

Odynophagia Flags Possibility of Lodged Food, Perforation

Esophageal Perforation Caused by Edible Foreign Bodies: A Systematic Review of the Literature.

Aronberg RM, Puneekar SR, Adam SI, et al:

Laryngoscope 2015; 125 (February): 371-378

Patients with lodged edible foreign bodies causing esophageal injury most commonly present with pain, odynophagia, and dysphagia. CT scan is 100% sensitive for identifying lodged food.

Background: Otolaryngologists are riddled with consults for food lodged in the esophagus. Most of these edible foreign bodies pass without any symptomatic sequelae. Although 90% of these cases do not require intervention, patients often complain of dysphagia as if the food remains stuck in the neck. Unlike ingestions of nonedible foreign bodies, edible foreign bodies that cause serious esophageal injury are uncommon. However, there are isolated reports of esophageal perforations from edible foreign bodies.

Design: Case report and literature review. **Case Report:** A 61-year-old woman who had been eating fish presented with severe throat pain that worsened with swallowing. CT scan showed a radiopaque focus in the cervical esophagus and precervical air indicative of possible esophageal perforation. Neither rigid endoscopy nor surgical exploration identified the source of the problem, although the esophageal perforation was repaired. On day 2, the patient continued to complain of pain, and a repeat CT again showed a radio-opaque focus at the same location. Rigid esophagoscopy was performed, and a fish bone was found and extracted. **Literature Review:** A systematic review of the literature identified 40 studies on 168 patients with edible foreign bodies causing esophageal injury. The most common presenting symptoms are pain, odynophagia, and dysphagia. Plain films are not reliably diagnostic, while CT scan shows a sensitivity of 100% for identifying lodged food. With this diagnosis, most studies show that esophagoscopy is sufficient to visualize the material. Complication rates in patients whose foreign body cannot be removed are quite high. The overall mortality rate is 10%, with complications ranging from mediastinitis, arterioesophageal fistula, and sepsis.

Conclusions: The authors recommend repeat CT imaging if the foreign body cannot be localized with esophagoscopy or open neck surgery.

Reviewer's Comments: This was a descriptive review of the literature with which otolaryngologists should be familiar. Although food/bone ingestion causing esophageal perforations is very uncommon, the clinical history should prompt clinical suspicions. One clue is odynophagia associated with signs of infection. CT scans can aid in the diagnosis and localization. Removal with formal esophagoscopy or open surgery is mandatory given the high rates of morbidity associated with this problem. (Reviewer-Young J. Kim, MD, PhD).

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Keywords: Esophageal Perforation Due to Edible Foreign Bodies, Diagnosis, Complications

Print Tag: Refer to original journal article

1 of 5 Patients Have Tertiary Bleeding After Tonsillectomy

Rapid Communication: The Risk of Additional Post-Tonsillectomy Bleeding After the First Bleeding Episode.

Bhattacharyya N:

Laryngoscope 2015; 125 (February): 354-355

The incidence of tertiary hemorrhage after tonsillectomy is nearly 20% in both pediatric and adult populations.

Background: Neil Bhattacharyya has mined the clinical database for the past decade to unearth important clinical information for otolaryngologists. Recently, he examined the incidence of pediatric and adult post-tonsillectomy bleeding rates, which were found to be 2.1% for kids and 4.8% for adults. He went back to this database and analyzed another clinical scenario in these patients who underwent tonsil surgery -- the rebleeding after a major post-tonsillectomy bleed. The author terms this type of bleeding as "tertiary hemorrhage."

Objective: To determine the tertiary bleeding rate and risks among children and adults who have undergone tonsillectomy.

Results: Among >1600 children who had a secondary hemorrhage, the tertiary hemorrhage rate was 17.5%. The relative risk for this tertiary hemorrhage was 10.2. Among children who presented with pain after secondary hemorrhage, the tertiary hemorrhage rate was only 3.5%. For adults, the tertiary hemorrhage rate was 21.3%, and the relative risk was 5.1. In the adult population that presented with acute pain after secondary hemorrhage, the relative risk for tertiary hemorrhage was only 1.1.

Conclusions: The rates of tertiary hemorrhage are higher than expected in both the pediatric and adult population.

Reviewer's Comments: Taken at face value, the implication of this report is that those who suffer from post-tonsillectomy hemorrhage should be admitted for observation. In both pediatric and adult populations, the author is stating that 1 of 5 patients will have a tertiary hemorrhage. However, the downside of this report is the lack of delineating what constitutes a tertiary hemorrhage. There are no records or data on the rate of trips to the operating room. These numbers would suggest a significant hemorrhage that would warrant a surgical intervention. Secondly, the database used in this study is extracted from only 4 states in U.S., suggesting a practice bias in diagnosis and management styles of those 4 states. Overall, however, this study is very provocative in setting up a discussion about whether these patients should be admitted after the secondary hemorrhage. (Reviewer-Young J. Kim, MD, PhD).

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Keywords: Tonsillectomy, Hemorrhage, Recurrent Bleeding Complications

Print Tag: Refer to original journal article

CTA, MRA Best Imaging Modalities for Unilateral PT

What Is the Best Imaging Modality in Evaluating Patients With Unilateral Pulsatile Tinnitus?

Ahsan SF, Seidman M, Yaremchuk K:

Laryngoscope 2015; 125 (February): 284-285

The mainstays of imaging for unilateral pulsatile tinnitus should be CT angiography and MR angiography.

Background: Tinnitus is a common complaint among patients, and the history should prompt questions regarding whether the tinnitus is pulsatile. About 20% of pulsatile tinnitus (PT) patients will have objective tinnitus (can be detected by the clinician). Unlike nonpulsatile tinnitus, structural pathologies can be detected in PT. The incidence of these structural findings range from 40% to nearly 90%, particularly if symptoms and signs are unilateral. In terms of pathobiology, PT can be explained by transmission of vibrations from blood flow turbulence to the nearby cochlea. For the clinician, therefore, the issue is which of the imaging tests to order.

Objective: To determine the best imaging modality for unilateral PT.

Methods: The authors examined 5 reports from the recent literature regarding imaging modalities for unilateral PT. Of course, the literature cannot be based on randomized clinical trials, so the level of evidence for these recommendation is 4.

