

# Essay Program 1

## Monday, April 18, 2005

#1 8:00 a.m.

NEWLY RECOGNIZED ORAL MANIFESTATIONS OF SCHIMMELPENNING SYNDROME. L. Ernst, P.D. Quinn, and F. Alawi. Children's Hospital of Philadelphia and U. of Pennsylvania, Philadelphia.

Schimmelpenning syndrome (SS) is an unusual disease that is characterized by mucocutaneous, central nervous system, ocular, and skeletal abnormalities. Nevus sebaceus, usually with broad involvement of the scalp and face, represents the classic skin finding associated with SS. We report a 6 year old female with SS who presented with a variety of oral lesions, including a number of intraosseous jaw findings that have not been previously described in patients with the syndrome. These findings include bilateral central giant cell granulomas (CGCG) – one lesion involving the left maxilla, which perforated into the soft tissues, and a second distinct lesion involving the right anterior hard palate. Both CGCGs were diagnosed at the patient's initial presentation. Although there have been two published reports of CGCG identified in patients with the syndrome, in both cases, the occurrence of the lesion was thought to represent a coincidental finding. We argue that CGCG represents a true clinical manifestation of SS. One year later, the patient presented again, this time with bilateral maxillary expansion. Microscopic review of the surgical specimens revealed bilateral benign fibro-osseous lesions, both complicated with foci of CGCG; typical appearing complex odontomas; and multiple, malformed teeth containing melanin. A hybrid adenomatoid odontogenic tumor-odontoma involving the anterior mandible was also removed at that time. The findings of pigmented teeth and a hybrid odontogenic neoplasm are novel and have not been previously reported in patients with SS. Although the genetic defect associated with SS has not been characterized, it is intriguing to speculate that a common gene may be important in the pathogenesis of tooth development, maxillofacial benign fibro-osseous disease, and CGCG.

#2 8:12 a.m.

INTRAORAL EPITHELIOID HEMANGIOENDOTHELIOMA: REPORT OF TWO CASES AND REVIEW OF THE LITERATURE. A.C. Chi, D.R. Weathers, A.L. Folpe, K. Rasenberger, and D. Dunlap. Medical U. of South Carolina, Charleston, and Emory U. Hospital, Atlanta, Georgia. The epithelioid hemangioendothelioma (EH) is an uncommon vascular neoplasm of borderline or intermediate malignant potential. Although EH may involve various anatomic locations, EH most commonly arises in soft tissue, liver, and lung. Involvement of the oral cavity is rare. A review of the English language literature reveals only twelve previously reported cases of intraoral EH. We present two additional intraoral cases—the first presenting as an asymptomatic radiolucency in the posterior mandible of a 23-year-old female, and the second presenting as an asymptomatic, erythematous gingival nodule in a 28-year-old female. The average age at presentation for EH is 28 years with a 2.5:1 female:male ratio. Intraoral tumors most commonly involve the gingival soft tissues and often are associated with adjacent alveolar bone resorption. Local recurrence was noted in four previously reported cases, and possible regional lymph node metastasis was described in one previously reported case. No cases of intraoral EH resulting in distant metastasis or death from disease have been reported. Wide local excision with close clinical follow-up appears to be the treatment of choice for these tumors of borderline malignant potential and somewhat unpredictable clinical behavior.

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#3 8:24 a.m.

FOREIGN BODY REACTION TO HYALURONIC ACID (RESTYLANE®): AN ADVERSE OUTCOME OF LIP AUGMENTATION. P. Edwards, J. Fantasia, and R. Iovino. Creighton U., Omaha, Nebraska, Long Island Jewish Medical Center, New Hyde Park, New York, and Private Practice, Southampton, New York.

Non-animal source hyaluronic acid (Restylane®) is a relatively new redefining dermal filler that is being employed with increasing frequency in the fields of dermatology and cosmetic/facial plastic surgery.

We report a case of a 74-year-old woman who presented with a firm submucosal nodule of the lower lip, which clinically was thought to represent a benign neoplasm. An excisional biopsy revealed the presence of multiple cyst-like vacuolated areas surrounded by granulomatous tissue composed predominantly of histiocytes and foamy macrophages, consistent with a foreign body reaction. Subsequent to the pathology findings, the patient acknowledged that she had received injections of Restylane® to the lips approximately 6 months before discovering the nodule.

Although hyaluronic acid-based dermal fillers reportedly have a low incidence of long term side effects, clinicians should be aware of the possible development of foreign body reactions to these injectable agents. The dermatology literature regarding this occurrence will be reviewed.

#4 8:36 a.m.

JUVENILE OSSIFYING FIBROMA: AN IMMUNOHISTOCHEMICAL STUDY. N.G. Nikitakis, R. Chaisuparat, G. Warburton, M.A. Lopes, O. Nicolatou, J.C. Papadimitriou, R.A. Ord. U. Maryland, Baltimore. Juvenile ossifying fibroma (JOF) is a non-metastasizing, but locally aggressive and highly recurrent fibro-osseous lesion of the craniofacial skeleton. Microscopically, JOF consists of a cellular fibrous stroma containing a mineralized component in a psammomatoid or trabecular pattern. JOF should be distinguished from other bone tumors, including ossifying fibroma (OF) and osteosarcoma (OS). This study presents five cases of biopsy-proven JOF, trabecular-type, affecting three male and two female patients with a mean age of 11.8 years. Three cases arose in the maxilla and two occurred in the mandible. All cases were treated by enucleation; two cases recurred and were retreated with wide surgical excision. Immunohistochemical study of the OS-associated molecules CDK4, MDM2, and p53 was performed in all cases in addition to five control cases of OF. CDK4 positivity was noted in all JOF cases; the staining pattern was diffuse and strong in four cases and focal and weak in one case. In contrast, four cases of OF were weakly and focally CDK4 positive. Immunostaining for MDM2 was observed in three JOF cases; all OF were MDM2 negative. All cases of OF and JOF were negative for p53, except one focally positive JOF case. Considering the combined results of our previously published immunohistochemical studies of 34 head and neck OS, CDK4 expression is noticed in a high percentage of JOF, OS and OF, although the latter shows diminished staining. MDM2 expression is seen only in JOF and OS, being absent in OF. Finally, p53 expression is detected almost exclusively in OS, with the exception of a single case of JOF. Although significant overlap exists, differential protein expression patterns can elucidate the pathogenesis and facilitate the determination of aggressive or malignant behavior of bone tumors in the head and neck region.

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#5 8:48 a.m.

A CASE REPORT: ORAL INVOLVEMENT AS AN EARLY MANIFESTATION OF WEGENER'S GRANULOMATOSIS. S. Kemp, G. Gallagher, and S. Kabani. Boston U., Boston, Massachusetts. A 17-year-old female presented for routine extraction of a third molar. The surgical site remained unhealed for over two weeks and on a subsequent follow-up visit, the patient developed "blebs" on her maxillary and mandibular marginal gingiva. A superficial biopsy of the lesions revealed epithelial hyperplasia with a mixed inflammatory cell infiltrate. The case was signed out descriptively as non-specific mucositis. The clinical impression was a reactive gingivitis secondary to antibiotic and oral steroid use for a "sinus infection" that was being treated by her ENT specialist. The patient was lost to follow-up but was later diagnosed with Wegener's granulomatosis at another institution. Oral lesions in Wegener's granulomatosis may be the only clinically evident sign of the disease. The disease is rare and approximately 30 new patients each year present with oral manifestations. Due to the poor prognosis associated with untreated patients, early diagnosis and treatment are important. Diagnosis on a superficial biopsy alone, without a strong clinical suspicion, may be difficult. This is complicated by the non-specific inflammation commonly seen in gingival biopsies. This case shows the importance of keeping the entity in a differential diagnosis of a biopsy that shows non-specific mixed inflammation without definitive vasculitis, even if there is not a strong clinical suspicion.

#6 9:00 a.m.

AUTOSOMAL DOMINANT MULTICENTRIC MYOFIBROMATOSIS PRESENTING AS A PALATAL MASS. C. Flaitz, M. Dishop, D. Metry, E. Friedman, M. Chintagumpala, and J. Hicks. UTHSC-Houston, Texas Children's Hospital, Houston. **Background:** Myofibromas are benign spindle cell proliferations composed of myofibroblasts that may mimic congenital infantile fibrosarcoma. These tumors occur in 3 forms: solitary (>50%), multicentric (33%), and multicentric with visceral involvement (<15%). Rare familial myofibromas have been reported. **Case history:** At 3 days of age, a Caucasian female had feeding difficulties due to a palatal mass that bled intermittently. A 10% weight loss was documented by the pediatrician at day 11. Besides a large palatal mass with surface ulceration, other soft tissue lesions were present including 2cm upper arm mass, 3cm red-purple back macule, 1 cm flank mass, and 3 cm thigh mass. CT images identified a destructive lesion involving the maxilla and sinus and a 2 cm focally calcified intracranial mass. Biopsy of the palatal mass was performed. **Pathology findings:** The palatal mass was composed of a cellular spindle cell proliferation with fascicular, nodular, and focal hemangiopericytoma-like patterns. Mitotic activity was moderate (3/10 HPFs), but there was no atypia, pleomorphism, or hyperchromasia. Smooth muscle actin was positive within tumor cells. Electron microscopy revealed spindle cells with longitudinal filaments with dense bodies and fibronexus structures. The tumor had a normal female karyotype without a t(12;15) translocation which is associated with congenital infantile fibrosarcoma. **Additional familial history:** Further investigation revealed an extensive family history of myofibromas that were diagnosed in 3 generations with an autosomal dominant inheritance pattern. **Conclusion:** An isolated spindle cell lesion in an infant or young child requires differentiation from congenital infantile fibrosarcoma, determination of tumor pattern, and consideration of family predilection when making a definitive diagnosis of myofibroma.

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**#7 9:12 a.m.**

**“INTRAOSSEOUS” SCLEROSING CARCINOMA OF POSSIBLE ODONTOGENIC ORIGIN. REPORT OF TWO CASES.** I.G. Koutlas, G. Warnock, and J.C. Manivel. U. of Minnesota, Minneapolis and Johns Hopkins Hospital, Baltimore, Maryland.

