



## S•P•O•H•N•C

A PROGRAM OF SUPPORT  
FOR  
PEOPLE WITH ORAL  
AND  
HEAD AND NECK CANCER

## SALIVARY GLAND CANCERS

DAVID W. EISELE, M.D., F.A.C.S.

### INTRODUCTION

The salivary glands consist of the two parotid glands, which are located on the side of the face in front of and below the ears; the paired submandibular glands, which are situated in the upper neck under the lower jaw; and the sublingual glands, which lie in the floor of the mouth. In addition, numerous minor salivary glands are located throughout the mouth and throat.

The salivary glands secrete saliva of varying consistencies. Saliva serves as a lubricant for the mouth and throat, helps to maintain healthy teeth, contains enzymes that aid in the digestion of food and other components that help maintain oral health. Radiation therapy adversely affects salivary gland function and may cause xerostomia, or dryness of the mouth and throat.

Both benign and malignant tumors may arise from the salivary glands. Salivary gland cancers are uncommon and account for less than 5% of head and neck malignant tumors. Salivary gland malignancies occur with an incidence of approximately 1 to 2 per 100,000 population per year in the United States. Men are afflicted slightly more often than women.

The factors responsible in the development of salivary gland tumors are poorly understood. In contrast to squamous cell carcinoma of the head and neck, tobacco and alcohol usage are not causative factors in salivary gland tumors. One exception is Warthin's tumor, a benign neoplasm, which is associated with smoking. Low-dose radiation therapy or cumulative radiation exposure, such as dental radiographs, have been implicated as causal factors for the development of both benign and malignant salivary gland tumors. In addition, exposure to hardwood dust has been associated with the development of minor salivary gland cancers of the nasal cavity and paranasal sinuses. The Epstein-Barr virus has been implicated in

the development of undifferentiated salivary gland carcinomas. The genetic factors responsible for the development of salivary tumors are presently being investigated.

### CLINICAL PRESENTATION

Most salivary gland tumors will present as a mass in the gland without symptoms. Benign tumors typically enlarge slowly and may be present for many years. Rapid growth of a new mass or a long-standing mass, however, is worrisome for malignancy. Other signs that are likely indicators of malignancy include fixation to surrounding structures, skin involvement, facial paralysis, sensory loss, or the presence of associated enlarged lymph nodes indicative of regional metastases.

Minor salivary gland tumors involving the oral cavity most often present as a painless, submucosal mass. Pain and tumor ulceration are unusual. Tumors of the nasal cavity may cause nasal obstruction or nasal bleeding. In addition, they may invade surrounding structures including the orbit, facial soft tissues or the cranial cavity.

### DIAGNOSTIC EVALUATION

Salivary gland tumor patients with a suspected salivary gland tumor should be thoroughly evaluated by a head and neck surgeon. The evaluation should include a detailed history and complete head and neck examination. Non-tumor causes for the glandular abnormality should be excluded and the clinical extent of the tumor determined. Commonly, a fine needle aspiration (FNA) biopsy is recommended to aid in the pathological diagnosis of the tumor. FNA is highly accurate when an adequate specimen is obtained and the specimen is evaluated by an expert cytopathologist. Some suspected tumors may be shown by FNA to be non-neoplastic, inflammatory disorders, enlarged benign lymph nodes, or benign cysts. If a malignant tumor is diagnosed by FNA, imaging studies such as CT scan or MRI are of value to obtain additional information regarding the extent of the tumor as well as to evaluate regional lymph nodes. A chest radiograph is also recommended to rule out metastases. Benign tumors that are large, fixed, or recurrent are also evaluated by imaging studies.

### TUMOR STAGING

Parotid gland and submandibular gland cancers are staged by a standardized TNM staging system. The T classification is based on tumor size and whether the tumor demonstrates extension into the surrounding skin, soft tissues, bone, or nerves. The N classification indicates regional lymph node involvement by metastatic tumor. The M classification indicates the presence or absence of distant metastases. There is no formal staging system for minor salivary

SALIVARY continued on next page



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**IN THIS ISSUE**

A Time For Sharing .....	4
Introduction to Gene Therapy.....	5
Pat's Pantry Provençal.....	7

**COMING IN WINTER, 2002**

Laser Surgery for Head and Neck Cancer  
Eugene N. Myers, MD & Johnathan C. Smith, MD

**SALIVARY** continued from page 1

gland malignances. Rather, they are staged using the staging system for squamous cell carcinoma for the relevant anatomic site.

