# JUVENILE NASOPHARYNGEAL ANGIOFIBROMA

HAYES MARTIN, M.D., F.A.C.S. HARRY E. EHRLICH, M.D., F.A.C.S.

AND
JULES C. ABELS, M.D.\*
NEW YORK, N. Y.

FROM THE HEAD AND NECK SERVICE, MEMORIAL HOSPITAL

JUVENILE NASOPHARYNGEAL ANGIOFIBROMA, though neither a common nor a malignant neoplasm, nevertheless presents serious problems because of the complications which are invariably associated with its growth and its treatment. This tumor, moreover, is of considerable scientific interest in that it is one of the few neoplasms which exhibit a marked sex predilection—etiologically related in this case, we believe, to a sex-endocrine imbalance. The present report is based on an analysis of 29 cases of juvenile nasopharyngeal fibroma observed on the Head and Neck Service at the Memorial Hospital from 1927 to 1946, inclusive.

### DEFINITION

Juvenile nasopharyngeal angiofibroma is a specific, highly vascular, non-infiltrating, essentially benign neoplasm, occurring in the nasopharynx or posterior nasal cavity of pubescent males. Symptomatically the tumor is characterized by nasal obstruction, repeated epistaxis, and by progressive growth throughout the period of adolescence, with a tendency toward spontaneous regression at about the time of sexual maturity.

While the term juvenile nasopharyngeal angiofibroma is anatomically specific and descriptive for the tumor, it is somewhat cumbersome, and for the sake of convenience in the remainder of this report, it will often be shortened to nasopharyngeal fibroma. Other terms which have been employed elsewhere to designate this neoplasm include myxofibroma, juvenile basal fibroma, nasopharyngeal fibroma of adolescence, fibroids of the nasopharynx, and bleeding fibromas of adolescence.†

<sup>\*</sup> Dr. Jules Abels died June 13, 1947.

<sup>†</sup> Historical Note.—The earliest Greek, Roman, and Arabian medical writers used the term nasal polyps (Zool—many footed) to designate all tumors or swellings within the nasal cavities or nasopharynx which caused obstruction to breathing. Subsequent medical writers employed the same term for several hundred years. As time passed, more than one variety of nasal polyps were recognized and by the 18th Century such lesions were often differentiated as soft or mucous and hard or fibrous nasal polyps; finally, they were classified into three groups—(1) soft (2) fibrous and (3) malignant. It is somewhat difficult to ascertain just when a specific form of nasopharyngeal fibroma of adolescence was first recognized, but as early as 1847 Chelius stated that fibrous nasal polyps "commonly occur in persons about the time of puberty."

#### ETIOLOGY

Nasopharyngeal fibroma is not a common tumor. In the Head and Neck Clinic of the Memorial Hospital about 2,000 new cases of neoplasms in the tissues of the head and neck are admitted annually, and of these there are usually one or two cases of nasopharyngeal fibroma. In the literature, most of the case reports number from one to three. A few fairly large series have been published, namely those of New and Figi<sup>21, 9</sup> from the Mayo Clinic — 63 cases, and of Shaheen<sup>6</sup> — 58 cases. Some aspects of the clinical material in these two reports, especially with regard to the ages of the patients and the fairly large proportion of females, suggest to us, for reasons to be considered later, that the cases have not been critically selected and that not all are actually juvenile nasopharyngeal fibromas as defined in the present report.

Age Incidence.—In our series of 29 cases, the age at the onset of symptoms varied from 7 to 19 years with an average age of 14 years. The age on admission averaged about 1½ to 2 years later—that is about 16 years, which is a little younger than Figi's figure of 18½ years at the time of the first examination. In one of our cases, the patient was admitted at the age of 36 years, but had symptoms since the age of 16.

The onset of nasopharyngeal fibroma always occurs during adolescence and is one of its most characteristic clinical features. While many observers,

Considerable space is given in the surgical texts of the early 19th Century to operations for the removal of bulky nasal polyps, especially when the tumors became so large as to produce what was known as a "frog face" deformity. Nevertheless, surgeons of that period, and some even up to the year 1900, appear to have been unaware of any age or sex predilection for these "fibrous nasal polyps." Legouest<sup>17</sup> in 1865 was one of the earliest to call attention to the selectivity of these tumors for males. Gosselin<sup>11</sup> in 1876 noted a tendency toward spontaneous regression after sexual maturity. The first comprehensive study of nasopharyngeal fibroma is to be found in a review on the general subject of nasal polyps in 1878 by Bensch,<sup>2</sup> who collected the scattered case reports and made an excellent morphologic and clinical description of this neoplasm. Chaveau<sup>3</sup> in 1906 suggested the term juvenile nasopharyngeal fibroma.

The first attempts at surgical removal of these tumors were made as early as the time of Celsus, by digital manipulations or by tearing off the tumor masses with forceps or snares. Later, injections of various escharotics and the actual cautery were employed.

About the middle of the 19th Century, several operative technics were devised to gain better access to the nasal cavities and the nasopharynx. Langenbeck<sup>16</sup> proposed an anterior approach through the skin of the cheek leaving the bone attached to the osteoplastic flap and temporarily resecting the maxilla. After removal of the tumor, the flap with the attached bone was replaced and the wound was sutured. To obtain access to the nasopharynx Rouge<sup>25</sup> reflected the nose upward and resected part of the septum by an incision in the upper gingivo-buccal gutter. Ollier<sup>22</sup> made a V-shaped incision with its base opposite the nasal ala, reflecting the whole nose downward. All of these operations were rather bloody and the mortality was high. Bilateral ligation of the external carotid arteries and tracheostomy were mentioned as preliminary surgical measures as early as the 1880's.

Most of the reports in the literature consist of three or less cases and the clinical data are often meagre and uncertain. In recent years several larger series have been published which we shall discuss later in greater detail.

as far back as Chelius<sup>4</sup> in 1847, have believed that this neoplasm occurs mainly in children, hence the eponym "juvenile," nevertheless such observers as New and Figi<sup>21, 9</sup> and Shaheen<sup>26</sup> have included cases with a supposed onset long after sexual maturity. Some of these apparent variations may arise by recording the age of the patient on admission rather than the age at the onset of symptoms. Shaheen<sup>26</sup> is the only recent observer who has reported the occurrence of this tumor during infancy and old age (2 and 4 years, 67 and 70 years, respectively). Since Shaheen appears to be unaware that his reports of cases occurring at the age extremes are at variance with those of most other observers and since he offers no histologic or other corroborant data, we feel that these particular cases are not all acceptable as genuine instances of juvenile nasopharyngeal fibroma.