Two cases of intraosseous carcinomas that share unusual characteristics are presented. The tumors involved a 72-year-old male and a 73-year-old female and occurred in the mandible and maxilla, respectively. Both tumors caused bone loss as became evident by radiography. They were characterized by small nests and slender cords of epithelial cells reminiscent of “American-Indian” files. Occasionally cytoplasmic clearing was encountered. Cytologically, there was no evidence of atypia and no mitoses. The most striking feature of malignancy was the tendency of the neoplastic nests and cords to infiltrate through muscle and peripheral nerves. The stroma was at areas characterized by very dense collagenous fibers. Initially and in both cases, metastatic disease was excluded after thorough clinical evaluation of the patients. Immunohistochemically, both tumors stained for cytokeratins 5/6, E-cadherin, and high molecular weight keratin. One of the tumors was positive for cytokeratin 7, while both were negative for cytokeratin 20. The male patient has been free of tumor for 3 years although his reconstruction was judged suboptimal. Presently there is no available follow-up of the female patient. The histogenesis of these tumors appears odontogenic. However, other possibilities, as well as relevant differential diagnosis, will be presented.

**#8 9:24 a.m.**

**PERIPHERAL ODONTOGENIC MYXOMA.** J. Whitt, B. Barker, and C. Cobb. U. of Missouri – Kansas City. Central odontogenic myxomas are uncommon odontogenic mesenchymal neoplasms associated with a significant recurrence rate. These neoplasms may present in a peripheral location either primarily, or by secondary extension of a primary central lesion. We report a case of a primary peripheral odontogenic myxoma, without evidence of bone involvement. A 41 year old female presented with a painless mass of the right anterior mandible that had been slowly enlarging over a period of three years. The firm, pink, bosselated, smooth-surfaced, 2 cm mass arose from a broad base on the facial gingival mucosa of the mandibular right canine, displacing it 0.75 cm to the lingual. The lesion extended distally over the facial surface of tooth #28 and anteriorly, moving tooth #26 into buccoverision. Radiographic examination showed no central bony involvement, with a normal trabecular appearance. When a complete excision of the lesion was performed, the superficial alveolar bone was described as having the consistency of balsa wood. Histopathologic examination revealed a proliferation of loose, myxoid tissue containing spindled and stellate mesenchymal cells with occasional epithelial rests, some of which were surrounded by an eosinophilic, hyalinized zone. A portion of the proliferation was arranged in a lobular pattern, separated by thin strands of fibrous tissue. There was a significant amount of bone formation associated with the myxoid areas. The diagnosis of peripheral odontogenic myxoma was unexpected, as the primary clinical differential diagnostic consideration was peripheral ossifying fibroma. The peripheral odontogenic myxoma is a rare lesion, based on the low number of cases reported.

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#9 9:36 a.m.

MAXILLARY MESENCHYMAL CHONDROSARCOMA: CASE REPORT AND REVIEW. R. Chaisuparat, N. Tien, R. Fernandes, E. Sarlani, J.C. Papadimitriou, R.A. Ord, N.G. Nikitakis. U. Maryland, Baltimore. Mesenchymal chondrosarcoma (MC) is a rare neoplasm that may present as a skeletal or extraskeletal mass. It exhibits an aggressive behavior with frequent recurrences and metastases, and a 10-year survival rate of approximately 25%. The craniofacial bones, including the jaws, represent a relative common location for skeletal MC. This report presents a case of MC in a 28 year old male who presented with a painless palatal swelling. CT and MRI showed a large mass in the left maxilla extending into the maxillary sinus and penetrating the orbital floor. Biopsy and histopathologic examination revealed a biphasic pattern, composed of an undifferentiated small round cell component that surrounded nodules of malignant cartilage; a pericytic vascular pattern resembling hemangiopericytoma was observed focally. Immunohistochemical studies showed moderate positivity for S-100 and weak positivity for CD99. The tumor was treated by extensive hemimaxillectomy followed by postoperative external beam radiation therapy. There was no evidence of disease at the 30 month follow-up. A comprehensive review of the clinical and histopathologic features of 31 previously described cases of MC of the maxilla was undertaken. The average age of patients was 25 years; male to female ratio was 1:1.2. The most common presenting symptom was a painless swelling. Treatment consisted of surgery alone or combination of surgery with chemotherapy or radiotherapy. The prognosis was not significantly affected by the selected treatment modality. The survival rate of 12 patients with long-term follow-up was 91% at 5 years and 42% at 10 years. Prognosis of MC in the maxilla appears to be better than in most other extra-osseous and osseous sites; however, a long term follow-up is necessary due to high rate of late recurrence and metastasis.

#10 9:48 a.m.

EXTRAOSSEOUS EWINGS SARCOMA OF THE TONGUE INITIALLY MISTAKEN FOR LYMPHOBLASTIC LYMPHOMA: KEYPOINTS IN DIAGNOSIS. J. Hicks, C. Flaitz, L. Trautwein, and D. Mahoney. TX Children's Hosp, Houston, UTHSC-Houston. **Background:** Ewings sarcoma typically presents as a bone tumor and less frequently at extraosseous sites. When presenting at unusual extraosseous sites, these peripheral primitive neuroectodermal tumors may be mistaken for other small round cell tumors. **Case history:** A 4 year-old female presented to her physician with difficulty swallowing. A polypoid mass at the base of the tongue was excised and the diagnosis of lymphoblastic lymphoma was made by a general pathologist. Based on the diagnosis, the child underwent oncologic management. With failure of the residual tumor to respond, referral was made to a children's hospital with a request for pathology review. **Pathology findings:** The tumor was composed of undifferentiated small round cells that had inconspicuous nucleoli and scant amphophilic cytoplasm. There was a fine capillary network, and the tumor cells appeared to be cohesive and closely apposed. Immunocytochemistry showed LCA and membranous CD99 reactivity, which occurs in lymphoblastic lymphoma/leukemia. CD3, CD20, desmin, myogenin, and NB-84 (neuroblastoma) were negative. Formalin-fixed paraffin-embedded tissue was recovered for electron microscopy. Ultrastructural examination identified primitive neuroectodermal features (rudimentary cell junctions, neurosecretory granules, neurite-like processes), suggesting extraosseous Ewings sarcoma. Tissue scrolls were taken from the paraffin blocks for RT-PCR. An EWS-FLI1 translocation [t(11;22)(q24;q12)] was discovered. **Conclusion:** Ewings sarcoma may be identified by a combination of routine, immunocytochemical, electron microscopic, and molecular techniques. A multimodal approach to pediatric small round cell tumors allows for the most appropriate diagnosis with difficult to distinguish childhood tumors that may occur in unusual sites.

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#11 10:00 a.m.

ASSESSMENT OF CD43 EXPRESSION IN ADENOID CYSTIC CARCINOMAS, POLYMORPHOUS LOW-GRADE ADENOCARCINOMAS, AND MONOMORPHIC ADENOMAS. V. Woo, R. Kelsch, and T. Bhuiya. Long Island Jewish Medical Center, New Hyde Park, New York. **Background:** CD43 is a sialoglycoprotein expressed on the surface of most hematolymphoid cells, including T lymphocytes. Expression of CD43 in T-cell malignancies and a subset of low grade B cell lymphomas has been established. We report differential immunostaining of CD43 in three types of salivary gland neoplasms: adenoid cystic carcinoma (ACC), polymorphous low-grade adenocarcinoma (PLGA), and monomorphic adenomas (MA). **Design:** Archived, formalin-fixed paraffin-embedded tissue was retrieved from the files of the Department of Pathology at LIJMC from 1990 to 2001. Forty tumors were selected, including 12 ACCs, 14 PLGAs, and 14 MAs. Immunohistochemical staining was performed employing standard techniques. Immunoreactivity was assessed using a scoring system based on percentage of positive cells (weak [10-25%], mild [26-50%], moderate [51-75%], and strong [76-100%]). **Results:** Immunoreactivity for CD43 was detected in 12/12 ACCs (6 with strong staining), 1/14 PLGAs, and 3/14 MAs (all weak staining). **Conclusion:** CD43 appears to be preferentially expressed in salivary gland ACCs in comparison with PLGAs and MAs. Distinguishing between ACC and PLGA can occasionally pose a diagnostic challenge. Our results indicate that use of CD43 immunostaining as an adjunct to histological examination may be helpful in differentiating ACC from other salivary gland neoplasms. The mechanism by which CD43 is favorably expressed in ACC remains obscure at this time. Further investigation of the role of CD43 in salivary gland and other epithelial neoplasms is warranted.

#12 10:12 a.m.

HEMIFACIAL HYPERTROPHY – COMPARISON BETWEEN TRUE AND PARTIAL INVOLVEMENT. N. Islam, K. Bober, J. Ojha, I. Bhattacharyya, and D. Cohen. U. of Florida, Gainesville and Private Practice, Omaha, Nebraska. **BACKGROUND:** Hemifacial hypertrophy (HFH) is a rare condition originally characterized by unilateral enlargement of all tissues of the face exhibiting enlargement of one half of the head and teeth on the involved side. It was first described by Meckel in 1822. In 1962, Rowe classified true hemifacial hyperplasia as a unilateral enlargement of the viscerocranium, and partial hemifacial hypertrophy as the condition in which not all structures are enlarged to the same degree. In 1947, Ward and Lerner similarly classified HFH into total and limited types of hypertrophy, where total HFH involved hyperplasia of all tissues of the face, while limited HFH did not involve all facial tissues. The vast majority of HFH in the literature are classified as true or total hyperplasias and only a very few cases involving solely muscular system have been reported. When limited to muscle involvement, this condition has been termed myohyperplasia. **PURPOSE:** We report one case of true or total HFH and compare and contrast it with a case of partial or limited HFH with only bony involvement. Comparison of teeth size, degree of involvement, and symmetry were performed. **CONCLUSION:** Partial HFH can cover a wide spectrum including those involving only muscle or bone. Contrary to previous reports, HFH can involve only limited tissues or locations. Previous cases reported as separate syndromes exhibiting enlargement of only the facial musculature may actually represent a forme fruste of partial HFH.

