequently than the plexiform variant, and tactile-like bodies was observed in both variants. These results demonstrated that neurofibromas, particularly, the plexiform type, can occur in the skin and oral mucosa as a isolated lesion, not associated with the NF-1. The benign clinical behavior of the isolated, neurofibroma unassociated with neurofibromatosis, in the head and neck region, suggests a hyperplastic hamartomatous rather than neoplastic in nature.

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EFFECT OF BLEACHING ON THE CEMENTOENAMEL JUNCTION

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The purpose of this study was to evaluate in Scanning Electronic Microscope (SEM) the effects of bleaching agents on the surface of human cementoenamel junction (CEJ). Thirty human teeth were selected and sectioned longitudinally so sixty specimens were obtained. Thirty specimens served as controls and the other ones were bleached by six protocols: Group I- external bleaching with 10% carbamide peroxide (Opalescence, Ultradent Products Inc.); Group II- external bleaching with 35% hydrogen peroxide (Lase Peroxide, DMC Equipments); Group III- external bleaching with 35% hydrogen peroxide (Opalescence Xtra, Ultradent Products Inc.); Group IV- internal/external bleaching with 35% hydrogen peroxide (Lase Peroxide, DMC Equipments); Group V- internal/external bleaching with 35% hydrogen peroxide (Opalescence Xtra Ultradent Products Inc.) and Group VI- intracoronal bleaching with paste of sodium perborate mixed with 9% hydrogen peroxide. All of the specimens were examined in SEM. It could be observed on the control specimens all of the relationships between enamel and cementum: cementum overlapping enamel, enamel and cementum edge-to-edge and a gap between both tissues, exposing dentin. It was also evident the three types of CEJ on the same specimen. When comparing the bleached to the control specimens in SEM, it could be observed that all of the bleaching agents and techniques promoted changes of the CEJ. The gap type was the most observed on the bleached specimens. The bleaching agents used in this study caused severe alterations on the shapes of the cementoenamel junction increasing the exposition of dentin in this area and separating the enamel and the cementum.

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ORAL MANIFESTATIONS IN HIV-POSITIVE PATIENTS IN PRISONERS FROM BAURU, BRAZIL

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The dental professional plays a fundamental role in the early diagnosis, treatment and control of serum-positive patients for the Human Immunodeficiency Virus (HIV). Considering the great number of opportunistic infections that affect these patients, which may present early manifestations in the oral cavity, some of which have a relevant diagnostic and prognostic value, the aim of this study was to compare the oral manifestations between male HIV-negative and HIV-positive prisoners, from the Penitentiary "Dr. Alberto Brocchieri" of Bauru, Brazil, and correlate the oral manifestations of HIV-positive prisoners with the results of laboratory exams on T CD4 lymphocytes count, CD4/CD8 ratio and quantification of serum viral load. The HIV-positive prisoners presented a higher percentage of oral manifestations compared to HIV-negative, being 79.17% and 16.67%, respectively ($P < 0.05$). The most frequent oral manifestation among HIV-positive patients was periodontitis ($P < .05$), followed by gingivitis, candidiasis, and hairy leukoplakia. The reduction in T CD4 lymphocyte counts and the increase in the serum viral load are associated to the immunodepression and to the increased degree of severity of oral manifestations. The dental professional may recognize the oral manifestations of Acquire Immunodeficiency Syndrome (AIDS) by clinical examination, requesting laboratorial screening tests in the routine care of patients whenever HIV positivity is suspected. The results revealed the importance to include the dental professional in a multidisciplinary team for management of HIV-positive patients in order to combine efforts to improve the quality of life of these patients, aiding in the diagnosis and evaluation of course of the disease, since the oral manifestations may represent early signs of the disease, because of its correlation with worsened serum parameters.
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TRADITIONAL AND UNUSUAL EPIDERMAL CYSTS – A STUDY OF 500 CASES FROM EASTERN NEPAL

