

## **Paparella: Volume III: Head and Neck**

### **Section 2: Disorders of the Head and Neck**

#### **Part 4: The Pharynx**

#### **Chapter 24: Cysts and Tumours of the Nasopharynx**

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The nasopharynx is a cuboidal compartment extending from the base of the skull to the soft palate. The superior and posterior walls of the nasopharynx are complete and are formed by the basisphenoid, the basiocciput, the atlas, and the axis. The anterior wall is penetrated by the posterior choanae, and the lateral walls are interrupted by the eustachian tube orifices. Each eustachian tube enters the nasopharynx through the sinus of Morgagni above the superior pharyngeal constrictor muscle, and the posterior lip of each tubal orifice is a prominent cartilaginous crescent known as the torus tubarius. The fossa of Rosenmüller is located immediately superior and posterior to the torus. The dorsal surface of the soft palate forms the anterior portion of the inferior nasopharyngeal wall, and posteriorly this wall opens into the oropharynx at the isthmus.

The soft tissue supporting structures of the nasopharynx are the pharyngobasilar fascia and the superior constrictor muscle, which are suspended from the basiocciput just anterior to the foramen magnum. The fascia is continuous with that of the foramen lacerum and is in close proximity to five other foramina, including the foramen ovale, the foramen spinosum, the carotid canal, the jugular foramen, and the hypoglossal canal. These relationships assume importance in the consideration of intracranial extension of nasopharyngeal disease.

The mucous membrane of the nasopharynx contains lymphoid tissue, epithelial tissue, and minor salivary glands. The lymphoid tissue component lies within and deep to the mucosa, is of the B-cell type, and contains follicles and germinal centers but does not possess a capsule or sinusoids. Efferent lymphatic flow is bilateral and is directed to the lateral retropharyngeal nodes of Rouviere, the jugulodigastric nodes, and the spinal accessory chain.

The epithelial component of the nasopharyngeal mucous membrane is variable and contains stratified squamous epithelium, ciliated pseudostratified epithelium, and indeterminate epithelium. The ciliated pseudostratified type predominates in infancy, but with time, metaplasia occurs and results in the transformation of the respiratory epithelium into the stratified squamous cell type. In adults, the superior and lateral walls of the nasopharynx are lined by ciliated pseudostratified epithelium, and the posterior wall is lined by stratified squamous epithelium.

Because the nasopharynx (including its epithelium, lymphoid tissue, and supporting structures) contains a wide variety of cell types, many different lesions may occur. These lesions range from embryologic anomalies to benign and malignant neoplasms.

## **Cysts of the Nasopharynx**

### **Tornwaldt's Cyst**

Tornwaldt's cyst, or the nasopharyngeal bursa of Tornwaldt, occurs in about 3 per cent of individuals and represents persistence of the embryonic communication between the caudal end of the notochord and the nasopharyngeal epithelium. This communication is usually lost in the second month of development but may be retained as the result of inflammation and adhesions. The cyst is located in the midline of the posterior wall of the nasopharynx and has an epithelial lining and nasopharyngeal mucosal coverage.

The symptoms of a Thornwaldt's cyst are variable. When there is no inflammation, the cyst may be asymptomatic. Infection of the cyst can cause nasopharyngeal bursitis with sore throat, purulent postnasal discharge, and eustachian tube dysfunction. The term *Thornwaldt's disease* refers to the syndrome of headache, frequent upper respiratory infections, asthma, and arthritis.

Physical examination by indirect and direct nasopharyngoscopy reveals a midline cyst on the posterior nasopharyngeal wall, and a central depression or pit may be visible.

### **Other Nasopharyngeal Cysts**

Branchial cleft cysts of the nasopharynx are rare. Derived from the first and dorsal portions of the second branchial pouches, these cysts are usually paired and are located on the lateral walls of the nasopharynx. Typically, they do not extend laterally into the soft tissues of the neck.

The intra-adenoid cyst is a retention cyst that results from chronic inflammation around the median pharyngeal recess. The cyst is located in the midline and is composed of lymphoid tissue only.

