



DIAGNOSIS • TREATMENT  
EDUCATION & RESEARCH

## American Academy of Oral and Maxillofacial Pathology

# ABSTRACTS

Essay Program I

Tuesday May 11, 2004

1:00 p.m. – 5:15 p.m.

Abstracts 1-21

Roy Eversole, Presiding

Essay Program II

Tuesday May 11, 2004

1:00 p.m. – 5:15 p.m.

Abstracts 22-42

Brad Neville, Presiding

58<sup>th</sup> Annual Meeting

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Continuing Education Program

May 8 – May 12, 2004

The Mills House

Charleston, South Carolina

ESSAY PROGRAM I  
Tuesday, May 11, 2004

#1 1:00 p.m.

AROMATASE EXPRESSION IN ORAL MUCOSA AND SQUAMOUS CELL CARCINOMA. Y.Cheng, J. Kusek, and J. Wright. Baylor College of Dentistry-TAMUSHSC, Dallas, Texas

Aromatase is a cytochrome P-450 enzyme that catalyzes the conversion of androgens to estrogens. It has been found to be expressed not only in the ovaries and testes but also the extragonadal tissues such as skin, muscle, fat, bone and brain which contribute to the local estrogen formation in these tissues. Its increased expression in breast carcinomas also leads it to be a promising target of chemointervention for hormonal-responsive breast carcinomas. Aromatase expression has never been investigated in normal oral mucosa or in squamous cell carcinomas. Using Western blot and a commercially-available aromatase antibody, we found two immuno-reactive bands of 53 and 60 kDa in disperse-separated oral epithelium obtained from crown lengthening procedures. The two bands were also detected in the primary culture of normal oral epithelial cells (NOEC) from different individuals as well as an oral squamous cell carcinoma (SCC) cell line. However, in NOEC the 60 kDa band was considerably more prominent, while in SCC the 53 kDa was more predominant. Our results indicate that normal oral epithelial cells as well as oral squamous cell carcinoma have the ability to synthesize estrogen. Further immunohistochemical and RT-PCR studies are in progress.

#2 1:12 p.m.

INTERNET and DVD-BASED INSTRUCTION IN ORAL PATHOLOGY FOR DENTAL STUDENTS. NJ D'Silva, CT Hanks, B Andrews. U of Michigan, Ann Arbor.

In the past two years, the Maxillofacial Pathology Laboratory course for dental students at the University of Michigan, has been converted from a microscope-based course to an internet accessible, case-based learning experience that includes a cutting-edge virtual histopathology "laboratory". Essentially this strategy moved the pathology microscopy course out of the physical laboratory to an online, virtual laboratory with an associated pathology workbook. This has saved the students class time, eliminated the need to maintain or replace expensive microscopes, eliminated the space requirement for the laboratory and dramatically improved the quality of slides that students view. The new web-based system, has also optimized utilization of faculty. One faculty member now spends one hour, every other week reviewing the assigned cases, and projecting network images of unknown cases in conjunction with high quality virtual "slides". Bacus laboratories (Lombard, IL) developed the "virtual microscope" technology that allows tissue sections to be scanned, digitized and visualized at different magnifications on a computer, as one would with a real microscope. Furthermore, we developed a DVD version of the case-based pathology course to provide all students, even those who do not have a rapid internet connection, with off-site access to the pathology course. *Conclusions:* The online virtual laboratory and workbook give students the opportunity to reinforce concepts that they have passively acquired, by challenging them to "examine" the lesion, develop a differential diagnosis, and discuss further evaluation. This teaching approach utilizes the behavioral, cognitive and socio-cultural learning lenses, thereby encouraging the future clinician to be more responsible for his/ her learning experience and hopefully, creating a lifelong learner. The successes and challenges of the virtual laboratory will be discussed.

### #3 1:24 p.m.

CENTRAL GIANT CELL GRANULOMA OF THE JAWS AND GIANT CELL TUMOR OF LONG BONES. A clinicopathological, cytometric and immunohistochemical comparative study M. Al Sheddi, H. Mosadomi and F. Al Dayel. King Saud U., Riyadh.

Central giant cell granuloma (CGCG) of the jaws and giant cell tumor of bone (GCT) share a number of similarities and dissimilarities with respect to their histopathological, cytometric and immunohistochemical features. In the present study the clinical, histopathological, cytometric and immunohistochemical features of 18 histologically diagnosed CGCG of the jaws and 22 GCT were compared. The findings on CGCG in particular were analyzed to see if they have any correlation with the so-called clinically aggressive variants of CGCG. CGCG of the jaw showed an early age (55.6% <25 years) compared to GCT (50% between 26-38 years). There was a female predilection in both lesions. The mandible was the more common location for CGCG, while the femur and tibia were equally affected by GCT. All the lesions were osteolytic in nature; 53.8% of the CGCGs were unilocular with root resorption in 46.2% of the cases. Radiographic features noted in GCT ranged from unilocular to multilocular. Pain and swelling were the usual complaints in both CGCG and GCT. Enucleation and curettage were the most common treatment modalities for both lesions. The recurrence rates of CGCG and GCT were 40% and 45.5% respectively. There were no significant histological differences, with the exception of necrosis that was higher in GCT. In addition, GCT showed higher mean number of giant cells per measurement field, higher number of nuclei per giant cell, greater fractional surface area and relative size index compared to CGCG. Both diseases showed similar cellular phenotype with respect to the following cell differentiation markers: Vimentin, S100 protein, CD68, and CD34. There was increased immunoreactivity of GCT to Ki-67, P53, and  $\alpha$ SMA. There were no clinical, histological, cytometric, and immunohistochemical differences between the aggressive and non-aggressive CGCGs, which could have been useful in predicting their clinical behavior. Our findings suggest that the GCT and the CGCG may be variants of the same disease entity. with age and site-specific features.

### #4 1:36 p.m.

GHOST CELL AMELOBLASTOMA; A NEW MICROSCOPIC VARIANT? F. Kratochvil and W. Yih, Oregon Health & Science U, Portland Oregon.

We are reporting a case of ameloblastoma with ghost cells as a prominent feature and support the acceptance of "ghost cell ameloblastoma" as a microscopic variant of ameloblastoma. Ameloblastoma is a common odontogenic tumor. Several microscopic subtypes including follicular, plexiform, acanthomatous, granular cell, desmoplastic, and basal cell have been described in the literature. Ghost cell ameloblastoma has not been reported as such, but ghost cells in ameloblastoma have been alluded to in the literature and has been suggested as a variant. A 69-year-old white female presented with a multilocular radiolucency from teeth #s 21 to 22. She had a history of enucleation of a lesion in the same area two years previously. The microscopic diagnosis of the previous lesion had been "ameloblastoma" and demonstrated the classic microscopic features of ameloblastoma. The lesion had recurred and had increased in size. Ghost cell elements appeared in the recurrence of this ameloblastoma. The nomenclature of ghost cell containing odontogenic neoplasms and the aggressiveness of these tumors will be discussed.

#5 1:48 p.m.

EXTRACRANIAL HEAD AND NECK CYSTICERCOSIS: REPORT OF 9 CASES WITH EMPHASIS IN SEROLOGIC ANALYSIS AND NATURAL HISTORY OF THE DISEASE. R. Carlos, E. Contreras and H. Rivera. Mariano Gálvez U/Centro de Medicina Oral de Guatemala and U. Central de Venezuela

Cysticercus cellulosae is the larval form of Taenia solium representing the second most common larval infection in humans produced by cestodes. It affects any tissue but is more common in skeletal muscle, CNS and eye. This infection has been known since 500 BC; in Guatemala it was first reported in 1877. It has no racial predilection but is rare in Jews and Moslems do not eat pork meat. Humans are definitive hosts for Taenia solium; pigs and wild hogs are intermediate hosts, but humans can manifest the sporadic larval form. Human cysticercosis is acquired by ingestion of infected pork or fecally contaminated foods. Cysticercosis is clinically characterized by the presence of solitary or multiple sub-mucosal/cutaneous firm nodule(s), which are circumscribed, movable, usually asymptomatic and measure 1 to 1.5 cms. Mature cysticercus are small translucent oval cysts containing the invaginated scolex which has four sucking openings each with a double crown of hooks. Macroscopic and microscopic features are both diagnostic. Living larvae with an intact membrane do not elicit an inflammatory reaction unless degenerated or dead. Anti-cysticercus serum titers are valuable for follow up and should be first determined before or immediately after diagnosis. MRI and/or CT are mandatory to rule out CNS involvement. The affected head and neck sites in our series are buccal mucosa (3), lower lip (2), upper lip (1), tongue (2), and temporal muscle (1). All of our cases represented single lesions, three of them without active CNS compromise. Systemic treatment is mostly recommended for CNS cysticercosis, Praziquantel being the most accepted drug.

#6 2:00 p.m.

EXPRESSION AND TOPOLOGICAL DISTRIBUTION OF CELL ADHESION MOLECULES CD44s, E-CADHERIN,  $\beta$ 4-INTEGRIN, DSG-2 AND ICAM-1 IN WARTHIN TUMORS OF SALIVARY GLANDS.

D.Antoniades D.Andreadis, K.Barbati K.Christidis, A.Epivatianos, A.Poulopoulos, G.Papazoglou, Aristotle U.of Thessaloniki & Hellenic Red Cross Hospital of Athens, Greece.

Background: Cell adhesion molecules participate in tissue development and maintenance by mediating interactions between cells and cells-extracellular matrix. E-cadherin in epithelial adherens junctions, dsg-2 in desmosomes,  $\beta$ 4 integrin in hemidesmosomes, CD44s in cell-matrix interactions and ICAM-1 are, mostly, essential for tissue integrity, architecture and function in normal salivary gland parenchyma. Aim: We studied the expression of cell adhesion molecules in Warthin's tumors in order to understand the structure of neoplastic epithelium and the interactions between them and the excessive lymphocytic stroma of this tumor. Material and Method: Immunohistochemistry using a 2-step Envision/HRP detection system was applied to paraffin-embedded specimens of 18 Warthin's tumors from parotid. Lobules from 7 cases of normal labial salivary glands were used as controls. Results: E-cadherin was strongly expressed only at the neoplastic epithelium, mainly at the inner layer of luminal epithelium composed of tall columnar cells (100%), dsg-2 to both luminal and non-luminal epithelial cells (100%),  $\beta$ 4 integrin was also positive only at epithelial cells (100%) and mainly at their basal pole, CD44s was stained at both epithelial cells, mainly luminal, and lymphocytic infiltration of the stroma (except lymphoblastic-germinal centers). Contrary to CD44s, ICAM-1 was mainly expressed in lymphocyte infiltration with a very strong positivity in germinal centers. In a number of cases a small portion of non-luminal epithelial cells was characteristically positive for ICAM-1. Conclusions: The structure of bilayered oncocytic epithelium in Warthin's tumors based on cells and cell-matrix interactions resembles normal salivary architecture composed of luminal and non luminal epithelial cells. Stroma may also interact with activated non luminal neoplastic epithelium depended on the longevity and the grade of lymphocytic infiltration of the tumor.

#7 2:12 p.m.

**OSTEONECROSIS OF THE JAWS ASSOCIATED WITH THE USE OF BISPHOSPHONATE MEDICATIONS: A REPORT OF 60 CASES.** S. Ruggiero, V. Woo, B. Mehrotra, and J. Fantasia. Long Island Jewish Medical Center, New Hyde Park, NY.

Bisphosphonates are non-metabolized analogues of pyrophosphate that function to disrupt osteoclast-mediated bone resorption. Pamidronate and zoledronic acid are intravenous bisphosphonates used in the treatment and maintenance of patients with symptomatic, osteolytic lesions of multiple myeloma and metastases of solid tumors; alendronate and risedronate are oral bisphosphonates commonly prescribed for the treatment and prevention of osteoporosis. *Objective.* We present 60 cases of osteonecrosis of the mandible and maxilla occurring in patients receiving bisphosphonate therapy. *Study design.* Patients with clinical evidence of osteonecrosis and a history of bisphosphonate use were referred to LIJMC from August 1999 to January 2004 for diagnosis, management, or entry into a bisphosphonate-related osteonecrosis database. These patients were evaluated for gender, age, symptoms at presentation, primary underlying diagnosis, site of necrosis, histopathological findings at biopsy or definitive management, and treatment rendered. *Results.* Sixty patients, 43 (72%) females and 17 (28%) males, were identified with a mean age of 68. The most common underlying oncologic diagnoses were multiple myeloma (28, 47%) and breast cancer (18, 30%). Thirty-eight (38) patients presented with mandibular disease and twenty-three (23) patients presented with maxillary disease; concurrent involvement of both sites has been noted. Cases examined histologically revealed the presence of necrotic bone and associated bacterial debris and granulation tissue, with no evidence of metastatic deposits. *Conclusion.* It appears that bisphosphonate therapy may be associated with development of osteonecrosis of the mandible and maxilla in certain patients; however the pathomechanism of this process remains unclear at this time. The goal of this report is to heighten the awareness of the dental and medical community regarding this possible complication of bisphosphonate use.