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An epidermal or epidermoid cyst is a common lesion formed by the downgrowth and cystic expansion of the epidermis, or of the epithelium forming the hair follicle. It should be differentiated from trichilemmal and dermoid cysts. A six and a half years year retrospective analysis of pathological record of cases diagnosed as cases of epidermal cyst in the Department of Pathology, B. P. Koirala Institute of Health Sciences, Dharan, Nepal was done. A comprehensive list of clinicopathologic findings were noted and the etiology of these cysts reported previously was reviewed. Total number of cases studied were 500. The age of the patient ranged from 1.5 to 87 years. There were 289 (57.8%) males and 211 (42.2%) females. Male to female ratio was 1.36:1. The mean age of the cases with traditional epidermal cysts was 50 years. History of traumatic episode was obtained in 9(1.8%) cases of cases. The mean size of traditional epidermal cysts was 1.7 cm. Common sites were hair bearing regions . Oral epidermoid cysts were seen in 9 (1.8%)cases.And epidermal cysts of lips were seen in 8 cases(1.6%). Only in 170 (34%) cases, clinical diagnosis of epidermal cyst was considered in the present study. 11% of the cases of traditional epidermal cysts showed focal absence of a granular layer .23% of the cases with traditional epidermal cysts revealed predominantly compact orthokeratotic cyst content. A hybrid feature, namely a combined feature of epidermal and so-called trichilemmal keratinization, was noted in 11% of the cases of traditional epidermal cysts. 17% of the cases of traditional epidermal cysts showed parakeratosis, whereas parakeratosis was found in all cases of epidermal cysts of the sole. Foreign body reaction around the cyst wall, namely granulomatous inflammation with foreign body-type multinucleated giant cells, was observed in, 1.8% cases of traditional epidermal cysts.

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ONCOCYTIC OR APOCRINE-LIKE APPEARANCE IN SALIVARY GLAND TUMOURS

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In order to clarify the polymorphism of salivary gland tumours, this retrospective study was performed to analyze the immunohistochemical distribution of oncocytic or apocrine-like cells in salivary gland tumours. Pleomorphic adenomas (PA), Warthin tumours (WT), adenoid cystic carcinomas (ACC) and mucoepidermoid carcinomas (MEC) were selected from the files of our laboratory. Primary antibodies used in the study were anti-mitochondria antibody (MIT) as an oncocyte marker and anti-growth cystic disease fluid protein-15 (GCDFP-15) as an apocrine marker. The positive immunoreactivity for MIT was identified in almost tumor cells of WT. The MIT-positive reactivity was also observed in ductal components of PA, MEC and ACC. In addition, positive immunoreactivity for GCDFP-15 was indicated only in the ductal components of PA. These results suggested that the oncocytic change was associated with the tumour growth not only in WT but also in PA, MEC and ACC. In addition, the apocrine-like change was related to polymorphism of PA, although no typical characteristics of GCDFP-15 were in WT, MEC and ACC.

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POLYMORPHOUS LOW GRADE ADENOCARCINOMA OF PAROTID GLAND: A CASE REPORT

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Purpose: Polymorphus low grade adenocarcinoma is rarely seen in the parotid gland.First case report from Nepal to best of our knowledge. **Methods:** A 63 years old female patient presented with the complaint of swelling in the right preauricular region for about 5 years which was gradually increasing in size. On examination, a firm mass measuring 5 x 3 cm was present. Clinical diagnosis of adenoid cystic carcinoma /pleomorphic adenoma was made. The mass was exised under general anesthesia.On gross examination the external surface was lobular in appearance,firm on touch and was measuring 5 x 4 x 3 cm in size. Microscopically the features were those of polymorphus low grade adenocarcinoma of parotid gland. **Conclusion:** The differential diagnosis includes benign mixed tumor, basal cell adenoma (both of which lack infiltrative features) and adenoid cystic carcinoma. The behavior of this tumor is that of a low grade malignancy. However it has been emphasized that first excision should be the most definitive and comprehensive as treatment of recurrent disease is rarely curative.

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AN ANGIOSARCOMA ON THE MAXILLA ACCOMPANYING WITH SEVERE BLEEDING - A CASE REPORT

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An angiosarcoma is relatively rare malignant vascular tumor that arises from various organs such as skin, liver, breast, bone and skeletal muscle. The oral and maxillofacial region is a rare site of angiosarcoma. We experienced a case of angiosarcoma in a 87-year-old man arising from maxillary bone. The patient complained of gingival swelling and bleeding at right upper canine area. First, the lesion was misdiagnosed as periodontal abscess by dental and medical clinicians of local clinic. Hematologic diseases were then suspected due to excessive spontaneous bleeding. Finally, surgical biopsy was performed for the diagnosis. Histologically, vascular structures with irregular arborizing pattern were surrounded by atypical polygonal endothelial cells. Immunohistochemical staining showed positive reaction for CD 31 and factor VIII and negative reaction for CD 34. The case was diagnosed as angiosarcoma, Grade II. We present this angiosarcoma with excessive gingival bleeding, concentrating on the importance of early differential diagnosis.

