2014 SITE REVIEW STUDY
HEAD AND NECK CANCER SITE REVIEW

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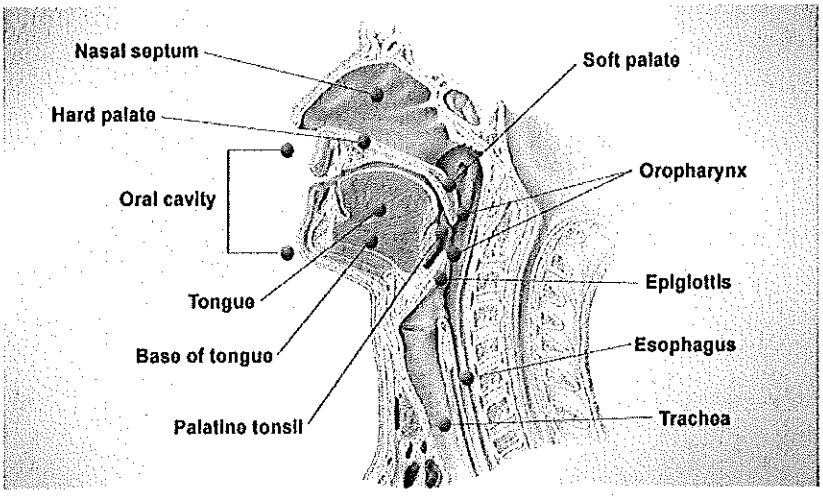
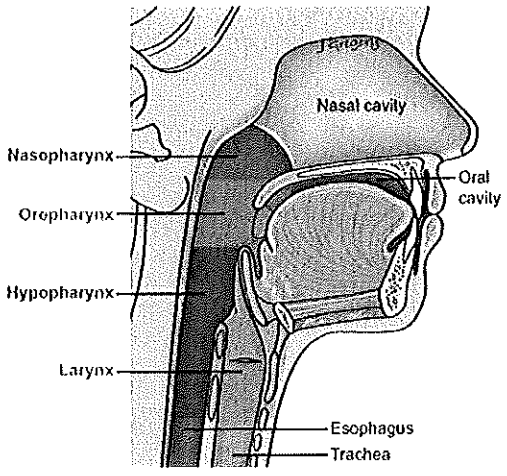
Presented to the Morton Hospital Cancer Committee on November 13, 2014.

Introduction: For the year of 2014, The Morton Hospital Cancer Committee selected to do an in-depth site review on head and neck cancer. There were 11 cases studies from the year 2013 diagnosed at the Morton Hospital that year.

Cancers of the head and neck area are primarily squamous carcinomas. The head and neck area is divided into three main subsites:

1. The oral cavity - which includes the lips, buccal mucosa, anterior tongue, floor of the mouth, hard palate, upper and lower gingiva, and retromolar trigone.
2. The nasopharynx – subdivided into the nasopharynx, the oropharynx, the tonsillar area, the base of the tongue, the soft palate and the posterior pharyngeal wall, and the hypopharynx - which is the lower part of the pharynx, including the piriform sinuses, posterior surface of the larynx, and the infero posterior and infero lateral pharyngeal walls.
3. The larynx – which contains the vocal cords and epiglottis. Internists divide it into the subglottic larynx, the glottic larynx (true vocal cords, anterior and posterior commissure), and the subglottic larynx.





We have had no cancers of the nasocavity and paranasal sinuses. I will not be dealing with the cancers of the salivary glands, because they are primarily adenocarcinoma, and have a different etiology and natural history.

With regards to staging, they are all staged by the TNM system. All of these areas have similar, but not identical, staging criteria. Likewise, the clinical approach is similar in all of these areas, but not identical.

In general, patients with localized disease, Stage 1 or 2, are treated with primary surgery or definitive radiation therapy. Results with regards to local control and survival are generally similar. Choice of treatment has to do with local expertise, specific site, and what may be the functional outcome or morbidity associated with either modality. Within the generalities are a couple of caveats. Cancers of the oral cavity are usually treated primarily with surgery. Should there be more extensive disease than thought initially, or should there be regional lymphadenopathy, chemoradiation therapy may be added as an adjuvant.

In any site, if radiation therapy is definitive, it may be external beam, brachytherapy, or more advanced techniques, including high conformational radiation techniques, such as intensity modulated radiation therapy (IMRT).

Where there is local or regionally advanced disease, usually Stage 3 or Stage 4, combined modality therapy is often offered. In our institution, this is usually concurrent chemoradiation therapy, and chemotherapy with a platinum-based regimen. Thereafter, after reimaging, physicians may then see the need for adjuvant surgery.

Although in most cases, platinum-based chemotherapy is given with radiation therapy, on occasion, the biological agent Cetuximab may be used, concurrent with radiation therapy. It does serve as a radiation sensitizer, although not as efficacious as Cisplatin. The benefit of Cetuximab, an EGFR inhibitor, is most pronounced when treated oropharyngeal cancers, which will be discussed later in this review.