Results: The authors recommend otoscopic and clinical examination to assess for paraganglioma or other neoplastic processes. If a mass is found, CT of the temporal bone is the first choice. If the patient has objective PT in which the clinician can also detect the PT, then CT angiography is recommended. If this is normal but there is still a high degree of suspicion, then a 4-vessel angiogram is needed to rule out aneurysm, dissection, or AV malformations. If the clinician has found only subjective PT, then the next step is usually CT angiography. If the history is more suggestive of idiopathic intracranial hypertension, then MRI/MR angiography is recommended.

Reviewer's Comments: This was a succinct review of the differential and the diagnostic management of unilateral PT. The readers should be aware of carotid duplex for patients with history of a transient ischemic attack (TIA) and stroke who present with unilateral tinnitus. For intracranial hypertension, the clinicians should look for venous sinus stenosis, empty sella, and flattening of the globes. Lastly, clinical distinction between venous PT versus arterial PT may be important to narrow the differential prior to ordering CT angiography. Overall, the mainstay of imaging should be CT angiography and MR angiography for this pathology. (Reviewer-Young J. Kim, MD, PhD).

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Keywords: Pulsatile Tinnitus, Imaging

Print Tag: Refer to original journal article

Topical Onion Extracts, Vit E May Not Reduce Scars

Do Topical Products Reduce Postincision Scars?

Hom DB, Hom KA:

Laryngoscope 2015; 125 (February): 282-283

Topical onion extracts, such as Mederma, and topical vitamin E products may not improve the appearance of surgical scars.

Background: Patients constantly ask their surgeons whether any topical products are available for improving postoperative incision scars.

Objective: To review the current literature to determine if good level-1 evidence exists for the use of topical medications to improve surgical scars.

Methods: The authors reviewed 5 recent randomized clinical trials that examined different methods to improve surgical scars. **Mederma:** Mederma® is a highly marketed onion-extract material for improving surgical scars. In a randomized controlled trial (RCT), the efficacy of Mederma was compared to that of petrolatum ointment. Both were applied three times/day for 8 weeks on the same type of surgical scar. The final results showed no differences in efficacy. The end point measured was the presence of hypertrophic scars. **Vitamin E:** In another randomized clinical trial, the efficacy of vitamin E was compared to that of a placebo cream. No differences in outcomes were seen. The results of these first 2 studies suggest that topical products do not improve surgical scars. However, the authors also reviewed 2 other studies that confused this issue. **Silicone Gel:** One RCT compared the efficacy of silicone gel with that of zinc oxide. In this study, the use of silicone gel was associated with improvement in hypertrophic scars and reduction of keloids. Another study compared silicone gel with cyanoacrylate application: both products improved final scar outcomes. **Paper Tape:** In yet another study, the prolonged use of paper tape (compared to no tape) improved the surgical scar.

Conclusions: Overall, the authors do not recommend the use of vitamin E and onion extracts for surgical scars.

Reviewer's Comments: Among the 5 studies cited in this review, otolaryngologists should be aware that all studies focused on different parts of the body. Therefore, technically, the efficacy of onion extracts and vitamin E on scars of the face and neck remains unknown. Nonetheless, the randomized clinical trials showed that vitamin E and onion extracts do not improve the surgical scars on different parts of the body, so it is unclear whether these results would be any different for the face and neck. Because of variations in the control groups used in the studies of silicone gel, it is still unclear whether silicone gels are effective. After reviewing these 5 randomized clinical trials, it remains unclear if something else can significantly improve surgical scars other than the practices we already know (meticulous closure and tension minimization). (Reviewer-Young J. Kim, MD, PhD).

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Keywords: Postincision Scar, Efficacy of Topical Products

Print Tag: Refer to original journal article

Regimented Swallowing Exercises Good for Rehab

Effects of 2 Different Swallowing Exercise Regimens During Organ-Preservation Therapies for Head and Neck Cancers on Swallowing Function.

Virani A, Kunduk M, et al:

Head Neck 2015; 37 (February): 162-170

Regimented swallowing exercises may be better than simple repetitive swallowing exercises for improving treatment-induced dysphagia in patients undergoing organ-preserving therapy for head and neck cancer.

Background: With the increase in the incidence of human papilloma virus (HPV)-associated squamous cell carcinoma (SCC), the use of chemoradiation therapy for these cases has also increased. Despite the improved prognosis of HPV-associated tumors, patients undergoing organ-preservation protocols are expected to experience dysphagia as a side effect. There are clear findings in the literature that these patients should be evaluated by speech pathologists to improve their posttreatment dysphagia and to improve the likelihood to removing their percutaneous endoscopic gastrostomy (PEG) tubes. Two different methods of swallowing therapies include (1) simple repetitive swallows and (2) regimented swallowing exercises.

Objective: To compare the efficacy of 2 swallowing rehabilitation methods (simple repetitive swallows vs regimented swallowing exercises) during and after either radiation alone or chemoradiation for the treatment of head and neck cancer.

Design: Prospective study.

Methods: 50 patients were assigned to 1 of 2 swallowing interventions: simple repetitive swallowing exercises or regimented swallowing exercises. Functional oral intake scale (FOIS) and PEG dependence were analyzed at posttreatment and again at 3 months.

Results: PEG dependence at 3 months was significantly lower in patients assigned to regimented swallowing exercises (16%) than in those assigned to simple repetitive swallowing exercises (50%). This relationship was also present when the authors examined only those who had been treated via the combination of chemotherapy and radiation.

Conclusions: The authors strongly recommend regimented swallowing exercises rather than simple repetitive swallowing exercises to manage posttreatment dysphagia in patients undergoing organ-preservation therapy for head and neck cancer.

Reviewer's Comments: The findings of this report are very intriguing from the standpoint of dysphagia rehabilitation. There are several caveats, however. One is that the study included all subsets of head and neck cancer patients. About 50% of the patients were oropharyngeal (OP) tumors, but segregating those only with OP tumors would have resulted in a low number of patients for analysis. The other caveat is that the study excluded patients who required PEG prior to treatment. In other words, the exercises may not improve swallowing in cancer patients with severe dysphagia, and the swallowing exercises may affect only those with treatment-induced dysphagia. Overall, however, this report validates the need to ensure that OP cancer patients undergo a speech pathology consult prior to the initiation of cancer treatment. Speech pathologists should be vital members of the treatment team. (Reviewer-Young J. Kim, MD, PhD).