#8 2:24 p.m.

**SEVERE/FREQUENT RECURRENT APHTHOUS ULCERS AND SALIVARY FLOW RATES** S. Zunt, Indiana University, Indianapolis.

The unstimulated salivary flow rate was measured in 79 consecutive patients referred for oral and maxillofacial pathology consultation because of severe or frequent recurrent aphthous ulcers (RAU). The unstimulated salivary flow rate (USFR) was measured using volumetric collection of whole saliva for 5 minutes and using the Modified Schirmer Test (MST) with a Schirmer tear test strip (Eagle Vision 1-800-222-7584) for three minutes. Results: 67 patients (60%) had RAU with USFR >0.1 ml/min, average age 34 years, range 6-78 years. 32 patients (40%) had RAU with USFR ≤ 0.1 ml/min, average age 48 years, range 17-80 years. Of the 67 patients with USFR >0.1 ml/min, 3/67 (4%) had abnormal saliva with 2 patients having sialorrhea (USFR >2 ml/min) and one patient with thick gelatinous saliva. Secretagogues, pilocarpine or cevimeline, were prescribed for patients with USFR ≤0.1 ml/min. The presence of adequate saliva protects the mucosa from minor irritation and reduces antigenic exposure, two triggers of RAU in susceptible patients. Conclusion: Diminished USFR due to salivary gland hypofunction may be a precipitating factor for RAU. Identification and management of diminished salivary flow should be helpful to identify an important precipitating factor and to recognize that the xerostomic patient is at risk for the complication of candidiasis in RAU patients treated with corticosteroids, a mainstay of RAU treatment. Often normal salivary flow rates can be re-established with secretagogue medications pilocarpine or cevimeline.

#9 2:36 p.m.

BASAL CELL ADENOCARCINOMA OF THE ORAL MINOR SALIVARY GLANDS: REVIEW OF THE LITERATURE AND PRESENTATION OF TWO NEW CASES. P. Parashar, E. Baron, JC Papadimitriou, RA Ord, NG Nikitakis. U. Maryland, Baltimore.

Basal Cell Adenocarcinoma (BCAC) is an unusual salivary gland malignancy with a predilection for the major salivary glands; involvement of the minor salivary glands is considered very rare. Here we present the clinical, histopathologic and immunohistochemical characteristics of two cases of BCAC arising in oral minor salivary glands. Both of our patients were female of 66 and 42 years of age, respectively. Their respective tumors were located in the left cheek and junction of hard and soft palate. Both tumors exhibited typical histopathologic characteristics of BCAC including infiltrative growth and perineural invasion, and assuming a tubular-trabecular and solid-membranous pattern, respectively. Both tumors showed immunopositivity for S-100, Bcl-2, p53 and cytokeratin 7, while being negative for vimentin, glial fibrillary acidic protein (GFAP), smooth muscle actin (SMA), and cytokeratin 20. One of the tumors was also immunopositive for epithelial membrane antigen (EMA) and carcinoembryonic antigen (CEA). Both patients were treated by surgery and remained tumor free during a follow-up of 96 and 22 months, respectively. A comprehensive literature review revealed only 17 previously reported cases of BCAC of oral minor salivary glands. Including the data of our patients, patients' age ranged from 24 to 73 years with a mean age of 54.5 years. Eleven of the patients were female and 8 were male. The most frequent location was the buccal mucosa (8 cases), followed by the palate (6 cases), lip (3 cases) and tongue (2 cases). Based on the current literature and our experience, BCAC of the oral minor salivary glands is an exceptionally rare salivary gland tumor presenting as a slowly growing but deeply infiltrating mass, which demands wide resection with adequate margins in order to achieve the best prognosis. Immunohistochemical studies may complement a thorough histopathologic analysis in discriminating BCAC from other benign and malignant salivary gland tumors.

#10 2:48 p.m.

MICROSCOPIC EXAMINATION OF BONE FROM 205 99M TECHNETIUM-MDP MAXILLO-FACIAL HOT SPOTS WITHOUT EVIDENCE OF ACTIVE DENTAL, PERIODONTAL OR SINUS DISEASE. J. Bouquot, K. Spolnik, K. Deardorf, W. Adams. The Maxillofacial Center, Morgantown, WV; Indianapolis, IN.

The Problem: To date, no study has evaluated microscopically "hot spots" in alveolar regions of pain without obvious radiographic evidence of infection. Purpose: Correlate a positive 99m-Tc scan with microscopic appearance of disease in a large group of individuals without radiographic or clinical evidence of periodontal, periapical or sinus disease. Material & Methods: Conservative exploratory surgery was performed in 205 regions of increase 99m-Tc radioisotope uptake, or hot spots, in a cohort of idiopathic facial pain patients without identifiable dental, periodontal or sinus disease, and with positive diagnostic anesthesia testing. 41 99m-Tc negative sites of pain were also explored in order to attempt to determine accuracy, sensitivity and specificity rates. Results: Of 205 surgically explored alveolar hot spots, 98.5% (n = 202) proved to have inflammatory or ischemic bone disease, demonstrating a highly significant (p<.0001) association. Diagnoses included: ischemic bone disease (n = 114) and chronic nonsuppurative osteomyelitis (n = 79), among others. Of 41 99m-Tc negative sites biopsied, 95.1% (n = 39) had positive biopsies (p<.0001). Accuracy (82.8%) and sensitivity (83.3%) were high, but specificity (40.0%) was low. Conclusion: A positive 99m-Tc scan is strongly correlated with microscopic bone and marrow disease in alveolar regions of pain, without dental, periodontal or sinus infection. The 99m-Tc hot spot should, therefore, not be discounted routinely but should be correlated with clinical findings, especially the presence of pain and a positive diagnostic anesthesia test. False negative tests are common and the presence of pain appears to be a stronger indicator of bone disease than a hot spot.

#11 3:00 p.m.

INFLAMMATORY MYOFIBROBLASTIC TUMOR OF THE ORAL CAVITY: REVIEW OF THE LITERATURE AND PRESENTATION OF AN ALK-POSITIVE CASE. NG Nikitakis, JK Brooks, BF Frankel, JC Papadimitriou, JJ Sauk. U. Maryland, Baltimore.

Inflammatory myofibroblastic tumor (IMT) is a controversial lesion composed of myofibroblastic spindle cells accompanied by varying numbers of inflammatory cells. Although various pathogenetic factors (i.e. reactive, infectious, autoimmune, or neoplastic) have been implicated, the etiology of most IMTs remains unknown. Here, we present a case of IMT arising from the mandibular alveolar mucosa of an 82-year-old female. The lesion presented as a 5 X 5 cm round, pedunculated, painless mass of 2 months duration, associated with a superficial resorptive defect of the mandible. The lesion was surgically removed and, on histopathologic examination, appeared to be composed of plump spindle cells set in a myxoid, vascular stroma admixed with an inflammatory component, consisting primarily of neutrophils and lymphocytes. Numerous large “ganglion cell-like” cells were dispersed throughout the lesion. Only occasional mitotic figures were encountered, in the absence of cytologic atypia. Ultrastructurally, prominent myofibroblastic features were seen. Immunohistochemical analysis revealed that the spindle and ganglion-like cells were diffusely positive for vimentin, smooth muscle actin and anaplastic lymphoma kinase (ALK), focally positive for CD68, and negative for desmin, bcl-2 and EBV-LMP. No evidence of recurrence has been noted at a 12-month follow-up. Including our patient, only 14 cases of oral IMT have been described in the literature. Patients’ age ranged from 2 to 82 years with a mean of 35 years, while a 1.6:1 female predilection was noted. The buccal mucosa was the most commonly affected site (50%), followed by the mandible (21%). None of the reported cases of oral IMT recurred or metastasized. The present case is the second reported ALK-positive oral IMT, which points to a potential neoplastic origin. Significant differences in the clinical behavior, immunohistochemical and genetic profile of lesions diagnosed as IMT may indicate that the term has been used to describe lesions with similar histology but variable etiopathogenesis and prognosis.

#12 3:12 p.m

MICROCYSTIC ADNEXAL CARCINOMA OF THE LOWER LIP: A REPORT OF A CASE AND REVIEW OF THE LITERATURE. D. Cox, E. Myers. U. of Pittsburgh, Pittsburgh Pennsylvania.

Background. Microcystic adnexal carcinoma is relatively uncommon skin appendage tumor, which shows evidence of both pilar and sweat gland differentiation. This locally aggressive and deeply infiltrative malignancy shows a strong predilection for the head and neck region, particularly the mid-facial area, and displays a high rate of recurrence if not completely excised. Clinically, these lesions present as firm, subcutaneous nodules that may mimic scars or other benign lesions. Characteristic microscopic features include islands of small basaloid keratinocytes with a bland cytologic appearance, keratin-filled cysts, eccrine ductal structures, deeply infiltrative growth, and perineural invasion, all within a background of desmoplastic stroma. The histologic differential diagnosis includes such neoplasms as syringoma and desmoplastic trichoepithelioma. Objective. The purpose of this study is to describe the incidence, and clinical and histologic features, of microcystic adnexal carcinoma and to present a case involving the lower lip.

Findings. We report a case of microcystic adnexal carcinoma presenting in the lower lip of a 71-year-old male. The lesion presented as a persistent scar-like subcutaneous mass of the lower lip without evidence of a skin or mucosal surface lesion. The patient was treated by surgical excision and remains disease-free 21 months after excision.

Conclusion. Although microcystic adnexal carcinoma is an uncommon skin appendage tumor, it shows a very strong predilection for the head and neck region. In addition, these lesions are very locally aggressive. The clinical and histologic presentations often mimic other, often benign, lesions and it is imperative that both the clinician and pathologist be aware of its features so that prompt diagnosis and adequate treatment occurs.

#13 3:24 p.m.

EXPRESSION OF G1/S PHASE MODULATORS OF CELL CYCLE, CYCLIN D1, CDK4, pRB, AND OF PROLIFERATION MARKER KI 67 IN PRIMARY MUCOSAL MELANOMA OF THE HEAD AND NECK. Y. Rawal, M. Prasad. The Ohio State University, Columbus.

Objective: Over-expression of Cyclin D1 and CDK4 genes and loss of pRb function are frequent events in many malignant tumors. Interestingly, Cyclin D1 and CDK4 expression is infrequent in cutaneous melanomas except for the acral melanomas and pRb expression is retained. The objective of this study was to ascertain the expression of these G1/S phase modulators of the cell cycle and the proliferation marker Ki 67 in the non-UV-light-related primary mucosal melanoma of the head and neck using monoclonal antibodies to Cyclin D1, CDK4, pRb and Ki 67. Findings: Archival tissue from 13 primary sinonasal and 4 oral mucosal melanomas from 12 men and 5 women (age range 60-86 years, median 76 years) were used for the study. Cyclin D1 expression was seen in 14 of 15 tumors (<5% positive cells=1, 10-50% positive cells=8, >50% positive cells=5 tumors). CDK4 expression was seen in all 17 cases (20% positive cells=1, >50% positive cells=16 tumors). pRb expression was also seen in all 17 tumors (<10% positive cells=1, 30% positive cells=2, >50% positive cells=14 tumors). The proliferation index as determined by Ki 67 expression was <20% in 6, 20-50% in 7 and >50% in 4 tumors and did not correlate with the expression of cyclin D1, CDK4 or pRb. Conclusion: Frequent over-expression of Cyclin D1 and CDK4 suggests deregulation of the G1/S phase of the cell cycle. This may be a critical step in the pathogenesis of mucosal melanoma. Loss of pRb is infrequent in mucosal melanoma and does not appear to be an important factor in its pathogenesis.

#14 3:36 p.m.