The duration of the tumor before it produces symptoms cannot of course be determined. From the observed rate of growth following the first examination in untreated patients, however, it is probable that a silent period of 2 to 3 years may elapse, bringing the onset of the tumor to between 11 and 12 years. We have not been able to find any comment on this probability in other reports.

Sex Relationship.—In the course of the present study, certain sex-endocrine factors of probable etiologic significance became apparent. These were:

- 1. The disorder was limited to young males.\*
- 2. These patients in most instances gave the clinical impression of undersexual development, both physically and emotionally.
- 3. In spite of roentgen-ray therapy the tumor significantly regressed only after secondary sex characteristics were developed fully; there was one exception in the 29 cases presented.
- 4. In two instances in which puberty was hastened by the administration of androgens, roentgen-radiation appeared to induce a more ready regression of the tumor.

<sup>\*</sup> All of our 29 patients with nasopharyngeal fibroma were males and we are of the opinion that this neoplasm never occurs in females. Beginning with Legouest<sup>17</sup> in 1865, many subsequent authors have recognized that the incidence of this tumor was considerably greater in males; but we are the first, so far as we know, to advance the proposition that juvenile nasopharyngeal fibroma is a completely sex-bound neoplasm. We realize that this point of view may not be generally accepted without question at this time, for all previous authors who have reported large series have given a definite percentage of female incidence (Figi and New, 7 per cent; Shaheen, 8 per cent). At the Memorial Hospital, up until about 10 years ago, we also believed that juvenile nasopharyngeal fibroma occurred occasionally in females, but since that time we have subjected all cases so diagnosed in female children to careful scrutiny. These investigations, based not only on biopsy but also on the subsequent clinical course, have failed to support the diagnosis of nasopharyngeal fibroma in a single female patient in our clinic. In three suspected cases in females the lesions on biopsy proved to be simple choanal polyps. In two other cases the eventual diagnosis was tuberculosis of a retropharyngeal lymph node and chondroma arising in a superior nasal turbinate, respectively. In none of these tentatively diagnosed cases of juvenile nasopharyngeal fibroma in females were found the characteristic symptoms and clinical course-progressive nasal obstruction, recurrent epistaxis, and spontaneous regression at sexual maturity.

These observations strongly suggest that juvenile nasopharyngeal fibromas may result from a deficiency of androgen activity or, perhaps, from an overproduction of estrogens. Unfortunately, little or no information is available concerning estrogen production by pubescent males from which conclusions might be drawn.

There is, however, considerable clinical and experimental evidence that vascular tissue can be influenced by certain of the sex hormones, but these effects are not always uniform. In cutaneous areas characterized by a large venous bed, the capillaries of castrated males are found widely dilated and this dilatation can be reversed by the administration of testosterone propionate. Likewise, the excitability of cutaneous blood vessels has been found to be more extensive in castrated men and this excitability to graded mechanical stimuli could be increased by estradiol and decreased by testosterone proprionate. 24

The observations of Soskin and Bernheimer<sup>27</sup> that relief of atrophic rhinitis was obtained by estrogen administration stimulated several studies concerning the relation of sex hormones to mucous membrane hyperemia. Of these, the work of Reynolds and his co-workers<sup>23</sup> bears most on the present clinical study. These investigators demonstrated that hyperemia of the mucous membranes was a function of blood estrogen content and could be induced by further estrogen administration. Furthermore, the mechanism of the hormone action was discovered to be due probably to the local production of acetylcholine. The clinical and experimental value of these observations have been demonstrated in the treatment of peripheral vascular disease. For example, gangrene induced by ergot drugs can be prevented by estrogen administration.<sup>18</sup>

During the course of further studies it is planned to give much more consideration to the sex linked character of this tumor. Particular attention will be given to:

- I. The determination of "developmental age" of these patients by roentgenray examination of ossification centers.
- 2. The excretion of total 17-ketosteroids; for this a considerable amount of work first must be done to establish the normal range for the 17-ketosteroid excretion of the pubescent male.
- 3. The effects of androgens alone in massive doses on the tumor before roentgen-radiation or surgery is applied.
  - 4. The effects of estrogens on the appearance of the tumor.

Histogenesis.—Histologic study in our cases reveals that in the tumors of younger subjects the angiomatous elements predominate and occasionally a microscopic picture of fully developed cavernous angioma is noted. It is probable, therefore, that in the beginning these growths are principally angiomatous rather than fibromatous. If estrogenic stimulation is a factor in the etiology of these tumors, their histogenesis can be reasonably explained as an overgrowth of vascular tissue in the nasopharynx, a result of an abnormal

stimulus to the local circulation. The fibromatous elements, at first being only supporting stroma of the tumor, develop as a structural component and become predominant as the estrogenic effect is lessened. An identical phenomenon is the gradual replacement of the angiomatous elements by fibrous tissue as seen in ordinary hemangiomas following spontaneous or therapeutically induced sclerosis of the blood vessels.

When the patient approaches sexual maturity, as will be later described, all tumors tend to become less vascular and often completely fibrous, which suggests that as the abnormal stimulus disappears the proliferation of blood vessels also ceases. This hypothesis, if correct, is sufficient to explain the histogenesis of this tumor.

Other genetic theories have been advanced which presuppose that the growth is of fibroblastic origin. The most prevalent and hitherto accepted explanation of the origin of nasopharyngeal fibroma, first advocated by Verneuil<sup>29</sup> and supported by Bensch,<sup>2</sup> Ewing,<sup>8</sup> and others, is that the growth is derived from embryologic fibrocartilage during development of the skull. The embryonal occipital plate, a cartilaginous structure, gives rise to the basilar portion of the occipital bone, body of the sphenoid bone, medial pterygoid process, and bones in the region of the foramen lacerum and ptervgopalatine space. Until early adult life the basilar portion of the occipital bone is joined to the body of the sphenoid bone by the remaining portion of embryonal cartilage. This cartilaginous plate becomes ossified by the 25th year. According to these authorities, perichondrium (fibrous connective tissue) covers the cartilaginous plate and from this or other perichondrium of the postnasal space juvenile nasopharyngeal fibroma is supposed to develop. This hypothesis is attractive in that it accounts for the phenomenon of spontaneous regression of the tumor about or after the 25th year, and also, for its various anatomic sites of origin. The latter theory, however, does not explain the sexual selectivity of this tumor nor does it take into consideration the presence of angiomatous elements which are integral and, perhaps, the more significant morphologic components of nasopharyngeal fibroma.