As with other head and neck cancers, advanced tumor stage for salivary gland malignancy is associated with a diminished prognosis. Large tumors, facial nerve paralysis, advanced nodal metastases, and distant metastases are poor prognostic signs for parotid carcinomas.

**TUMOR TYPES**

There is tremendous diversity of salivary gland tumors. The World Health Organization recognizes twelve benign and twenty-two malignant tumors arising from the salivary glands. In addition, lymphoma can arise in the parotid gland and other malignancies, particularly the skin cancers, squamous cell carcinoma and melanoma, can metastasize to intraglandular parotid lymph nodes.

Because of the many various types of salivary gland tumors and their varied clinical behavior, a proper pathological diagnosis is important to guide proper treatment for an individual patient.

The majority (80%) of neoplasms arising in the parotid gland are benign. Pleomorphic adenoma (benign mixed tumor) is the most common benign tumor. Warthin's tumor is the second most common benign tumor of the parotid gland. Cancerous tumors are predominately mucoepidermoid carcinomas, followed by acinic cell carcinoma and adenoid cystic carcinoma. Other tumor types include adenocarcinoma, undifferentiated carcinoma, carcinoma ex-pleomorphic adenoma, and squamous cell carcinoma.

The salivary glands that are smaller than the parotid glands have larger proportions of cancerous tumors. This proportion increases with decreased gland size so that 40-50% of submandibular tumors and about 70% of minor salivary gland tumors are malignant. The most common submandibular malignancy is adenoid cystic carcinoma followed by mucoepidermoid carcinoma. Adenoid cystic carcinoma is also the most common minor salivary gland carcinoma, followed by low-grade polymorphous adenocarcinoma.

**TUMOR BEHAVIOR**

Malignant salivary gland tumors have varied behavior depending on their tumor type. Low-grade mucoepidermoid carcinoma, acinic cell carcinoma, and polymorphous low-grade adenocarcinoma are considered low-grade malignancies. The low-grade carcinomas are generally diagnosed at a low stage and they have a minimal tendency to metastasize. Low-grade carcinomas generally have favorable treatment outcomes.

The remaining salivary gland cancers are designated high-grade carcinomas. The high-grade carcinomas tend to be locally invasive, present at higher stages than low-grade carcinomas, and have a higher propensity to metastasize to regional lymph nodes. In general, the high-grade carcinomas have a less favorable prognosis compared to low-grade carcinomas.

Malignant salivary gland tumors may recur many years after initial treatment. Therefore, long-term follow-up of patients is recommended in order to diagnose recurrent disease. Unlike squamous cell carcinoma of the head and neck, survival rates for malignant salivary gland tumors continue to decline after five years

SALIVARY continued on next page

SALIVARY continued from page 2

for all tumor types except for the low-grade malignancies and squamous cell carcinoma.

**BENIGN NEOPLASMS****Pleomorphic Adenoma**

The pleomorphic adenoma (benign mixed tumor) accounts for 65% of all salivary gland neoplasms. These tumors are found most frequently in the parotid gland, followed by the submandibular gland and the minor salivary glands. Pleomorphic adenoma also represents the most common tumor for each type of salivary gland. Microscopically, pleomorphic adenomas show incomplete encapsulation. These features account for the high rate of tumor recurrence after surgical enucleation of these tumors. Adequate surgical therapy requires resection with an adequate margin of normal gland surrounding the tumor.

**Warthin's Tumor**

Warthin's tumor is the second most common benign neoplasm of the parotid gland. Most cases occur in older men between the fourth and seventh decades of life, although the incidence appears to be increasing among women probably related to increased smoking rates in women. The tumor usually presents as a slowly growing mass in the lower portion or tail of the parotid gland. Approximately 10% of Warthin's tumors occur bilaterally. Treatment of Warthin's tumor is complete surgical excision. Recurrence after surgical resection is uncommon.