Overall, surgery is the primary modality in the oral cavity, and definitive radiation therapy or concurrent chemoradiation therapy are often the choice in the pharynx and the larynx. All decisions are however individualized.

Of particular importance is management of the neck. Head and neck cancers commonly metastasize to the cervical lymph nodes without distant metastatic disease. Where there has been complete regression, as documented by PET scan and CT scan, we may choose observation with salvage surgery for progression. Where there has not been complete regression by PET scan and CT scan, the patient will process directly to salvage surgery. Where the risk of occult metastases is high, 15 to 20%, one may proceed to prophylactic neck dissection anyway.

When disease is metastatic, it is, in almost all case, incurable. Where it presents as metastatic, quite infrequent, one uses a platinum based regimen. In those patients are whom a platinum based regimen may not be used, regimens based on Paclitaxel and Gemcitabine, may give responses over 50%, and prolong overall survival. The inhibitor of Epidural Growth Factor Receptor (EGFR) Cetuximab, when added to platinum based regimens, improve overall survival, when compared to chemotherapy alone. It is also active as a single agent. The toxicities of agents such as Cetuximab are quite different than those associated with chemotherapy. While we do not commonly see the neuropathy and the hematologic toxicities, one does see severe skin reactions, low magnesium, infusion reactions, and sepsis.

In all stages, the diagnosis and treatment of head and neck cancers, it is important that there be a multi-modality approach, with input from surgery, radiation oncology, and medical oncology. The role of ancillary services is also crucial. These patients often have severe damage to the salivary glands, and the dentition, so all of these patients should be seen by a dentist before any intervention. They are also seen by nutrition, and will have swallowing evaluations. It has been the practice at the Morton Hospital that all patients at nutritional risk have a feeding tube placed. There are studies that show that interruption of radiation therapy decreases the likelihood of cure. Patients with nutritional comprises are susceptible to poor healing, increasing pain, and concurrent infections, all of which may prolong the course of therapy, and compromise the results.

All of the above generalities hold, there are regarding particular areas, particular cancers.

The human papilloma virus, known to cause cervical cancer, vaginal cancer, and penile cancer, has been shown to be the causative agent for over half the squamous cell cancers arising in the oropharynx (tonsil and base of the tongue). Surveillance data shows that HPV positive cancers comprise up to 70% of oropharyngeal carcinoma. While one can do a polymerase chain reaction with these (PCO) to attempt HPV DNA, there are biomarkers that serve as surrogates. The most common biomarker used is P16 protein, which is overexpressed in HPV associated cancer.
This is a rather recent change. Although we treat these patients the same way, they have an improved prognosis compared with the HPV negative, tobacco associated, cancers. There are trials underway at this time, to see if these cancers require the intense treatment that we usually offered for head and neck cancers. Any treatments in such situations however should only be done, at this time, in a clinical trial.

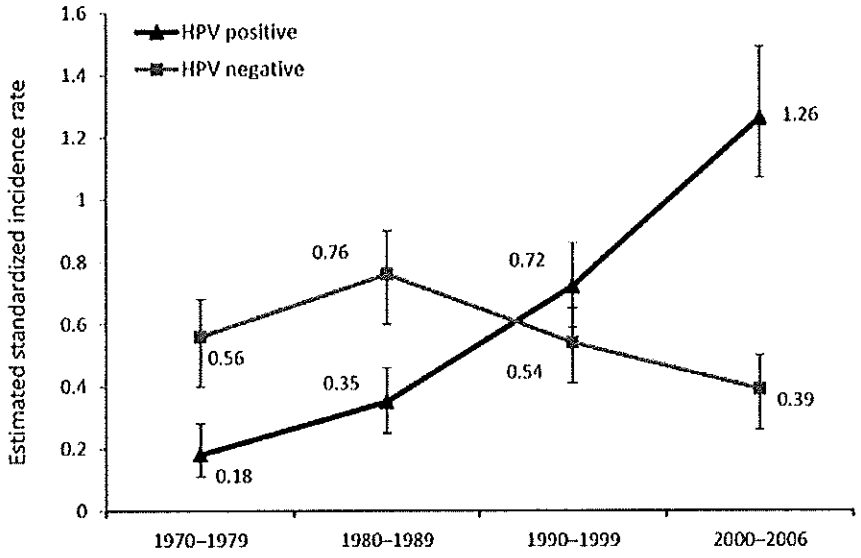
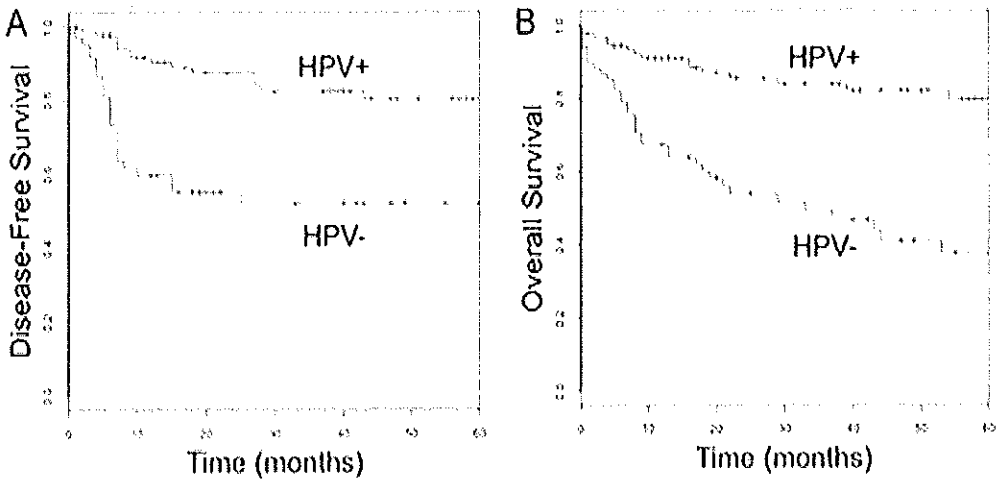