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Keywords: Oropharyngeal Cancer, Treatment-Induced Dysphagia, Rehabilitation

Print Tag: Refer to original journal article

Sorafenib Monotherapy Not Beneficial for Advanced ACC

Phase II Trial of Sorafenib in Advanced Salivary Adenoid Cystic Carcinoma of the Head and Neck.

Thomson DJ, Silva P, et al:

Head Neck 2015; 37 (February): 182-187

Sorafenib monotherapy does not appear to be efficacious for the treatment of recurrent and/or metastatic adenoid cystic carcinoma. More than 50% of patients experience grade 3 toxicity at a dose of 400 mg twice daily.

Background: Salivary gland tumors are primarily treated with surgery followed by adjuvant radiation. Whether chemotherapy has a role for the treatment of these pathologies remains unclear. Among the salivary gland pathologies, adenoid cystic carcinoma (ACC) has attracted attention for its ability to recur and progress, and it comprise 25% of salivary gland cancers. Only 20% of surgically treated patients remain disease-free at 15 years, and nearly 50% develop distant metastases to the lung decades after the treatment of the primary tumor. Molecular expression analysis has demonstrated that these tumors can express c-kit and vascular endothelial growth factor receptor (VEGFR), so oncologists have tested multiple tyrosine kinase inhibitors in several clinical trials, and not one of the tested agents was found to be effective.

Objective: To determine the efficacy of sorafenib, an oral tyrosine kinase inhibitor, in the treatment of advanced ACC that has either recurred or metastasized. Sorafenib can target multiple oncogenic pathways to include c-kit, VEGFR, and EGFR.

Participants: 23 patients with metastatic and/or recurrent ACC.

Methods: After a phase I trial to test its safety, the authors performed a single-arm phase II clinical trial to test the potential clinical efficacy of sorafenib as monotherapy for advanced ACC. Patients were followed up for median progression-free survival (PFS), overall survival (OS), and toxicity profile.

Results: The median PFS was 11 months, and the median OS was 19 months. More than 50% of patients had grade 3 toxicity with a sorafenib dose of 400 mg twice daily. Overall, at 12 months, clinical activity was limited, and sorafenib induced significant toxicity.

Conclusions: The authors do not recommend the clinical use of sorafenib as monotherapy for the treatment of metastatic and/or recurrent ACC.

Reviewer's Comments: The field of oncology is littered with failed clinical trials, and sorafenib is another victim of this. Sorafenib has been tested for other cancers with molecular phenotypes similar to that of ACC. However, this phase II trial demonstrated that single agents that target unregulated serine/threonine kinases does not work as a monotherapy for ACC. Now, this does not preclude its use as part of a combination therapy, but these negative clinical trials would prevent much enthusiasm for its future use. (Reviewer-Young J. Kim, MD, PhD).

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Keywords: Advanced Adenoid Cystic Carcinoma, Sorafenib

Print Tag: Refer to original journal article

HNSCC -- High PLR, Low NLR Predict Poor Prognosis

Systemic Inflammatory Markers as Independent Prognosticators of Head and Neck Squamous Cell Carcinoma.

Rassouli A, Saliba J, et al:

Head Neck 2015; 37 (January): 103-110

A high platelet-to-lymphocyte ratio and a low neutrophil-to-lymphocyte ratio are associated with a poor prognosis in patients with head and neck squamous cell carcinoma.

Background: With the wealth of molecular analysis of head and neck cancer, some expected molecular analysis to provide prognostic information for these malignancies. However, for most head and neck cancers, prognostic biomarkers are limited. The authors hypothesized that cancer and tissue inflammation are intimately related.

Objective: To determine if simple pretreatment inflammatory markers correlate with prognosis in patients with head and neck squamous cell carcinoma (HNSCC).

Design: Retrospective analysis.

Participants: 273 patients with HNSCC.

Methods: Platelet-lymphocyte ratio (PLR) and neutrophil-to-lymphocyte ratio (NLR) served as the parameters for inflammation. These ratios were correlated with mortality and recurrence rates.

Results: A PLR >170 was associated with increased mortality rates, while an NLR >4.2 correlated with increased recurrence rates. A PLR >170 combined with an NLR ≤3 correlated with greater T-stage and greater mortality rates. From these correlative analyses, the authors found that these 2 ratios were comparable to TNM staging in providing prognostic information. Specifically, PLR was found to be an independent predictor of mortality, and NLR was predictive for recurrence.

Conclusions: The authors recommend the use of PLR and NLR for pretreatment staging of patients with HNSCC.

Reviewer's Comments: The authors have touched on an important topic in cancer biology at a clinical level. There is now a wealth of information showing that the tumor microenvironment can modulate outgrowth of the aggressive or metastatic phenotype in cancer biology. These authors have produced an early clinical parameter to measure how the inflammatory environment of the patient can potentially dictate the prognosis of the cancer. They selected 3 cell populations to measure in the peripheral blood: platelets, neutrophils, and lymphocytes. Unfortunately, there are clear subsets of neutrophils and lymphocytes that are both pro- and anti-carcinogenic, so it would have been more useful had the authors measured other subsets of cells in their analysis. While the use of these ratios is not ready for clinical use, it is clear that they are on the right path. (Reviewer-Young J. Kim, MD, PhD).

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Keywords: Head and Neck Squamous Cell Carcinoma, Prognosis, Inflammatory Markers

Print Tag: Refer to original journal article

Proton Therapy for ACC -- Initial Outcomes Encouraging

Proton Therapy for Head and Neck Adenoid Cystic Carcinoma: Initial Clinical Outcomes.

Linton OR, Moore MG, et al:

Head Neck 2015; 37 (January): 117-124

Proton therapy for the treatment of unresectable or recurrent adenoid cystic carcinoma of the head and neck appears to have an acceptable toxicity profile.

Background: Adenoid cystic carcinoma (ACC) is generally considered to be a surgical disease, but surgery has its limitations in many scenarios. For patients with unresectable or recurrent disease, radiation therapy has been reported to reduce disease progression. Even for resected disease, patients with perineural invasion or close or positive margins are treated with postsurgical external beam radiation. Some centers have adopted neutron beam radiotherapy to deliver a more potent dose of radiation therapy, and there appears to be some biological effect without any curative benefit.