CLINICALLY AGGRESSIVE CENTRAL GIANT CELL GRANULOMAS IN TWO PATIENTS WITH NEUROFIBROMATOSIS 1. P. Edwards, T. Rosenberg, S. Ruggiero, S. Sachs, J. Wu, Long Island Jewish Medical Center, New Hyde Park, NY. Background: Neurofibromatosis 1 (NF1) is an autosomal dominantly inherited genetic disorder caused by a spectrum of mutations affecting the NF1 gene, a gene located at 17q11.2 and spanning more than 350 kilobases. Affected patients develop a number of benign and malignant tumors at an increased frequency. Clinical findings include multiple café-au-lait spots, neurofibromas, axillary freckling, optic gliomas, benign iris hamartomas, scoliosis, and poorly defined hamartomatous lesions of the skeleton. Kerl (1971) first reported the association of NF1 with central giant cell granuloma (CGCG) of the jaws. There have since been 4 additional reports of NF1 patients with multiple CGCG of the jaws (molecular analysis of one of these cases uncovered a novel NF1 splice mutation in the proband). An additional case involving the occipital bone and one of a patient with multiple peripheral giant cell granulomas have also been reported. Clinical Cases: We report on 2 patients who presented with NF1 and aggressive CGCG of the jaws. In both cases, the clinical course was characterized by numerous recurrences despite surgical treatment. Conclusions: While the association between NF1 and CGCG could represent a genetic linkage, this association could also be coincidental since both NF1 and CGCG of the jaws are relatively common. For example, NF1 demonstrates phenotypic overlap with Noonan syndrome (short stature, ocular hypertelorism, pulmonic stenosis, webbed neck) in approximately 12% of patients. Watson syndrome, characterized by overlapping mild features of both NF1 and Noonan-like syndrome is linked to the NF1 gene. NF1-Noonan syndrome, an entity of its own right, is believed to be the result of the independent segregation of a both classical NF1 phenotype and a Noonan syndrome phenotype. Interestingly, multiple giant cell lesions have also been reported in a number of patients with Noonan syndrome.

#15 3:48 p.m.

ELEVATED CYSTATIN EXPRESSION IN METASTATIC ORAL CANCER CELLS CONFERS GREATER RESISTANCE TO TRAIL-INDUCED APOPTOSIS: N. Vigneswaran, J. Wu & W. Zacharias (U.TX-Houston and U. Louisville). TRAIL (tumor necrosis factor-related apoptosis-inducing ligand) preferentially induces apoptosis of cancer cells without toxicity in normal cells. TRAIL plays an important role in host immunosurveillance against tumor metastasis. Cathepsin B (CB) is a mediator of apoptotic cell whose activity is regulated by its inhibitors known as cystatins (CY). OBJECTIVE: To relate the TRAIL sensitivity of clonally related primary and metastatic oral cancer (OC) cells with their CB and CY levels. FINDINGS: Two pairs of primary (686Tu and 101Tu) and metastatic (686Ln and 101Ln) OC cell lines were treated with various concentrations (10 – 1000 ng/ml) recombinant human TRAIL protein for 14-hours. Cell viability was quantified by MTT assay. Apoptosis rate among TRAIL-treated cells was measured using the TUNEL and M30 CytoDEATH immunodetection assays. CB and CY (A, B, C and M) levels in these cells lines were analyzed by RT-PCR and Western blots. Primary cells revealed greater susceptibility to TRAIL-induced killing (ED<sub>50</sub> of 50 and 250 ng/mL for 686Tu and 101Tu, respectively) than their metastatic clones (ED<sub>50</sub> of 250 and 1000 ng/mL for 686Ln and 101Ln, respectively). Primary cells in the presence of CB-specific chemical inhibitor CA074 revealed markedly increased resistance to TRAIL (ED<sub>50</sub> > 1000 ng/mL). Expression levels of CY were markedly higher in metastatic OC cells than in their respective primary cells whereas CB levels remain unchanged. CONCLUSION: CB is a mediator of TRAIL-induced apoptosis in OC cells. Elevated levels of cystatins in metastatic OC cells correlate with their greater resistance to TRAIL-induced apoptosis. Our data suggest that overexpression of CY in OC cells may confer a metastatic phenotype by enhancing their resistance to TRAIL.

#16 4:00 p.m.

GRANULAR CELL LEIOMYOMA OF THE ORAL CAVITY. I. Bhattacharyya, DJ Summerlin, D.M. Cohen, G.L. Ellis, J.B. Bavitz, L.L. Gillham. U.of Florida, Gainesville, Indiana U., Indianapolis, ARUP Labs, Utah, U. of Nebraska, Lincoln and U. of Virginia, Richmond.  
Leiomyoma involving the oral cavity is an uncommon, but histologically distinct neoplasm. Granular cytoplasmic change is a reported, but uncommon, finding in leiomyoma. In other sites, leiomyoma has been recognized to demonstrate granular cytoplasmic change. To our knowledge, this phenomenon has not been previously reported in the oral region. Two cases of oral granular cell leiomyomas are presented along with the immunohistochemistry and ultrastructural findings. These tumors were positive for HHF-35, desmin, smooth muscle actin, vimentin and alpha-1 antitrypsin and unreactive for myoglobin, S-100 protein, cytokeratin (AE1/AE3) and factor VIII. The importance of recognizing this variant lies in the potential for misdiagnosis. Accordingly, the clinical and histologic differential diagnosis, pathogenesis, and the occurrence of granular cell change in other oral tumors will be discussed.

#17 4:12 p.m.

ATYPICAL CENTRAL ODONTOGENIC FIBROMA RECURRING AS AMELOBLASTOMA. F. Alawi and P. Quinn University of Pennsylvania, Philadelphia.

Central odontogenic fibroma (COF) is a benign neoplasm that appears to have a limited potential for recurrence. However, we describe an example of an atypical COF that recurred as a cystic ameloblastoma. A 65 year old male presented in 1998 with a 6x5 cm mixed, radiolucent-radiopaque mass in the right posterior mandible. A peripheral ostectomy was performed and the mass was submitted for microscopic examination. The unencapsulated tumor was composed of a hypercellular epithelial component made up of numerous cords and islands of odontogenic epithelium and clear cells. In areas, the tumor islands were seen in very close proximity to nerves. In focal areas, nuclear hyperchromasia and pleomorphism were also seen, yet there was no evidence of any mitoses. The surrounding connective tissue was also hypercellular and composed of a benign-appearing, fibroblastic proliferation. Numerous round, droplet-like calcifications, trabeculae of bone, and foci reminiscent of giant cell granuloma were scattered throughout the stroma. Due to the unusual nature of the epithelial component, a diagnosis of "atypical COF" was rendered. In 2002, the patient returned complaining of a small, painless swelling in the right angle of the mandible. An excisional biopsy revealed a cystic neoplasm composed of hypercellular, atypical-appearing ameloblastic epithelium. The wall of the tumor was composed of mainly mature fibrous tissue which is characteristic of most ameloblastomas. However, the stroma immediately subjacent to the epithelium contained focally scattered multinucleated giant cells and extravasated hemorrhage, which was reminiscent of the original neoplasm. There were no calcifications or compressed odontogenic cords or islands within the wall of the tumor. Thus, a diagnosis of ameloblastoma was rendered. To date, there has been no evidence of any additional recurrences.

#18 4:24 p.m.

PALATAL PERFORATION RESULTING FROM INTRA-NASAL PRESCRIPTION NARCOTIC ABUSE. W. Jewers, Y. Rawal, C. Allen, J. Kalmar, E. Fox, G. Chacon, P. Sedghizadeh. The Ohio State U., Columbus.

Background: Palatal perforation resulting from insufflation of cocaine has been well- documented. In comparison, reports of destructive oro-facial lesions resulting from intra-nasal abuse of prescription narcotics are rare. We present the clinical and histopathologic findings in a case of palatal perforation arising in a patient abusing a prescription opioid drug. The patient denied any history of cocaine use, but admitted to habitually crushing and snorting a hydrocodone/acetaminophen preparation. Methods: The patient presented to our clinic seeking resolution of speech difficulties associated with an oro-antral fistula. Surgical repair of the defect had been attempted unsuccessfully in the past. Endoscopic examination and blood and chemistry panels were conducted prior to surgical attempt at repair. During the surgery, several biopsy specimens were removed for histopathologic evaluation and flow cytometry from lesional and peri-lesional sites in both the oral and nasopharyngeal cavities. Culture and cytology for fungal organisms were also performed. Results: Histopathologic examination revealed normal mucosa with diffuse and focal inflammatory changes and no evidence of malignancy. Polarizable foreign material was noted in the specimens. The absence of lymphoid neoplasia was confirmed by flow cytometric analysis. The toxicology panel was positive for the presence of opiates in the blood. Culture and cytology were positive for candidal organisms. A palatal obturator was fabricated for the patient, producing significant improvement in the quality of speech. Conclusions: This is the first reported case of palatal perforation resulting from abuse of a drug other than cocaine. The potential for drugs other than cocaine to produce destructive oro-facial lesions should be considered.

#19 4:36 p.m.

PLASMABLASTIC LYMPHOMA IN A NON-HIV POSITIVE PATIENT: A CASE REPORT AND REVIEW OF THE LITERATURE. M.A. Scheper, N.G. Nikitakis, R. Fernandes, C.D. Gocke, R.A. Ord, J.J. Sauk.

University of Maryland, Baltimore

Plasmablastic lymphoma is an HIV-associated non-Hodgkin lymphoma primarily affecting the oral cavity and jaws. The purpose of this study is to report a case of plasmablastic lymphoma occurring in a 49-year-old non-HIV positive African American male. The patient presented with pain and swelling of the right mandible of two weeks duration, with a single enlarged lymph node. A computed tomography scan revealed a destructive mass centered on the right posterior mandible. Histopathologic examination of an incisional biopsy revealed a dense, diffuse lymphocytic infiltrate of non-cohesive large lymphocytes with plasmacytoid features. Immunohistochemical analysis revealed positivity for the B-cell marker CD79a, Epstein Barr virus latent membrane protein (LMP), and lambda light chain restriction; in contrast, the neoplastic cells were negative for leukocyte common antigen, CD20, CD3, CD10, BCL-2, desmin, actin, EMA, S-100, HMB45, and cytokeratins. The final diagnosis of plasmablastic lymphoma was made with a recommendation for HIV testing, which was negative. There are six previously reported cases of plasmablastic lymphoma in non-HIV positive patients, including three immunosuppressed, two immunocompetent and one of unknown immune status. The present case represents the first reported oral plasmablastic lymphoma in a non-HIV positive as well as non-immunocompromised individual. The features of this rare disease are summarized based on a comprehensive review of the epidemiologic, clinical and immunohistochemical findings of previously reported cases.

#20 4:48 p.m.

PERIPHERAL ODONTOGENIC KERATOCYST: A CASE REPORT AND REVIEW OF THE LITERATURE.

A. Chi and S. Muller. Emory University Hospital, Atlanta, Georgia.

We report a case of an 81-year-old female with an asymptomatic, fluctuant, gingival nodule occurring in the area of the left mandibular first premolar and canine. The clinical impression was that of a gingival cyst of the adult. However, microscopic examination revealed features of an odontogenic keratocyst, including a parakeratinized stratified squamous epithelial lining with a palisading basal cell layer and an absence of rete. A review of the literature revealed twelve previously reported cases of peripheral odontogenic keratocyst with an average age of 51 years and a 1.5:1 female:male ratio. Among these cases, there was a striking predilection for the gingiva in the canine-premolar region (n=9), a presentation similar to that of the gingival cyst of the adult. Two cases were associated with superficial erosion of the underlying alveolar bone. However, all reported lesions fulfilled the histopathologic criteria for an odontogenic keratocyst. One case occurred in a patient with nevoid basal cell carcinoma syndrome. Recurrence was seen after 6 months in the present case and after 7 years in one of the previously reported cases. Although there is some controversy in the literature as to whether to consider this lesion a variant of the gingival cyst of the adult or the soft tissue counterpart of the central odontogenic keratocyst, we favor the latter view given the distinct histopathologic features, recurrence potential, and occasional association with nevoid basal cell carcinoma syndrome.

#21 5:00 p.m.

**ALVEOLAR RIDGE KERATOSIS: A CLINICO-PATHOLOGIC ENTITY. E.Natarajan, J Rheinwald, S.Woo**

Harvard School of Dental Medicine, Harvard Medical School, Boston, MA.