The paired nasopharyngeal pseudocysts are postulated to occur as a consequence of longus capitis perimyositis. Like the intra-adenoid cyst, the pseudocysts contain no epithelial elements. Mucous retention cysts can occur in the nasopharynx, and they possess characteristics typical of those found in other regions of the upper aerodigestive path.

## **Benign Tumours of the Nasopharynx**

### **Choristoma**

Choristomas are congenital lesions and are not true neoplasms. Also known as heterotopic tissue or aberrant rests, choristomas are composed of histologically normal tissue for a part of the body other than the site at which they are found. The nasopharyngeal choristoma, a rare lesion, presents as nasopharyngeal obstruction in the newborn. Physical examination reveals a

laterally based nasopharyngeal mass, and radiographic studies do not reveal intracranial communication. Treatment is surgical excision, and pathologic examination reveals a mass of fat and fibrovascular tissue covered with skin and hair.

### **Hamartoma**

Like the choristoma, hamartomas are not true neoplasms but instead are malformations or simple spontaneous growths made up exclusively of locally derived tissue. Hamartomas are generally self-limiting because as their cells reach maturity they do not reproduce. Although their occurrence in the nasopharynx is unusual, their presentation can mimic that of a neoplasm. Treatment involves surgical removal.

### **Teratoma**

The teratomas are a group of germ cell tumors of embryonic origin. They are thought to be derived from an ectopic primitive streak that has been segregated by errors of fusion. In the nasopharynx, they arise from the lateral wall or the basisphenoid in the midline. These growths are usually present at birth, and girls are affected six times more often than boys. Teratomas are classified as dermoids, teratoids, and epignathi.

The dermoid is the most common nasopharyngeal teratoma. Also known as a hairy polyp, the nasopharyngeal dermoid is a mass of poorly differentiated ectoderm and mesoderm covered with epidermal appendage-bearing skin. The dermoid arises from the basisphenoid and sometimes possesses an intracranial component attached to the main mass through a defect in the base of the skull.

Teratoids and true teratomas are composed of ectoderm, mesoderm, and endoderm and, like dermoids, they arise from the basisphenoid. Teratoids are poorly differentiated, whereas true teratomas are differentiated to the extent that organs can be identified histologically. Both of these growths are frequently associated with skull deformities, such as palatal defects, hemicrania, and anencephaly. Teratoids occurring in other sites have a 30 per cent incidence of malignant degeneration, but this phenomenon has not been reported in the nasopharynx.

The epignathus is the least common variety of nasopharyngeal teratoma. Arising from the basisphenoid or the fossa of Rosenmüller, the epignathus consists of ectoderm, mesoderm, and endoderm. The three germ layers are well differentiated and manifest the gross development of fetal organs and limbs. An epignathus is rarely compatible with survival of the host.

### **Miscellaneous Benign Tumours**

The nasopharyngeal mucosa contains minor salivary glands, and infrequently benign glandular neoplasms arise. They include pleomorphic adenomas, Warthin's tumors, and oncocytomas. Chondromas are benign cartilaginous growths that have been described grossly as smooth, round, submucosal masses originating from the base of the skull or the eustachian tube.

Finally, paragangliomas have been reported to occur rarely in the nasopharynx. These vascular neoplasms, described as blue, pulsatile, submucosal masses, are thought to arise from the paraganglionic tissue surrounding the terminal part of the maxillary artery in the pterygopalatine fossa or from the nodose ganglion.

The indications for treatment of the preceding benign nasopharyngeal cysts and tumors include recurrent inflammation, eustachian tube dysfunction, and upper airway obstruction. Treatment is removal, and the transoral approach is preferred. When wider exposure is necessary, the soft palate can be divided.

### **Angiofibroma**

Angiofibromas are the most common benign neoplasms of the nasopharynx, yet they account for only 0.05 per cent of head and neck tumors and for as few as 1 in 50,000 otolaryngologic admissions. The term *juvenile nasopharyngeal angiofibroma* is misleading because the tumor occurs in older patients and is not limited to the nasopharynx; the simple term *angiofibroma* is preferred.