**MALIGNANT NEOPLASMS****Mucoepidermoid Carcinoma**

Mucoepidermoid carcinoma is the most common malignant salivary gland tumor in adults and in children. Women are more commonly afflicted than are men. Most patients are asymptomatic and present with a slow-growing, painless mass. Mucoepidermoid carcinomas are usually classified as low-grade or high-grade tumors. Low-grade tumors behave like benign neoplasms but are capable of local invasion and metastasis. High-grade tumors are aggressive neoplasms with a high propensity for metastasis. Low-grade mucoepidermoid carcinomas are usually small and partially encapsulated. High-grade mucoepi-

dermoid carcinomas are usually larger and locally invasive.

**Acinic Cell Carcinoma**

Acinic cell carcinoma is a low-grade malignancy. Ninety percent of these tumors arise in the parotid gland, with the remainder found in the submandibular gland. Acinic cell carcinoma of the minor salivary glands is rare. Acinic cell carcinoma occurs most commonly in women. These tumors occur most frequently in patients in the fifth decade of life. Acinic cell carcinomas generally demonstrate a benign course in early years, but long-term follow-up studies have shown a decline in survival approaching 50% at 20 years after therapy. There appears to be a subset of these tumors with a poor prognosis.

**Adenoid Cystic Carcinoma**

Adenoid cystic carcinoma accounts for about 6% of all salivary gland neoplasms. Adenoid cystic carcinoma occurs less commonly than mucoepidermoid carcinoma in the parotid gland, but it represents the most common malignancy of the submandibular gland and the minor salivary glands. Adenoid cystic carcinoma occurs with equal frequency in men and women, usually in the fifth decade of life. This tumor most often presents as an asymptomatic mass. Facial paralysis and pain occur as initial symptoms in only a small percentage of the cases. Perineural invasion, or growth around and along nerves, is a typical feature of adenoid cystic carcinoma. This feature explains the difficulty in tumor eradication despite extensive surgical excision. Complete gross tumor excision and post-operative radiation therapy is recommended for the management of this tumor. Because adenoid cystic carcinoma may progress in a slow relentless fashion, long-term follow-up is mandatory for the assessment of therapy results and for monitoring for metastatic disease development.

**Adenocarcinoma**

Adenocarcinoma most commonly occurs in the minor salivary glands, followed by the parotid gland, and represents about 15% of malignant parotid neoplasms. These tumors occur equally in both sexes and usually present

as a palpable mass. Adenocarcinomas arising within the salivary glands are aggressive tumors that are likely to recur and metastasize.

**Polymorphous low-grade Adenocarcinoma**

Polymorphous low-grade adenocarcinoma is the second most common malignancy of the minor salivary glands. This neoplasm most commonly occurs in the palate, buccal mucosa, and upper lip. Women are affected more commonly than men, and most of these neoplasms occur in the sixth decade of life. These tumors usually present as a firm painless mucosalized mass. Tumor growth rates are variable. Prognosis for this tumor is generally favorable after complete surgical resection.

**Carcinoma Ex-Pleomorphic Adenoma**

Carcinoma ex-pleomorphic adenoma (carcinoma ex-mixed tumor) represents a malignant tumor that has arisen from a pre-existing pleomorphic adenoma. This malignancy represents 2% to 5% of salivary gland tumors. Clinically, carcinoma ex-pleomorphic adenoma typically presents as a slowly growing mass, which has usually been present for many years and suddenly increases in size. Local and distant metastases are common with this tumor. Compared with other malignant salivary gland neoplasms, this tumor is associated with a very poor prognosis.

**Squamous Cell Carcinoma**

Squamous cell carcinoma of the salivary glands represents a neoplasm that constitutes 0.3% to 1.5% of salivary gland tumors. Squamous cell carcinoma occurs more commonly in the submandibular gland than in the parotid gland. Proper diagnosis of salivary gland squamous cell carcinoma requires exclusion of contiguous spread of a squamous cell carcinoma into the gland, metastases to the gland, and high-grade mucoepidermoid carcinoma. These tumors usually present as firm indurated masses and occur more commonly in males, usually in the seventh decade of life. There is a high incidence of regional and distant metastases with this tumor and the prognosis is generally poor.