Alveolar ridge keratosis (ARK) is a common benign white papule or plaque that occurs on the keratinized gingiva of the maxillary or mandibular alveolar ridge with characteristic histologic features. This is a retrospective study of 70 consecutive cases of ARK accessioned over a 26-month period. Detailed information was available on 27 cases through a mail-in questionnaire. The male:female ratio was 3.6:1. The retromolar pad was involved in 69 % of cases, with 30% of such cases being bilateral. All lesions were less than 2 cm in greatest dimension. A tobacco habit was noted in 50% of cases. Histologically, the lesions were characterized by moderate to marked hyperorthokeratosis, with wedge-shaped hypergranulosis, slight surface papillomatosis, acanthosis in the form of long, tapered rete ridges and none to mild inflammatory cell infiltration. These features are similar if not identical to what is reported as lichen simplex chronicus of the skin, a benign condition caused by chronic irritation. Ten cases were stained immunohistochemically for p16INK4A(p16) a tumor suppressor protein commonly expressed in oral intraepithelial neoplasia (OIN) grade II and III, carcinoma-in-situ and invasive fronts of squamous cell carcinomas. All lesions were negative for p16, demonstrating the benign nature of the lesion. All the cases that were excised (17/27) did not recur. None developed malignancy at the site.

ARK is a specific clinico-pathologic entity that should be removed from the category of leukoplakia and placed in its own category of ARK, as is currently the practice for clinical white lesions with a specific, well-recognized histologic pattern such as lichen planus and morsicatio buccarum.

## READ BY TITLE

**ORAL MANIFESTATIONS OF AMYLOIDOSIS: REPORT OF TWO CASES**

A.Kolokotronis, P.Stefanopoulos, M.Xohellis, D.Antoniades.

Aristotle u. Thessaloniki, Greece.

Amyloidosis represents a group of conditions in which there is extracellular deposition of amorphous fibrillar proteins, termed amyloid. There are many biochemically distinct forms of amyloid proteins that have been identified. Two of the most common forms are: AL type that is derived from immunocytes and contains immunoglobulin light chains; and AA type that is a unique non-immunoglobulin protein.

The current classification of amyloidosis is based on the biochemical composition of amyloid. One third of the patients with either the AA or AL amyloidosis are reported to have oral amyloid deposits.

We present the oral involvement in two cases of amyloidosis.

Case 1: A patient under investigation for multiple myeloma with oral lesions was referred for oral consultation. The lesions consisted in enlarged tongue with red and smooth surface and purpuric exanthema of perioral skin. Biopsy of the tongue demonstrated amyloid deposits and the diagnosis of AL amyloidosis had been made.

Case 2: A patient suffering from AA amyloidosis with oral lesions was referred for oral consultation. The patient was complaining of pain in the oral cavity (burning mouth), especially on the tongue, and difficulty in chewing and swallowing foods. Oral examination revealed a few papules on the dorsum of the tongue associated with xerostomia. In addition small ulcers, localized on the vestibule of the mouth were observed. Biopsy of the tongue demonstrated amyloid deposits.

IMMUNOHISTOCHEMICAL INVESTIGATION AND STUDY OF THE EXPRESSION AND TOPOGRAPHY OF CELL ADHESION MOLECULES IN CASES OF ACINIC CELL ADENOCARCINOMA OF SALIVARY GLANDS D.Antoniades, D.Andreadis, K.Christidis, A.Epivatianos, A.Poulopoulos, G.Papazoglou, K.Barbati

Aristotle U. of Thessaloniki & Hellenic Red Cross Hospital of Athens, Greece.

**Background:** Diagnostic difficulties can arise because of the architectural diversity of acinic cell adenocarcinoma based on both growth -solid, microcystic, follicular, papillary-cystic- and cellular -acinar, intercalated ductal, vacuolated, clear and nonspecific glandular- patterns. Immunohistochemical detection systems may be helpful for the definition of the diagnosis. Cell adhesion molecules participate in tissue development and maintenance by mediating interactions between cells and extracellular matrix. E-cadherin in epithelial adherens junctions, ds2 in desmosomes,  $\beta$ 4 integrin in hemidesmosomes, CD44s in cell-matrix interactions and ICAM-1 are, mostly, essential for tissue integrity, architecture and function in normal salivary gland parenchyma.

**Aims:** We used immunohistochemical methods to investigate the neoplastic cellular profile of acinic cell adenocarcinoma and to study the expression of cell adhesion molecules in order to understand the structure and the possible interactions between cellular patterns and cell-matrix in different tissue architecture.

**Material and Method:** Immunohistochemistry using a 2-step Envision/HRP detection system was applied to paraffin-embedded specimens of 5 acinic cell adenocarcinomas from parotid. Lobules from 7 cases of normal labial salivary glands were used as controls. Cellular profile was examined by staining with p53, Ki67, bcl-2, A1AT, CEA, EMA, Vim, SMA, cytokeratins, GFAP, and S-100 protein. We detected cell adhesion by utilizing antibodies against CD44s, E-cadherin,  $\beta$ 4-integrin, Dsg-2 and ICAM-1.

**Results:** p53, Ki67 and bcl-2 positivity was associated with the degree of tumor invasion. Neoplastic epithelial cells were positive for A1TA, CEA, CKs (except CK 18), LP34 (not all cases), MNF, S-100, GFAP (locally) and Vim (basal pole). E-cadherin and  $\beta$ 4 integrin were positive in neoplastic epithelium only, upon cell surface (100%), ds2 was also moderately positive but mainly intracellular. In a case of acinic cell adenocarcinoma all neoplastic epithelium was ICAM-1 positive, and finally CD44s, was strongly, positive in all types of cells and architecture patterns. **Conclusions:** Immunohistochemistry may be a useful tool for the diagnosis of acinic cell adenocarcinoma. On the other hand, the study of cell adhesion explains the origin of neoplastic cells and helps in the describing of the structure of different growth patterns.

HISTOPATHOLOGIC DIAGNOSTIC DISAGREEMENT BETWEEN CONTRIBUTING PATHOLOGISTS AND CONSULTATIVE PATHOLOGISTS IN ORAL AND MAXILLOFACIAL PATHOLOGY. D. Wells, E. Childers, A. Nelson. Armed Forces Institute of Pathology (AFIP), Washington DC.

**Background:** The Armed Forces Institute of Pathology's trifold mission is consultation, education, and research. In order to focus educational objectives, this investigation determined which diagnoses are most often designated as a clinically significant disagreement (Code 4) or no contributor's diagnosis (Code 1) between the contributing pathologist and the Department of Oral and Maxillofacial Pathology.

**Materials and Methods:** The central database was queried for the previous 5 years by diagnosis, anatomic site, and diagnostic agreement code. Eighty-eight diagnoses and 9 distinct intraoral and perioral sites were queried. **Data:** The diagnoses most commonly Code 4 were basal cell adenocarcinoma (19%), polymorphous low-grade adenocarcinoma (18%), adenoid cystic carcinoma (13%), and adenomatoid odontogenic tumor (13%). When the data was filtered by site, the majority of diagnoses Code 4 were salivary gland malignancies. The diagnoses most commonly Code 1 were leiomyoma (40%), canalicular adenoma (27%), myoepithelioma (27%), benign fibrous histiocytoma (25%), and neurofibroma (20%). Although a large number of squamous cell carcinomas were identified (497), those with diagnostic Code 4 were less than 5% of all squamous cell carcinomas submitted.

**Conclusions:** Malignant neoplasms of salivary gland origin were the most common source of clinically significant diagnostic disagreement between contributors and the Department of Oral and Maxillofacial Pathology, AFIP. A wide variety of diagnoses were Code 1, and included a number of soft tissue spindle cell neoplasms.

**THE EXPRESSION OF PIM-1 AND ENDOTHELIN -1 IN OSTEOLYTIC AND OSTEOLASTIC METASTATIC CARCINOMA TO BONE. N. Said-Al-Naief, M. Roh, C. Song, I. Eltoun, B. Gary, R. Azuero and S. Abdulkadir. UAB, Birmingham, AL.**

Certain tumors are known to induce an osteoblastic response when metastasizing to bone but the exact mechanism by which the neoplastic cells stimulate new bone formation is only partially understood. The selective orthotropism in these neoplasms has been investigated and numerous factors have been implicated. Endothelin-1 is a potent peptide produced by endothelial cells. It is also produced by and affects bone cells and this is thought to play a role in osteoblastic metastasis. Independently, Pim-1, a serine/threonine protein kinase is involved in the regulation of cell growth, differentiation and apoptosis. The overexpression of this protooncogene is linked to the development of lymphoma and recent studies have demonstrated that it also plays an important role outside of hematopoietic system. Recently, Roh & co workers at our institution have demonstrated (*Cancer Research* 63, 8079-8084, December, 2003) that overexpression of Pim-1 promotes genomic instability in prostate carcinoma, one of few types of carcinomas that are characteristically known to induce osteoblastic response when they metastasize. The exact role of Pim-1 in osteoblastic tumor metastasis and its expression in various tumor types have not been characterized. A search of our files returned 19 cases of metastatic carcinomas to bone with documented osteoblastic/osteolytic host response. We are currently investigating the expression of Pim-1 and endothelin-1 by immunohistochemical staining.

**WEGENER GRANULOMATOSIS: A CASE REPORT WITH PRIMARY ORAL MANIFESTATION. SV Lourenço, MMS Nico. Division of Dermatology, Hospital das Clínicas, São Paulo, Brazil.**

Background: Wegener's granulomatosis (WG) is a form of systemic leukocytoclastic vasculitis of small and medium vessels leading to granuloma formation. Oral manifestations are uncommon and may include palatal and lingual ulceration, aphthae and non-healing extraction sockets. History: A 45-year-old white female presented with an 8-month history of an exophytic and haemorrhagic mulberry-like growth, with granular surface involving the gingiva from the mandibular lateral incisor to the 1<sup>st</sup> molar on the left side. The teeth involved showed significant mobility. Periapical and panoramic X-rays presented bone destruction with imprecise limits. Extra-oral examination showed no particularities. Haematologic and serologic tests including complete blood cell counts, anti-nuclear antibodies, p-ANCA and c-ANCA, renal functions, erythrocyte sedimentation rate, were all within normal range. Chest X-ray showed no abnormality, urinalysis was unremarkable. Incisional biopsy revealed acute proliferative gingivitis with pseudoepitheliomatous hyperplasia, focal epithelial degeneration and presence of micro-abscesses. The inflammatory infiltrate in the lamina propria, consisted of a histiocytic component admixed with plasmacytes, neutrophils, numerous eosinophils and scattered multinucleate cells. There was no evidence of granuloma formation. Focal necrosis, haemorrhage and vascular dilation were observed. Vascular wall necrosis and inflammation were lacking. No fungi or bacilli were seen with special stains. These features are compatible with oral manifestation WG. Conclusion: Gingival lesions are extremely rare in WG, but when present, are pathognomonic of the early stages of the disease, preceding any other systemic signs. In these cases ANCA might be negative. Case discussion with literature review is presented.

THE POTENTIAL FOR SAMPLING ERROR IN INCISIONAL BIOPSIES OF ODONTOGENIC KERATOCYSTS. R. Padilla and V. Murrah. U. of North Carolina, Chapel Hill.

Incisional biopsies of large lytic jaw lesions are commonly performed in order to obtain a pre-treatment diagnosis. Odontogenic keratocyst (OKC) is a frequent entity in the differential diagnosis of such lesions and mandates a relatively more aggressive surgical approach. Preliminary analysis of incisional biopsies of OKCs revealed that often, in areas of inflammation, samples did not show the classic histopathologic diagnostic features. Instead, the epithelial lining displayed a squamous-type metaplasia that precluded such diagnosis if that was the only area of epithelium sampled. The purpose of this study, therefore, was to determine the likelihood of sampling error resulting in a non-diagnosis of OKC in cases which truly were OKCs. Fifteen cases of totally excised inflamed OKCs were histomorphometrically analyzed to determine the total area of epithelium in each cyst that was diagnostic or non-diagnostic, respectively, utilizing classic histopathologic criteria. The mean for the total area of lining epithelium was  $0.098\text{mm}^2$ , with non-diagnostic and diagnostic epithelium comprising  $0.033\text{mm}^2$  and  $0.063\text{mm}^2$  respectively. Standard deviations were 0.025 for the total areas, 0.026 for non-diagnostic areas, and 0.016 for diagnostic areas. Standard errors of the mean were 0.007, 0.007 and 0.004, respectively. Results show that 33.6% of the area sampled when incisionally biopsying an inflamed OKC is likely to be non-diagnostic. We conclude that in order to minimize the risk of sampling cystic lining non-diagnostic for OKC, large lytic lesions should be sampled away from sites associated with inflammation, such as those in proximity to sulcular regions, to partially impacted teeth, or in areas exposed to the oral cavity. The caveat is also given that the smaller the incisional biopsy, the greater the chance for sampling error.