Objective: To explore the use of proton beam therapy for ACC, which is an indolent but aggressive disease. Proton beam therapy can focus the energy delivery to the tumor site and minimize the radiation dose delivered to the surrounding tissue.

Design: Retrospective analysis.

Participants: 26 patients with ACC with either an unresectable primary tumor or a recurrent tumor.

Methods: The median radiation dose delivered via proton beam therapy was 72 Gy. The authors examined progression-free survival, overall survival, local control, and toxicity rates in these patients.

Results: The median follow-up was 25 months. The 2-year overall survival rate was 93% for patients with primary tumor and 57% for those with recurrent disease. The 2-year local control rate ranged from 86% to 95%. Among these 26 patients, grade 3 to 5 toxicity occurred in only 4, while 22 had either grade 1 or 2 toxicity.

Conclusions: From these preliminary data, the authors concluded that proton therapy may be a viable option for unresectable or recurrent ACC.

Reviewer's Comments: Given that ACC is a slow-growing tumor, this study measured survival rates in terms of 2 years, which is not very meaningful. However, what was meaningful in this report was that the toxicity of proton therapy was tolerable. Most patients had only grade 1 or 2 toxicity, so the potential for using proton therapy to treat ACC is moderate. Better response parameters measured in terms of at least 5 to 10 years may help bring proton therapy's acceptance to the community at large. Furthermore, this study did not have a control group that received standard external beam radiotherapy or neutron therapy. These control groups should be included in future studies to demonstrate whether proton therapy is more or equally effective compared to the standard of care (external beam radiotherapy). (Reviewer-Young J. Kim, MD, PhD).

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Keywords: Adenoid Cystic Carcinoma of Head & Neck, Proton Therapy, Outcomes

Print Tag: Refer to original journal article

NPC Progression May Be Linked to Inflammation

Pretreatment Neutrophil-to-Lymphocyte Ratio as Predictor of Survival for Patients With Metastatic Nasopharyngeal Carcinoma.

Jin Y, Ye X, et al:

Head Neck 2015; 37 (January): 69-75

Neutrophil count may have prognostic significance in patients with metastatic nasopharyngeal cancer.

Background: Chronic inflammation as measured by neutrophil count has been associated with a poor prognosis for many types of cancer. For lung, renal cell, colorectal, and gastric cancers, an elevated neutrophil-to-lymphocyte ratio (NLR) has been associated with the prognosis.

Objective: To determine if pretreatment NLR correlates with clinical prognosis in patients with metastatic nasopharyngeal carcinoma (NPC) in China.

Participants: Patients with disseminated NPC who were receiving palliative cisplatin chemotherapy.

Methods: For each of the 229 patients with metastatic NPC, the authors determined the peripheral blood neutrophil count, lymphocyte count, and neutrophil-to-lymphocyte ratio (NLR). These parameters were correlated with disease progression using hazard ratios.

Results: Pretreatment neutrophil count, neutrophil percentage, and NLR were associated with a poor prognosis. The median survival was 15.3 months when NLR was >3.6 and was 23.5 months when NLR was ≤ 3.6 (difference statistically significant). After examining multiple clinical parameters in this population (including number of metastases, initial chemotherapy response, age, and gender), only Karnofsky performance status and NLR ratio >3.6 were associated with overall survival in both univariate and multivariate analysis.

Conclusions: Pretreatment NLR is prognostic for metastatic NPC.

Reviewer's Comments: In this fascinating study, the authors examined an often-overlooked variable among head and neck cancer patients. Biological studies have shown the presence of tumor-associated neutrophils to have a pro-cancer effect, but these clinical results suggest that these neutrophils may have clinical relevance. Of course, one thing that is not clear is whether the NLR affects responsiveness to palliative chemotherapy. The authors examined this, but these data are very preliminary. It would have been more interesting had they examined early stage versus late-stage NPC. (Reviewer-Young J. Kim, MD, PhD).

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Keywords: Metastatic Nasopharyngeal Carcinoma, Prognosis, Neutrophil-to-Lymphocyte Ratio

Print Tag: Refer to original journal article

Extent of Parotid Surgery Affects Postop Nerve Weakness

Impact of Extent of Parotid Resection on Postoperative Wound Complications: A Prospective Study.

Tuckett J, Glynn R, Sheahan P:

Head Neck 2015; 37 (January): 64-68

Compared with more extensive parotid surgery, less extensive surgery is associated with an increased incidence of postoperative wound complications and a reduced incidence of nerve weakness.

Background: The complications for parotidectomies should be familiar to otolaryngologists: Frey syndrome, sialocele, fistula, wound complications, numbness, and facial nerve weakness. While dealing with facial nerve weakness has been a major focus, the complications of sialocele and fistula have not been addressed to the same degree. This is probably due to the fact that both of these complications are managed conservatively, and they resolve with little intervention. The extent of parotidectomy has been reported to be associated with these wound complications.

Objective: To determine whether the extent of parotidectomy is associated with the types of complications.

Methods: The authors prospectively examined and analyzed their series of 66 consecutive parotidectomies, which were subdivided into partial/extracapsular parotidectomy versus superficial/total parotidectomy.

Results: When these 2 groups were followed prospectively, there was a clear separation in terms of types of postoperative complications. Partial/extracapsular parotidectomy was associated with greater rates of sialocele, fistula, and other wound complications than was superficial/total parotidectomy. However, partial/extracapsular parotidectomy had a lower incidence of facial nerve paresis than did superficial/total parotidectomy. Patients undergoing extensive surgery to remove bone and skin were excluded from this series.

Conclusions: A greater extent of parotidectomy is associated with a reduced incidence of sialocele and fistula but with an increased rate of nerve weakness.

Reviewer's Comments: Although the results of this report are not surprising, it is worth noting that the wound complications of sialocele and fistula stem from the remnant salivary tissue present in the surgical bed. One criticism of this study is that the authors included all tumor types, both benign and malignant. This may have been due to the low number of cases accrued in this prospective analysis, but it is unclear whether facial nerve paresis is related to the oncologic surgery. Of course, a malignant lesion would render the surgery more extensive, but a segregation of the pathology involved would have ensured that this would not bias the study's results. (Reviewer-Young J. Kim, MD, PhD).