In 1943 a case of chondrosarcoma of the nasopharynx occurring in an adolescent boy was reported by Wirth.<sup>28</sup> Although this tumor finally metastasized to the lungs as chondrosarcoma, the initial biopsy was compatible with a diagnosis of juvenile nasopharyngeal angiofibroma. The presence of cartilage even in the first biopsy specimen, the lack of response of the growth to large doses of external and interstitial radiation, and subsequent biopsy reports (vascular embryonal chondroma; chondrosarcoma) mitigate against this growth being a genuine nasopharyngeal fibroma in the beginning, as Wirth admits. If it could be proved, however, that chondrosarcomatous transformation can occur in a pre-existing nasopharyngeal fibroma, it would favor the prechordal plate genetic theory of Verneuil.

Other Causative Factors.—Further analysis of our data reveals no evidence of any systemic disturbances. The majority of patients were investi-

gated for syphilis, tuberculosis, and other infections and were found to be free from these diseases. Allergy or trauma did not appear to be etiologic factors. Congenital anomalies, mal-developments and other associated tumors were not encountered and in no case were either neurofibromatosis or hemangiomatous tendencies present. The boys were not retarded, either physically or mentally, and except for evidence of underdevelopment of secondary sex characteristics in over one-half of the cases, they appeared normal in all other respects.

No tendency toward racial or familial predilection was noted in the present series or in any previously reported cases.

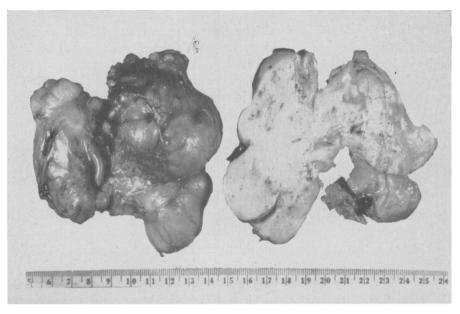


Fig. 1.—Surgical Specimen of Nasopharyngeal Fibroma. This bulky, lobulated, cartilaginous-like mass was removed from the nasopharynx and posterior nasal cavity of an 11-year-old boy by a radical Weber-Ferguson type of resection of the maxilla. Note that the tumor is dumb-bell shaped; one portion projected into the posterior nasal cavity and the other beneath the soft parts of the cheek in the infrazygomatic and temporal areas.

#### **PATHOLOGY**

Gross Pathologic Anatomy.—Nasopharyngeal fibroma is an unencapsulated, fungating, vascular tumor. The surface of the growth, if not traumatized by operative intervention or packing to control hemorrhage, is covered by intact mucous membrane, highly injected and deep red in color in younger subjects and pale pink in older patients or those in whom the vascularity has been reduced by radiation or sex hormone therapy. If there has been hemorrhage with the attendant trauma of packing, ulceration and necrosis occur and the surface of the tumor may become granular.

In our cases, with one execution, the growth ranged from 2 to 5 cm. in

greatest diameter and the average size was 3 cm. One tumor was so large (10 cm.) as to be out of proportion to the standard variation in this series.

In the specimens available for gross morphologic study, unusual variations and combinations were noted. Although the shapes of the tumors differed widely, the commonest types were ovoid or club-shaped. The surface was either smooth or definitely lobulated (Fig. 1). Some of the tumors were rubbery or cartilaginoid in consistency while others were soft, edematous and occasionally friable. On section the color of the neoplasms ranged from pinkish white to grayish yellow to reddish brown, and translucent tissue was seen as often as homogeneous tissue. All growths were solid with no areas of



Fig. 2.—Vascular Phase of Nasopharyngeal Fibroma. In this microphotograph of an extremely vascular nasopharyngeal fibroma in a 10-year-old boy, the microscopic appearance is that of a fully developed cavernous angioma in a fibrous stroma. Some of the blood vessels have become sinusoid. This tumor had no previous sex hormone or radiation therapy.

cystic degeneration. Older tumors or those which had been subjected to radiation therapy were usually densely fibrous and pale; younger and untreated tumors were soft and deeply vascular.

Histopathology.—Nasopharyngeal fibroma is composed essentially of connective tissue and blood vessels. In microscopic appearance it may vary from that of a fully developed cavernous angioma in a fibrous stroma (Fig. 2) to that of a densely cellular or occasionally myxomatous fibroma (Fig. 3). The usual histologic pattern consists of connective tissue stroma containing numerous spindle-shaped immature fibroblasts and thin-walled blood vessels in

varying proportions. In fact, spindle- and star-shaped fibroblasts may be so numerous as to suggest fibrosarcoma or angiosarcoma, with which juvenile nasopharyngeal angiofibroma is often confused. In younger subjects and in untreated tumors, the angiomatous elements are in abundance, the vessels becoming large, irregular and even sinusoid; in older tumors or in those which have been subjected to radiation therapy or intensive treatment with androgens, the vascular components are less prominent or they may disappear altogether and fibrous elements predominate. Foci of lymphocytes and plasma cells may be present, especially in those tumors which are ulcerated or traumatized. Myxomatous changes in varying proportions are frequently found,

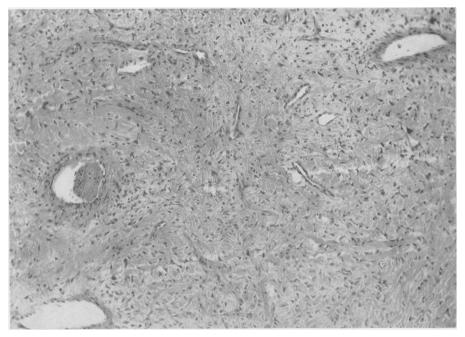


Fig. 3.—Avascular Phase of Nasopharyngeal Fibroma. The microscopic appearance of a relatively avascular nasopharyngeal fibroma consists of sparsely scattered blood vessels in a densely cellular stroma. This histologic pattern of replacement of angiomatous elements by connective tissue (involution) can frequently be brought about by androgenic therapy and irradiation.

as are areas of necrosis. Hyalinized thrombi are occasionally seen, especially in older or treated tumors, together with areas of hyalinized stroma.