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#13 10:24 a.m.

A 60 YEAR-OLD MAN WITH FOUR POORLY DIFFERENTIATED MALIGNANCIES IN HEAD AND NECK REGION WITHIN 8 YEARS. Y. Chen, Y. Cheng, H. Kessler, and J. Wright. Kaohsiung Medical U., Kaohsiung, Taiwan and Baylor College of Dentistry-TAMHSC, Dallas, Texas. A 51 year-old Chinese male was first seen for a left nasal mass in 1996. The lesion was biopsied and revealed coalescent islands of poorly differentiated epithelioid cells. It was diagnosed as non-keratinizing undifferentiated carcinoma and the patient received surgery and radiotherapy. Follow-up after the treatment was uneventful until he developed a swelling in the left submandibular gland in 1999. That lesion was excised and histological evaluation revealed groups of dark-stained epithelioid cells in a myxomatous, highly cellular spindle cell stroma. Several duct-like structures of various sizes, possible rosette formation, focal squamous differentiation, and areas of necrosis could be found within the groups of epithelioid cells. Immunohistochemical studies showed positivity for cytokeratin, S100, CD56, and NSE; focal positivity for synaptophysin and chromogranin in the epithelioid cells; and scattered positivity for SMA in the spindle cells. Tumor cells were negative for myogenin and desmin. This lesion was diagnosed as carcinoma ex pleomorphic adenoma. He later developed a swollen lymph node in his neck in 2001, showing sheets of round, polygonal, and spindle cells with variable amounts of cytoplasm. Immunohistochemical studies revealed diffuse positivity for NSE; focal positivity for cytokeratin, CD56, myogenin, desmin, and SMA; and negative results for synaptophysin and chromogranin. This third lesion was diagnosed as metastatic carcinoma. He came back with a left mandibular lesion and the clinical diagnosis was osteomyelitis in 2004. The biopsy tissues showed a poorly differentiated malignancy. The original diagnoses, our diagnoses, and diagnoses from AFIP for this case will be discussed.

#14 10:36 a.m.

ORAL TUBERCULOSIS AS A POTENTIAL ADVERSE REACTION FROM TREATMENT WITH ANTI-RHEUMATIC DRUGS. A. Kolokotronis, E. Avramidou, T. Zaraboukas, K. Mandraveli, S. Alexiou, D. Antoniadis. Aristotle U., Thessaloniki, Greece.

Infections are common in people with rheumatoid arthritis (RA). The use of immunosuppressive medication is a dominant risk factor for infection in patients with RA. Methotrexate (MTX) is one of the traditional disease-modifying anti-rheumatic drugs. Adalimumab (a human anti-tumor necrosis factor - a monoclonal antibody) represents an important advance in the treatment of RA and has recently come in use. TNF plays a role in the host defense against *Mycobacterium tuberculosis* and notably in granuloma formation. Infections occur at a high rate among those who use one of the combinations of the two medications. Tuberculosis (TB) disease is a potential adverse reaction from treatment with adalimumab and/or MTX. Approximately 60% of TB patients develop extra-pulmonary disease after the beginning of treatment. We present a case of oral TB that was manifested as an adverse reaction from treatment with adalimumab and MTX in a patient who suffered from RA.

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#15 10:48 a.m.

ORAL MUCOSAL LESIONS IN PATIENTS WITH PSORIATIC ARTHRITIS: A REVIEW OF CLINICAL FINDINGS AND RESPONSE TO VARIOUS TREATMENT REGIMENS. E. Philipone, J. Wu, and J. Fantasia. Long Island Jewish Medical Center, New Hyde Park, New York. **Background:** Psoriatic arthritis is a chronic, heterogeneous disease whose background is unknown, although genetic, environmental, and immunologic factors likely play major roles. Psoriatic arthritis can follow an aggressive course, and differentiating it from other arthropathies is sometimes difficult. Understanding the pathogenesis of psoriatic arthritis has led to the use of several biologic agents (e.g., etanercept) that modulate T-cell signaling, or by inhibiting cytokines involved in inflammation, such as tumor necrosis factor (TNF). The oral manifestations of this disease are not widely documented, nor is the impact of systemic treatment on the mucosal lesions well documented. **Objective:** We sought to demonstrate the clinical variability of psoriasiform oral mucosal lesions that could be encountered in patients with a history of psoriatic arthritis, and report the influence that treatment regimens had on oral mucosal lesions. **Methods:** The clinical histories of three patients with psoriatic arthritis and oral mucosal lesions that were symptomatic were reviewed. The effect the arthritis treatment regimens had on the oral lesions was documented. **Results:** The oral manifestations of psoriatic arthritis were variable, consisting of diffuse mucosal erythema of palatal and buccal mucosa, erythematous gingivitis, and migratory glossitis. Etanercept appeared to have a favorable effect on some, but not all, of the mucosal lesions identified.

#16 11:00 a.m.

BISPHOSPHONATE OSTEOCHEMONECROSIS: CLINICAL FINDINGS AND TREATMENT THEORIES MAY RELATE TO A POSSIBLE ANALOGY WITH "PHOSSY" JAW. J. Hellstein and C. Fielding. U. of Iowa, Iowa City and Armed Forces Institute of Pathology, Washington, DC.  
The use of bisphosphonates, both injectable and orally administered, continues to escalate and problems of the oral region associated with their use continue to be seen. Currently, in our clinical practice and mail-in histopathology service, we have seen 3 cases of suspected osteochemonecrosis in patients receiving "chronic" oral bisphosphonate therapy and an additional 24 associated with injectable bisphosphonates. Alendronate and risidronate are in the top 75 most prescribed drugs. With such large numbers, oral bisphosphonates may yet prove to be of significant clinical concern, but risk ratio may be extremely low. However, for those affected, the morbidity may be high. The preponderance of cases associated with injectable bisphosphonates, such as pamidronate and zoledonic acid, makes it clear that the risk ratio associated with these drugs will be much greater than the oral bisphosphonates. Historical review of phossy jaw cases may help with understanding the current cases. Histopathologic review of a historical case of phossy jaw, as well as current cases, show varied findings, such as variability of reversal lines. A hypovascularity is generally not appreciated, although the vascular spaces are often congested. Osteoclasts are present, but in diminished numbers. When increased reversal lines are seen, this may represent areas of increased bone turnover prior to exposure. Risk factors, therapy, and treatment will continue to evolve, but some rationales are being implemented. Identification of "hot spots" by nuclear medicine studies should be taken seriously. Extractions on high risk patients should be avoided. Removal of sequestra with minimal epithelial manipulation and the goal of reestablishing epithelial coverage with topical and systemic antibiotics seem to be desirable.

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**#17 11:12 a.m.**

FIRST REPORT OF INTRAORAL CELLULAR BLUE NEVUS WITH REVIEW OF LITERATURE. J. Ojha, J. Akers, J. Akers, I. Bhattacharyya I, and D. Cohen. U. of Florida, Gainesville.

Intramucosal melanocytic nevi are rare lesions and make up more than one half of all reported oral nevi. The common blue nevus is the second most common variant of intraoral nevi. The first case of intraoral blue nevus was reported by Scofield in 1959. The blue nevus is most commonly seen on the skin of the hands, feet, and buttocks area, and in rare instances has been reported on oral mucous membrane. Three types of blue nevi are recognized: the common blue nevus, the combined blue nevus, and the cellular blue nevus. Among these the cellular type is less frequent than the common variant. We present a rare case of cellular blue nevus occurring on the mucosa of the hard palate in a 66 year old white female. The lesion presented as an asymptomatic discrete bluish grey lesion with a pinkish white border. An exhaustive search of the English language literature yielded a single report of an intraoral cellular blue nevus on the palate. However, this case, on re-examination by us and in an extensive review of intraoral nevi by Buchner et al., was re-classified as a common blue nevus. Due to the clinical resemblance of the cellular blue nevus to melanoma and the rarity of this lesion in the oral cavity, recognition and accurate diagnosis are critical.

**#18 11:24 a.m.**

MELANOCYTIC LESIONS OF THE ORAL CAVITY: CLINICOPATHOLOGICAL AND IMMUNOHISTOCHEMICAL ANALYSIS. M. Magalhães, V. Araújo, S. Lourenço, and F. Sousa. U. of São Paulo, São Paulo, Brazil.

Nonmalignant melanocytic lesions and melanomas are uncommon in the oral cavity. Our study was undertaken to review clinicopathologic aspects of oral melanocytic lesions and to analyze specific melanocytic markers in these lesions. A total of 121 cases of benign melanocytic lesions and 8 malignant melanomas of the oral cavity were retrieved. Immunohistochemical analysis was performed against the melanocytic markers S-100, HMB-45, anti-melan-A (A-103), and anti-tyrosinase (T311). We demonstrated that both benign and malignant melanocytic lesions from oral mucosa showed immunostaining with anti-S-100 protein, HMB-45, A103, and T311 antibodies. S-100 protein was the most sensitive protein in these lesions. It was noted that melanomas were intensely immunoreactive when compared with benign melanocytic lesions. In our experience, substitution of diaminobenzidine, a brown-colored chromogen, by new fuchsin (red in color) was an essential step in the technique to avoid misinterpretation of the actual antibody with endogenous melanin.

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#19 11:36 a.m.

PERIVASCULAR EPITHELIOID CELL TUMOR (PECOMA) OF THE HARD PALATE. IG Koutlas, R Gopalakrishnan, and SE Pambuccian. U. of Minnesota, Minneapolis.