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Keywords: Parotidectomy, Extent of Surgery vs Postop Complications

Print Tag: Refer to original journal article

Presentation, Imaging of Inflamed Parotid Lesions

Inflamed Benign Tumors of the Parotid Gland: Diagnostic Pitfalls From a Potentially Misleading Entity.

Mantsopoulos K, Psychogios G, et al:

Head Neck 2015; 37 (January): 23-29

The clinical presentation and imaging findings of parotid lesions may be useful for differentiating inflamed benign lesions from malignant lesions.

Background: Inflamed benign tumors of the parotid gland are uncommon, and these lesions are included in those scenarios that do not fit neatly into a well-defined presentation of classic salivary gland pathology. These inflamed benign tumors can arise from pleomorphic adenomas, Warthin tumor, or monocytic adenoma, and their acute inflammation can render them to be suspicious for malignancy.

Objective: To characterize the clinical presentation, radiographic findings, fine-needle aspiration (FNA) findings, and final pathologic findings associated with inflamed benign tumors of the parotid gland.

Methods: The authors of a tertiary center in Germany reviewed their series of patients (n=16) with benign tumors of the parotid gland confirmed on final pathology. The clinical presentation, radiographic findings, FNA findings, and final pathologic findings were reviewed.

Results: Most cases presented with acute pain or acute tenderness to palpation. The charts did not have blood tests, such as WBC counts or sedimentation rates, to aid in the diagnosis. US findings typically had blurred tumor margins that made them suspicious for malignancy. MRI was done in only 4 cases, and FNA was done in only 4 cases. In 1 case, facial nerve paresis was noted, albeit slight. Of 16 cases, 11 were Warthin tumors, 4 were pleiomorphic or monomorphic adenomas, and 1 was an oncocytic cystadenoma.

Conclusions: The authors recommend an algorithm in which US is instituted first. If a distinct tumor is detected, patients should be given antibiotics to resolve the inflammation. If the acute pain and inflammation resolve, then US should be repeated in 3 weeks, making definitive plans for surgery at that time. If the inflammation does not resolve, lesions should be imaged with MRI. The authors did not include FNA in their algorithm.

Reviewer's Comments: This report comes from Europe, so there may be some differences in management styles. For example, some centers in the United States prefer imaging via CT scans rather than US, and they may use US-guided FNA as an important diagnostic tool for this pathology. Although the US images in this series showed blurred tumor margins, which may be suspicious for malignancy in most cases, the authors still have adopted US as their mainstay imaging method, even for these inflamed parotid lesions. Overall, the algorithm they have presented may work for clinicians who would like to avoid CT-associated radiation or in settings in which the clinician does not trust the cytopathologist. (Reviewer-Young J. Kim, MD, PhD).

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Keywords: Parotid Gland, Inflamed Benign Tumor, Diagnosis

Print Tag: Refer to original journal article

Pharyngeal Wall SCC -- Survival Similar for TLM, Open Surgery

Oncologic Results of Transoral Laser Microsurgery for Squamous Cell Carcinoma of the Posterior Pharyngeal Wall.

Canis M, Wolff HA, et al:

Head Neck 2015; 37 (February): 156-161

In patients with posterior pharyngeal wall carcinomas, local control after transoral laser microsurgery is better for T1/T2 tumors than for T3/T4 tumors.

Background: Transoral laser microsurgery (TLM) is mostly known for its applicability in the treatment of glottic cancer. Its use in the treatment of squamous cell carcinoma (SCC) of the posterior pharyngeal wall has not been described extensively.

Objective: To describe clinical outcomes following TLM for SCC of the posterior pharyngeal wall of the hypopharynx or oropharynx.

Design: Retrospective cohort study.

Methods: Charts of patients who had undergone TLM for primary treatment of posterior oropharyngeal and/or hypopharyngeal SCC between 1986 and 2006 were reviewed. TLM was carried out to achieve resection margins of at least 5 mm, with repeat resection for positive margins. Patients were excluded if they had second primaries, distant metastatic disease, and N3 neck disease.

Results: 25 patients were included in this study, including 20 men and 5 women. Median age was 58 years, and median follow-up was 41.6 months. Posterior wall SCC was oropharyngeal in 12 patients and was hypopharyngeal in 13. Most patients had tumor extension into both subsites. The authors classified the tumor origin based on the location of the main tumor bulk. The American Joint Committee on Cancer stage classification was as follows: stage I, 4%; stage II, 28%; stage III, 24%; and stage IVa, 44%. Sixteen patients (94%) underwent bilateral neck dissections, while 13 (52%) received adjuvant radiation. Although local control at 5 years was higher for T1/T2 tumors (90%) than for T3/T4 tumors (68.8%), overall survival was almost similar for T1/T2 tumors (36.5%) and T3/T4 tumors (41.2%). Local control at 60 months did not vary significantly according to tumor subsite. No patient required a permanent gastrostomy tube, while 1 required a temporary tracheotomy.

Conclusions: The outcomes for local control and survival associated with TLM are comparable to those for open surgery and primary chemoradiation in patients with SCC of the posterior pharyngeal wall of the hypopharynx or oropharynx.

Reviewer's Comments: This is a relatively small case series compared to the larger volumes for TLM in glottic cancer previously reported by Dr Steiner's group. Posterior pharyngeal wall SCC is a less common subsite for laryngeal cancer, and survival data in this study are comparable to existing survival data for open surgery. The authors make the case for advantages of TLM to include improved visualization for preservation of surrounding vasculature and muscles through the use of magnification, and they highlight the absence of permanent tracheostomies or feeding tubes. Further validation of the data in this study will require a much larger study population from multiple centers. (Reviewer-Zhen Gooi, MD).

© 2015, Oakstone Publishing, LLC

Keywords: Pharyngeal Carcinoma of Posterior Wall, Transoral Laser Microsurgery

Print Tag: Refer to original journal article

Immunocompromised State Prognostic for Oral Cavity SCC

Histologic and Systemic Prognosticators for Local Control and Survival in Margin-Negative Transoral Laser Microsurgery Treated Oral Cavity Squamous Cell Carcinoma.