The tumor possesses no true capsule. A pseudo-capsule which actually consists of pharyngeal or nasal mucosa, occasionally stretched and atrophic, is noted in non-ulcerated specimens (Fig. 4).

Although malignant transformation has been reported by others (Shaheen, 26 Jackson, 15 Dabney 5) the presented evidence is inadequate and unconvincing, in our opinion. No tumor in the present series underwent malignant

transformation, anatomically or clinically, with the exception of a single case in which one of numerous recurrences revealed unusual cellularity and localized areas of malignant transformation; subsequent recurrences, however, during a period of three years were reported as benign and there have never been any clinical manifestations of malignant behavior. This case will be referred to again under prognosis.

# SYMPTOMS, MORBID ANATOMY AND CLINICAL COURSE

The first symptom of nasopharyngeal fibroma is probably always nasal obstruction which, if only moderate in degree, may for a time pass unnoticed.



Fig. 4.—Surface Appearance of Nasopharyngeal Fibroma. The neoplasm has no true capsule. In this microphotograph intact mucosa may be seen stretched over the tumor, forming a pseudocapsule.

While in a few of our cases the patients at first gave epistaxis as the initial symptom, closer questioning almost always elicited a preceding history of nasal obstruction to which little attention had been paid. In order to produce nasal obstruction, we estimate that a tumor in the nasopharynx must reach the size of about 2.5 cm. in diameter, although in the choana a smaller mass could undoubtedly produce this symptom. At any rate there is probably a silent period of at least several months before a growing nasopharyngeal fibroma becomes large enough to cause some obstruction to breathing.

The second symptom of nasopharyngeal fibroma and the one which most often causes the patient to seek medical advice is recurrent epistaxis. Hemor-

rhage probably occurs either as a result of trauma to the tumor, incident to sneezing or to forcibly blowing the nose, or from pressure necrosis of the expanding growth as it meets with the resistance of the confining bony walls. Once initiated, hemorrhages occur at increasingly frequent intervals, especially when their control necessitates tamponage or nasal packing. These manipulations, when repeated, almost always result in sepsis which may extend to the paranasal sinuses, the middle ear, and even the mastoid. With recurrent hemorrhages, the patient becomes anemic and since proper nutrition is interfered with by local manipulations, usually loses considerable weight.

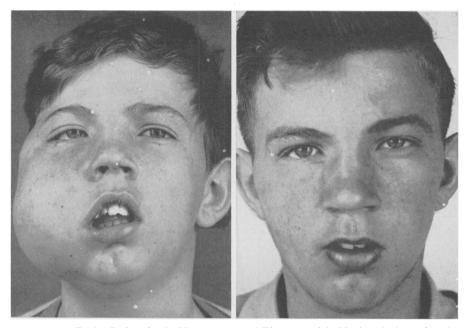


Fig. 5.—Facial Deformity in Nasopharyngeal Fibroma. (a) Marked facial deformity may be produced by a bulky nasopharyngeal fibroma as the mass grows outward compressing the antrum and pushing the soft parts of the cheek ahead of it. Removal of this tumor necessitated resection of the anterior wall of the maxilla and corresponding alveolus after reflecting a cheek flap. (b) Postoperative photograph.

If hemorrhage is not an early or frequent symptom and the nasal obstruction is ignored, the tumor may attain sufficient size to cause "frog face" deformity so often mentioned in the surgical literature of the 19th Century.\* Such a degree of facial deformity, consisting of prominence of the cheeks and

<sup>\* &</sup>quot;Frog-face" deformity is a clinical manifestation associated with lesions other than juvenile nasopharyngeal angiofibroma. Benign and malignant neoplasms of the nasal cavity, nasopharynx, and maxilla not infrequently occur in children, such as ossifying fibroma, sarcoma of the soft parts, lymphomatous tumors, and central myxoma. As the growth expands and advances, the floor of the orbit is elevated (unilateral or bilateral), producing "frog-face" deformity.

nose, obliteration of the naso-labial groove, and prominence of the eyes, was present in about one-quarter of our cases on admission (Fig. 5). The character of the deformity results not only from the expansion of a growing bulky tumor but sometimes from the particular direction that a growth has taken from its point of origin.

Most of the tumors appear to have origin in the vault of the nasopharynx or at least mainly in the vault and the immediately adjacent lateral or posterior nasopharyngeal walls. The base of attachment of the growth is usually rather broad (2–3 cm. or more) so that the exact point of origin and extent of attachment is difficult to delineate either by clinical examination or operative exposure.

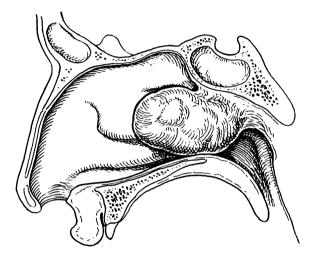


Fig. 6.—Anterior Growth of Nasopharyngeal Fibroma. Diagram of nasopharynx (sagittal view) showing a common location for nasopharyngeal fibroma. The tumor arises from one of the walls of the nasopharyngeal cavity or posterior nasal space and grows downward and forward blocking one or both choanae.

As the tumor enlarges and expands it may grow forward into the nasal cavity (Fig. 6), often presenting at one anterior naris as an edematous partly necrotic mass; in other cases the growth extends backward to protrude below the free edge of the soft palate; some proceed laterally, perforating by pressure necrosis the maxilla to enter the antrum and even appearing in the subcutaneous tissues of the cheek (Fig. 7). A large growth occasionally produces pressure on the floor of the orbit and causes elevation of the globe with resultant unilateral exophthalmos. In any case, the main mass is always in the nasopharynx.

The osseous walls of the nasopharynx are formed by the body of the sphenoid bone, the basilar portion of the occipital bone, the medial pterygoid

plate, and the cervical portion of the vertebral column. The union of these bones, the fascial and tendonous structures which are attached to them, together with variously sized recesses produced by numerous mucosal folds and the cartilages of the eustachian tube (torus tubarius, fossa of Rosenmüller, etc.), contribute to the unusual irregularity of the walls of the nasopharyngeal cavity. This irregularity makes complete surgical removal of a densely adherent broadly attached tumor, like nasopharyngeal fibroma, difficult if not impossible. The peculiarities of the surgical anatomy of nasopharyngeal fibroma will again be referred to in the section on treatment.