**MANAGEMENT**

A multi-disciplinary, team approach to the SALIVARY continued on page 6

## A TIME FOR SHARING

I'm doing and feeling great! It's been more than two and a half years since I completed my treatments and I can now say that I am finally back to doing all the things I love. But as I think back, there are definitely some dates I will not soon forget, if ever. The first was August of 1999. That was the month that I discovered the growth in my mouth. I later found out that it was actually my left tonsil. The growth was as large as my thumb. The second date was in October of that year when I was told that I had cancer; squamous cell carcinoma of the left tonsil. I remember thinking, "What the hell is that?" Never heard of such a thing. Cancer was always in the lungs, skin, breast or prostate not in a person's mouth. I was wrong.

The third date that I remember is the day I had the modified radical neck dissection. I was not prepared for this either. All the discussions I had with my ENT surgeon did nothing to prepare me for this. We had discussed what he was going to do; what he hoped to accomplish; what I should expect and what the worst case scenarios might be. However, about the only thing I can really remember about those meetings was asking the doctor "You've done this before, right?" He just kind of smiled and told me that he was not going to lose any sleep over it. He did not know what to tell me to make me feel at ease, but he did his best. It was only a while later that I found out that this surgeon was involved in the management of about 90% of all the head and neck cancer cases at the hospital where I was being treated. I was being cared for by the best.

December 7<sup>th</sup> 1999, the first day of my radiation treatments, and if I may borrow a famous line, "A day that will live in infamy." Because the biopsies showed that the cancer had spread to two lymph nodes, it would be necessary to have 35 treatments of radiation. There was just no way that the radiation oncologist could have prepared me for what was to come. This was by far, the most difficult time of my life. I guess it was about the tenth treatment when I really began to feel terrible. I was extremely fatigued to the point that all I wanted to do was sleep. Then with only five treatments remaining, I came down with an infection. I couldn't tolerate anything in my mouth. It was like a fire was raging beyond description. Fortunately, the doctor

was able to get it under control and it has never returned. I never did find out what the infection was, nor did I care. All I wanted to do was be finished with the treatments.

The day after I started radiation therapy, back on December 8<sup>th</sup> 1999, my uncle in Craig, Colorado, began his own treatments for cancer. When I was about half way through mine, a letter arrived in the mail from his wife telling me about Tom and his cancer. I called him right away and told him what I was experiencing.

I had not seen my uncle in years. Craig, Colorado is a four hour drive, and driving that far to visit with someone you hardly know is seldom done. However, Tom was having treatments here in Denver; chemo at one hospital and radiation at another. So we started calling one another on the phone, to talk about our "war stories" and lean on each other for support. And boy, was that ever needed. When things got too much for either him or me, all we had to do was pick up the phone and we

*....We can't live our lives from inside a doctor's office or inside a protective shell of some kind, but we can keep up with our checkups and keep informed of all the new developments that are happening daily in the field of head and neck cancer research.*

had support. We met for lunch, dinner, heck we even had a family reunion, first one in years. I had never been close to my uncle; I always liked him, but we just were not "buddy, buddy." But this cancer experience brought me closer to him as never before.

Unfortunately, on October 13<sup>th</sup> 2001, my uncle lost his battle with cancer. This caused more pain for me than the treatments. He fought well for more than two years, but it was not to be. I had lost my cancer buddy, the one man I could turn to for support. When I was diagnosed with the cancer, I had told no one, and I mean no one. I could not bring myself to talk about it. In fact my own family and friends did not find out until the day of the surgery, when the surgeon had to tell them because I could not. Every one was shocked to say the least. And that is one thing I have

never forgiven myself for. I should have told every one, but I just couldn't.