Angiofibromas occur almost exclusively in males, and the most common signs and symptoms are nasal obstruction, epistaxis, and a nasopharyngeal mass. Obstruction of the eustachian tube orifice or orifices may produce serous otitis media. Extension of the tumor beyond the nasopharynx into the paranasal sinuses, pterygomaxillary fossa, infratemporal fossa, temporal fossa, orbit, and cranium may produce purulent sinusitis, facial deformity, proptosis, and dysfunction of cranial nerves II, III, IV, V, and VI. Physical examination typically reveals a pale, reddish blue, smooth mass in the nasopharynx and frequently in the posterior part of the nose. Microscopic examination demonstrates a rich vascular network in a fibrous stroma. The vascular channels are of variable size and are lined by endothelial cells that lie directly against the stromal cells. The lack of an intervening smooth muscle layer between these two cell types contributes to the capacity for profuse bleeding.

**Diagnosis.** The clinical diagnosis of angiofibroma is based on a thorough history and physical examination, and the extent of the growth is assessed with contrast-enhanced computed tomography (CT) scans. Sessions and co-workers proposed that the CT scan be used to standardize reporting and staging of patients, and Chandler and associates described an angiofibroma staging system similar to that proposed for cancer by the American Joint Committee (Table 1). Some surgeons consider arteriography to be a necessary part of the diagnostic evaluation because of the information obtained about the source and the degree of the tumor's blood supply. However, although there may be contributing vessels from the internal carotid artery or the contralateral external carotid system (or both), the dominant arterial supply is the ipsilateral maxillary artery. Because of this predictable blood supply and the risks associated with arteriography - including death, blindness, transverse myelitis, and hemiplegia - arteriography is not essential in most patients. However, it can be helpful in instances of suspected intracranial extension and is necessary to assess candidacy for preoperative embolization.

**Table 1. Angiofibroma Staging**

Stage I	Tumor limited to posterior nares or nasopharyngeal vault (or both)
Stage IIA	Minimal lateral extension through sphenopalatine foramen into pterygomaxillary fossa
Stage IIB	Fills pterygomaxillary fossa, displacing posterior wall of antrum, or extends superiorly, eroding bone of orbit (or both)
Stage IIC	Extends through pterygomaxillary fossa into cheek and temporal fossa
Stage III	Intracranial extension.

**Treatment.** Optimal treatment planning requires an appreciation of the point of origin of the tumor and its pathways of extension, as described by Neel and co-workers. The point of origin is the junction of the sphenoid process of the palatine bone with the horizontal ala of the vomer and the root of the pterygoid process of the sphenoid bone; this junction forms the superior margin of the sphenopalatine foramen on the posterolateral wall of the roof of the nose. From this point, the tumor may extend anteriorly into the nose, posteriorly into the nasopharynx, superiorly into the sphenoid sinus, laterally into the pterygomaxillary fossa, or in more than one of these directions. From the pterygomaxillary fossa, the tumor has access anteriorly to the antrum, laterally to the infratemporal and temporal fossae, and superiorly to the orbit through the inferior orbital fissure. Intracranial involvement may occur as a result of direct extension along one of two pathways: from the sphenoid sinus through the sella (medial to the internal carotid artery and lateral to the pituitary gland) or through the floor of the middle cranial fossa (anterior to the foramen lacerum and lateral to the cavernous sinus).

Primary surgical excision is the treatment of choice for the vast majority of patients with angiofibromas, and the particular approach used depends on the preoperative diagnostic assessment and the surgeon's experience with a given technique. Regardless of the specific approach, however, brisk bleeding must be anticipated, sufficient blood for replacement must be available, and the use of preoperatively donated blood for autologous transfusion can be considered.

The various techniques include the transoral approach, the transpalatal approach, the transhyoid approach, the transmandibular and transzygomatic approaches, the craniotomy-rhinotomy approach, facial degloving, and the lateral rhinotomy. The lateral rhinotomy is preferred because it allows swift, direct, and *wide* exposure of the body of the tumor. When extension of the growth make exposure lateral to the infraorbital foramen desirable, the incision can be extended through the upper lip and along the superior buccogingival sulcus. The lateral rhinotomy and its variations permit removal of tumor from the nose and nasopharynx, the paranasal sinuses, the pterygomaxillary fossa, the infratemporal and temporal fossae, the orbit, and the middle cranial fossa. Respect for the natural curvatures of the face while the incision is made and meticulous wound closure result in reliably satisfactory cosmesis.