Sinha P, Mehrad M, et al:

Head Neck 2015; 37 (January): 52-63

An immunocompromised state strongly correlates with local control and survival rates in patients with oral cavity squamous cell carcinomas treated via margin-negative transoral laser microsurgery.

Background: TNM staging is currently used for oral cavity squamous cell carcinoma (SCC), and many clinicians accept its use while acknowledging its limitations. For example, TNM staging does not address the systemic factors that can affect prognosis, such as a patient's immune status. Some use tumor's depth-of-invasion for staging oral cavity SCC, but this is not widely accepted. Another proposed prognostic test for oral cavity SCC is the Brandwein-Gensler score (BGS) derived from histological findings (tumor invasion patterns, lymphocytic infiltration, and perineural invasion).

Objective: To determine if the BGS as well as systemic signs of an immunocompromised state provide prognostic information regarding local control and survival in patients with oral cavity SCC who underwent TLM.

Methods: The authors reviewed their series of 60 cases with ≥ 2 -years follow-up after treatment of oral cavity SCC with TLM (negative margins). The BGS and immune status of these cases were determined and then correlated with recurrence and survival rates.

Results: In multivariate analysis, an immunocompromised state was predictive for recurrence and local control. Patients were deemed to be "immunocompromised" if they had a history of medical disease that would render them as immunocompromised, such as patients with a history of autoimmune disease, steroid use, chemoradiation, or immunodeficiencies, etc. A high BGS risk category correlated only with overall survival rates, while T-grade and an immunocompromised state were prognostic for disease-specific survival and overall survival rates. The strongest predictive parameter was an immunocompromised state. The authors recommend improved delineation of the determinants or parameters that establish an immunocompromised state.

Conclusions: An immunocompromised state and a high BGS risk category best correlate with local control and survival rates among patients with oral SCC after treatment with margin-negative TLM. In the authors' series of patients, the overall local recurrence rate was 18%.

Reviewer's Comments: This report has an interesting finding: immune compromise strongly correlates with local control and survival rates. However, the authors' definition of this systemic immunocompromised state is not clear. They deemed a patient to be immunocompromised by using only history, but they did not use objective laboratory data. Despite this poorly defined parameter, they found that the immunocompromised state was the strongest predictor for recurrence and survival rates, which I think is very interesting. The study is limited by the low number of participants. While the findings should prompt more investigations on how the immune system modulates oral cavity tumors, it is unclear how these findings can be translated into prognostic information in patients treated for oral cavity SCC. (Reviewer-Young J. Kim, MD, PhD).

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Keywords: Squamous Cell Carcinoma, Laser Microsurgery, Local Control, Prognostic Factors

Print Tag: Refer to original journal article

Serial Biopsies Explain Acquired Resistance to Everolimus

Response and Acquired Resistance to Everolimus in Anaplastic Thyroid Cancer.

Wagle N, Grabiner BC, et al:

N Engl J Med 2014; 371 (October 9): 1426-1433

Everolimus, an mTOR inhibitor, was temporarily effective for a patient with anaplastic thyroid cancer, but *MTOR* eventually mutated, and the tumor acquired resistance to the drug.

Background: Despite treating about 2 patients per year who have anaplastic thyroid cancer, I have never cured 1 of them. The median survival is 5 months. Like many of my peers, I cringe when a referral is made. Therefore, when something positive is reported, I am all ears. Everolimus is an oral medication that inhibits mTOR (mammalian target of rapamycin). Specifically, mutations in the tumor-suppressor genes *TSC1*, *TSC2*, and *STK11* cause activation of the mTOR pathway and are targets for everolimus.

Objective: To document a near-complete response to everolimus in a patient with metastatic anaplastic thyroid cancer.

Design: Case report.

Methods: This patient participated in a phase 2 trial of everolimus for thyroid cancer. To better understand the initial sensitivity and subsequent resistance to everolimus, whole-exome sequencing was performed on the tumor while it was sensitive to everolimus and again after the tumor became resistant to everolimus. **Case**

Report: 7 patients with anaplastic thyroid cancer have been treated with everolimus to date, with only 1 having a response. The patient who responded was a 57-year-old woman with a 3.8-cm anaplastic thyroid cancer. The patient underwent a total thyroidectomy with central neck dissection and had positive margins with involvement seen in 3 of 12 nodes. Three weeks postoperatively, the patient's thyroglobulin (Tg) level was 17.2 ng/mL and she received external radiation with concurrent paclitaxel and carboplatin. Four weeks later, her Tg level dropped to 12.0 ng/mL. Three months later, a hilar mass developed. She enrolled in the everolimus protocol (10 mg daily), and at 6 months, the hilar mass had gone from 3.0 x 2.6 cm to 1.1 x 0.8 cm. By 18 months, the mass had progressed and was removed. Pathology showed anaplastic thyroid cancer. **Mutations:** In the pretreatment tumor, genomic sequencing showed a somatic nonsense mutation of the tumor-suppressor gene *TSC2*. The inactivated *TSC2* allowed the mTOR pathway to be activated, explaining the effectiveness of everolimus for treating the hilar mass. On posttreatment biopsy (after mass once again began to progress), the *TSC2* nonsense mutation persisted, but pS6 (a downstream target of mTOR) was also seen. This suggested that the mTOR pathway had re-established itself despite treatment with everolimus. Further analysis showed a new mutation in *MTOR*. The prevalence of the *MTOR* mutation was 0% in the pretreatment tumor and was 98% to 100% on the posttreatment specimen. The mechanism for mTOR resistance was replicated in kidney cancer cells.

Conclusions: Serial biopsies led to better understanding of everolimus sensitivity.

Reviewer's Comments: It's hard to believe a case report merits 20 authors. *TSC2* mutations have been reported for kidney and bladder cancers as well as for hamartomas and perivascular epithelioid tumors in patients with tuberous sclerosis complex. (Reviewer-Jonathan J. Beitler, MD, MBA, FACR, FASTRO).

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Keywords: Anaplastic Thyroid Cancer, Everolimus, Mechanisms of Resistance

Print Tag: Refer to original journal article

Smoking Increases Second-Cancer Risk Among Survivors

Cigarette Smoking Prior to First Cancer and Risk of Second Smoking-Associated Cancers Among Survivors of Bladder, Kidney, Head and Neck, and Stage I Lung Cancers.