Somewhere along the road through all this, I found SPOHNC and became a member, receiving their newsletter. I also started talking with others about cancer. And since then have talked so much about it that people think I'm never going to shut up. I found that talking about it made a difference, to me at least. I could cope with the disease and recovery better. Talking turned out to be a good thing and that's why I decided that there should be a place for people to come together and talk about their experiences. I am indeed proud to say that here, in Denver, we now have a chapter of SPOHNC. If you live in the area or are here just to visit, look us up, we'll be talking.

Granted, not everything is hunky-dory. My sense of taste is still a roller-coaster, that comes and goes, and the stiffness in my neck causes cramps every now and then. But I'm moving forward, I guess the most difficult thing to cope with is the dry mouth. I have tried to get the saliva working again, through acupuncture and herbs. Last September I even flew to California for acupuncture. It worked for the first four treatments, but then it stopped. I brought the technique back to town with me to a doctor here in Denver and tried again for a while. However, there was still no lasting results. But this does not mean that I have given up, I will keep searching and trying new things. I truly believe that someday, something will be found that can really help.

As I write this story, I think of all my family members who have fought a cancer battle and lost. I dedicate this story to them and to all others who have fought bravely and lost the battle. I also dedicate this story to the survivors. For me, it will be another two and one half years until my five year anniversary. I know as well as any of you that does not mean it can't come back, but I will keep a eye out for it's possible return for the rest of my days. We can't live our lives from inside a doctor's office or inside a protective shell of some kind, but we can keep up with our checkups and keep informed of all the new developments that are happening daily in the field of head and neck cancer research.

I'm doing and feeling great! Best wishes to all.

Virgil Holdridge  
Denver, CO

## Introduction to Gene Therapy by Janet E. Gregory, MD

### What is a Gene?

Cells of the human body carry a master blueprint of information called "DNA". This blueprint has all of the information necessary to direct the characteristics and functions of each cell and for the organization of the cells into organs and systems within the body. DNA itself is organized into segments called "genes" that carry the information or "genetic code" that directs the production of proteins within the cell. Most genes carry the code for a single protein chain. Through production of specific proteins, genes determine visible traits, such as hair and eye color, as well as more subtle characteristics, such as the ability of the blood to carry oxygen. Sometimes the DNA of genes is altered or "mutated" by environmental factors such as carcinogens or exposure to radiation or through errors made in the duplication of DNA as cells divide. Mutated genes can produce defective proteins; missing genes do not produce proteins. Gene defects are the sole cause of some diseases (i.e. cystic fibrosis or hemophilia), and are thought to be contributing or predisposing factors for others (i.e. cancer, cardiovascular disease).

### Why is Gene Therapy Useful?

Drug discovery and development advanced into a new era approximately twenty years ago when scientists discovered how to manipulate and transfer genetic information from one organism to another. The ability to "cut and paste" DNA between organisms, called "recombinant DNA technology," first led to the development of new drugs in which human genes were introduced into simple organisms (such as yeast and bacteria) in order to produce proteins like insulin for the treatment of diabetes and other diseases. By the 1980s, technology had developed to the point where recombinant DNA methods could be used to manipulate the genes of human, insect, and rodent cells. These technologies have allowed scientists to develop new animal models for specific diseases and expanded their ability to use genes as treatments for these diseases.

Gene therapy is one of the approaches that is used to enhance the normal protein production of a cell or to enable cells to perform additional roles beyond their normal ones. In studies of gene therapy for cancer, for example, scientists are working to improve the body's natural ability to fight the disease or to make the cancer cells more sensitive to other kinds of treatment, such as chemotherapy and radiation. In order to deliver the disease-fighting gene to the cells of a patient, the gene must be linked to a gene transfer system called a "vector". Vectors may be based on viruses that have been modified to reduce their own ability to cause disease (viral systems) or may be chemically synthesized (nonviral systems). The choice of each gene and vector to be used depends on the disease to be treated. Types of viral vectors include adenoviruses and retroviruses. Adenoviruses are transient viruses that allow for short-term treatments such as those appropriate for cancer treatment; retroviruses can lead to a permanent change to the cell's own DNA and may be suited for situations where long-term effects are needed. Nonviral vectors are frequently based on fatty materials that resemble the membranes that cover cells. However, there are currently a limited number of vectors for use in gene therapy, and more are needed to expand and improve this approach for disease treatment.