## ESSAY PROGRAM II

Tuesday, May 11, 2004

#22 1:00 p.m.

INTRAOSSSEOUS KAPOSI'S SARCOMA OF THE MANDIBLE. J. Rinaggio, K. Noel, G. Mardirossian, L. Schneider. U. of Medicine and Dentistry of New Jersey, Newark.

Kaposi's sarcoma (KS) is a common mucocutaneous manifestation of AIDS. Primary bone lesions have been reported, but are rare. A 38-year-old HIV-positive African-American male presented for the evaluation of a 1.5 cm diameter well-defined radiolucency of the mandibular midline that had been noted on routine radiographic examination. The adjacent central incisors were asymptomatic, non-mobile, and vital. The overlying mucosa and cortical plate were intact. Excision of the lesion revealed a fleshy, pink-red soft tissue mass with a uniform consistency. Histologic examination showed a malignant vascular neoplasm characterized by proliferating spindle cells occasionally exhibiting a fascicular arrangement. They were associated with numerous extravasated erythrocytes and granules of hemosiderin pigment. The tumor cells showed positive immunohistochemical staining for CD 31, CD 34, and HHV 8. This case represents one of the few reported instances of primary intraosseous involvement of the jaws with KS. One year after surgery, the surgical defect shows radiographic evidence of repair and there is no sign of recurrent tumor.

#23 1:12 p.m.

STUDENT PERCEPTIONS OF RISKS ASSOCIATED WITH CIGARETTE SMOKING AND SMOKELESS TOBACCO USE. Tilashalski K, Rodu B, Barnes C, Cole P. University of Alabama at Birmingham (UAB), and University of Nebraska Medical Center (UNMC).

This study documented the perception among student health professionals of the relative health risks from cigarette smoking and from smokeless tobacco (SLT) use. Subjects consisted of dental students, internal medicine residents, and public health graduate students at UAB, and dental students at UNMC. The subjects completed a questionnaire indicating their view of the relationship between cigarette smoking or SLT use and "general health", "cancer", and "oral cancer". Response was on a 10-point scale ranging from zero ("not at all harmful") to ten ("deadly"). A comparison of responses was made between groups for each health category. Individual responses were categorized to indicate whether one product was perceived to be more harmful than the other (or equal). SLT use was perceived by 30% of respondents to be either equally or more harmful than smoking in relation to general health. The corresponding results for cancer and oral cancer were 38 and 72%. However, when focusing on the responses of the 3<sup>rd</sup> and 4<sup>th</sup> year dental students, these numbers dropped to 8%, 9%, and 35%, respectively. Students in the health professions overestimate health risks from SLT use. However, the dental school curriculum at these schools, including the core oral pathology courses, results in a more accurate perception of the lower risks from SLT than from smoking.

#24 1:24 p.m.

**METACHRONOUS MALIGNANT PRIMARY SALIVARY GLAND NEOPLASMS.** J. Whitt, D. Schafer, M. Callihan, Naval Medical Center San Diego, California and National Naval Dental Center, Bethesda, Maryland. Multiple primary salivary gland neoplasms are rare. When they do occur, they are most frequently both benign and of the same histologic type. While there are a number of reports in the literature of individuals with multiple benign, or both a benign and a malignant primary salivary gland neoplasm, there are few reports of individuals with multiple malignant primary salivary gland neoplasms. Although primary malignant neoplasms of salivary glands are not uncommon, multiple primary malignant salivary gland neoplasms, occurring synchronously or asynchronously, are exceedingly rare. We report a case of an adult male that presented with a mucoepidermoid carcinoma involving the minor salivary glands of the palate at age 57 years, followed by an adenoid cystic carcinoma of the floor of mouth at age 63 years. The patient later succumbed to non-Hodgkin's lymphoma of unknown type at age 79 years. An autopsy was not performed. The palatal mucoepidermoid carcinoma was treated surgically by a hemi-maxillectomy. The floor of mouth adenoid cystic carcinoma was treated surgically by wide local excision, including a marginal excision of the mandibular lingual cortex and a neck dissection. The histopathology of the palatal lesion exhibited an intermediate grade mucoepidermoid carcinoma, composed of sheets and nests of intermediate cells containing foci of mucous cells and little cytologic atypia. The adenoid cystic carcinoma was of the typical cribriform type. Individuals with a history of malignancy are at risk for the development of additional malignant tumors and should receive appropriate clinical follow-up.

#25 1:36 p.m.

**IMMUNOHISTOCHEMICAL EXPRESSION OF BID IN ORAL SQUAMOUS CELL CARCINOMA:** B. Singh, J. Borke and G. Caughman. Medical College of Georgia, Augusta  
Bcl-2 and its congeners play a key role in controlling programmed cell death (PCD-apoptosis). We and others have reported the status of anti-PCD proto-oncogenes Bcl-2, Bcl-X<sub>L</sub>, Mcl-1 and Bag-1 as well as Bax and Bak (pro-PCD) in oral cancer. The objective of this study was to examine the expression of Bid (allosteric regulator) in oral carcinomas. For this purpose, 5 micron thick sections from archival paraffin blocks were examined using polyclonal antibodies to Bid oncoprotein. A finely granular Bid immunoreactivity was observed primarily in the cytoplasm of 60% (12 out of 20) carcinomas. A varying degree of zonal or diffuse heterogenous reaction was observed generally based on the degree of neoplastic cell differentiation. The mechanisms involving the role of Bid in regulation of apoptosis remain unclear. It has been considered that: (1) full length Bid translocates Bax to the outer mitochondrial membrane. Bax activation results in induction of mitochondrial permeability transition, (2) caspase 8 cleaved Bid (t-Bid) induces conformational change in Bak and (3) other mechanisms. These processes enable cytochrome-c release from mitochondria. Cytochrome-c forms apoptosome with caspase 9 leading to caspase activation. Initiating caspases 9 and 8 activate downstream caspase #3 leading to apoptosis. It appears that Bid plays an effector role by inducing functional status to other oncogenes. The elucidation of Bid in oral carcinomas as well as caspase 8 and 3 (previously reported by us) indicate a potential for apoptosis. A higher apoptotic index has been shown to confer favorable response to treatment; therefore the induction of apoptosis (inherent in tumor cells) could be a valuable tool for oral cancer therapy.

#26 1:48 p.m.

**INTERTUMORAL ANGIOGENIC HETEROGENEITY: BIOLOGIC AND THERAPEUTIC IMPLICATIONS.**

R. Hasina, W. Kuo, L. Ohno-Machado, M.W. Lingen. University of Chicago, Chicago, IL, and Harvard University, Boston, MA.

It has been largely assumed that tumors within a given histological type induce angiogenesis via the same mechanisms. While such concepts neatly compartmentalize angiogenesis, it is not consistent with other critical tumor phenotypes. The literature contains numerous references describing heterogeneity for tumor phenotypes including cell proliferation, invasiveness, metastatic potential and response to therapies. At this time, data regarding angiogenic heterogeneity are limited. In order to investigate this possibility, normal, dysplastic and malignant oral keratinocytes were harvested using laser capture microdissection (LCM). Total RNA was extracted and subjected to RTQ-PCR analysis. IL-8 and VEGF messages were highly variable within the tumor samples. Validation of the RTQ-PCR data via immunohistochemistry on human tumor samples also found highly variable expression of VEGF and IL-8. Finally, using mouse tumor xenografts, anti-VEGF treatment of HNSCC lines secreting VEGF markedly inhibited the growth of the tumor xenografts. Conversely, anti-VEGF treatment had no effect on the growth of xenografts tumors containing cells that do not produce VEGF. These findings underscore the concept of tumor angiogenic heterogeneity. They imply that there are differences with regard to the specific mechanism by which individual tumors within the same histologic type induce angiogenesis. Moreover, they demonstrate the need for a more in depth understanding of the variability of the angiogenic phenotype within a given type of neoplasm when designing anti-angiogenic therapies.

Supported in part by the NIH grants: DE12322 (MWL) and DE00470 (MWL)

#27 2:00 p.m.

**PRIMARY INTRAOSSEOUS ODONTOGENIC CARCINOMA ARISING IN AN ODONTOGENIC CYST OR DE NOVO: A CLINICOPATHOLOGIC STUDY OF FIVE NEW CASES.** R Chaisuparat, D Coletti, RA Ord, NG Nikitakis. U. Maryland, Baltimore.

The term primary intraosseous odontogenic carcinoma (PIOC) has been primarily used to describe a squamous cell carcinoma within the jaws arising either from a previous odontogenic cyst or, more rarely, *de novo*. Diagnostic criteria of PIOC require absence of initial connection with the overlying mucosa or skin and exclusion of metastasis from a distant primary tumor by physical and radiographic examination during at least a 6-month follow-up. Here, we report five patients with PIOC treated at the University of Maryland, Baltimore during the period from 1997 to 2004. Three of the patients were female and two were male. Their age ranged from 18 to 84 years, with a mean age of 52.8 years. One case involved the anterior maxilla, while four cases occurred in the mandible, three of them being located posteriorly. One patient complained of pain and paresthesia, while the remaining patients were asymptomatic. The typical radiographic presentation of our cases was that of a radiolucent lesion with well-defined or irregular margins. Histopathologically, four cases were diagnosed as PIOC arising from previous odontogenic cysts (including two odontogenic keratocysts and two periapical cysts); all four were well differentiated, keratinizing carcinomas. The remaining case, a poorly differentiated non-keratinizing squamous cell carcinoma, was not associated with a cystic component and appeared to have arisen *de novo*. Four patients underwent surgical removal with postoperative radiotherapy, whereas one patient was treated with surgery only. Lymph node involvement and distance metastasis were not present in any of our patients at the time of diagnosis and did not develop during a follow-up period ranging from 15 to 77 months. To date, all patients are alive and free of disease. Knowledge of the clinical, radiographic and histopathologic features of PIOC will allow accurate diagnosis and appropriate treatment of this rare malignancy.

#28 2:12 p.m.

ARTEMISININ: AN ALTERNATIVE TREATMENT FOR ORAL CANCER. D. Oda, T. Habte, E. Yamachika. University of Washington, Seattle.

Artemisinin (AR), a sesquiterpene lactone, is a widely used antimalarial drug with minimal or no toxic side effects. Recently, additional uses for AR were discovered, including anticancer treatment for a number of in vitro cancer models. It is therefore possible that AR can kill human oral cancer cells through apoptosis. Using an HPV 16 immortalized/transformed human oral epithelial (IHOK) cell line, we evaluated the effect of AR and 5FU, a known chemotherapy agent. Using TUNEL, immunohistochemistry (IHS) markers, and flow cytometry techniques, we investigated the mechanism by which AR kills IHOK cells. Dose response was performed for optimal concentrations and time. A 400 $\mu$ M concentration over a 48-hour period yielded the optimal results. The results of TUNEL showed that AR-treated IHOK cells were over 80% strongly positive cells, while 5FU-treated cells were less than 20% positive. The majority of AR treated cells maintained their integrity while 5FU treated cells were mostly necrotic. The IHS markers demonstrated strong positive staining with Bax, p53, CD40 and CD40L in AR treated cells and negative with Bcl2. 5FU-treated cells demonstrated a profile similar to AR but with less intensity. Control cells exhibited focal positive staining with all five antibodies. Cell cycle by flow cytometry results showed that cells treated with AR demonstrated a slight, but not statistically significant, increase in S phase—21% compared to the control rate of 16%. 5FU treated cells, however, demonstrated a significant increase in S phase of 45%. In conclusion, our results indicate that AR kills transformed oral epithelial cells and does so through apoptosis with no toxicity while 5FU kills mostly through toxicity. We therefore suggest that artemisinin may be useful as an alternative treatment for oral cancer.

#29 2:24 p.m.

CLINICO-PATHOLOGIC FEATURES OF ORAL PLASMABLASTIC LYMPHOMA. G. Folk, S. Abbondanzo, R. Foss, and E. Childers. Armed Forces Institute of Pathology (AFIP), Washington DC.