In the most recent review of the Mayo Clinic experience with angiofibroma, the lateral rhinotomy approach and its extensions resulted in a mortality rate of 0 per cent and surgical cure

rates of 95.5% per cent in patients with extracranial disease and of 50 per cent in patients with intracranial extension. Other studies report a 10 to 20 per cent incidence of intracranial extension and a 10 to 18 per cent incidence of recurrence. The issues of recurrence and intracranial extension, then, are closely associated and controversial.

Jafek and colleagues recommended a combined otolaryngologic-neurosurgical approach for patients with intracranial extension and postoperative external beam radiation therapy for angiographically verified residual disease. In contrast, Sessions and Humphrey favored primary treatment with radiation for patients with known intracranial extension, and Goepfert and associates advocated systemic chemotherapy in some patients. We have been unable to demonstrate that intracranial extension justifies craniotomy, and we prefer to treat these patients with an extracranial approach through a lateral rhinotomy. Almost all tumors are extradural and can be safely dissected free from dural attachments by progressive packing between dura and tumor. The postoperative course is marked by expectant observation; radiation therapy and embolization are reserved for symptomatic intracranial recurrence. For asymptomatic patients with residual or recurrent disease, we advise close observation without intervention, since the natural history of angiofibroma includes the possibility of spontaneous regression.

A noteworthy exception to primary surgical treatment is the series of patients from the Princess Margaret Hospital in Toronto, in whom primary external beam radiation was advocated as the preferred method of treatment. Briand and co-workers reported control rates of 80 per cent with on 3000 to 3500 cGy course of therapy and of 94 per cent with two courses of therapy. In young patients, primary radiation therapy is of concern because of the potential consequences, including atrophic rhinitis, osteomyelitis, arrest of facial growth centers, and radiation-induced neoplasia; for this reason, lifelong follow-up is necessary after radiation therapy.

Interest in adjunctive measures such as cryotherapy, sclerotherapy, electrocoagulation, and brachytherapy has waned. Endocrine therapy has met with limited success to date, but its application continues to be investigated. The perioperative use of intra-arterial embolization to reduce vascularity has received considerable attention, but as in the case of hypotensive anesthesia, we have no evidence that it decreases blood loss or permits more nearly complete tumor removal.

## **Malignant Tumours of the Nasopharynx**

### **Nasopharyngeal Carcinoma**

Nasopharyngeal carcinoma (NPC) originates from epithelial cells of the nasopharynx. This definition is restrictive and excludes all other nasopharyngeal malignancies, including minor salivary gland carcinomas, lymphomas, and sarcomas. NPC is a fascinating disease of interest to many medical and other scientific disciplines.

Head and neck clinicians appreciate NPC as a tumor that can occur in any age group and that can confuse examiners with an array of subtle symptoms and signs. Epidemiologists have

performed many detailed investigations of NPC, focusing on its high incidence among certain Chinese, its reduced incidence in North American-born Chinese, and the role of environmental factors. NPC is of interest to pathologists because, despite its origin from microscopically uninteresting tissues, it has a variety of histologic types. Radiation oncologists maintain a keen interest in NPC because external beam therapy is the mainstay of treatment. More recently, immunovirologists have intensively investigated the relationship between NPC and Epstein-Barr virus (EBV).

**Epidemiology.** NPC accounts for only 0.25 per cent of all cancers among North American whites, but among the Chinese of North America, it constitutes approximately 18 per cent of all malignant tumors. This incidence is higher among Chinese in the southern states. Among the Chinese of Taiwan, NPC is the most common cancer in males and the third most common cancer in females. There is a significant increase in HLA-A2 and HLA-B-SIN<sub>2</sub> in Chinese patients with NPC, but this strong affiliation with Chinese DNA is not absolute; the incidence of NPC among Chinese born in the USA is consistently lower than that among native-born Chinese but not as low as the incidence in most populations. These findings have led to the identification of other potential etiologic factors, including EBV, exposure to polycyclic hydrocarbons, dietary ingestion of nitrosamines, chronic rhinosinusitis, and poor hygiene. It is probable that NPC is etiologically a multifactorial disease.