Figure 3. Estimated age-standardized incidence of human papillomavirus (HPV)–positive and HPV-negative tonsillar cancer squamous cell carcinoma cases per 100,000 person-years, Stockholm, Sweden, 1970–2006. Error bars indicate 95% confidence intervals. Data from Näsman et al. (*13*), with permission of John Wiley and Sons (www.Interscience.wiley.com).



Nasopharyngeal carcinoma, also a squamous cell cancer, also has a natural history different from other cancers of the head and neck area. It is different in its geographic variability. Uncommon in the United States, and Western Europe, but endemic in Southern China, Hong Kong, and areas of Southeast Asia and the middle east. Epstein Barr virus infection is felt to be critical in developing these cancers, and is modulated by a genetic predisposition or other environmental factors. They tend to occur in a younger population. Radiation therapy is the primary modality. The additional of concurrent platinum based chemotherapy has improved survival in advanced disease. Depending upon anatomical location, surgery is not usually employed.

The paranasal sinuses are predominantly squamous cell carcinomas, but they may also have adenocarcinoma. These are quite uncommon cancers. Salivary cancers are primarily adenocarcinoma, and tend to be more benign or low-grade tumors, and tend to be treated primarily with surgery.

Lastly, squamous cell carcinomas may be found in cervical lymph nodes, and factors may suggest an occult oropharynx primary, although none may be identified. These patients are treated primarily with chemoradiation therapy to the oropharyngeal and nasopharyngeal mucosa and to the neck. The prognosis is actually better than that for squamous cell carcinomas from a defined primary.

If the lymphadenopathy is from a lower cervical chain, it is still likely due to a head and neck primary, but one must search for other sites of origin, especially lung or esophagus.

With all head and neck cancers, after initial treatment, it is imperative that the patients undergo life long surveillance. They are at high risk for recurrence, second primaries, and other cancers of the aerodigestive tract, such as esophageal or lung cancers.

Data available to us on the 11 patients diagnosed with head and neck cancer at the Morton Hospital in 2013 is incomplete. Of the 11 patients, nine were of the oropharynx, including three oral tongue, base of tongue, one tonsil, one uvula, and one of the oral cavity near the mandible. Those that were not of the oral cavity include a cancer of the piriform sinus, and one of the hypopharynx. This reflects national trend. We are seeing fewer cancers of the pharynx as the percentage of people smoking decreases. We are however seeing increasing cancers of the oropharynx, due to the HPV epidemic.

There were four patients who had some portion of their treatment, chemotherapy, performed at Morton, MSOT/SMG. Three were of the oropharynx, base of the tongue, the tonsil, and uvula. We had one cancer of the piriform sinus.

It is impossible to say anything statistically about such a small group, especially as the majority were treated elsewhere. The cancer of the tonsil was Stage IIIC, and the other three cancers, base of the tongue, piriform sinus, and the uvula, were all Stage IV. All patients received concurrent chemotherapy and radiation therapy, the chemotherapy being Cisplatin single agent. Three of the patients, the ones with the cancer of the uvula, cancer of the tonsil, and piriform sinus, all obtained complete remissions. The fourth patient, for a cancer of the base of the tongue, was receiving Cisplatin and radiation therapy. She had what appeared to be a cerebral hemorrhage during treatment, and that hemorrhage caused her death. All three of the cancers of the oropharynx treated at the Morton Hospital were HPV positive. One would have expected good results with treatment, as the response rates of HPV positive cancers are almost double those of HPV negative cancers. It is of interest that all three of the patients who had complete responses, although they were HPV positive, were also smokers. All had appropriate staging with direct laryngoscopy, and PET scans. As noted above, HPV testing was done.