Background: Plasmablastic lymphoma (PBL) is an uncommon type of B-cell derived lymphoma that displays distinctive affinity for extranodal presentation in the oral cavity. PBL is strongly associated with human immunodeficiency virus (HIV) infection, but has been reported in HIV negative individuals. PBL pursues an aggressive clinical course and the prognosis is poor, despite therapy. Plasmablastic lymphoma can be the presenting finding in a previously undiagnosed HIV positive patient. Materials and Methods: Five cases of oral cavity lymphomas conforming to the current WHO morphologic criteria for PBL were retrieved from the consultation files at the AFIP. An immunohistochemical panel consisting of CD3, CD20, CD30, CD38, CD45RB (LCA), CD79a, CD138, Bcl-2, Bcl-6, Alk-1, Ki-67, and LMP-EBV was performed. Clinical follow-up, including HIV status, was pursued for each case. Results and Conclusions: Morphologically, sheets of large immunoblast-like cells with a high mitotic rate characterize PBL. The nuclei are eccentrically placed with a single prominent nucleolus. The abundant cytoplasm is deeply basophilic with a paranuclear hof. Scattered tingible body macrophages and necrosis are present as well. PBL is immunoreactive with CD38, CD138, and CD79a, but shows minimal or absent expression of CD45RB (LCA) as well as CD20. Follow-up information was also pursued. Recognition of this distinctive type of lymphoma, confined mostly to the oral cavity, is important to avoid confusion with other malignancies.

#30 2:36 p.m.

HEAD AND NECK SQUAMOUS CELL CARCINOMA (HNSCC) MANIPULATES IMMUNE RESPONSE. Z. B. Kurago, A. Lam-ubol, B. Stone, J. Untrauer, C. De La Mater, U. Iowa, Iowa City.

Most surface epithelial pre-cancers do not progress to advanced HNSCC, suggesting that host factors, such as the immune system, may interfere with HNSCC progression. HNSCC is believed to be “immunosuppressive”, although the mechanisms of HNSCC-immune system interactions are poorly understood. Dendritic cells (DC) play a central regulatory role in anti-tumor immunity. DC differentiate from monocytes and other precursors, and depending upon DC ability to mature, they induce immunity or tolerance. Hypotheses: Manipulation of host response is important for HNSCC progression. HNSCC factors regulate DC and DC precursor phenotype and activity. Methods: 1) In vitro co-cultures and migration-function assays using HNSCC lines, normal monocytes and DC, analyzed by flow cytometry and ELISA for cell phenotypes and cytokine production. 2)

Immunohistochemical evaluation of oral HNSCC specimens for DC, monocyte and macrophage populations. Results: In vitro, HNSCC lines produce cytokine interleukin-6 (IL-6) and Langerhans cell chemoattractant macrophage inflammatory protein-3 (MIP-3), etc., as detected by ELISA. High IL-6-producing HNSCC further synergize with monocytes in IL-6 production, which correlates with monocyte differentiation into macrophages and leads to great synergism in VEGF production. In two-chamber migration-function assays using DC and HNSCC introduced into separate chambers, high HNSCC MIP-3 production correlates with high DC numbers in HNSCC chambers, suggesting DC are recruited to HNSCC. However, DC maturation appears impaired. In co-cultures, HNSCC support and expand specific DC populations. Monocyte-macrophage-DC populations in HNSCC specimens are also evaluated. Conclusions: HNSCC factors manipulate DC and DC precursor differentiation, migration and function, which may support cancer progression. Supported in part by American Cancer Society Grant #IN-122V, administered by The Holden Comprehensive Cancer Center.

#31 2:48 p.m.

ORAL KOILOCYTIC DYSPLASIA ASSOCIATED WITH SQUAMOUS CELL CARCINOMA. M.Fornatora, J.Ghannoum, R.F.Reich, P.Freedman Temple U. Philadelphia, N. Y. Hosp. Med. Center of Queens Oral koilocytic dysplasia (KD), described in 1996 as an entity of unknown biologic potential, exhibits histologic features of both human papillomavirus (HPV) infection and oral epithelial dysplasia. Histologic features of HPV infection include koilocytosis, acanthosis, multinucleated keratinocytes, and atypical mitoses. HPV 6/11 may be present in KD, but high risk HPV types including HPV 16/18/31/33 were consistently found in cases shown to be HPV positive in the original study. Being reported are two cases of oral KD found to be in continuity with squamous cell carcinomas (SCCa). A 41yo non-smoking male dentist with a negative history for regular alcohol intake presented with a 2.7cm lateral tongue leukoplakia. Clinical impression was oral appliance related traumatic hyperkeratosis. Diagnosis on biopsy was epithelial dysplasia, mild, with features of HPV (KD). SCCa was found at re-excision and a lateral neck lymph node was positive for metastases. The biopsy specimen was positive for HPV DNA using PCR. Sequencing for HPV subtype identification was unsuccessful, interpreted to be due to infection with multiple HPV subtypes. A second case of KD with histologic transition to SCCa was identified in a 64yo male, also as a lateral tongue leukoplakia (2.5cm). Social history was positive for smoking (2.5ppd) and daily alcohol intake. Clinical impression was epithelial dysplasia without appreciable lymphadenopathy. Biopsy revealed SCCa in transition from KD. The biopsy specimen was positive for HPV 16 DNA (PCR and DNA sequencing). Definitive conclusions cannot be drawn regarding the role of HPV in the pathogenesis of these SCCas. However, the intimate associations of SCCa with lesions fulfilling the histologic and microbiologic criteria for oral KD document the potential for KD to be associated with oral cancer.

#32 3:00 p.m.

SCLEROSING MYOEPITHELIAL NEOPLASM: IMMUNOHISTOCHEMICAL AND ULTRASTRUCTURAL FEATURES IN A UNIQUE CASE. ZB Kurago, J Hicks, C Flaitz, B Kloberdanz. U Iowa, Iowa City; UTHSC-Houston, Tx Children's Hosp, Baylor College of Medicine, Houston; St. Charles, IL.

Background: Histopathologic features of myoepithelial tumors may vary, and include spindled, plasmacytoid, epithelioid and clear cells, as well as mucoid to hyalinized matrix. Purpose: We present a unique myoepithelial neoplasm with dense sclerosis. Case History: A 19 yr-old male presented with a 2yr history of a right buccal lesion. A poorly circumscribed submucosal lesion without ulceration or tenderness was located near Stenson's duct. Contributor's impression was "lipoma". Pathologic Features: The specimen was 2.1x1x1cm, very firm and varied from tan-brown to yellow. Microscopic examination revealed very dense fibrous stroma that infiltrated striated muscle, adipose tissue and minor salivary gland lobules. Small strands and irregular islands of cells with poorly defined plasma membranes, abundant pale eosinophilic fibrillar to vacuolated cytoplasm and oval to round nuclei were embedded in, and often compressed by the dense stroma. Ductal structures and chondroid matrix were not present. Tortuous thin-walled vascular channels were common. The cellular strands and nests reacted with antibodies for S-100, pancytokeratin (AE1/AE3) and GFAP, but not for SMA, CD34 or CD68. There was mild expression of CD99 and bcl-2. Electron microscopy revealed occasional intermediate filament aggregates, hemidesmosomes, rare structures representing myofilament attachment plaques, basement membranes and basal lamina material. Neural processes, neurosecretory granules, neurofilaments and glial differentiation were not identified. Myoepithelial origin was supported by the histopathologic, immunohistochemical and ultrastructural findings. Conclusion: Dense sclerosis may be associated with myoepithelial neoplasms and both immunohistochemical and ultrastructural examination may help define the cell of origin.

#33 3:12 p.m.

EXPRESSION PATTERNS OF INTEGRINS ON PLEOMORPHIC ADENOMA AND ADENOID CYSTIC CARCINOMA: STUDY ON SPECIMENS AND *IN VITRO* INVESTIGATION OF THE EFFECTS OF EXTRACELLULAR MATRIX ON THE EXPRESSION OF THESE ADHESION MOLECULES. SV Lourenço, S Kapas, K Leite, VC Araújo. Instituto de Medicina Tropical de São Paulo and Dermatology Department, Medical School, University of São Paulo, Brazil

Background: Pleomorphic Adenoma (PA) and Adenoid Cystic Carcinoma (ACC) are neoplasms of distinct behaviour, showing similar origin, cell components and marked presence of extracellular matrix (ECM). Interactions between cells and ECM are important in the biology of tumours, being partially mediated by integrins. This study investigated these interactions on PA and ACC using paraffin-embedded tissue and an *in vitro* model. Methods: Expression of integrins in paraffin-embedded samples was assessed by immunohistochemistry. Cells from PA and ACC were characterised using immunofluorescence, and integrin patterns of expression were investigated on cells cultivated on different ECM proteins. Results: Luminal cells of both PA and ACC were more intensely positive for integrins than myoepithelial cells. *In vitro* studies revealed that PA cells expressed more integrins than ACC cells regardless the ECM protein present. Conclusions: This study revealed the patterns of integrin expression in both specimens and *in vitro* models of PA and ACC. This might be useful to a better understanding of the biology of these lesions.

#34 3:24 p.m.

METASTATIC TUMORS TO THE JAWS: RETROSPECTIVE STUDY OF 101 CASES. NJ D'Silva; DJ Summerlin; R Abdelsayed, CE Tomich, CT Hanks; KC Cordell; S Meyrowitz. U. of Michigan, Ann Arbor and Indiana U., Indianapolis.

Metastatic tumors to the jaws are rare lesions that often present with innocuous symptoms mimicking dental infection. In this study, we report two cases of prostatic adenocarcinoma metastatic to the mandible and review >100 cases of metastatic cancer from the archives of the oral pathology biopsy services of the U. of Michigan and Indiana U. Schools of Dentistry. Methods: After IRB approval at both institutions, cases diagnosed as metastatic disease to the jaws were retrieved. Data collected from these cases included gender, age, clinical signs and symptoms, location and primary tumor diagnosis. Results: Case 1: The lesion presented as an expansile, bony mass in the mandible of a 76 year old male with a history of prostatic adenocarcinoma. Case 2: An 82 year male with a history of prostatic adenocarcinoma presented with a lesion causing bone destruction and swelling of the mandibular alveolar ridge. In a retrospective analysis of archival cases there was an equivalent gender distribution and a 5:1 mandibular predilection. The breast and lungs were the most common primary tumor sites for females and males respectively. When all metastatic tumors were considered, regardless of gender or location, the breast was the most common site of origin. Pain was the most common presenting symptom, followed by paresthesia. There was a wide age distribution, but women exhibited twice as many jaw metastases as men in the 31 – 40 age group and one third as many in the 71-80 year age group. Conclusions: Metastatic jaw disease presents at an earlier age in women than in men and exhibits an equivalent distribution in both genders. Patients presenting with dental symptoms and with a history of malignancy should be evaluated for the possibility of metastatic disease. (This information was presented in part at the 1994 AAOMP meeting.)

#35 3:36 p.m.

MASSIVE OSTEOLYSIS WITH HISTOLOGIC FEATURES OF EOSINOPHILIC ANGIOCENTRIC FIBROSIS. T.Gibson, J. Neugarten, J. Fantasia, R. Kelsch, and S. Sachs. Long Island Jewish Medical Center, New Hyde Park, NY.

Background: Massive osteolysis (MO) is a rare destructive process of unknown etiology, first described by Gorham and Stout in 1954. This condition is exceedingly rare with approximately 150 cases described in the literature with 20 percent involving the jaws and skull. The disease is characterized by a proliferation of thin-walled vasculature channels and inflammation with regional osteolysis. Eosinophilic angiocentric fibrosis (EAF) is a newly described entity also of unknown etiology. Previously reported cases of EAF have been restricted to the nose and upper airway tract. The histology of EAF is characterized by a perivascular fibrosis and associated tissue eosinophilia. A sixteen-year-old girl with MO affecting the right mandible and bilateral maxilla and histological features of EAF is described. Objective: We attempt to determine whether similarities exist between MO and EAF and if these two entities can be distinguished based on the clinical, radiographic, or histopathologic features. Methods: A comprehensive search of the Medline database from 1966 through 2003 and a review of the reference lists of relevant articles of MO and EAF formed the basis of this study. These data are compared to the aforementioned case of MO with histological features of EAF. Results: The case report has clinical and radiographic features of MO. The process was progressive, with uncontrolled osteolysis despite aggressive surgery and radiation therapy. The histological features identified are comparable to that described for EAF. However our literature review could not identify clinical and radiographic similarities between this case and those of EAF reported in the literature. Conclusion: The clinical and radiographic features of this case are consistent with a diagnosis of MO, yet the histopathology is more typical of EAF. The relationship between these two poorly understood conditions, if any, remains obscure.