**Clinical Presentation.** NPC frequently arises in the fossa of Rosenmüller, and therefore it is not surprising that hearing loss and lumps in the neck are the most common presenting symptom and sign. A tumor in the fossa of Rosenmüller frequently impairs eustachian tube function and results in serous otitis media. The nasopharynx is richly endowed with a network of lymphatics with access to both sides of the neck; in a study of 151 North American patients, 46 per cent had unilateral adenopathy at diagnosis and 22 per cent had bilateral adenopathy.

A primary tumor of the nasopharynx may obstruct the posterior choana or choanae, and it may bleed. Hence, blood-tinged nasal drainage and nasal stuffiness occur in about 30 per cent of patients.

Cranial neuropathy occurs as a result of superior extension of the tumor, and the "petrosphenoidal crossway", formed by the foramen lacerum and the foramen ovale, provides an unimpeded pathway from the fossa of Rosenmüller into the cranium. In one study of North American patients, 20 per cent had cranial nerve involvement at diagnosis. Xerophthalmia reflects involvement of the greater superficial petrosal nerve at the foramen lacerum. Facial pain, facial paresthesia, or a characteristic ache high in the neck indicates infiltration of cranial nerve V. Abductor paralysis of the eye causes diplopia and results from involvement of cranial nerve VI. Ophthalmoplegia reflects involvement of cranial nerves III, IV, and VI and indicates disease in the cavernous sinus or superior orbital fissure. More extensive skull base disease leads to lower cranial nerve (IX, X, XI, and XII) deficits, and involvement of the cervical sympathetic chain causes Horner's syndrome.

Distant metastatic lesions are clinically evident in less than 3 per cent of North American patients at the time of presentation, but in most parts of the world, distant disease is present in about 35 per cent of patients. The most frequently involved sites are the lungs, the skeleton, and the liver.

**Diagnosis.** The basis for the diagnosis of NPC is a complete history and physical examination of the head and neck. Indirect nasopharyngoscopy can be supplemented with direct flexible or rigid fiberoptic examination. The gross appearance of NPC is variable, with some tumors appearing as friable exophytic growths, others as smooth submucosal masses, and still others with no identifiable abnormalities. Invasion of the skull base occurs in 25 percent of patients, and contrast-enhanced high-resolution CT scanning of the head and nasopharynx is the imaging study of choice in most instances for definition of the extent of disease and for treatment planning. Nuclear magnetic resonance imaging may define the extent of soft tissue involvement more accurately, although its precise role has not yet been determined.

The diagnosis of NPC is confirmed by microscopic examination of tissue from the nasopharynx. Pathologists can quite consistently segregate NPC by light microscopy into three categories on the basis of fundamental morphologic differences and the *predominant* histologic type. The three categories have been defined by a committee of the World Health Organization (WHO), and the resulting classification has been accepted around the world. The three groups are squamous cell carcinoma (WHO type 1), nonkeratinizing carcinomas (WHO type 2), and undifferentiated carcinomas (WHO type 3).

The WHO type 1 carcinoma account for 25 per cent of NPCs among white patients in North America. The tumors are well to moderately differentiated; have large cells with eosinophilic cytoplasm, obvious keratin production, and intercellular bridges; and are morphologically similar to other squamous carcinomas of the upper aerodigestive path. The WHO type 2 carcinomas account for 12 per cent of NPCs, have cells that range from mature to anaplastic, and have little or no keratin production by light microscopy. These lesions resemble urinary tract carcinomas and are sometimes called transitional cell carcinomas. The WHO type 3 carcinomas account for 63 per cent of NPCs. This is a heterogeneous group that includes lymphoepitheliomatous, anaplastic, clear cell, and spindle cell variants. The cells are moderately large and have basophilic cytoplasm, indistinct borders, and distinctive, large, single nuclei. Because these tumors often resemble large-cell lymphomas, electron microscopy and special stains for epithelial and lymphocytic cell markers can be of assistance. Both the WHO type 2 and the WHO type 3 tumors have the typical anti-EBV serologic profile, whereas the relationship of the WHO type 1 tumors to EBV by serologic testing is weak.