Perivascular epithelioid cell tumors (PEComas) comprise a family of tumors that are defined by the co-expression of melanocytic and muscle markers. Examples have been reported in many organs as well as soft tissues and bone and are seen frequently in patients with tuberous sclerosis complex (TSC). Further expanding the list of locations, we report a case arising in the hard palate of a 46-year-old female without evidence of TSC. The lesion measured 4x2 cm. Histologically, it presented as sheets of large, elongated or epithelioid cells with granular, eosinophilic to clear cytoplasm. A limited collagenous component was present. Tumor cells were positive for HMB-45, Melan A/MART-1, and CD-10 as well as smooth muscle actin, desmin, and calponin. Melanocytic markers were positive especially in epithelioid cells while muscle markers generally stained the area close to the cytoplasmic membrane. Additionally, faint reactivity was obtained for estrogen receptors while KP-1 antibody immunostaining correlated to increased lysosomal content. Tumor cells were negative for S-100, CD34, and cytokeratin antibodies. Ki-67 highlighted less the 1% of nuclei. Ultrastructurally, tumor cells featured stage I melanosomes in addition to thin filaments and dense plaques consistent with those present in smooth muscles. Recurrence has not been reported after 20 months. Lesions diagnosed as PEComas should be differentiated from granular cell tumor, rhabdomyoma, epithelioid leiomyoma, alveolar soft part sarcoma, clear cell sarcoma, and melanoma. To our knowledge, this is the first detailed example in the mouth.

#20 11:48 a.m.

IMMUNOHISTOCHEMICAL DIAGNOSIS OF SUBMENTAL TOXOPLASMA LYMPHADENITIS.

Y. Rawal, J. Kalmar and C. Allen. The Ohio State U., Columbus.

Objectives: The diagnosis of toxoplasmosis is rarely made on the basis of microscopic findings. Since the microorganisms are sparse and infrequently identified in patient biopsy material, the diagnosis is typically based on positive serologic findings. We present a case of submental lymphadenopathy in a 26-year-old male with microscopic features that lead to the immunohistochemical (IHC) detection of *Toxoplasma gondii* and the diagnosis of toxoplasma lymphadenitis.

Findings: Routine microscopic examination of the biopsy specimen revealed a lymph node with prominent follicular hyperplasia, proliferation of monocytoid B-cells in the paracortical and sinus areas, and clusters of epithelioid histiocytes. Using an antibody probe to *Toxoplasma gondii*, focal cytoplasmic staining was noted within scattered sinus histiocytes, and a reactive cluster of *Toxoplasma* trophozoites was identified. The diagnosis of toxoplasmosis was subsequently confirmed by serum analysis, with an elevated serum IgG concentration (106 IU/ml). The patient was treated with pyrimethamine and sulfadiazine for 8 weeks and has been disease-free for over 2 years.

Conclusions: Although often an asymptomatic condition in immunocompetent hosts, toxoplasmosis can be a life-threatening infection in immunocompromised patients. A variety of reactive and neoplastic conditions must be considered in the microscopic differential diagnosis. IHC testing may aid in the detection of rare tissue microorganisms and allow appropriate antibiotic therapy to be initiated at the earliest time point.

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### Monday, April 18, 2005

**#21 12:00 p.m.**

**RAPID GROWTH OF UNICYSTIC GRANULAR CELL AMELOBLASTOMA.** J. Whitt, C. Dunlap, H. Wallin, and L. Gonzales, U. of Missouri – Kansas City.

The granular cell ameloblastoma is an uncommon histologic variant of ameloblastoma that has been reported to be clinically aggressive. We report a case of a young adult male who exhibited destructive growth of a unicystic granular cell ameloblastoma over a period of four years. A 23 year-old male presented with pain and mobility of tooth #18. Clinically, there was moderate expansion of the left posterior mandible and lingual displacement of erupted tooth #18. Radiographically, tooth #17 was displaced to the inferior border of the mandible near the angle by a 4 cm pericoronal radiolucent lesion that had partially resorbed the roots of teeth # 18 and #19. The lesion extended anteriorly to the second premolar and superiorly within the ascending ramus to just below the mandibular notch. The lucency exhibited several variations of radiographic density giving the radiographic appearance of multilocularity. The lesion, enucleated via an intraoral approach, consisted of a unilocular cystic cavity partially filled with brownish, translucent fluid. The lumen contained a 1 cm, firm, yellowish-white mass that arose from the lining on a broad base. The lining separated easily from the bony crypt with blunt dissection. Histopathologic examination revealed a unicystic ameloblastoma with an intraluminal plexiform granular cell proliferation. A panoramic radiograph taken four years earlier showed tooth #17 impacted and without evidence of pathosis. The patient had been advised to have the impacted tooth removed. The destruction produced by this lesion over a short four-year interval reinforces the need for periodic imaging of the jaws.

**#22 12:12 p.m.**

**CYSTIC VARIANT OF CALCIFYING EPITHELIAL ODONTOGENIC TUMOR (CEOT).** R. Gopalakrishnan, IG Koutlas, and S. Simonton. U. of Minnesota School of Dentistry, Minneapolis, and Children's Hospitals and Clinics, Saint Paul, Minnesota.

Calcifying epithelial odontogenic tumor (CEOT) is a benign, locally aggressive odontogenic neoplasm, characterized by sheets and nests of epithelial cells with deeply eosinophilic or occasionally clear cytoplasm, varying amounts of calcification, and eosinophilic amorphous material that is positive for amyloid staining. Although many cases of CEOT are associated with impacted teeth and occasionally present radiographically as dentigerous cysts, a cystic variant of CEOT has not been previously reported. We report a 15-year-old white male with a large cystic left maxillary lesion in the area of tooth # 15 that features characteristics of CEOT. The cystic mass filled most of the left maxillary sinus and contained an unerupted molar and several delicate calcifications. It deformed the medial maxillary sinus wall, the inferior orbital floor, and caused narrowing of the left inferior meatus. The epithelial lining showed classic CEOT characteristics. Focally, it was in continuity with very thin epithelium indistinguishable from that of a dentigerous cyst. Hyalinized amorphous material that gave positive staining for Congo red and apple-green birefringence after polarization was identified in the lining and in sheets of tumor cells apparently deriving from cystic contents. These contents included typical solid CEOT areas. Areas of possible mural extension of the tumor were present. Follow-up is less than 6 months, therefore, any meaningful long-term prognosis is impossible although the patient has not reported any symptoms or signs of recurrence.

## Essay Program 2

### Tuesday, April 19, 2005

#23 1:00 p.m.

HOMEBOX mRNA IN ORAL SQUAMOUS CELL CARCINOMA. F.D Nunes, D.S.Pinto Jr., M.D.Durazzo, T.N.L.Santos, F.C.S.Almeida, L.F.Matizonkas, and M.G.S.Valenzuela. U. of São Paulo, São Paulo, Brazil.

Homeobox is an important group of genes involved in morphogenesis and cellular differentiation. Involvement of homeobox with carcinogenesis has been recently discussed in the literature. In this study, the possible expression of some homeobox transcripts is verified in oral squamous cell carcinoma (OSCC) using reverse transcriptase polymerase chain reaction (RT-PCR) and in situ hybridization.

Frozen tumoral tissues and adjacent non-tumorous oral mucosa specimens were obtained from 29 patients with OSCC. Histopathological diagnosis was previously established and the tumors were graded as well, moderately, or poorly differentiated. The amplicons were visualized by electrophoresis on a 1% agarose gel with ethidium bromide. Expression was correlated with UICC staging, pT stage, pN stage, tumor location, tumor thickness, adjacent tissues involvement, vascular and perineural invasion, and tumor differentiation.

There was RT-PCR amplification of HOXB13, HOXB5, PITX, TGIF, and HOXA7, and a positive statistical correlation was found between amplification of HOXB13 and tumor thickness, neural invasion, and vascular invasion. In situ hybridization signal was seen in some tumoral cells population, however no relation was found between cells showing signal and their morphology. These results show the presence of homeobox genes in oral squamous cell carcinomas, suggest a correlation between homeobox gene amplification and important OSCC prognostic indicators, but no relation to neoplastic cell morphology.

#24 1:12 p.m.

PROTEOMIC ANALYSIS OF HEAD & NECK SQUAMOUS CELL CARCINOMAS. B. Herr, M. Beachamp, and M.W. Lingen. U. of Chicago, Chicago, Illinois.

The objective of this work was to develop protein expression profiles of normal, dysplastic, and malignant oral keratinocytes. Our hypothesis was that the comparison of these profiles would allow for the identification of potential biomarkers that could be tied to tumor critical phenotypes and/or neoplastic progression. Whole cell extracts were analyzed using two-dimensional polyacrylamide gel electrophoresis (2D-PAGE) using the PROTEAN 2D IEF system (Bio-Rad). Using the PDQuest 2D gel image analysis system, the profiles from normal oral keratinocytes were then compared to profiles of immortal, but non-tumorigenic (dysplastic), and malignant cell lines. Proteins identified as over or underexpressed were then harvested using the Genomics Solutions ProPic robotic spot retrieval system, and identified using matrix-assisted laser desorption/ionization mass spectrometry (MALDI-MS). Two proteins, Annexin-III and alpha-soluble N-ethylmaleimide-sensitive factor attachment protein (alpha-SNAP), were found to be up-regulated in multiple HNSCC cell lines when compared to immortal/dysplastic keratinocytes. These findings suggest that Annexin-III and Alpha-SNAP may be biologically important in the progression of dysplasia to HNSCC. Furthermore, these proteins may serve as potential biomarkers for predicting the progression from dysplasia to HNSCC.

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

## Essay Program 2

### Tuesday, April 19, 2005

#25 1:24 p.m.