Shiels MS, Gibson T, et al:

J Clin Oncol 2014; 32 (December 10): 3989-3995

Survivors of stage I lung cancer, bladder cancer, kidney cancer, and head and neck cancer who are current smokers have second-cancer risks that are up to 5 times higher than that for never-smokers.

Background: Second cancers represent about 20% of new cancer diagnoses. The association between tobacco use and the risk of a second smoking-associated cancer is poorly described.

Objective: To determine if baseline smoking in 5-year survivors of a previously treated primary smoking-associated cancer affects the risk of developing a second smoking-related cancer at a different site than the first cancer.

Design: Retrospective cohort study.

Methods: Analysis of data from 5 prospective cohort studies utilizing medical record review and cancer registry linkage.

Results: Smoking-associated second cancers were diagnosed in 80 of 2552 lung cancer survivors, 385 of 6386 bladder cancer survivors, 139 of 3179 kidney cancer survivors, and 262 of 2967 H/N cancer survivors. In each group, survivors diagnosed with a second cancer were more likely to be current smokers at first-cancer diagnosis than were survivors without second cancers. Second-cancer risk increased in each of the first-cancer groups as the number of cigarettes smoked per day increased (compared with never-smokers). For example, smoking >20 cigarettes/day was associated with the following risks of developing a second smoking-related cancer: lung cancer group, HR 3.26; bladder cancer group, HR 3.67; H/N cancer group, HR 4.45; and kidney cancer group, HR 5.33. Second-cancer risk was significantly associated with greater smoking intensity and ever-smoker status among kidney and H/N cancer survivors, but not among lung or bladder cancer survivors. There was a significant inverse association between time since quitting and second-cancer risk for bladder and kidney cancer survivors, but not for H/N or lung cancer survivors. Current smokers (>20/day) compared with never-smokers had increased mortality risk among survivors of lung cancer (HR, 3.08), bladder cancer (HR, 2.48), kidney cancer (HR, 1.57), and H/N cancer (HR, 1.68). Among stage I lung cancer survivors, current smokers were more than twice as likely as never-smokers to die (5-year cumulative incidence of death, 51.2% vs 25.0%, respectively). In the other groups, 5-year cumulative incidences of death for current and never-smokers were: bladder, 26.0% versus 15.5%; kidney, 42.2% versus 31.7%; and H/N, 38.4% versus 30.0%.

Conclusions: Smoking increases both mortality and second-cancer risk among survivors of 4 common smoking-related cancers.

Reviewer's Comments: Cancer survivors who smoke need ongoing encouragement to quit. According to the authors, only 58% of American Society for Clinical Oncology member providers advise patients to quit, and only 39% routinely provide smoking cessation assistance. (Reviewer-Alan B. Grosbach, MD, FACP).

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Keywords: Smoking-Related Cancers, Effect of Smoking on Risk of Second Cancer

Print Tag: Refer to original journal article

Combination Therapy Superior for Advanced Melanoma

Combined Vemurafenib and Cobimetinib in BRAF-Mutated Melanoma.

Larkin J, Ascierto PA, et al:

N Engl J Med 2014; 371 (November 13): 1867-1876

Adding MEK inhibition to BRAF inhibition in V600-mutated melanoma improves outcome with little additional toxicity.

Background: A number of new targeted agents for the treatment of metastatic melanoma have revolutionized the treatment of this disease. PD-1 inhibitors and inhibition of tumors with the V600 mutation of *BRAF* have stood out. Cobimetinib is one of a number of new mitogen-activated protein kinase MEK inhibitors that show promise as well.

Objective: To determine whether combining BRAF and MEK inhibition improves outcomes for patients with metastatic melanoma.

Design: Randomized trial.

Participants: Patients had either locally advanced surgically incurable or metastatic *BRAF* v600 mutation-positive malignant melanoma.

Methods: Patients were randomly assigned to receive either monotherapy with vemurafenib (a BRAF inhibitor) or combined therapy with vemurafenib and cobimetinib (an MEK inhibitor). The primary end point was progression-free survival (PFS).

Results: Median PFS was 6.2 months in the monotherapy group and was 9.9 months in the combination group (hazard ratio for progression, 0.51; $P < 0.001$). Complete response (CR) or partial response rate was 68% with combination group versus 45% with monotherapy group. The CR rate was 10% with combination therapy versus 4% with monotherapy. At 9 months, the overall survival rate was 81% with combination therapy versus 73% with monotherapy. Grade 3 or higher toxicity rates were 65% with combination therapy versus 59% with monotherapy. Dropout from the study because of toxicity was low in each group.

Conclusions: Combination therapy with BRAF and MEK inhibitors in *BRAF*-mutated tumors results in superior results than seen with BRAF inhibitors alone.

Reviewer's Comments: The authors acknowledge that progress in treating melanoma is so rapid that this study may shortly be dated. Nonetheless, it shows proof of principle that blocking a cascade of enzymatic steps encoded by separate genes is superior to blocking a single gene. The differences in outcome are substantial as melanoma studies go. (Reviewer-James J. Stark, MD, FACP).

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Keywords: Metastatic Melanoma, Targeted Therapy

Print Tag: Refer to original journal article

Otolaryngology—Head & Neck Surgery

Volume 25 Number 4: April 30, 2015

Quiz Code: 33228P

To complete the quiz for credit, log onto www.practicalreviews.com. If you have not previously registered at the site, click on “New Customer Registration” located in the right navigational bar and follow the directions. You will need your account number (located above your name on the Table of Contents) and your mailing zip code. To access the quiz, click on the “Take a Quiz” link located in the right navigational bar. Enter the quiz code and select your answers. Once you click Submit, you will receive immediate notification of your score.