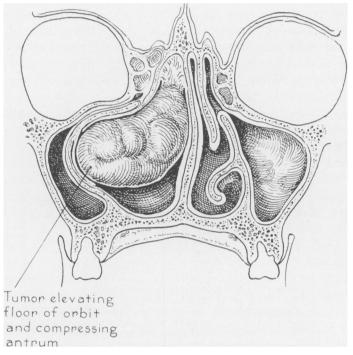


Fig. 7.—Lateral Growth of Nasopharyngeal Fibroma. Diagram of nasopharynx (coronal section) showing direction of growth frequently taken by nasopharyngeal fibroma. After plugging the posterior nasal cavity, the tumor compresses the antum, expands laterally into the maxilla, and may eventually reach the soft tissues of the cheek.

As an expanding tumor closes off the nasopharynx, voice changes may occur (*rhinolalia clausa*) and, also, a loss of sense of smell. In our series, there is no instance of erosion of the base of the skull, although it has been described by Goldsmith.<sup>10</sup>

The usual history in patients with juvenile nasopharyngeal fibroma applying to Memorial Hospital followed a rather definite pattern: an acute onset of recurrent epistaxis in boys from 12 to 15 years of age, usually preceded by

progressive nasal obstruction to which little or no attention had been paid. With each incidence of epistaxis, the nose had been packed and the hemorrhage temporarily arrested, only to recur with increasing frequency and severity. In most of the protracted cases there was marked local sepsis and sometimes partial necrosis of the tumor.

In about one-half of the cases in our series, previous operative attempts to remove the tumor had been made, frequently through the mouth and sometimes by splitting the soft palate. Usually two or three and in one case five operative efforts had been made. In almost every instance where surgical removal had been undertaken, the operator admitted that he had abandoned the attempt to completely remove the growth because of ensuing hemorrhage. In about 50 per cent of these failures, the diagnosis of "sarcoma" was made, the case was given up as hopeless, and the patient was referred to Memorial Hospital for palliative roentgen-ray therapy. In some of the cases, prior to referral to us, snare removal of a "nasal polyp" had been tried, or the bleeding point had been cauterized, or, in five cases, tonsillectomy and adenoidectomy had been performed in the belief that the tonsillar hypertrophy was the cause of the symptoms. All of these efforts had been followed by an increase in nasal bleeding.

In advanced and complicated cases such as described above, especially after incomplete surgical removal, there is usually an ill-defined, bulky, infected, partly necrotic, vascular tumor filling the nasopharynx and extending into one or both nasal cavities. The picture is sometimes one of subacute sepsis, pansinusitis, otitis media, mastoiditis, anemia, and malnutrition which, if unrelieved, results fatally despite the fact that the neoplasm is essentially benign and self-limited in growth.

In contrast to the tragic picture of the advanced and neglected cases, many others, properly managed, follow a relatively benign course provided that the symptoms of an expanding growth and hemorrhage can be kept under control. It is probable that some cases of nasopharyngeal fibroma of moderate size occur and regress spontaneously without ever being discovered or producing any marked symptoms. We have under observation at Memorial Hospital a case in which a nasopharyngeal tumor, undoubtedly a nasopharyngeal fibroma, was discovered by us on routine physical examination in a 15-year-old boy. The growth was not large enough to produce nasal obstruction and there had been no epistaxis. No treatment has been given. The tumor has been observed for two and one-half years and has remained about stationary in size. It is probable that such asymptomatic nasopharyngeal fibromas may often occur and regress when sexual maturity is reached.

# DIAGNOSIS

The histories of the 29 cases in the present series reveal that the correct diagnosis was seldom made by the physician first consulted. In many instances a clinical diagnosis of malignant tumor was made and without further inves-

tigation radiation therapy was advised; in other cases, after an unsuccessful attempt to remove the growth or the adenoids had been made, resulting in profuse hemorrhage, the patient was referred to us for treatment of "sarcoma." Such defeatist attitudes were the rule if the boy presented appreciable facial deformity or proptosis. Only occasionally, when a biopsy had been performed, had an accurate diagnosis of juvenile nasopharyngeal fibroma been made.

Although the tumor is admittedly rare and on the basis of incidence will not be recognized by the casual examiner, nevertheless the unique anatomic and clinical setting of this neoplasm should plainly suggest the possibility of nasopharyngeal fibroma. The clinical syndrome of rapidly progressive nasal obstruction, recurrent severe nosebleeds in *pubescent and adolescent males*, plus the presence of a discrete, ovoid or club-shaped, smooth, vascular and usually bulky nasopharyngeal mass, which has grown forward to block one or both choanae, justifiably warrants a clinical diagnosis of nasopharyngeal fibroma. It should be emphasized, however, that only by mirror examination of the nasopharynx through the open mouth, occasionally supplemented by direct rhinopharyngoscopic examination through the anterior nares, can the tumor be visualized and its essential character appreciated.

Stereoscopic radiographic examination of the base of the skull, paranasal sinuses, and nasopharynx is not only of value in determining the exact location and extent of the tumor, but is especially important in the differential diagnosis where a bulky growth in the head has brought about considerable deformity of the face or unilateral exophthalmos.

Differential Diagnosis. There are several extra-nasopharyngeal lesions which produce either nasal obstruction, epistaxis, unilateral exophthalmos, deafness, or facial asymmetry, singly or in combinations. Asymptomatic tume-factions may also be encountered in the nasopharyngeal or posterior nasal cavity which are occasionally mistaken for juvenile nasopharyngeal fibroma.

Choanal polyps can be distinguished from nasopharyngeal fibroma even when they occur in boys. These growths are frequently multiple, bilateral, pedunculated and tend to appear in individuals suffering from an allergy. They rarely exceed 1.5 to 2 cm. in diameter and resemble in every way the common and well-known pale, edematous polyps found in the anterior nasal cavities. Microscopic examination of the tissue conclusively establishes the diagnosis.

Pharyngeal tonsil (adenoids) is a common cause of nasal obstruction and nasal speech in juveniles. Hyperplastic lymphoid or granulation tissue in the nasopharynx may even be responsible for recurrent nosebleeds, although rarely profuse. There should be no difficulty in differentiating this condition from nasopharyngeal fibroma inasmuch as aggregates of lymphadenoid tissue, generally on the posterior nasopharyngeal wall, present a typical appearance consisting of irregular, conglomerate, soft, grayish-red masses which are distributed along the mucosa.