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RETIFORM HAEAMANGIOENDOTHELIOMA ARISING FROM TONGUE

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Retiform heamangioendothelioma or hobnail heamangioendothelioma listed in a new WHO classification is a very rare

variant of intermediate vascular neoplasms. It mostly affects skin or subcutaneous tissue of distal extremities, but no case involving oral mucosa except for composite type. We report a case of retiform haeamangioendothelioma of tongue. The patient was a 31-year-old Japanese male who visited our dental hospital with a chief complaint of a tumour in the anterior part of tongue. He noticed this tumour three years ago, but he had no treatment because of a painless mass. However, it rapidly grew before visiting our hospital. Clinical examinations revealed a smooth,reddish and elastic hard exophytic nodule. Excisional biopsy was performed under the local anesthesia. The excised tumour, measuring 15x10x6mm, showed solid and light brown in the cut surface. Formalin-fixed and paraffin-embedded specimen was routinely processed for histological examinations including immunohistochemistry using commercially available antigens: CD3, CD20, CD31, CD34, factor VIII-related antigen (FacVIII) and D2-40. Histological examinations revealed the proliferation of arborizing, narrow vascular channels. This nodule was covered by squamous epithelium without capsulation. Retiform vessels were lined with protuberant plump endothelial cells which had hyperchromatic nuclei demonstrating infrequent mitotic figures. These vascular networks were supported by prominent stroma with lymphocytic infiltration and a few lymphatic follicles. Immunohistologically, neoplastic cells were positive for CD31and Fac VIII, CD34 and D2-40. Infiltrating lymphocytes were somewhat CD3-dominant. Current case showed a characteristic ''retiform'' architecture mimicking retiform testes with peculiar tombstone or hobnail appearance and immunophenotypes, especially CD34 and D2-40 reactivities. It is thought that this case is the first report of pure retiform haeamangioendothelioma arising from oral mucosa.

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TWO CASES OF ACINIC CELL CARCINOMAS ARISING IN THE RANULA

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Acinic cell carcinoma, which is a malignant salivary gland tumor, is characterized by serous cell differentiation. In the literature, about 80% of acinic cell carcinoma occurs in the parotid gland, and less than 1% arises in the sublingual gland. In this paper, two cases of acinic cell carcinoma appeared as ranula and mucous cyst in the oral floor were examined histologically and immuno-histochemically. **Case 1:** The patient, a 42 year-old man, was admitted a painless swelling at the right side of floor of mouth. Clinically, fenestration of the cyst wall was performed under the diagnosis of ranula. However, recurrence of swelling was distinct eight month after the operation, and cystic lesion was resected surgically. In the pathological specimen, solid tumor mass of proliferating serous cells was recognized in the mucous cyst wall, continuing lining epithelium. **Case 2:** The patient, a 65-year-old woman, was clinically diagnosed ranula at the left side of floor of mouth, and fenestration of the cystic lesion was performed. In the resected tissue, solid tumor mass was observed at the cyst wall. These tumor cells showed clear cytoplasm and solid proliferative pattern with ductal structure. Immuno-histochemically, those tumor cells showed positive reaction for amylase and lactoferrin. Our pathological diagnosis of both case were acinic cell carcinoma, microcystic variant composed of acinar cells and intercalated duct cells type. On the histogenesis of this tumor, it is suggested that, tumor masses of the acinic cell carcinoma proliferate in the sublingual gland duct or at the portion close to the duct, and obstruct to form retention mucous cyst at the floor of mouth, in both cases.