GALANIN RECEPTOR 1 AND 2 SIGNALING IN ORAL KERATINOCYTES: NOVEL FINDINGS IN ORAL CANCER. B. Henson, R. Neubig, I. Jang, T.E. Carey, and N.J. D'Silva. U. of Michigan, Ann Arbor. Studies have shown that aberrations of chromosome 18q develop with tumor progression and are associated with significantly decreased survival in head and neck cancer patients. The G-protein coupled receptor (GPCR), Galanin Receptor 1 (GALR1), maps to this region of chromosome 18q. Galanin (GAL), a 30 amino acid neuropeptide, engages GALR1 and two other galanin receptors, GALR2 and GALR3. GAL binding to the galanin receptors induces several regulatory functions in neuronal cells, including growth and development. However, the mitogenic function of GALRs has not been investigated in oropharyngeal squamous cell carcinoma (SCC) where it may have implications for patient survival. Objective: To explore the role of GAL and GALRs in proliferation in keratinocytes and SCC. Methods: GAL secretion in keratinocyte and SCC cell lines was quantified using a competitive ELISA. Galanin receptor expression was determined by immunoblot analysis and RT-PCR. The role of GAL, GALR1 and GALR2 in proliferation and MAPK activation was investigated in human SCC and keratinocytes. Rap1 and Rho activation were evaluated using pull-down assays. Results: GALR1, GALR2, and GALR3 protein and mRNA expression and GAL secretion were detected in immortalized keratinocyte and SCC cell lines. Inhibition of GALR1 or stimulation of GALR2 enhanced proliferation in immortalized keratinocytes. Furthermore, GALR1 inhibits proliferation via rap1-mediated inhibition of MAPK, whereas GALR2 activates MAPK via rho activation. These findings suggest antagonistic role for GALR1 and GALR2. Conclusions: GALR1 and GALR2 have antagonistic effects on proliferation in epithelial cells and disruption of this balance may lead to neoplastic transformation.

#26 1:36 p.m.

RETICULAR MYOEPITHELIOMA: A CLINICOPATHOLOGIC CORRELATION STUDY. M. Stokes, R. Foss, S. Williams. Armed Forces Institute of Pathology (AFIP), Washington DC.

Background: The reticular myoepithelioma (RM) is a benign epithelial salivary gland tumor which may fall within the spectrum of phenotypically myoepithelial tumors. It represents one of the most frequently misinterpreted salivary gland tumors reviewed at the AFIP.

Materials and Methods: AFIP diagnostic files of adenoma (NOS), pleomorphic adenoma, basal cell adenoma, myoepithelioma, and canalicular adenoma were reviewed, revealing 39 examples of tumors classifiable as RM. Clinical, histomorphological, and immunohistochemical evaluation was performed on the cases and follow-up data was obtained. For purpose of comparison, eight cases of canalicular adenoma were reviewed.

Results and Conclusions: The patients' ages at diagnosis ranged from 34 to 88 years with mean and median ages of 63.7 and 66.0 years, respectively. There were 25 females and 9 males (5 Unk). Tumors involved the parotid gland (37), submandibular gland (1), and buccal mucosa (1). Morphologically, RM is a multinodular and partially cystic salivary gland neoplasm composed of eosinophilic polygonal to columnar cells arrayed in cords and anastomosing trabeculae. Among 28 cases with submitted diagnoses, 7 were interpreted as malignant tumors. Four of 26 tumors recurred locally but did not further progress. Immunopositivity for the following antigens was identified: CK7 30/30, Kermix 29/29, S100 29/29, Vimentin 28/28, CEA 28/28, CK8 28/28, CK18 28/28, K903 28/28, GFAP 28/29, CK5/6 27/29, EMA 24/27, Calponin 25/29, P63 21/26, SMA 17/30, and CK20 0/30. This immunophenotype supports the inclusion of RM in the spectrum of myoepitheliomas. Awareness of this uncommon tumor may avoid its misclassification as a malignancy.

## Essay Program 2

### Tuesday, April 19, 2005

#27 1:48 p.m.

INFLUENCE OF EGF IN pAKT EXPRESSION AND CELL PROLIFERATION PROTEINS IN CULTURED ORAL SQUAMOUS CELL CARCINOMA CELLS. F.T. Salles; D.S. Pinto Jr. U. of São Paulo, São Paulo, Brazil. EGF is a growth factor that plays a main role in progression of many neoplasms, and its receptors are more expressed in head and neck tumors than in the normal mucosa. EGF-mediated radioresistance is probably related to p-Akt activation, but few studies regarding this pathway in oral squamous cell carcinoma have been performed. In order to evaluate p-Akt expression, cell cycle and apoptosis related proteins in response to EGF stimulation, five cell lines were used: HN6, HN19, HN30, HN31 and HaCat as normal keratinocytes. 10ng/ml EGF was applied to the cell cultures in serum-free medium during 18h periods, and the expressions of p-Akt, cyclin D1, PTEN, Bad, and CtBP, and evaluated through Western blot, immunofluorescence, and co-immunoprecipitation. The results revealed an increased p-Akt expression in all cell lines, as well as cyclin D1. PTEN exhibited a decreased expression in all cell lines except for HN31, the same occurring with CtBP and Bad. Through co-immunoprecipitation, we could observe an interaction between p-Akt and Bad, especially in HN6. These results suggest a main role of p-Akt in EGF-stimulated cells, promoting cell cycle progression through cyclin D1 and blocking apoptosis by interacting with Bad in oral squamous cell carcinoma. These data may provide evidence for cancer treatments targeting the EGF pathway, as well as drugs promoting PTEN and CtBP overexpression, since these molecules play crucial roles in blocking Akt phosphorylation and cell cycle progression.

#28 2:00 p.m.

CAN TISSUE INHIBITOR OF METALLOPROTEINASES-4 (TIMP-4) AFFECT BLISTER FORMATION IN A PEMPHIGUS VULGARIS MODEL? A PRELIMINARY REPORT. V. Woo, J. Fantasia, and M.Y. Celiker. Long Island Jewish Medical Center, New Hyde Park, NY. The matrix metalloproteinases (MMPs) are a group of multi-functional proteinases that collectively act to hydrolyze components of the extracellular matrix (ECM). The accelerated degradation of the ECM underlies various pathological processes, including certain inflammatory and ulcerative diseases. Tissue inhibitor of metalloproteinases (TIMPs) are endogenous proteins that specifically bind to and inhibit MMPs. Recently, it has been demonstrated that TIMP-4 reduces inflammation by downregulation of the cytokines interleukin-1 $\alpha$  (IL-1 $\alpha$ ) and tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ). *In vitro* and *in vivo* evidence support a role for IL-1 and TNF- $\alpha$  in the pathogenesis of pemphigus vulgaris (PV), possibly through cytokine modulatory effects on plasminogen activator and complement expression. **Objective.** We aimed to investigate the effects of TIMP-4, and secondarily IL-1 $\alpha$  and TNF- $\alpha$ , on blister formation in a PV model. **Study design and methods.** An *in vivo* model was initially employed; PV was induced in neonatal BALB-c mice by passive transfer of IgG fractions isolated from the serum of patients with mucocutaneous PV. Mouse cells had been previously transduced with an adenovirus construct containing the TIMP-4 plasmid 1 day earlier. Successful development of the PV phenotype was confirmed by histologic and immunofluorescent examination of lesional skin. However, overexpression of serum TIMP-4 compared to controls was not achieved. Currently we are utilizing a tissue culture model whereby punch biopsies of murine skin will be exposed to PV IgG and purified TIMP-4 protein under culture conditions, with appropriate controls. Preliminary studies done thus far have demonstrated successful induction of acantholysis in cultured murine skin following exposure to PV IgG alone.

## Essay Program 2

### Tuesday, April 19, 2005

#29 2:12 p.m.

LYMPHOEPITHELIOMA-LIKE CARCINOMA OF HEAD AND NECK SKIN: A REPORT OF 11 CASES & REVIEW OF THE LITERATURE. P. Welch, S. Williams, R. Foss, M. Tomaszewski. Armed Forces Institute of Pathology (AFIP), Washington, DC. Lymphoepithelioma-like carcinoma of the skin (LELCS) is a rare cutaneous tumor of low malignant potential that is histologically similar to high grade carcinomas with lymphoid stroma in other anatomic sites including the nasopharynx, salivary glands, and tonsils. LELCS presents as flesh-colored, firm nodules or plaques on the face, scalp, or shoulder of middle-aged to elderly individuals. **Objective:** To retrospectively review the AFIP files concerning the morphology, behavior, and histogenesis of LELCS. **Methods:** 11 cases of LELCS were identified in the AFIP files. Microscopic and clinical features were reviewed. **Findings:** All lesions were located on sun-exposed areas of the head and neck in middle aged to elderly individuals. There were 8 male and 3 female patients with a median age of 74 (range 47-84 years). Clinical impressions included BCC, SCC, and adnexal tumors. Submitted diagnoses included poorly differentiated SCCA, LELCS, undifferentiated malignancy, and lymphoma. Two separate growth patterns were identified. One was characterized by multinodular growth of syncytial sheets, islands, and/or nests of poorly differentiated epithelial cells with pale cytoplasm, indistinct cell borders, round to oval pleomorphic nuclei, and 1-2 eosinophilic nucleoli. The second pattern was diffuse growth of more typical, undifferentiated lymphoepithelial carcinoma. Adnexal and squamous differentiation was noted in some cases. The tumor cells were consistently associated with a dense stroma composed primarily of lymphocytes with occasional plasma cells. **Conclusions:** Our findings are similar to past studies that favor an adnexal origin for LELCS. Morphologic and IHC features may help distinguish this tumor from similar appearing high grade carcinomas.

#30 2:24 p.m.

INTEGRIN EXPRESSION IN DEVELOPING HUMAN SALIVARY GLANDS. S.V. Lourenço, M.M.S. Nico, and S. Kapas. U. of São Paulo, São Paulo, Brazil. The development and complete differentiation of salivary glands is a complex process which involves a large number of coordinated events. Little is known about the molecular basis for salivary gland development, however, we have reported previously that integrins appear to be important. Integrins are heterotrimeric transmembrane receptors consisting of one  $\alpha$  and one  $\beta$  subunit that play a pivotal role in the interaction of cells with the extracellular matrix. Such interactions regulate the organization of cells of tissues and organs during development as well as cell proliferation and differentiation. Using immunohistochemistry, western, and northern blot analysis, we have mapped the localization and expression of integrins  $\beta 1$ ,  $\beta 3$ , and  $\beta 4$  in human salivary glands obtained from fetuses ranging from weeks 4 to 24 of gestation and compared them to adult salivary glands. Integrin  $\beta 1$  first appeared during canalization stage and during the differentiation stage. Message first appeared at week 6 of development. The expression of  $\beta 4$  integrin protein and message was observed only in late stage of differentiation. Integrin  $\beta 3$  was not detected. Integrins  $\beta 1$ ,  $\beta 3$ , and  $\beta 4$  were all expressed in adult salivary gland tissues. The data suggest that integrins, particularly  $\beta 1$ , are important in salivary gland development and differentiation.