Quiz Questions

1. CT scan is 100% sensitive for identifying lodged food, such as a fish bone, causing esophageal perforation.
Circle one: True False
2. The rate of tertiary hemorrhage after tonsillectomy is significantly lower for adults than for children.
Circle one: True False
3. For pulsatile tinnitus patients suspected of having idiopathic intracranial hypertension, CT angiography is the best imaging modality for obtaining a diagnosis.
Circle one: True False
4. Topical application of vitamin E significantly improves the appearance of surgical scars.
Circle one: True False
5. Regimented swallowing exercises may be better than simple repetitive swallowing exercises for improving treatment-induced dysphagia in patients undergoing organ-preserving therapy for head and neck cancer.
Circle one: True False
6. Sorafenib monotherapy is well tolerated among >50% of patients with recurrent and/or metastatic adenoid cystic disease.
Circle one: True False
7. The neutrophil-to-lymphocyte ratio appears to be an independent predictor of mortality in patients with head and neck squamous cell carcinoma.
Circle one: True False
8. Proton therapy may be a viable option for the treatment of unresectable or recurrent adenoid cystic carcinoma of the head and neck.
Circle one: True False
9. Neutrophil count may have prognostic significance in patients with metastatic nasopharyngeal cancer.
Circle one: True False
10. Compared with less extensive parotid surgery, more extensive parotid surgery is associated with a lower incidence of postoperative facial nerve paresis.
Circle one: True False
11. Ultrasound is universally accepted as the imaging method of choice for inflamed parotid lesions.
Circle one: True False
12. For the treatment of posterior pharyngeal wall squamous cell carcinomas, transoral laser microsurgery is associated with significantly lower survival rates than is conventional open surgery.
Circle one: True False
13. In patients with oral cavity squamous cell carcinoma, the Brandwein-Gensler score highly correlates with local control rates after treatment with margin-negative transoral laser microsurgery.
Circle one: True False
14. A study by Wagle et al found that everolimus, an mTOR inhibitor, was temporarily effective for a patient with anaplastic thyroid cancer until *MTOR* mutated and the tumor became resistant to the drug.
Circle one: True False
15. Smoking at the time of a primary smoking-related cancer diagnosis increases the risk of developing a second cancer among survivors.
Circle one: True False
16. Adding MEK inhibition to BRAF inhibition does not improve outcomes in patients with metastatic melanoma.
Circle one: True False

Otolaryngology—Head & Neck Surgery
Answers for Volume 25 Number 3: Patient Safety & Telemedicine 2015
Quiz Code: 33206P

1. T According to a 2015 article published in *Consumer Reports*, the risk of experiencing a medical error while hospitalized is 2.5 times more likely in patients who say they rarely receive respect from medical staff than in those who report being treated respectfully.
2. T As computers and handheld devices are being used more frequently during patient care, providers may tend to look more at the screen rather than at the patient.
3. T Hospitalized patients who believe they are not being heard by the care team will not ask questions, point out mistakes, or communicate in other ways to help improve care.
4. T Emerging evidence shows that outcomes are generally better for hospitalized patients who are actively involved in their own care.
5. T When the physician uses a handheld device to document medical records, patients tend to feel like they should not interrupt the physician to ask questions.
6. T Among recently hospitalized patients surveyed by *Consumer Reports*, <50% knew that a patient relations person was available to help address ongoing concerns about their care.
7. F According to a 2014 survey, >50% of adults base their definition of provider quality on health care delivery and outcomes.
8. T Angie's List is an online resource that provides the user with information about physician availability, punctuality, staff friendliness, and effectiveness of treatment.
9. T According to the Centers for Medicare and Medicaid Services, telehealth involves the provision of real-time telemedicine between a provider in 1 location and a patient in another location (a qualifying rural area).
10. T Currently in the U.S., telemedicine providers wanting to treat patients located in a different state must apply for a license in that state.
11. F Although privacy and data security requirements vary from state to state, patient data can be transmitted from one state to another without compliance issues or adjustments.
12. T One of Medicare's requirements for reimbursement of telehealth services is that the patient receiving care is located in a rural health professional shortage area.
13. T As a best practice, each telemedicine program should purchase appropriate professional liability insurance that covers its providers and its institution in each state where telemedicine services will be provided.
14. F In liability cases, whatever is written in a telemedicine services contract between 2 institutions regarding liability for the issuing of second opinions will supersede the laws regarding what constitutes the practice of medicine in the state where medical care was rendered.
15. F In the U.S., online telemedicine programs are heavily regulated regarding what medical conditions can be treated.
16. T Although larger institutions can afford to donate telemedicine equipment and technology to smaller hospitals, federal anti-kickback statutes limit these donations.
17. T In the U.S., telepediatrics helps improve access to specialized care in the face of a major shortage of pediatric subspecialists.
18. F Most telemedicine patients state that they prefer the traditional form of health care in which they meet in person with the provider compared to the virtual health care offered by various telemedicine programs.

Otolaryngology—Head & Neck Surgery
Answers for Volume 25 Number 2: Expert Witness: A Physician's Perspective 2015
Quiz Code: 33205P

1. T Because of the nature of legal cases, the time commitment required of an expert witness can be ambiguous.
2. T As an expert witness, physicians can issue opinions only in medical areas in which they practice and have expertise.
3. F All states require lawyers to file a Certificate of Merit at the same time that they file a malpractice claim.
4. T The lawyer who hires the expert witness should be the one writing the check to pay him for his services.
5. T When formulating an expert opinion, the physician must ensure that he is basing his opinion on the best information that applies at the time the care was delivered.
6. F In a malpractice case, the medical expert should never review the opposing expert's opinions about standard of care.
7. T In a malpractice case, the physician serving as an expert witness is responsible for ensuring that the content of the opinion report matches his/her views.
8. F Supplemental opinion reports should be written only when an expert witness's opinions have been changed after reviewing new information.
9. T Before a trial, the expert witness must know his opinions and the facts that support those opinions so well that he can answer any question accurately while under duress.
10. F When giving courtroom testimony, the main job of an expert witness is to sway the decisions of the jury.
11. T Although the standards vary between states, a physician must have ongoing contact with medicine as part of the qualifications to be considered an expert witness.
12. F The standard of care for a given situation differs for the care administered in a quaternary care hospital versus that administered in a rural hospital.
13. F Visual aids are not allowed as part of an expert witness's testimony in the courtroom.
14. T Because expert witnesses have "good-faith immunity," they cannot be sued for what they say when testifying in good faith.
15. T The information received by an expert witness to evaluate a case is considered confidential.
16. F To qualify as an expert witness, a physician must have subspecialty training.