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FREQUENCY OF DENTAL RESORPTIONS IN PATIENTS WITH ENDOCRINOPATHIES

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Some dental resorptions, especially those occurring during the use of orthodontic devices, were empirically related with systemic disorders, emphasizing the endocrinopathies. The endeavor of this research was to determine the dental radiographic profile of patients with endocrine disorders who had not undergone orthodontic treatment, in order to verify the correlation to the pathological etiology of root resorptions compared to the dental radiographic profile of healthy patients. The experimental sample consisted of ten experimental groups submitted to clinical and radiographic assessment. Nine groups were constituted of 10 patients each, respectively distinguished as: normal, with hypothyroidism, hyperthyroidism, hyperparathyroidism, diabetes mellitus type 1, diabetes mellitus type 2, menopause, micropolycystic ovaries syndrome and patients under use of oral contraceptives. The tenth group consisted of only one patient with hiperparathyroidism. The patients were individually analyzed. Systemic conditions, hormonal seric grades, as well as Ca, P, acid and alkaline phosphatases were compared according to an established clinical and diagnostic endocrinological protocol. Multiple root resorptions were not found in any patient. Some teeth presented isolated root resorptions due to chronic periapical lesions, classified as 1 or 2, considered questionable and incipient, respectively. The results allowed to conclude that endocrinopathies do not influence the etiopathogenesis of root resorption.

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IS ORAL LICHEN PLANUS A PRE-MALIGNANT LESION? EVIDENCE FROM A CASE REPORT

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It has been argued that Oral Lichen Planus (OLP) may increase the risk of oral cancer. Patients with OLP may be at an increased risk for developing of OSCC (Oral Squamous Cell Carcinoma) but a clear estimation of this risk is not available. Here we report a case of OLP initially presenting with a clearly benign LP(Lichen Planus) lesion that transformed into OSCC over a course of 16 months. This report provides a clear evidence for (LP) lesion as a potential pre-malignant state.

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OSTEOGLOPHONIC DYSPLASIA – ORAL AND DENTAL IMPLICATION
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Aims and Objectives: Documentation of oral and dental implications of osteoglophonic dysplasia. **Settings and Participants:** We had recently reviewed the oral and dental manifestations of a female with Osteoglophonic Dysplasia, aged 39 years who was first documented three decades ago. **Results:** This rare genetic disorder showed gross stunting of stature and was associated with severe craniofacial malformation and multiple unerupted teeth. Radiographically, multiple lucent lesions were present in the tubular bones and mandible and several impacted teeth were inverted. **Conclusion:** We concluded that prosthetic dental replacement in our patient would be difficult because of the distorted bony relationships and large alveolar ridges. Equally, craniofacial reconstruction might be compromised by obstruction of the nasal airways, difficulty in intubation and post-operative respiratory problems.

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POST RENAL TRANSPLANT ULCERATION; CASE REPORT AND MANAGEMENT
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Case presentation: A 24-year old Indian man who had preemptive living non-related renal transplantation in India, came in with painful oral ulcers, 3 months post renal transplantation. His primary kidney disease was Diabetic Nephropathy secondary to type 1 Diabetes Mellitus. He was on triple therapy: Prednisolone, Cyclosporine A and Mycophenolate Mofetil (MMF). The ulcers were initially thought to be due to Cyclosporin A, thus Cyclosporine A was switch to Tacrolimus. After a trial of 3 weeks on Tacrolimus, the ulcer did not resolved and he was admitted for ulcer biopsy. In the ward, we noticed that his absolute neutrophil count was as low as 0.8 x 109/L and he needed granulocytes colony stimulating factor (GCSF). His MMF was then discontinued. Histopathology showed a non-specific ulceration with deep-seated gram negative bacteria. He was treated with appropriated antibiotic and the ulcers gradually became less. **Diagnosis:** This case, report the incidence of severe oral ulceration with concomitant neutropenia secondary to MMF in renal transplant patient. Therapeutic management includes the use of anti fungal, antibiotics, wound healing promoter and symptomatic relief of ulcers. **Discussion:** Severe oral ulceration in an immunocompromised patient are generally due to heamatological disorder, malignancy, viral infection and drug induced. Cocktails of immunosuppresive drug had induced oral ulceration in this patient. This factor combined with severe leukopenia secondary to MMF, work synergistically to promote the progression of his oral ulcers. Withdrawal of MMF led to regression of the oral lesions suggesting that there was a strong causal relationship. Few similar case reports claimed that the resulting leukopenia could prolong the ulcerations up to 2-3 weeks. We concluded that in rare cases, MMF could induce severe oral infective ulcers secondary to profound leukopenia.