Detailed immunologic and biochemical investigations have confirmed that EBV is associated with NPC worldwide, and we have incorporated some of these studies as routine components of the initial evaluation and follow-up of our patients. Serum is assayed for antibodies to viral capsid antigen (IgA) and to the diffuse component of the early antigen; these two tests are the most specific for diagnosis, and the viral capsid antigen (IgA) test is the more specific of the two. We use the viral capsid antigen (IgA) and early antigen tests to complement



the process of diagnosis and have found them especially useful for directing attention to the nasopharynx in patients with occult or small NPCs.

The antibody-dependent cellular cytotoxicity (ADCC) assay is used to titrate sera for antibody to the EBV-induced membrane antigen complex, and this test seems to be predictive of the clinical course and prognosis of patients with WHO types 2 and 3 NPC. Low ADCC titers at diagnosis signify a poor prognosis, and declining titers after treatment indicate the likely development of recurrent disease.

**Staging.** The purpose of staging is to allow more meaningful end-results reporting and interpretation. Several staging systems are in various degrees of use throughout the world, including the system of the American Joint Committee for Cancer Staging and End-Results Reporting (AJC), the system of the International Union Against Cancer, and the Ho system. Each of these extent-of-disease schemes has liabilities as well as assets, and there is no consensus about which system is best.

The most commonly used system in the USA is the AJC. The primary tumor (T) is classified as shown in Table 2; the N and M classifications and the stage grouping for NPC are the same as those for other regions of the pharynx. Major criticisms of this system have been made about the descriptions of the primary tumor and the regional lymph nodes. Submucosal spread beneath a normal-appearing mucosa is common, and the extent of the primary lesion is frequently difficult to determine. Additionally, because the definitions of posterosuperior and lateral walls are imprecise and because tumors often arise in the fossa of Rosenmüller, which is the junction of the posterior and lateral walls, any attempt to classify the primary tumors as T<sub>is</sub>, T<sub>1</sub>, or T<sub>2</sub> is not meaningful. Furthermore, as a tumor becomes extensive within the nasopharynx or extends beyond the nasopharynx, the chance of survival decreases, but the AJC does not distinguish among tumors that have contiguous regional extension; T<sub>3</sub> refers to nasal cavity or oropharynx extension, and T<sub>4</sub> refers to skull invasion or cranial nerve involvement (or both). In our experience, regional extension and cranial nerve involvement are important prognostic signs, but skull invasion does not necessarily indicate a poor prognosis. Finally, we have determined that prognosis is poor when lower cervical nodes are involved, but there is no significant difference in survival of patients with unilateral or bilateral involvement of upper neck nodes and of patients with disease limited to the nasopharynx. Because the nasopharynx is a midline structure, the concept of homolateral versus contralateral is unworkable.

**Table 2. American Joint Committee Staging System: T Classification**

T <sub>is</sub>	Carcinoma in situ
T <sub>1</sub>	Tumor confined to one site of nasopharynx or no tumor visible (positive biopsy only)
T <sub>2</sub>	Tumor involving two sites (both posterosuperior and lateral walls)
T <sub>3</sub>	Extension of tumor into nasal cavity or oropharynx
T <sub>4</sub>	Tumor invasion of skull or cranial nerve involvement (or both).

The deficiencies of the extent-of-disease (TNM) staging systems prompted Neel and co-

workers to develop a prognostic scoring system based on disease characteristics that have been determined to have a significant impact on prognosis, as in thyroid cancer and lymphoma. These characteristics included symptoms (type, number, and duration) at presentation, tumor site and extent (local extent, nerve involvement, skull base involvement, level of nodes in neck, fixation of nodes, and diameter of nodes), and miscellaneous characteristics (WHO type, ADCC titer, and age). Application of the Cox regression "step-down" method reduced the list of characteristics to those shown in Table 3. The resulting score predicts more precisely than disease extent systems the risk of death from NPC as one proceeds from low to high scores; the ADCC titer makes the least significant contribution and eventually may be deleted.