## Essay Program 2

### Tuesday, April 19, 2005

**#31 2:36 p.m.**

**EXPRESSION OF PCNA, KI-67, BCL2, AND P53 IN ODONTOGENIC CYSTS.** H. Rivera, M. Correnti, M. Avila, and A. Guzman. Central U. of Venezuela, Caracas.

The aim of the present study was to evaluate the immunohistochemical expression of proliferation, apoptosis, and oncogene markers in the epithelial lining of odontogenic cysts (OC). Eighteen cases of OC were retrieved from our files. Six cases of dentigerous cyst (DC), seven cases of odontogenic keratocyst (OKC), four cases of periapical cyst (PAC), and 1 case of glandular odontogenic cyst (GOC) were selected. 3  $\mu$ m sections were obtained for immunohistochemical technique. PCNA (1:200), ki-67 (1:50), p53 (1:50), and bcl2 (1:25) were used as primary antibodies. Our results showed that PCNA was expressed in 4/6 cases (66.67%) of DC, while ki67 was expressed in 3/6 cases (50%), and bcl2 and p53 in 2/6 cases (33.33%) respectively. Additionally, PCNA was positive in 4/7 cases of OKC (57.16%), while the rest of the markers were uniformly expressed in 1/7 cases, representing 14.28%. However, 2/4 (50%) of the PAC cases were immunopositive for PCNA, and the rest of the cases expressed only bcl2. The only case of GOC expressed similar positivity for all markers. We may conclude from the present study that PCNA was the most common proliferation marker expressed in all OC. DC and OKC expressed all markers, in contrast to PAC, which exhibited positivity for only PCNA and bcl2, probably due to its inflammatory etiopathogenesis. The only case of GOC showed a strong expression of the four markers along the epithelial lining and within the mucous cells, evidencing the proliferative activity and the potential for neoplastic transformation of this entity.

**#32 2:48 p.m.**

**ULCERATIVE UREMIC STOMATITIS ASSOCIATED WITH UNTREATED CHRONIC RENAL FAILURE. REPORT OF A CASE.** D.Z. Antoniadis, A.K. Markopoulos, I. Balaskas, E. Patrikalou, and D. Grekas. Aristotle U., Thessaloniki, Greece. Uremic stomatitis represents a relatively uncommon intraoral complication of uremia, seen mostly in cases of end-stage or undiagnosed/untreated chronic renal failure. However severe uremia is rare and this explains why reports on uremic stomatitis are exceedingly rare. Two types are generally distinguishable; the most common type is the erythemoplaceous or non-ulcerative type, while the second ulcerative type is more rarely seen. The objective of this article is to report an 83-old female patient with untreated chronic renal failure who developed the ulcerative type of uremic stomatitis as a complication of the sudden relapse of uremia. Based on the literature's data, we will discuss the clinical and microscopic findings along with the pathogenesis of the disease.

## Essay Program 2

### Tuesday, April 19, 2005

#33 3:00 p.m.

RT-PCR AND IMMUNOHISTOCHEMICAL STUDIES OF AROMATASE EXPRESSION IN NORMAL ORAL KERATINOCYTES AND SQUAMOUS CELL CARCINOMA. Y. Cheng, G. Mues, D. Wood, and J. Ding. Baylor College of Dentistry-TAMHSC and Baylor U. Medical Center, Dallas, Texas. Aromatase is a cytochrome P-450 enzyme that is responsible for estrogen synthesis. Its expression has been found to be dramatically increased in breast carcinoma tissues leading to the use of aromatase inhibitors as a major treatment for hormone-dependent breast carcinomas in postmenopausal women in recent years. Aromatase expression has never been investigated in oral mucosal tissues or oral cancers. We previously reported evidence from immunocytochemistry and Western blot analysis suggesting aromatase protein expression in normal oral keratinocytes and oral squamous cell carcinoma (SCC) in cell culture. In our current study, we investigated aromatase mRNA expression of the common coding region (exon 2-3) and the various first exons (I.1, I.4, I.7, I.3, and PII) in oral keratinocytes from three normal donors and oral SCC cells in culture by RT-PCR. We found that both normal oral keratinocytes and carcinoma cells expressed the common coding region of aromatase. Carcinoma cells expressed exon I variants I.7, I.3 and PII, while none of the three normal samples expressed I.3 or PII variants, and only one expressed exon I variant I.7. We also investigated aromatase expression in archival human normal and neoplastic oral tissues by immunohistochemistry. Aromatase expression was detected in oral epithelium in fibromas and in tumor islands of well-differentiated SCC, but not in tumor islands of poorly differentiated SCC cells. Our current results indicate that, compared to normal oral keratinocytes, oral SCC cells utilize more promoters for aromatase expression. This may lead to an increased amount of aromatase expression in oral SCC, similar to the situation in breast carcinoma cells.

#34 3:12 p.m.

NEUROENDOCRINE MARKERS IN AMELOBLASTOMA: AN IMMUNOHISTOCHEMICAL STUDY OF THIRTY-TWO CASES. E.Gagari, E Deligianni, D. Z. Antoniadis, and R. Goode. Tufts U., Boston, Massachusetts and Aristotle U., Thessaloniki, Greece.  
Ameloblastoma is a benign, biologically aggressive odontogenic tumor of epithelial origin.  
Objectives: Given the neuroectodermal origin of dental lamina, we decided to test the hypothesis that ameloblastoma may demonstrate neuroendocrine differentiation immunohistochemically.  
Materials and Methods: Immunohistochemistry for CD 99, chromogranin, neuron-specific enolase, synaptophysin, S-100, keratin, and vimentin was performed in thirty-two ameloblastomas diagnosed in our biopsy service. The ameloblastomas showed the characteristic age, sex, and location predilection reported in the literature.  
Findings: Strong positivity for CD99 was observed throughout the epithelial structures of all ameloblastomas tested. Synaptophysin exhibited strong focal positivity in the ameloblast-like peripheral layer, whereas neuron-specific enolase and S-100 demonstrated equivocal positivity in the ameloblastomatous islands. Chromogranin was uniformly negative in all cases tested. Keratin and vimentin were used as controls in order to confirm the preserved antigenicity of the tissue tested.  
Conclusions: This study presents the first evidence that ameloblastomas possess a neuroendocrine immunohistochemical profile. This evidence may prove valuable in elucidating the origin of this neoplasm as well as in establishing a pathogenetic link between neuroendocrine and odontogenic tumors.

## Essay Program 2

### Tuesday, April 19, 2005

#35 3:24 p.m.

**MALIGNANT MELANOMA METASTATIC TO THE MANDIBLE PRESENTING AS PERIAPICAL DISEASE.** L. Perez, O. Yoris, H. Fuenmayor, and V. Murrah. U. of Zulia, Maracaibo, Venezuela and U. of North Carolina, Chapel Hill.

Malignant melanoma, an aggressive melanocytic malignancy, normally occurs on sun-exposed areas of the skin, but can occur anywhere melanocytes are present. It is rare in the oral cavity as a primary tumor, but even more unusual as a metastasis to the jaws. The pathogenesis of metastatic jaw lesions is considered to be hematogenous dissemination with deposition and growth in areas of hematopoietic marrow. We present a case of a 64 year-old male with pain in the lower right jaw. Clinical exam revealed slight bony expansion in the area with an intact mucosa. An initial periapical radiograph revealed a demarcated radiolucency extending from the mandibular right canine to the mandibular 2<sup>nd</sup> premolar containing a retained root tip from the first premolar. The initial clinical differential included lesions associated with a periapical infectious process. The three teeth were extracted and the curetted tissue submitted for microscopic examination. The initial microscopic diagnosis was "large cell malignant neoplasm." Subsequent medical history review, examination, and consultation revealed a past history of malignant melanoma of the heel two years earlier. Head and neck exam revealed multiple large palpable supraclavicular lymph nodes on the right side. A panoramic radiograph revealed a moth-eaten appearance to the mandibular bone at the previous surgical site. S-100 and Melan A immunostains performed on the original tissue were positive in tumor cells. The patient was dead of disease four months after diagnosis. This case illustrates the importance of a thorough medical history, consideration of metastatic disease in the differential diagnosis for jaw lesions, and submission of all curetted periapical tissues for microscopic examination.

#36 3:36 p.m.

**LICHEN SCLEROSUS AND ATROPHICUS. REPORT OF TWO CASES.** A.K. Markopoulos and D.Z. Antoniadis. Aristotle U., Thessaloniki, Greece. Lichen sclerosus and atrophicus is a chronic inflammatory disease preferentially affecting the skin and genitalia. Involvement of oral mucosa is extremely rare. However, in some cases manifestations are restricted to oral mucosa. It is predominantly observed in women and the mean age of onset is the 5<sup>th</sup> to 6<sup>th</sup> decade of life. The cause of the disease is unknown and may be multifactorial including disorders of autoimmunity, genetic and hormonal abnormalities, trauma, infections, and metabolic diseases. Oral manifestations, exclusively or accompanied with skin and anogenital diseases, are unusual. We report two cases of lichen sclerosus and atrophicus documented histopathologically. The first one had oral manifestations exclusively, while the second case had oral manifestations with pre-existing skin lesions. We also summarize the etiologic, clinical, and histopathologic aspects of this unusual oral disease.

## Essay Program 2

### Tuesday, April 19, 2005

#37 3:48 p.m.

MASPIN EXPRESSION IN ORAL LEUKOPLAKIA. S. Sousa, A. Fontes, V. Araújo, and M. Martins. U. of São Paulo, São Paulo, Brazil.