Benign minor salivary gland tumors, carcinoma, and malignant lymphomas, though uncommon in the head and neck of children and adolescents,

occur with much greater frequency in the nasopharynx and posterior nasal cavity than nasopharyngeal fibroma and, although they may produce symptoms similar to those of nasopharyngeal fibroma, in no way resemble it on clinical examination.

Chordoma of the upper cervical vertebrae, malignant tumors of the nasal accessory sinuses, and primary osseous neoplasms of the maxilla may produce nasal obstruction, epistaxis, and facial asymmetry, but by careful physical and roentgenographic examination these lesions can be tentatively diagnosed and differentiated from nasopharyngeal fibroma with little difficulty. We have seen chondroma in the posterior nasal cavity, tuberculosis of a retropharyngeal lymph node, and olfactory aesthesioneuroblastoma in the postnasal space, which clinically resembled nasopharyngeal fibroma in every way.

Biopsy.—An effort should always be made to establish the diagnosis by biopsy. It is prudent to hospitalize the patient for this procedure so that, if necessary, satisfactory anesthesia and facilities for control of profuse hemorrhage and for blood transfusions can be available. Deferment of biopsy is often wise if the patient is either bleeding actively or still recuperating from severe epistaxis or if there is appreciable infection in the nasopharynx, paranasal sinuses, or middle ear.

A straight biopsy forceps inserted directly backward through the nasal cavity or a curved forceps inserted through the open mouth may be used to remove a specimen from a nasopharyngeal tumor. The manipulations in either instance should be guided visually by a mirror or digitally by a finger.

Although biopsy is highly desirable and usually essential in the diagnosis of neoplasms, it must be conceded that in some cases of nasopharyngeal fibroma, despite the best of intentions, a positive histologic report cannot be obtained. In some cases, a recurrent growth, after several operative attempts, is largely necrotic and the local condition in the nasopharynx is one of advanced sepsis. Repeated biopsies in such instances may show nothing more than necrosis or granulation tissue. If the case is clinically typical in all other respects (age, sex, characteristic sequence of symptoms, anatomic location, gross appearance of the tumor), the diagnosis of nasopharyngeal fibroma may fairly be made even though not confirmed by a positive biopsy.

In our clinic where primary histologic confirmation is insisted upon, we nevertheless felt justified in making a diagnosis of nasopharyngeal fibroma in five cases in which a positive microscopic report on the biopsy specimen could not be obtained, despite repeated attempts at biopsy in three of these. The subsequent clinical course of these patients confirmed our initial belief that we were unquestionably dealing with nasopharyngeal fibroma.

## TREATMENT

A basic consideration in the treatment of nasopharyngeal fibroma is the fact that this tumor is anatomically and clinically benign, that with few exceptions it will begin to regress spontaneously at about the time of sexual maturity, and from then on will cause no further trouble. The real hazards consist

of the complications—hemorrhage, sepsis, facial deformity, and last but not least the effects of injudicious and over-aggressive attempts at complete eradication of the growth by surgery or radiation therapy. Provided that the aforementioned complications can be kept under reasonable control during the period of adolescence by moderate irradiation or limited surgery, and sex hormone therapy, spontaneous regression almost uniformly occurs at the time of sexual maturity.

The types of deforming surgical procedures particularly to be avoided in nasopharyngeal fibroma are approaches through the skin of the middle of the cheek (Langenbeck<sup>16</sup>), temporary detachment of bone (Ollier<sup>22</sup>) or exposure of the nasopharynx by splitting the soft palate. We shall discuss the more restrained and judicious forms of surgical procedure later in this report.

By over-aggressive and injudicious radiation therapy we mean any dose of interstitial radium (or radon) which is likely to produce radionecrosis in the tumor or adjacent palate, skin of the face or bones of the skull, or the application of roentgen-radiation in such dosages and through ports so located and of such size as to arrest or markedly retard the growth of the maxillae and other facial bones.

Once a diagnosis of nasopharyngeal fibroma is made, a systematic plan of management should be instituted, consisting of a combination of at least two and sometimes more methods of treatment. First, if epistaxis has been marked, both external carotid arteries should be ligated and measures taken to improve the local hygiene, dispensing, if possible, with any nasal packing or tamponage which inevitably incites a vicious cycle of further hemorrhage, repeated tamponage, and sepsis. Next, the administration of androgens adequate to induce the development of secondary sex characteristics without undue emotional imbalance should be instituted. The amounts of testosterone propionate and/or methyl testosterone required probably are very different for each individual and may be a function of his chronologic and "developmental" ages. At the same time radiation therapy (radium or roentgen-ray or both) should be given. Lastly, if the tumor is so large as to produce complete blockage of the nasal cavity with an edematous, partly necrotic mass or with symptoms of pansinusitis, then some form of partial surgical removal should be considered. The rationale and technic of these several therapeutic programs will next be discussed separately and in detail.

Ligation of the External Carotid Arteries.—This is one of the most direct and useful procedures in controlling arterial hemorrhages from any portion of the mouth, middle or upper pharynx, and nasal cavities. It is an entirely safe and harmless procedure to ligate permanently both external carotid arteries at one operation. Ligation of these blood vessels will not always completely control hemorrhage from the nasal cavities and nasopharynx, but it will markedly reduce it.

While a portion of the arterial supply of the nasal cavities is derived from the internal carotid artery by way of the ophthalmic artery and its anterior and posterior ethmoidal branches, this source can hardly cause any major difficulty. A much more troublesome source of hemorrhage from the nasopharynx and nasal cavities is venous—from the pterygoid plexus which communicates not only with the anterior facial vein but also with the veins of the cranial cavity by way of the superior ophthalmic vein. In any case, as compared with arterial hemorrhage, venous bleeding tends to be less profuse and the relatively low venous pressure may more easily be controlled by temporary light tamponage.

Sex Hormone Therapy.—This form of therapy can be started immediately in all cases without interfering with any other treatment measure. A clinical evaluation of the status of sexual development should be made by frequent examinations to determine any change possibly brought about by androgenic therapy. The state of the ossification centers, the level of urinary excretion of 17-ketosteroids, careful evaluation of secondary sex characteristics and emotional changes should be made at frequent intervals.