### Types of Gene Therapy

The field of gene therapy encompasses two main strategies for treating disease. The first of these uses genes to repair a mutated gene or replace a missing gene and is generally used to treat rare diseases such as cystic fibrosis and hemophilia. The second of these approaches, and the one that has made the most clinical progress so far, uses genes more like conventional drugs to block disease processes or to kill diseased cells outright. One advantage to gene-based treatments over conventional drugs, however, is their specificity, that is, they can be selected to solve a particular cellular problem while having little impact on

unrelated processes. This reduces the frequency and severity of their side effects relative to those found with many conventional drugs.

One of the most advanced clinical programs in gene therapy to date uses a cancer-suppressing gene, the p53 tumor suppressor gene, as a drug to treat cancer. Among the cancer-fighting capabilities of p53 are its abilities to kill cancer cells outright through a cell suicide pathway called "apoptosis", to inhibit the division of cancer cells through a process called "growth arrest", and to block the development of the blood vessels necessary to feed growing tumor cells through mechanisms called "anti-angiogenesis". p53 is a normal cellular gene that uses these processes to keep cancer from developing. If the p53 gene is mutated or its action is blocked, however, it is unable to carry out these processes and the probability for cancer increases. More than half of human cancers have mutations in the p53 gene, and many others have blocks to its normal activity. Clinical studies have shown that vectors delivering normal copies of the p53 gene can trigger these processes and lead to cancer cell death and growth arrest without harming normal tissue.

Another type of gene therapy in clinical study uses genes to enhance the activity of the immune system ("immunomodulatory gene therapy"). This is a method to induce immune responses to tumor cells that have spread from their primary location (metastatic or secondary tumors). The benefit to the patient is the specificity of these immune responses in that only cancer cells are targeted and destroyed by the immune system, leaving normal cells intact.

### Advantages of Gene Therapy

While the next generation of gene therapy may need improvement in targeting and efficiency of gene transfer, there are many advantages in applying gene therapy tools to the treatment of human disease. These include:

- sustained production of a therapeutic

GENE continued on page 7

SALIVARY continued from page 3

treatment of salivary gland malignancies is recommended. Initial treatment for these tumors is usually surgery ensuring complete surgical excision of the tumor. The type of surgery will vary according to tumor location and tumor extent. Surgery is tailored for the individual patient on the basis of clinical information, imaging studies and the findings at the time of surgery. For parotid tumors, a parotidectomy is performed. Parotidectomy involves identification and preservation of the facial nerve, which innervates or supplies the facial muscles and courses through the substance of the parotid gland. The tumor is then removed with an adequate margin of normal gland surrounding it to insure complete tumor removal. Tumors that extend beyond the parotid gland into surrounding tissues require more extensive surgery.

Preoperative facial paralysis or intra-operative identification of facial nerve invasion by cancer are indications for resection of the facial nerve. Facial nerve reconstruction with a nerve graft is then performed during the same surgery. In addition, a neck dissection is recommended if regional neck node metastases are present or suspected. Complete surgical resection is sufficient treatment for benign parotid tumors and for small low-grade cancers (acinic cell carcinoma and low-grade mucoepidermoid carcinoma) without local extension or regional metastases. Postoperative radiation therapy is recommended as additional therapy for all other parotid malignancies.

For submandibular gland tumors, submandibular gland excision is recommended for small low-grade malignancies confined to the gland. For all other cancers, removal of the soft tissue contents of the neck space that surrounds the submandibular gland, the submandibular triangle, is recommended. Included in this removal are the submandibular triangle lymph nodes. Adjacent nerves including the marginal mandibular branch of the facial nerve, the lingual nerve, and the hypoglossal nerve are preserved unless invaded by tumor.

For locally invasive submandibular gland tumors, the surgical resection is extended with adequate resection of involved structures. Postoperative radiation therapy is recommended

for most submandibular gland cancers except small low-grade malignancies.