Leukoplakia is the most common potentially premalignant condition in the mouth. Clinically, this lesion is represented by white patches or spots which cannot be easily scraped away, and may affect any site of the oral mucosa. Histologically, these entities may present a large variety of features with cases showing from hyperkeratosis without atypia to any degree of atypia. Some leukoplakias may actually be “in situ” carcinoma (ISC) or, confirming its malignant potential, superficially invasive carcinoma. Maspin is a serine protease and functions as a tumor suppressor through inhibiting cellular invasion, cellular motility, and angiogenesis. It also has an anti-metastasis effect. This study had the aim of evaluating the maspin expression in oral leukoplakia by streptavidin-biotin method of immunohistochemistry. Seventy cases clinically diagnosed as leukoplakia were retrieved from our files. The cases were represented by 28 hyperkeratosis without atypia, 18 mild atypia, 12 moderate atypia, 8 severe atypia, and 4 cases of ISC. 3  $\mu$ m sections from formalin-fixed, paraffin-embedded tissue were submitted to anti-maspin antibody (BD PharMingen, 1:100). Immune-staining was graduated: 0 (no staining), 1 (weak), 2 (moderate), and 3 (intense). Results were: hyperkeratosis - 1: 42.8%, 2: 53.6%, 3: 3.6%; mild atypia - 1: 55.5%, 2: 27.8%, 3: 16.7%; moderate atypia - 1: 8.3%, 2: 33.3%, 3: 58.4%; severe atypia - 1: 25%, 2: 62.5%, 3: 12.5%; and ISC - 0: 50%, 1: 25%, 2: 25%. Thus, maspin expression is scarce in the lesions without or with mild atypia, it is increased in lesions with moderate atypia, and it becomes scarce once more in severe atypia and ISC. In conclusion, maspin is related with the atypia degree in oral leukoplakias, being intensely expressed in moderate atypia, which may indicate a decisive moment in pathology progression.

#38 4:00 p.m.

RAP1GAP INHIBITS TUMOR GROWTH IN HUMAN OROPHARYNGEAL SQUAMOUS CELL CARCINOMA. N.J. D'Silva, Z.C. Zhang, R.S. Mitra, B. Henson, N.S. Datta, L. McCauley, P. Kumar, J. S-J. Lee, and T.E Carey. U. of Michigan, Ann Arbor.

Rap1, a growth regulatory protein that is strongly expressed in human squamous cell carcinoma (SCC), is inactivated by rap1GAP. Recent evidence in normal rat cells suggests that rap1GAP regulates proliferation. The objective of the current study was to investigate whether rap1GAP functions as a tumor suppressor in SCC. Using a pull-down assay, we observed that active GTP-bound rap1 is upregulated in SCC compared to normal or immortalized keratinocytes. Since both rap1A and rap1B, isoforms of rap1, are expressed in SCC, we verified that rap1GAP inactivates both rap1 isoforms using cells transfected with either EGFP-rap1A or EGFP-rap1B, or co-transfected with FLAG-tagged rap1GAP. Our results demonstrate that expression of rap1GAP in oropharyngeal SCC, downregulates active rap1, ERK activation, and proliferation. Incubation of stably transfected SCC cells with nocodazole, an inhibitor of mitosis, caused an accumulation of rap1GAP transfected cells in S-phase in comparison to the vector control, indicating that rap1GAP transfected cells have slower progression through the cell cycle. This was supported by downregulation of cyclin D1, cdk4, and cdk6 in rap1GAP transfected SCC cells. Furthermore, SCC cells transfected with rap1GAP produced significantly smaller tumors in nude mice as compared to controls ( $p < 0.005$ ). These novel findings show that rap1GAP acts as a tumor suppressor protein in SCC.

## Essay Program 2

### Tuesday, April 19, 2005

#39 4:12 p.m.

BETA-CATENIN IN SQUAMOUS CELL CARCINOMA. D.S. Pinto, Jr., F.D. Nunes, and S.C.O.M. Sousa. U. of São Paulo, São Paulo, Brazil.

The aim of this study was to verify the participation of  $\beta$ -catenin in oral squamous cell carcinomas (OSCC). Thirty-nine cases of squamous cell carcinoma were retrieved from the files of the Department of Oral Pathology, School of Dentistry, University of São Paulo. Besides biopsy material, cell lines of OSCC were used and treated with LiCl for simulation of Wnt pathway. Of the 39 cases, 27 (69.2%) showed loss of expression of  $\beta$ -catenin in focal areas, especially in isolated invasive cells along the active front of the tumor. This loss of expression was demonstrated by faint visualization of  $\beta$ -catenin or even a total loss of the protein in the cell membrane. Accumulation of  $\beta$ -catenin in the cytosol was observed in 15 cases (38.5%), especially in tumors with evident invasion. In the cell nucleus, the labeling occurred in 11 cases (28.2%); 10 cases (25.6%) showed simultaneous labeling in both the nucleus and cytoplasm.

The immunofluorescence reactions against  $\beta$ -catenin in the cell lines showed only membrane expression. In the basal poles there was no labeling. The cell lines with medium supplemented with LiCl demonstrated a higher proliferative rate than the control ones and showed nuclear labeling of  $\beta$ -catenin.

In Western blot reactions, the amount of  $\beta$ -catenin was almost similar among all cell lines and the control, and the immunoprecipitation with E-cadherin provided evidence of assembling of cellular contacts among the cells, with exception of HN12.

Our results suggest a real participation of  $\beta$ -catenin in OSSC, not only in invasion but also in carcinogenesis.

#40 4:24 p.m.

A PERSISTENT INFRAORBITAL SWELLING IN A 45 YEAR OLD MALE. N. Said-Al-Naief and V. Reddy. The U. of Alabama at Birmingham. The most common periapical pathologies encountered are of dental origin. However, other common and rare, benign and malignant entities of variable biological behavior may also mimic periapical pathology, including lymphoproliferative disorders. In general, dentists, especially endodontists, consider that most periapical radiolucencies of dental etiology can be cured by root canal treatment. Therefore, fewer teeth with periapical radiolucencies are initially treated surgically and no material is available for histomorphological interpretation. We present a case of a destructive, radiolucent lesion that involved the maxillary sinus in a 40 year old male, who initially presented with several month history of a left infraorbital swelling associated with cellulitis of the left maxillary vestibule. The patient had pain and sensitivity to percussion in several teeth in the area, which were justifiably treated endodontically in multiple visits after failure to respond to pulp vitality testing. A representative biopsy originally showed a mixed inflammatory cell infiltrate, with plasma cells and an increase in T cell subsets. The infiltrate was focally atypical. A battery of immunohistochemical stains (CD3, CD5, CD20, CD56, CD 57, CD138, TIA, kappa, and lambda), as well as T cell rearrangement studies, were not contributory in delineating the nature of the focal atypical cells observed. Therefore, a suggestion was made to excise the lesion for better characterization. Excision of the lesion revealed a "solitary plasmacytoma" of the left maxillary sinus. Flow cytometry was positive for a clonal plasma cell population. Clinicopathological and radiographical correlation and potential diagnostic pitfalls of periapical radiolucencies are discussed.

## Essay Program 2

### Tuesday, April 19, 2005

#41 4:36 p.m.

**PYOSTOMATITIS VEGETANS AS AN ORAL MANIFESTATION OF ULCERATIVE COLITIS. REPORT OF TWO CASES.** A.K. Markopoulos, D.Z. Antoniadis, and E. Gagari. Aristotle U., Thessaloniki, Greece and Tufts U., Boston, Massachusetts. Pyostomatitis vegetans is a rare pathologic entity considered to be a harbinger or sign of gastrointestinal disease such as ulcerative colitis or Crohn's disease. The pathogenesis of pyostomatitis vegetans is unclear. Clinically, it is characterized by the presence of snail-trail-like white-yellowish micro-abscesses that may affect the entire oral mucosa. Histopathologic examination of the oral lesions reveals the presence of epithelial edema and abscesses. The epithelium and the underlying connective tissue are usually infiltrated by eosinophils. Eosinophilia may be present in blood test counts (eosinophils 6-25%). In certain cases, autoantibodies against basement membrane may be present in the peripheral blood. The final diagnosis is established by the clinical findings and the exclusion of other diseases by histopathologic examination and direct immunofluorescence testing. The treatment of pyostomatitis vegetans consists mainly of topical administration of corticosteroids. The lesions resolve but tend to recur after termination of treatment. Complete resolution of the symptoms usually occurs when the underlying gastrointestinal disease is successfully managed. We report two cases of pyostomatitis vegetans. The first case was a 42-year-old male and the second a 68-year-old female with characteristic oral lesions of pyostomatitis vegetans. Both patients suffered from ulcerative colitis. The second patient had an intestinal biopsy that was positive for ulcerative colitis. Blood tests in both cases revealed the presence of eosinophilia, and histopathologic examination showed characteristics of pyostomatitis vegetans. Dexamethasone was administered topically and the patients were referred to a gastroenterologist for treatment of ulcerative colitis.

### Abstracts Read-By-Title

#42

**PFAPA SYNDROME: CASE REPORT AND DESCRIPTION OF CONJUNCTIVITIS AS A NEW SIGN.** A.K. Markopoulos, A. Kolokotronis, D.Z. Antoniadis. Aristotle U., Thessaloniki, Greece.

PFAPA or FAPA or Marshal syndrome is a relatively new, rare, and little-known entity, since the first description was made in 1987. No more than about 150 cases have been documented in the literature. The syndrome is characterized by periodic episodes of high fever, aphthae, pharyngitis, and cervical adenitis. Other described signs and symptoms include chills, headache, and digestive symptoms (mild abdominal pain, diarrhea, nausea, and vomiting). In very rare cases, arthralgias or cutaneous exanthema may be observed.

We report a new case in which, for the first time, a mild conjunctivitis was observed. Since specific laboratory abnormalities have not been shown, the diagnosis of PFAPA syndrome in this patient was based on diagnostic criteria of the syndrome. Other conditions with similar clinical symptoms, such as cyclic neutropenia, hyper-IgD syndrome, TNF $\alpha$  receptor associated syndrome, and familial cold autoinflammatory syndrome, were excluded.