We had hoped at first to be able to control nasopharyngeal fibroma by endocrine therapy alone. This has not proved possible in the few instances in which its limited use has been employed. We have noted in these instances a definite and gradual elimination of the hemorrhagic tendency of the tumors associated with an acceleration of sexual maturation. In particular this association was observed in the case of an 18-year-old male who was treated for several months with limited benefit by radiation therapy. The intramuscular administration of 25 mg. of testosterone proprionate four times each week effected a marked change of his secondary sex characteristics and a rapid disappearance of the tumor in the space of one month.

Roentgen-ray Therapy.—Practically all hemangiomatous lesions are at least moderately radiosensitive. Fibrous tissue and fibromas in general are not radiosensitive. In our opinion radiation therapy is useful in nasopharyngeal fibroma mainly as a measure to reduce the angiomatous component of the tumor, thereby assisting in the control of the hemorrhage and to some extent in the arrest of its growth. We think it doubtful that radiation therapy in justifiable dosage can have much direct effect on the fibromatous elements of this neoplasm.

Radiation therapy is immediately indicated in bleeding nasopharyngeal fibroma but is of less value as initial treatment in bulky (6–8 cm.) edematous tumors in which the clinical picture is mainly one of facial deformity and nasal obstruction from an expanding tumor. Roentgen-ray therapy can be instituted promptly, preferably through the open mouth and hard palate in posteriorly placed growths. Additional roentgen therapy may also be given externally through the maxillae, but here some thought should be given to the possibility of permanent damage to the development of the facial bones. We have never been able to determine exactly what dose of roentgen therapy can be given safely over the germinal centers of growing bones. In general, we suggest in nasopharyngeal fibroma not more than 1000–1500 r in divided doses through circular portals 5 cm. in diameter over each maxilla (200–250 K.V., 50 cm. T.S.D., 1–1½ mm. copper filtration). Even this dose may result in some

flattening of the cheeks as the boy reaches full stature. The dose through the hard palate may be greater (2000–2500 r) with less danger of late deformity, employing peroral circular or oval portals 3–4 cm. in diameter. By cross-firing the tumor through these three portals, a significant roentgen-ray dose can be delivered into the tumor site.

Radium Therapy.—If the growth is bulky (5 cm. or more in diameter), no significant radiation dose which may be considered safe can be distributed throughout the mass by interstitial radium or radon. If the tumor is extremely vascular, the insertion of a trocar for implantation of seeds or the introduction of a radium needle is attended by profuse hemorrhage, necessitating immediate and firm tamponage. Under such conditions, the procedure appears to cause as much harm as good even though the radiating sources remain in place.

Radium therapy in the form of gold radon implants is one of the most useful methods for control of nasopharyngeal fibroma provided the tumor is less than 5 cm. in diameter and the dosage is fractionated and combined with other forms of treatment such as supplemental roentgen-radiation to the cheeks and palate and hormone therapy. Seeds in doses of 5–6 mcs. (unit strength I–I.5 mcs.) can be inserted either through the nasal cavity and/or the soft palate with the aid of the exploring finger passed behind the soft palate into the nasopharynx. The dose may be repeated once or twice at intervals of about a month. Delevan<sup>6</sup> and Figi<sup>9</sup> have recommended that the main reliance be placed on this method of treatment. Radon seeds are also useful for the treatment of residual tumor or re-growth after surgical removal of large neoplasms which were too bulky for control by radiation therapy in the beginning.

Surgical Excision.—It is not possible to obtain even a moderately wide surgical exposure of the nasopharynx except by operative procedures which are not only immediately hazardous but also permanently deforming and disabling. Whether the surgical approach is made through the maxilla anteriorly, the alveolar process, or the palate, the permissible size of the opening through the bone is limited to 3-4 cm., and the destination of the approach, that is the cavity of the nasopharynx, is at a depth of 9-10 cm. from the surface. Deliberate and continued surgical dissection at such a depth in a highly vascular zone and through such a narrow aperature is simply not possible. For these technical reasons, and the almost inevitable postoperative recurrence, surgical removal of nasopharyngeal fibroma, except when absolutely necessary, has never been regarded enthusiastically by experienced observers. Nevertheless, in the larger tumors with marked facial deformity and progressive destruction of the maxilla or other adjacent bony structures by pressure necrosis, the bulk of the tumor should be removed or at least reduced by some expedient other than radiation therapy. To this end several methods have been employed by others, such as avulsion by wire snare through the nasal cavity or mouth, destruction of the tumor in situ by endothermy, and by the direct trans-maxillary surgical approach.

We have used several methods for the surgical removal of these and other varieties of tumors in the naso-pharynx, the selection depending mainly on the position and surgical anatomy of the growth. In some cases where the nasopharyngeal fibroma was not too large, we have employed the wire snare or simple avulsion by digital manipulations through the anterior nares and mouth. Such simple maneuvers have at least the advantage of being nondeforming. In others, we have approached the nasal cavity and nasopharynx through an incision in the upper gingivobuccal gutter (Rouge), but have found that unless a considerable portion of the nasal bones and nasal septum are rongeured away this approach has little advantage over simple dilation of the anterior nares. In some cases where the tumor extended directly forward through the antrum and anterior wall of the maxilla, we have developed and reflected a cheek flap (Weber-Ferguson incision), exposing the tumor directly from the front. One of the most useful, least deforming, and least disabling approaches to the nasal cavity and nasopharynx is through the alveolar process anteriorly, just to one or the other side of the midline. If teeth are present, about 4 or 5 are extracted, and the entire thickness of the alevolus removed exposing both the antrum and nasal cavity on that side. The party wall between the nasal cavity and the antrum is then rongeured away and a fairly wide exposure of the nasopharynx obtained with adequate accessibility to the ethmoid and sphenoid sinuses. The latter operation is followed by surprisingly little disability. The opening in the alveolus shrinks down to about 2 cm. in diameter and a dentist can provide a prosthesis which completely covers the defect, inconveniencing the patient no more than would an ordinary full upper dental plate.

After the anterior aspect of the tumor has been exposed by an adequate trans-maxillary approach, the growth must be further mobilized from its attachment at the base. If it were possible to dissect the mass from the underlying bone, periosteum, or fascia, it would then be feasible to enucleate the tumor in its entirety. Due to the irregular bony walls of the nasopharyngeal cavity, however, in addition to the generally broad dense attachment of nasopharyngeal fibroma, complete surgical removal of the neoplasm cannot be effected, unless it is limited to the basilar portion of the occipital bone where the surface is smooth. Residual tumor, therefore, will almost always be left behind, despite the good intentions of the surgeon. In many cases appreciable recurrences, frequently ulcerated and infected, will appear and have to be treated with interstitial radiation.