Surgery for minor salivary gland tumors varies according to tumor location. Tumors involving the oral cavity and oropharynx can usually be resected through the mouth or transorally. Tumors that invade the hard palate require partial maxillectomy. Extensive oropharyngeal tumors usually require an external surgical approach to provide adequate exposure for safe tumor removal. Minor salivary gland tumors involving the larynx are removed using conservative laryngeal surgery. Massive and highly invasive tumors usually require total laryngectomy.

Tumors of the nasal cavity and paranasal sinuses may require a partial or total maxillectomy. Tumors extending into the orbit can sometimes be removed with preservation of the eye if there is limited tumor invasion. More extensive invasion requires removal of the orbital contents. Tumors extending into the cranial cavity require craniofacial resection, a two-team procedure performed by a head and neck surgeon and a neurosurgeon. Indications for postoperative radiation therapy for minor salivary gland carcinomas include large tumor size, high-grade tumors, lymph node metastases, incomplete tumor removal, and deep tumor infiltration.

At the present time, there is no proven benefit of chemotherapy for improving locoregional tumor control or survival for malignant salivary gland tumor patients. The primary role of chemotherapy in the management of these malignancies is the palliation of symptomatic, unresectable recurrent disease. Patients who have advanced unresectable disease and achieve a response to chemotherapy often have significant pain control. New chemotherapeutic agents with better activity toward these malignancies are needed.

#### SUMMARY

Salivary gland cancers are uncommon cancers of the head and neck. They constitute a diverse group of tumors with varied clinical behavior best managed by a multidisciplinary team of physicians and other health professionals. Clinical information, results

of imaging studies, and pathological diagnosis are important factors that allow for treatment recommendations for an individual patient. Treatment is primarily surgical with radiation therapy given postoperatively to select patients. Chemotherapy is beneficial to some patients for palliation.■

*Editor's Note: David W. Eisele, M.D., F.A.C.S. is Professor and Chairman of the Department of Otolaryngology-Head and Neck Surgery at the University of California, San Francisco, San Francisco, California.*



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GENE continued from page 5

protein without the need of repeated treatments;

- higher local concentrations of therapeutic proteins than could be achieved by conventional therapies without serious side effects;

- insignificant side effects with gene therapies when compared to traditional drugs;

- the potential to fix the underlying cause of disease (killing cancer cells or repairing genetic defects);

- potential for use in combination with other therapeutic treatments without increasing overall side effects;

- ability to express the protein in selected organs or tissues.

With gene therapeutics in late stage development, including phase 3 clinical trials, gene therapy is well on the way to providing the next generation of medicines to treat a variety of human diseases.■

*Editor's Note: Janet E. Gregory, MD, is the Senior Director of Clinical Development for a Houston based biotechnology company currently working on a gene therapy treatment (INGN201, ADVEXIN) in clinical testing for head and neck cancer.*

*Comment: For information concerning clinical trials utilizing gene therapy, please visit SPOHNC's clinical trials webpage at www.spoync.org.*



from PAT'S PANTRY  
PROVENÇAL

Minestrone Soup

- |   |   |
|---|---|
| 1 lb. ground beef or stew beef or steak, etc.         | 2 cloves garlic                             |
| 1 16 oz. can lima beans                               | 1/4 lb. angel hair pasta or couscous grains |
| 1 large onion   | 1 tsp. sage                                 |
| 3 carrots   | 1/2 cup grated parmesan cheese              |
| 2 stalks celery                                       | Water                                       |
| 2 tomatoes or a small can of chopped tomatoes (8 oz.) | Milk  |
|   | Salt to taste                               |

Crumble the ground beef or chop the stew beef or steak. Chop the vegetables. Put everything in the stew pot except for the pasta or couscous, milk and parmesan cheese. Add water to cover, not more. Bring to a boil and reduce heat. Simmer 1 hour. Add the pasta or couscous and simmer 1/2 hour more or until the vegetables are cooked and the meat is tender. Blend with milk and 1/2 cup grated Parmesan cheese.

*November's Tip: This soup has crossed southern Europe. From Italy, it traveled to southern France and became Pesto Soup, made with basil and tomato pesto. Its value is in its many ingredients which offer a wealth of nutrients in one meal. Adding the pasta completes the food grouping and consequently provides a full meal in a bowl of soup!*

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