**Essay Program 2 – Abstracts Read-By-Title**  
**Tuesday, April 19, 2005**

**#43**

**DETECTION OF EPSTEIN-BARR VIRUS (EBV) IN NORMAL ORAL MUCOSA OF RENAL TRANSPLANT PATIENTS.** P. Silva, N. Rezende, F. Nunes, and M. Magalhães. U. of São Paulo, São Paulo, Brazil.

The Epstein-Barr virus (EBV) is associated with both malignant and benign diseases in the head and neck region. It has been implicated in the pathogenesis of oral hairy leukoplakia and possibly other oral diseases in immunocompromised patients. The aim of this study was to determine the prevalence of EBV-DNA in healthy oral mucosa of renal transplant patients and verify the efficiency of rinse with phosphate buffered saline (PBS) to eliminate the detection of EBV due to salivary contamination. Lingual, gingival, and buccal cytobrushings were obtained from clinically normal oral mucosa of 10 renal transplant patients and 10 normal subjects for examination by polymerase chain reaction (PCR), before and after rinse with PBS. EBV-DNA was detected in 86.6% of renal transplant recipients and 46.6% of healthy people. There was no significant difference between after and before rinse with PBS in detection of EBV-DNA in oral scrapes. Our results suggest that the use of the polymerase chain reaction to detect the presence of Epstein-Barr virus DNA in oral mucosa in the absence of specific lesions gives rise to the problem of identifying the real viral replication sites. Rinse with PBS was not efficient to minimize contamination with saliva.

**#44**

**CANINE ORAL MALIGNANT MELANOMA: CLINICAL, HISTOLOGIC, AND IMMUNOHISTOCHEMICAL ASPECTS OF 268 CASES.** C. Felizzola, V. Araújo, N. Araújo, D. Pinto, Jr, and S. Sousa. U. of São Paulo, São Paulo, Brazil.

Melanoma is the most frequent oral malignancy occurring in dogs. These melanomas may present a wide range of histopathologic features, usually requiring immunohistochemical studies of associated antigens. Thus, in the present study, 268 cases of canine oral melanomas were retrieved from the files of the Oral Pathology Department at the University of São Paulo. Clinical analysis showed that most of the cases occurred in male and mongrel dogs, while both mandible and maxilla were equally affected. Histologically, most tumors were composed of sheets of epithelioid cells (180 cases, 67.2%), followed by spindle cells (29 cases, 10.9%), dendritic cells arranged in fascicles (17 cases, 6.3%), and a mixed type, composed by epithelioid and spindle cells (42 cases, 15.6%). For immunohistochemistry (streptavidin-biotin-alkaline phosphatase), commercially available antibodies were used, and vimentin, S-100, and neuron-specific enolase were detected in 97%, 80%, and 77% of the 268 cases, respectively. Of the melanocyte-specific antibodies tested, Melan A, HMB-45, and tyrosinase were detected in 66%, 62.5%, and 40% of the cases, respectively. It was concluded that melanocyte-specific antibodies, in combination with S-100 and neuron-specific enolase are helpful for the histopathologic diagnosis of oral canine melanoma variants.

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## Essay Program 2 – Abstracts Read-By-Title

### Tuesday, April 19, 2005

#45

HEMANGIOENDOTHELIOMA OF THE HEAD AND NECK. REPORT OF 2 CASES AND REVIEW OF THE LITERATURE. N. Said-A-Naief, S. Sittitavornwong, and M. J. Klein. The U. of Alabama at Birmingham. Hemangioendotheliomas are rare vascular tumors that belong to a heterogeneous group of vascular neoplasms of intermediate biological behavior and histomorphological appearance between benign and frankly malignant lesions. Since its original description in 1982, a spectrum of histomorphological patterns has been recognized including the epithelioid and Kaposiform variants. Approximately 10-15% of cases of epithelioid hemangioendothelioma occur in the head and neck area with a tendency to involve soft tissue and bone. Our review of the literature revealed the presence of a total of 31 cases of the epithelioid hemangioendothelioma of the head and neck area, including one case from our institution that presented as a destructive anterior mandibular radiolucency in a 60 year old African-American male. The lesion was treated with total block excision and the surgical margins were free of tumor, and there is no evidence of recurrence after 7 month follow-up. The occurrence of Kaposiform hemangioendothelioma in the head and neck is even rarer with a total of 14 cases identified in the literature, including one case from our institution that involved the left lateral nasal wall in a 14 year old female who presented with several month history of nasal obstruction and distant history of epistaxis. Diagnostic nasal endoscopy with completion medial maxillectomy was subsequently performed and did not reveal any residual tumor. The clinicopathologic and radiographic features of hemangioendothelioma of the head and neck are discussed, including an analysis of the reported cases of epithelioid and the Kaposiform hemangioendothelioma of the oral and maxillofacial region.

#46

ACTINIC CHEILITIS: COMPARATIVE STUDY OF HISTOPATHOLOGICAL ASPECTS OF INCISIONAL BIOPSIES AND VERMILIONECTOMY – STUDY OF 20 CASES. M.M.S. Nico, S.V. Lourenço, and E.A. Rivitti. U. of São Paulo, São Paulo, Brazil.

Actinic cheilitis is the incipient and superficial squamous cell carcinoma of the lip vermilion. In this study, 20 cases of actinic cheilitis were initially biopsied and a vermilionectomy was then performed. The cases comprised those with diffuse and homogeneous clinical alterations. Serial sections of the products of vermilionectomies were histologically analyzed and compared with the biopsies. Histopathological changes were classified as: normal epithelium, mild, moderate, and severe dysplasia/carcinoma *in situ*, superficially invasive squamous cell carcinoma (SISCC), and invasive well-differentiated squamous cell carcinoma (ISCC). Biopsy findings included: epithelial dysplasia – mild (4 cases), moderate (10 cases), severe/carcinoma *in situ* (3 cases), SISCC (8 cases), ISCC (1 case). The most severe findings at vermilionectomy included: dysplasia - mild (2 cases), moderate (6 cases), severe/carcinoma *in situ* (3 cases), SISCC (9 cases). A comparison between biopsies and most severe findings at vermilionectomy revealed coincidental findings in 8 cases, more severe findings on biopsy in 3 cases, and more severe findings on vermilionectomy in 9 cases. SISCC was observed in 9 cases: of these, 2 had already been diagnosed at biopsy, 6 had shown milder aspects at biopsy, and 1 biopsy had shown a more severe aspect. Histopathological epithelial changes were not uniform along the vermilion in most cases and the biopsies did not reveal the most severely affected area in many cases.

## Essay Program 2 – Abstracts Read-By-Title

### Tuesday, April 19, 2005

#47

THE ROLE OF DIRECT IMMUNOFLUORESCENCE (DIF) IN THE DIAGNOSIS OF ORAL LICHEN PLANUS. N. Musa, A. Aguirre, W. McCall, V.Kumar, and M.Neiders. U. at Buffalo, State U. of New York, and IMMCO Diagnostics Inc.

Lichen planus is a common chronic mucocutaneous disease that affects 1%-4% of the population; it is a disease of females (60-65%) in the age range of 30-60 years. The diagnosis of oral lichen planus (OLP) is based on the consensus of clinical, histological, and DIF findings. The role of DIF in the diagnosis of OLP has been questioned by many researchers. **Objective:** To evaluate the role of DIF technique in OLP diagnosis.

**Methods:** This is a retrospective study of 392 consecutive cases taken from the files of IMMCO Diagnostics Inc. The clinical diagnosis was established by the contributing clinicians. The histological examination was established by the consensus of three oral pathologists. The DIF diagnosis was established by staining for fibrin, immunoglobulins, and C3. **Results:** 392 cases were evaluated. Seventy five (75) cases were positive for OLP by both H&E and DIF, 65 cases were not suggestive of OLP by H&E and found to be positive for OLP by DIF, and 36 cases were suggestive of OLP by H&E but ruled out by DIF. From the 65 cases which were positive for OLP by DIF, one case of dysplasia, one case of carcinoma *in situ* (CIS), and one case of squamous cell carcinoma (SCC) were found to be suggestive of OLP by DIF, yet ruled out by H&E. **Conclusions:** DIF is *very valuable* in establishing the diagnosis of OLP in cases where histology had failed to do so. DIF is *very valuable* in ruling out OLP when it is not present. Some cases of SCC, dysplasia, and CIS maybe misdiagnosed by DIF as OLP, and combinations of histology and DIF are important to reach the final diagnosis.

#48

ORAL AND MAXILLOFACIAL MANIFESTATIONS OF GRANULOMATOUS DISEASES. A RETROSPECTIVE STUDY OF 21 CASES. A.K. Markopoulos, D.Z. Antoniadis, E. Deligianni, and A. Kolokotronis. Aristotle U., Thessaloniki, Greece.

The term granuloma implies a histopathologic condition which is characterized by the presence of circular formations that contain epithelioid cells, giant cells, lymphocytes, and plasma cells. In certain occasions, necrotic areas co-exist. Granulomatous diseases are defined as the diseases that contain granulomas. They include (1) infections (tuberculosis, leprosy, syphilis, systemic fungal infections, cat scratch disease); (2) diseases of unknown etiology (Melkersson-Rosenthal syndrome, granulomatous cheilitis, Crohn's disease, sarcoidosis, Wegener's granulomatosis, orofacial granulomatosis); (3) foreign body reaction; and (4) hairy cell leukemia.

The study group comprised 21 patients with granulomatous diseases seen in the Oral Medicine Clinic of the University of Thessaloniki, Greece. Eleven patients suffered from Melkersson-Rosenthal syndrome or granulomatous cheilitis, four from tuberculosis, four from syphilis, and two from sarcoidosis. The clinical picture, histopathologic findings, and the results from laboratory tests were analyzed for every case.

In conclusion, granulomatous diseases are rare, they clinically appear with a non-pathognomonic picture, and the final diagnosis is established with the combination of clinical, histopathologic, and laboratory findings.