**Table 3. Prognosis Score\* in Nasopharyngeal Carcinoma**

Characteristic	Score	
	If yes	If no
Extensive tumor in nasopharynx	1	0
Nodes in lower neck region	1	0
WHO type 1 tumor	1	0
ADCC titer < 1:7680 (WHO types 2 and 3)	1	0
Seven or more symptoms	1	0
Age > 40 yr	1	0

\* Prognosis score = sum of item scores (range, 0 to 6).

**Treatment.** The mainstay of treatment for patients with NPC is external beam supervoltage radiation. A commonly used treatment plan for small tumors limited to the nasopharynx involves inclusion of the primary tumor and the primary echelon of lymph nodes in large lateral opposed portals. This volume of tissue is treated in fractions of 175 to 200 cGy/day to a dose of 6500 cGy. Larger tumors are "boosted" with electrons to 7000 cGy through smaller fields. The lower cervical and supraclavicular areas are treated to 5000 cGy through direct anterior fields. Intracavitary brachytherapy may be used to "boost" the nasopharynx as part of the initial treatment, or it may be reserved for the treatment of recurrent or residual disease.

The role of surgery in the treatment of patients with NPC has been limited. Radical neck dissection has been reserved for patients in whom radiotherapy has controlled the primary tumor but has failed in the neck; this situation occurs infrequently. Recently, however, aggressive surgical approaches to the nasopharynx have been described. Fisch has advocated an infratemporal fossa approach, and Panje and McCabe and Panje and Gross have described a multistage, multiteam transparotid temporal bone approach. Fisch has reported both palliation of patients with T<sub>4</sub> NPC and surgical salvage of patients with T<sub>1</sub> and T<sub>2</sub> NPCs. Panje and associates have reserved surgery for palliation of carefully selected patients in whom radiation therapy has failed.

Adjuvant chemotherapy has been advocated in some centers, but its role has not been established by prospective randomized studies. Chemotherapy can provide palliation of pain and prolong life in some cases. It is hoped that radiation and chemotherapy or immunotherapy in combination may provide better results.

**Prognosis.** As discussed earlier, the prognosis of patients with NPC depends on the extent of disease in the nasopharynx, the level of disease in the neck, the histopathologic findings, the age of the patient, the number of symptoms, and the ADCC titer. In a prospective study of 182 patients treated with radiotherapy at major medical centers, survival was 60 per cent at 3 years after diagnosis and 50 per cent at 5 years after diagnosis. Of the patients with WHO type 1 NPC, 30 per cent survived to 3 years, and less than 20 per cent survived to 5 years; of the patients with WHO types 2 and 3 NPCs, 70 per cent survived to 3 years, and 59 per cent survived to 5 years. Thus, there is a striking trend toward more and earlier deaths in patients with WHO type 1 tumors.

Overall survival to death from NPC are shown. Survival as observed diverges continually from the survival expected so that there is a continuing high risk of death at least up to 6 years. NPC appears to be a chronic disease, and the risk does not appear to level off in a few years as it does for many other cancers.

**Prevention.** The potential development and application of vaccines in EBV-associated disease is exciting. Neutralizing and cytotoxic antibodies can be induced by purified EBV-specific membrane glucoprotein, and eventually it may be possible to investigate the efficacy of a vaccine in areas with a high incidence of NPC.

### **Miscellaneous Malignant Tumors**

Most lymphomas of the nasopharynx are of the B-cell type and have a diffuse large-cell organization. These tumors can closely resemble WHO type 3 NPCs, and electron microscopy and immunostaining may be required for accurate diagnosis. The treatment of nasopharyngeal lymphoma is radiation or chemotherapy, or both, the details of which depend on cell type, disease stage, and other factors.

Although nasopharyngeal sarcomas are quite rare, embryonal rhabdomyosarcoma in children can also resemble WHO type 3 NPC. Because the treatment and prognosis of these lesions differ, distinction is important and may require electron microscopy and special stains.

Chordomas can appear to be nasopharyngeal lesions, but they are actually tumors of bone. Finally, most nasopharyngeal salivary gland malignant lesions are adenoid cystic carcinomas.