#36 3:48 p.m.

EXTRAPLEURAL SOLITARY FIBROUS TUMOR OF THE ORAL CAVITY: PROLIFERATION MARKERS, TUMOR SUPPRESSOR GENE EXPRESSION AND ULTRASTRUCTURAL FEATURES. C Flaitz, B Neville, J Hicks, UTHSC-Houston Dental Branch, Medical U So Carolina, Tx Children's Hosp, Baylor College Medicine.

Background: Extrapleural solitary fibrous tumors (ESFT) were previously classified as hemangiopericytomas (HPC). With the current WHO classification, HPCs have been incorporated within ESFTs. A myopericytic category includes tumors with pericytic differentiation. Purpose: Proliferation markers, tumor suppressor gene expression, and ultrastructural features were evaluated with cellular oral ESFTs. Case History: Two females (53yrs, 52yrs) presented with recurrent oral masses (1cm, 1.8cm) involving the anterior facial gingiva and buccal mucosa. Pathology: These cellular tumors were composed of a bland plump spindle cell proliferation embedded in a vascular background. The cells were arranged in a storiform pattern. The adjacent soft tissues were infiltrated by tumor with extension to the margins. Tumor cells were diffusely positive for CD34, bcl-2 and MCM-7, moderately to focally positive for CD99, mildly positive for mib-1, and focally positive for p53. Smooth muscle actin, muscle-specific actin and S100 protein were negative. Electron microscopy revealed bland spindle cells with occasional areas of extracellular collagen precipitation. Glycocalyx material coated the cell surfaces. Attachment plaques and smooth muscle differentiation were lacking. Dermatofibrosarcoma protuberans [t(17;22), COL1A1-PDGFB] and pericytic tumor [t(7;12), GLI-ACTB] translocations were not detected by RT-PCR. Conclusions: With these cellular oral ESFTs, proliferation markers (bcl-2, MCM-7) were expressed diffusely in a high proportion of cells, and p53 was also identified focally. Morphology alone does not predict which ESFTs have aggressive or metastatic potential. Complete excision of ESFTs with close clinical follow-up is the recommended treatment.

#37 4:00 p.m.

CO-EXPRESSION OF p16INK4A AND LAMININ 5 GAMMA 2 IN KERATINOCYTES: A NORMAL WOUND HEALING RESPONSE THAT GOES AWRY DURING NEOPLASTIC PROGRESSION  
E.Natarajan<sup>1,2</sup>, A.Lazar<sup>2,3</sup>, S.Woo<sup>1,2</sup>, J.Omobono<sup>2</sup>, S.Browne<sup>2</sup> and J.Rheinwald<sup>2,3</sup>. <sup>1</sup>Harvard School of Dental Medicine, <sup>2</sup>Brigham and Women's Hospital, <sup>3</sup>Harvard Medical School, Boston, MA.

We recently reported that p16INK4A (p16) and the gamma 2 chain of Laminin 5 (Lam5g2) are coordinately expressed in early invasive regions of neoplastic epithelium in vivo, at the edges of wounds made in confluent cultures of normal primary keratinocytes, and by senescent keratinocytes, associated with directional hypermotility (Natarajan et al. (2003) Am J Path 163: 477-491). These results led us to investigate whether p16/Lam5g2 coexpression occurs in wounds in vivo and to determine the cause and effect relationships between expression of these proteins and the hypermotile phenotype. We examined 16 skin ulcers immunohistochemically for p16 and Lam5g2. In 13 of the specimens, p16 and Lam5g2 were coordinately expressed at the normal epithelium/ulcer border and in reepithelialized regions lacking normal basal cell layer morphology. To investigate causal relationships between Lam5 and p16 expression and hypermotility, we plated keratinocytes at low density on surfaces coated with extracellular matrix proteins secreted by the tumor cell line 804G, shown by others to be comprised predominantly of Lam5. Normal keratinocytes plated on such a surface expressed p16, arrested growth, and exhibited enhanced directional motility. Two cell lines cultured from neoplastic epithelium---one p16-deleted and the other expressing mutant p16, became directionally motile when plated on such Lam5 surfaces. In contrast, precoating culture dishes with serum, which contains fibronectin, produced no effect. We conclude that contact with endogenous or exogenous Lam5 induces p16 expression and hypermotility in normal keratinocytes, but that p16 is not essential for the hypermotile phenotype. These results suggest that p16/Lam5g2 co-expression is an important feature of normal epidermal wound healing, causing growth arrest of the motile cells that lead wound closure. Loss of p16 during neoplastic progression permits motile cells to continue proliferating, thereby resulting in invasive growth.

#38 4:12 p.m.

SALIVARY GLAND LYMPHOMA. REVIEW OF 11 CASES. N. Said-Al-Naief, V. Reddy, M. Roh, R. Azuero and S. Abdulkadir. UAB, Birmingham, AL.:

Malignant Lymphomas of the salivary glands are uncommon. Historically, they comprise 1.7 to 3.1 % of all salivary neoplasms. The parotid glands are the most common site of occurrence but submandibular, sublingual, and minor salivary gland involvement is well documented. A mass in the salivary gland, especially the parotid, may represent the initial manifestation of malignant lymphoma or it may be part of a more, generalized disease. Additionally, the vast majority of major salivary gland lymphomas are non Hodgkin's lymphoma of B-cell lineage. In our review of 11 cases of salivary gland lymphoma at our institution, 8 patients were women and 3 were men. All were Caucasian with the exception of one African-American. Age ranged from the 3<sup>rd</sup> to the 8<sup>th</sup> decade with the average being 66 years. Nine out of eleven cases involved the parotid glands and all, with the exception of one case, represented primary disease. The other two cases involved the submandibular glands. A total of four patients had an underlying Sjogren's syndrome who went on to develop lymphoma (three in the parotid and one in the submandibular gland). One patient was diagnosed with T cell rich B cell lymphoma. A second was diagnosed with small lymphocytic lymphoma/ chronic lymphocytic leukemia and a third with lymphoplasmacytoid lymphoma. Two patients were diagnosed with low grade follicular lymphoma, one of which represented metastatic disease to the parotid which underwent subsequent transformation to an intermediate grade. Another patient was diagnosed with Mantle zone lymphoma while the remaining five patients were diagnosed with mucosa associated lymphoid tissue (MALT-lymphoma) and in one of those; transformation into large B cell lymphoma was documented. The clinicopathological features, utilizing special and ancillary studies, treatment and follow-up and are presented.

#39 4:24 p.m.

PERICYTIC TUMOR WITH *GLI* ONCOGENE AND *BETA-ACTIN* TRANSLOCATION [T(7;12)]. J Hicks, C Flaitz. Texas Children's Hospital, Baylor College of Medicine, UTHSC-Houston Dental Branch, Houston, Tx.  
Background: Pericytic tumor with a t(7;12) translocation is a recently described spindle cell neoplasm that affects a wide age range and has an oral cavity predilection (Am J Pathol 2004 in press). Purpose: We present a pericytic tumor of the tongue with translocation of *Gli* oncogene and *beta-Actin* in a 10 year-old male. Case History: A 10 year-old male presented with a 5.5 cm right tongue mass that occupied over 50% of the tongue volume. Following biopsy, the patient underwent chemotherapy to reduce the tumor volume and allow for excision. The patient is currently without recurrence at 32 months following definitive resection. Pathology: The tumor was multilobulated with an infiltrative growth pattern and comprised of spindle cells arranged around small thin-walled vessels. Mitotic rate was relatively low (1/10 HPFs and <5% proliferation index with mib-1). Immunocytochemistry showed CD34 reactivity for endothelium only. Smooth muscle actin and laminin were focally positive with tumor cells. Myogenin, muscle-specific actin, desmin, keratin, EMA and type IV collagen were negative. Electron microscopy showed spindle cells arranged around capillary-sized vessels. The tumor cells had attachment plaques, abundant glycocalyx material lining their surfaces, intracytoplasmic glycogen, and rudimentary cell junctions. Cytogenetics revealed a translocation, t(7;12)(p21q15) at a locus that involved *Gli* oncogene and *beta-Actin*. Conclusion: This unique spindle cell neoplasm possesses pericytic differentiation based upon histopathologic, immunocytochemical and ultrastructural evaluation, and will most likely be classified as a separate entity within the WHO myopericytic neoplasm category. This unique pericytic tumor has a tumor-defining reciprocal translocation and lacks aggressive features.

#40 4:36 a.m.

DENTAL FORENSIC SUPPORT OF OPERATION IRAQI FREEDOM. W. Henry, E. Childers, R. Foss. Armed Forces Institute of Pathology (AFIP), Washington DC.

*Background:* The AFIP's trifold mission is consultation, education, and research. Through the Office of the Armed Forces Medical Examiner (OAFME), investigating unnatural deaths including deaths during combat operations, is an additional tasking. The Department of Oral and Maxillofacial Pathology (OMFP) provides support to the OAFME at the Carson Mortuary, primarily in the form of dental identification of casualties. Dental identification support provided during Operation Iraqi Freedom (OIF) from 26 March 2003 through 31 December 2003 is reviewed and discussed. *Materials and Methods:* Data collected by the OMFP and the OAFME were examined. For purposes of discussion, the mission was broken into three phases: the preparatory phase, from October 2002 until 19 March 2003, the surge phase, from 20 March to 30 April 2003, and the sustained operations phase (SUSTOP), from 1 May 2003 to 31 December 2003. Total identifications, methods of identification, identifications based on panoramic radiographs versus records, turnaround rates, and manning requirements were evaluated. *Data:* Mission planning occurred during the preparatory phase. During the surge phase, 145 postmortem dental examinations were performed and 120 forensic dental identifications were made. During the SUSTOP, 360 postmortem examinations were performed and 284 forensic dental identifications were made. *Conclusions:* Forensic dental identification is an expedient method of identification for human remains. Fifty four percent of casualties were identified the same day the postmortem examination was performed and an additional 16% were made within 24 hours.

#41 4:48 p.m.

EXTRANODAL HODGKIN'S LYMPHOMA OF THE ORAL SOFT TISSUE

M.Fornatora, R.F.Reich, P.Freedman. Temple U. Philadelphia, N. Y. Hospital Medical Center of Queens  
Cervical lymphadenopathy is the most common head and neck presentation for Hodgkin's lymphoma (HL). Although uncommon, extranodal HL observed at the time of diagnosis is well documented and is typically associated with generalized disease and a consequence of local spread from adjacent lymph nodes. Extranodal HL of the upper aerodigestive tract soft tissue is extremely rare, but has been reported to involve the oral cavity, oropharynx, nasopharynx and larynx. Two cases of extranodal HL of the oral soft tissue are being reported. A 32yo male presented with a 5.0cm ulcerated lateral palatal swelling and a history of recently diagnosed HL. Clinical impression was palatal abscess, r/o HL. Diagnosis on biopsy was malignant lymphoid infiltrate, consistent with HL. The patient was determined to have stage IV HL, with involvement of the low pelvic area, oral cavity and cervical lymph node chain. A second case of extranodal HL of the oral soft tissue was identified in a 70yo female as a swelling of the floor of the mouth. Clinical impression was mucocele, r/o salivary gland tumor. The biopsy specimen was diagnosed on routine microscopy as consistent with lymphocyte predominate HL. The diagnosis was confirmed by immunohistochemical analysis. A diagnosis of stage I HL was made based on the absence of any detectable sites of involvement outside of the oral cavity. After treatment, the patient was considered free of disease at six month follow-up. These two cases contribute to the paucity of cases documented in the literature of extranodal HL of oral soft tissues.

#42 5:00 p.m.

SOME PITFALLS OF MEDLINE SEARCHES USING KEYWORD AND MESH PROTOCOLS.

K. Summersgill, U. of Pittsburgh, Pittsburgh, Pennsylvania.

Objectives: The use of computerized databases has revolutionized how we perform literature searches. However, some methods are more efficient and fruitful than others. This research was performed to identify some pitfalls of literature search protocols. Methods: Using the Medline database from 1996 to November 15, 2003 in the OVID interface, I performed keyword and Medical Subject Heading (MeSH) searches of commonly misspelled words, British versus American English spelling, and words containing diacritical markings such as umlauts and tildes.