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MANDIBULAR METASTASIS OF THE BREAST CARCINOMA: A FOLLOW-UP OF 11 YEARS
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The oral metastases are rare and correspond only to 1% of all malignant tumors affecting the oral cavity. Breast and lung cancer are the neoplasms most frequently involved in this condition. At the diagnosis, the majority of the patients with metastatic tumors in the mouth present metastases in other parts of the body, being the palliative treatment the choose management. The main treatment of mandibular metastasis is radiotherapy to decrease the pain and lost function prevents. The follow-up of these patients has showed a poor prognosis with a mean general survival of 6 months.The patient AMS, female, 48 years old, with an invasive ductal breast carcinoma diagnosed in 1991 was treated with surgery and adjuvant radiotherapy. She developed mandibular and cervical column metastases 33 months after the diagnosis of the primary tumor. The mandibular metastasis was confirmed by incisional biopsy. At this time, the patient complained of difficult to open the mouth and pain in the mouth and cervical region. Tamoxifen were used for four years with the control of the metastases and the patient was asymptomatic. Then, the tamoxifen was cancelled and the patient presented very slowly progression of the mandibular metastasis for 7 years, without progression of the cervical metastasis. In 2005, there was an important progression of the mandibular metastasis and both cervical and mandibular metastases were treated with local radiotherapy. There were pain and trismus resolution and decreased the facial asymmetry. The follow-up is maintained and the patient is controlled until at the moment.

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BIOLOGICAL SIGNIFICANCE OF bcl2 IN THE DEVELOPMENT AND PROGRESSION OF ORAL SQUAMOUS CELL CARCINOMA
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Advances in molecular medicine have led us to understand that neoplastic cell growth results from disruption of normal mechanisms that regulate cellular proliferation, differentiation and cell death Apoptosis is a genetically determined process playing an active role in tissue size regulation, morphogenesis and in removal of cells that are infected or damaged that are potentially dangerous to their host. Normally, the elimination of genetically damaged cells by apoptosis precludes the development of tumors and plays a role in effective cancer therapy. However, an imbalance if the apoptotic pathway contributes to immortalization of replicating cells, thus favoring the accumulation of sequential genetic damage. Aberrations of the apoptotic

pathways in tumorigenesis as the potentially lead to reduced cell death promote resistance to therapy and favour the onset of transforming mutations. Various regulatory molecules play a role in apoptotic pathway. The bcl2 family of molecules orchestrates the apoptotic pathway. This family consists of pro-apoptotic molecules (e.g. BAX, BAK, and BID) and anti apoptotic molecules (e.g. Bcl2, BCL –XL) The anti apoptotic molecule Bcl2 are localized to membranes primarily of mitochondria, but also smooth endoplasmic reticulum and nucleolemma. Over-expression of bcl2 reflects on suppression of programmed cell death and extension of tumor cell life span This paper aims to explore the interplay of bcl2 family of molecules and its immunohistochemical expression during the development and progression of Oral Squamous cell carcinomas.

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ROLE OF FINE NEEDLE ASPIRATION CYTOLOGY (FNAC) IN DIAGNOSIS OF PLEOMORPHIC ADENOMAS

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Purpose: To determine difficulties encountered in the diagnosis of pleompophic adenoma on FNAC. **Methods:** This retrospective study was carried out in B.P Koirala Insitute of Health sciences from January 1999 –January 2005 to review the cases diagnosed as pleomorphic adenoma in major or minor salivary glands and determine the difficulties encountered on typing this tumour on fine needle aspiration cytology (FNAC). Over a 5-year period 48 pleomorphic adenomas were diagnosed on FNAC from different sites (parotid) – 27 cases, submandibular – 12 cases; oral cavity – 9 cases). Histology was available in 12 cases. On review 4 cases of the 12 cases were only initially diagnosed as pleomorphic adenoma is difficult to identify on FNAC. **Conclusion:** FNAC is an ideal, fairly accurate preoperative procedure for the diagnosis of pleomorphic adenomas.

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CEMENTOBLASTOMA : REPORT OF A CASE WITH A LONG PERIOD OF PAIN

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Cementoblastoma has shown to be a rare benign neoplasm of cementoblast origin which usually represents itself with distinct swelling and severe pain. According to the histopathologic evaluation in addition to radiographic findings, the case presented illustrates a benign cementoblastoma related to the first mandibular molar with a long period of dull pain. The etiology of this long period of dull pain in the case we reported may be the gradual compression of the inferior alveolar nerve by the neoplasm.