Findings: Misspelled words or variants such as “boney”, “persistance”, “inflammation”, and “erythematosis” occurred 16, 51, 10, and 19 times, respectively, and were far outnumbered by entries with the correct spelling. In general, diacritical markings are ignored in keywords, authors’ names, and MeSH headings. The American form of a keyword greatly predominated over the British spelling of a keyword, and was much more likely to map more specifically to MeSH headings. Those entries with a misspelled word often also contained the correctly-spelled version. The use of MeSH headings usually yielded more-specific results than the use of keywords.

Conclusions: Although using keywords in literature searches is sometimes easier than using MeSH, one is likely to miss numerous relevant citations. In performing Medline database searches, we must be aware of the particular quirks of spelling and usage of the program.

## READ BY TITLE

SUBMUCOSAL CALCIFIED NODULE OF THE LOWER LIP. REPORT OF A CASE.

D. Antoniadou, A. Markopoulos, Aristotle U. Thessaloniki, Greece

Background. The subepidermal calcified nodule is a form of idiopathic calcinosis cutis that affects children and is occasionally present at birth. The most common locations are the extremities and the face. The oral and perioral regions are very rarely affected by calcinosis cutis of any type. Method. A 1-year-old white girl was referred to the department of Oral Medicine and Maxillofacial Pathology of the School of Dentistry, Aristotle University of Thessaloniki, Greece for evaluation of a white hard nodular lesion that had been present on her lower lip since birth. The patient had no history of connective tissue disease or calcium and phosphorus abnormalities. The nodule was surgically excised and was histopathologically and immunohistochemically examined. The sections stained with H&E revealed a cystic lesion filled with calcified material. A thin layer of inflammatory and epithelioid cells was arranged around the calcium deposits. Immunohistochemically these cells were CD 68 positive and negative to keratins. These findings were compatible with a diagnosis of submucosal calcified nodule.

Conclusion. The subepidermal calcified nodule is characterized by the presence of calcified material which is usually located in the uppermost lamina propria. The calcium is present as irregular granules and globules. The exact mechanism that leads to excessive calcification is not clear.

**MUCOUS RETENTION CYST WITH DEVELOPMENT OF BASAL CELL ADENOMA: REPORT OF A CASE.**

**D. Antoniadis, A. Markopoulos, T. Zaraboukas, A. Epivatianos** Aristotle U. Thessaloniki, Greece.

**Background:** Mucus retention cyst is a relatively uncommon lesion of the salivary gland. Unlike the more common mucus escape reaction, it is a true cyst that is lined by epithelium consisting of a uniform layer of cuboidal to low columnar cells. However, a uniform thin layer of non-keratinizing stratified squamous epithelium is common, and occasional mucus cells within the epithelial lining of the cyst can be observed. Some authors have mentioned that in some cases the epithelium demonstrates papillary folds into the cystic lumen, when these lesions are misdiagnosed as papillary cystadenoma. Other authors contend that mucus retention cysts do not show piling up of cells in the wall of the cyst and neither proliferation nor infiltration of islands of epithelium into the connective tissue is a feature. These histological features with connection to the absence of multicystic structures and of areas of solid epithelial proliferations are particularly important to rule out cystic neoplasms. Also, in the literature review, we could not find any reported case of mucus retention cyst with development of a neoplasm from the lining epithelium.

**Method:** A 68-year-old man was referred to the Oral Medicine and Oral Pathology Department of the Dental School of Thessaloniki because of a painless swelling that was periodically fluctuated in size. Intraoral examination revealed a well demarcated mass, soft to palpation, measuring 1.5 x 1cm which was located in the submucosa of the upper lip. The covered mucosa was reddish-blue in color. Under local anesthesia the lesion was totally excised. Histological examination showed the presence of a monocystic lesion lined by atrophic epithelium in proximity to normal minor salivary glands. Islands consisting of single layered cuboidal or columnar epithelial cells were also observed in contact with the lining epithelium and floating into the cystic cavity. These cell islands, when examined immunohistochemically, reacted positively in keratin 7 and S-100 protein and negatively for vimentin.

**Conclusion:** The histological and immunohistochemical findings supported diagnosis of mucus retention cyst with development of basal cell adenoma. Differential diagnosis of the tumor is discussed.

**CLINICOPATHOLOGIC STUDY OF 174 EPULI IN DOGS.** **C. Felizzola, N. Araújo, V. Araújo, D. Pinto Jr, S. Sousa.** University of São Paulo, School Dentistry, Brazil.

Epulis is a clinical term that has longed been used to diagnose gingival lesions occurring in dogs. Attempts have been done to individualize these lesions, and classifications have been proposed, some of which attempt to correlate dog lesions to those occurring in men. Studies have shown that although some resemblance does exist, the lesions tend to be different in histological aspects and clinical behavior in dogs and men. Among these lesions, most are of odontogenic origin or hyperplastic reactive lesions. Presently, histological characteristics of 174 oral dog tumors with clinical appearance of epulis were reviewed. The lesions originally diagnosed as fibromatous, acanthomatous and ossifying epulis were reclassified taking the currently available criteria into account. The lesions most frequently diagnosed were: peripheral odontogenic fibroma (53,5%), fibrous hyperplasia (32%), peripheral ameloblastoma (11,5%) and odontoma (3%). The average ages of dogs presenting focal fibrous hyperplasia, peripheral odontogenic fibroma, and peripheral ameloblastoma were 8.7, 7.7 and 7, years, respectively, and for odontomas the medium age was 5 months. There were slight breed differences among the types. Only in peripheral odontogenic fibroma, males were more affected than females. The other tumors were equally frequent in males and females. Since clinical behavior and clinical management varies among the oral lesions, it is important to properly diagnose them.

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DERMAL CHORISTOMA OF NASOPHARYNX. J. Whitt, A. Sanderson, D. Brewster. Naval Medical Center San Diego, California

The dermal choristoma of the nasopharynx is a developmental tumor that has been reported under a variety of different terms, including accessory auricle, hairy polyp and dermoid. Although the majority of these lesions arise from the vault of the nasopharynx near the region of the eustachian tube orifice, they have also been reported to arise within eustachian tube itself, from the nasopharyngeal surface of the soft palate, the oropharynx in the tonsillar region and, rarely, even in the middle ear and mastoid area. We report a case of an otherwise healthy 15 month-old female who presented with a one year history right-sided clear rhinorrhea. Nasopharyngoscopy revealed a 1 cm, firm, pinkish-white, smooth-surfaced, spherical, pedunculated mass arising from the left nasopharyngeal wall. The left-sided lesion acted as a ball valve to produce intermittent right-sided obstruction of the nasal passage. Imaging studies demonstrated a homogenous, solid mass of the density of adipose tissue. It was excised without complication using cautery.

Histopathologic examination revealed a solid mass of fibroadipose tissue that was surfaced by essentially normal skin. The keratinized, stratified squamous epithelial surface exhibited a granular layer and numerous dermal appendage structures, including hair follicles, sebaceous glands and sweat glands. The lesion did not exhibit elastic cartilage. These clinical and histologic findings support the diagnosis of dermal choristoma, a lesion that should be included in the differential diagnosis of nasopharyngeal masses in young individuals.

LYMPHOEPITHELIAL CYSTS OF THE ORAL CAVITY.LITERATURE REVIEW AND REPORT OF 4 CASES; ONE CASEWITH CO-EXISTENCE OF EPIDERMAL CYST.

D.Antoniades,A.Epivatianos,T.Zaraboukas Aristotle U.of Thessaloniki, Greece

Background: The lymphoepithelial cysts of the oral cavity (LCs) are uncommon lesions that present as small, raised, painless and movable submucosal masses. Epidermoid cysts are very rare small lesions with clinical characteristics similar to those of LCs. The aim of the present study was to present 4 cases of oral LCs adding 144 cases reported in the literature which are reviewed. In one out of 4 cases an epidermoid cyst co-existed.

Method: Four cases of LC were retrieved from the files of the department of Oral Pathology. New serial sections were cut and stained with hematoxylin and eosin and were reviewed. From the histories of the patients the clinical characteristics were recorded and added to those of 144 reported in the literature.

Conclusions: Analysis of the clinical data showed that the predominant location of oral LCs is the floor of the mouth (65.3%), followed by the posterolateral surface of the tongue (13.7%) and the ventral surface of the tongue (9.7%). The age of occurrence ranges between 4 and 81 years and the lesion most often occurs in the 3<sup>rd</sup> decade of life. There is a slight predilection for males (1.3:1) and the size of the lesion ranges between 1 mm to 20 mm in diameter and seldom exceeds 15 mm. Accidental injury of the oral cavity may produce the formation of epidermoid cysts as well as in areas when oral tonsils are present the formation of LCs.

**ORAL CARCINOMA IN SITU WITH EXTENSIVE DENDRITIC MELANOCYTIC COLONIZATION.** N Said-Al-Naief, J. Holmes & J. Hackney. UAB and Saint Vincent Hospital, Birmingham, Alabama:

A 49 year old, well nourished, well developed, African American man presented by referral to the oral and maxillofacial surgeon's office for the evaluation and management of a 2 X 2 cm, deeply pigmented lesion with an erythematous border located in his left soft palatal mucosa. The lesion was superficial but contained a small area of central ulceration. Review of his past medical history was significant for peripheral vascular disease and diabetes. Review of his social history revealed a 30 pack a year history of smoking and daily consumption of alcoholic beverages. An incisional biopsy showed carcinoma in situ with extensive dendritic melanocytic colonization. The dysplastic changes also focally involved salivary gland ductal epithelium. Immunohistochemical staining with anti HMB45 and anti-S-100 protein antibodies clearly delineated the dendritic melanocytes and melanocytic processes. Staining with broad spectrum cytokeratin was strong and diffuse. An outside expert was consulted and agreed with our interpretation. The lesion was excised with clear margins and the resection specimen showed identical findings to the biopsy. Melanocytic colonization is a well recognized occurrence in various primary and metastatic tumors including oral and cutaneous squamous cell carcinoma, but the incidence remains low and the significance of such finding remains to be determined. Various theories have been proposed to explain the proliferation and colonization of melanocytes including the liberation of cytokines, growth factors or other unknown factors by cancer cells. It has been also suggested that in ulcerated lesions, the presence of the melanocytes may represent cells that migrated into the existing lesion. In this case report, we review the literature and theories of etiology. The keratinocyte/melanocyte relationship is also investigated in this interesting entity.

**GLANDULAR ODONTOGENIC CYST OF THE ANTERIOR MAXILLA. REPORT OF A CASE AND LITERATURE REVIEW.** S. Sittitavornwong, J. Koehler, and N. Said-Al-Naief. UAB, Birmingham, Alabama: Glandular odontogenic cyst (GOC) is a rare odontogenic entity that has gained special attention primarily due to 1) its potentially aggressive behavior, with a propensity toward local recurrence if inadequately treated and 2) the overlap in histomorphological features with lateral periodontal & botryoid odontogenic cysts and central mucoepidermoid carcinoma of the jaws. An additional case of GOC in the anterior maxilla of a 57 y.o Ethiopian female is presented, bringing the total number of reports in the English literature (from 1966 till present) to 63 cases. Our review confirmed that GOC occurred over a wide age range, extending from the 1<sup>st</sup> to the 9<sup>th</sup> decades and showed slight predilection for males (52.4%) and prevalence for mandibular rather than maxillary involvement (79.4% vs. 20.6%, respectively). 84.6% of the maxillary cysts occurred in the anterior segment. The majority of cases (53.6%) presented with asymptomatic swelling. Radiographically, 50.8% of lesions were multilocular radiolucencies while 36.5% were unilocular. Out of the 63 cases, 38 had good post-treatment follow-up records. Out of twenty-two cases that were treated with enucleation, 8 recurred during the follow-up period which ranged from 12 - 44 months. Two out of the seven cases that underwent curettage recurred between 29 - 84 months. The remaining 2 cases that were managed with either en-bloc resection alone or with en-bloc with cryosurgery also recurred, while none of the seven cases that have undergone more aggressive treatment showed signs of recurrence during a follow-up period ranging from 1 - 14 years. Our review confirms the need for more aggressive management of GOC. The similarities and differences between GOC and other entities entertained in its differential diagnosis are discussed.