The indication for any given method of surgical removal must be decided by the clinical setting in each case. The selection of the proper time for operation may also be important. In general, we suggest deferment of any surgery in cases without marked deformity, hemorrhage, or sepsis. Such cases should be continued indefinitely under sex hormone and radiation therapy. Where hemorrhage is a serious complication or where surgical removal of the tumor is contemplated, a bilateral ligation of the external carotid arteries should first be made, hormones given, and radiation therapy instituted. By these less aggressive measures, the hemorrhages may be arrested and the tumor reduced in size or at least brought under control. In any case, these preliminary precautions will markedly reduce the amount of bleeding at operation, if this finally becomes necessary.

Table I.—Juvenile Nasopharyngeal Fibroma			
Tabulation of Methods of Treatment and Their Complications			

Method of Treatment	Number of Cases	Case Number	Complications
A. X radiation	9	4 8** 9** 11 12 13** 15** 19**	Dryness of nasopharynx Atrophy of maxilae None Dryness of nasopharynx None None Otitis media; coarse feature: Otitis media Died of rheumatic fever
B. Interstitial radiation	5	3 5 *7 21 29**	Necrosis of palate Dryness of nasopharynx Pansinusitis None None
C. Interstitial and X radiation	2	2 6	Dryness of nasopharynx Dryness of nasopharynx
D. Surgical excision	4	*22 *24 *25** *26	None None None None
E. Surgical excision combined with X radiation	1	*27	None
F. Surgical excision combined with interstitial radiation	2	1 *28	Died of brain abscess None
G. Surgical excision combined with interstitial and X radiation	4	*10 *16** *17 *18**	Died of brain abscess Necrosis of hard palate Otitis media None
H. Hormones only	1	14	None
I. No treatment, observation only	1	23	None

<sup>\*</sup> Ligation of external carotid arteries.

## METHODS OF TREATMENT SUMMARIZED AND COMPARED

Once the diagnosis of juvenile nasopharyngeal fibroma has been established, a therapeutic program should be adopted, subject to change as required by ensuing clinical developments. As already mentioned, there is no one type of treatment which is a panacea for any given case and in practically all instances a combination of methods must be employed. Obviously, aside from

<sup>\*\*</sup> Received hormone therapy.

periodic examination, an active therapeutic regimen is not indicated for the occasional case where the tumor is discovered during routine physical examination with no symptoms referable to it. In the absence of nasal obstruction, nose-bleeds, impairment of hearing, infection of the paranasal sinuses or middle ear, facial deformity, exophthalmos, headache or any discomfort about the head, or evidence of progressive enlargement or significantly increased vascularity of the neoplasm, a policy of watchful waiting is justified. This policy was followed in the case of one of our patients, age 15 on admission, and during a two-year period of observation the growth has remained stationary and asymptomatic.

Endocrine therapy was the only form of treatment which was prescribed in one case. In ten others it was combined with some form of radiation therapy, surgery, or both. With the combination of methods, sex hormone therapy was either utilized alone as the initial treatment and, following its failure to control the growth satisfactorily, radiation therapy was instituted, or both forms of treatment were begun simultaneously. While no definite regression of the tumor was noted in any case in which the patient received only male sex hormone, it was our clinical impression that hemorrhages usually diminished in frequency and severity following the use of hormones. The basis for this observation may be due to the considerations included under etiology.

In our series, some form of radiation therapy, either alone or combined with one or more surgical procedures, was resorted to in 23 cases (Table I). In nine of these, roentgen therapy was the only form of radiation employed and in this group late complications (dryness of nasopharynx, atrophy of maxillae, coarsening of features), attributable to the high dosages used to control the tumor, were frequent, indicating that no one method of treatment can be depended on without courting the hazards of over-aggressiveness. Because of its possible effect on the growth centers of the facial bones, roent-genradiation should preferably be reserved for patients 18 years of age or older.

Interstitial radiation therapy was employed alone in five cases and was followed by serious complications in three instances. In one, necrosis of the hard palate resulted, due to an unnecessarily large dose of gold seeds (total of 34 mcs. inserted at three sittings over a period of two years). In two, even more unfortunate developments followed massive doses of interstitial radiation (total dose of 32 mc. in one; 20 mc. in another after administration of 3000 r of 200 K.V. therapy through a single 6 cm. cheek portal). Both patients developed extensive osteonecrosis extending into the sphenoid bone and finally succumbed to brain abscess. At that time, about 20 years ago, we believed it essential to eradicate the growth completely in order to cure the patient and were not cognizant of the fact that simple control of tumor activity until sexual maturity had been attained was all that was necessary.

From an analysis of our data, it is noteworthy that as a rule smaller doses of interstitial and roentgenradiation will effectively control symptoms if the patient is receiving continued and adequate endocrine therapy, that bulky tumors producing facial deformity or exophthalmos are followed by no complications when treated by primary surgical excision (four cases), and that residual tumors can be readily controlled with small doses of gold seeds inserted at frequent intervals.

During the period of radiation therapy, suppuration in the nasal accessory sinuses or middle ear occasionally supervenes and rarely mastoiditis may occur. Such sepsis, together with the untoward systemic effect of radiation therapy in general, makes hospitalization for the treatment of many of these patients mandatory. In this way local hygienic care, adequate nutritional therapy, blood transfusions, and chemotherapy are made available.

### PROGNOSIS

As has been previously stated, if complications of hemorrhage, sepsis (pansinusitis, otitis media, etc.), and facial deformity by an expanding tumor can be prevented or even markedly reduced, little or no harm can come to the patient with nasopharyngeal fibroma and the growth will regress spontaneously in practically all instances. From a study of our cases it is plain that many of the most serious complications are brought on primarily by aggressive and ill-conceived therapeutic measures, such as poorly planned attempts at surgical removal without preliminary arterial ligation and inadequate exposure of the nasopharynx and secondarily by unduly vigorous endeavors to control further growth by radiation therapy. In such cases the patients would have been much better off without any treatment whatever.

Juvenile nasopharyngeal fibroma is not essentially a malignant tumor. It does not invade adjacent tissues and its destructive capacities are entirely due to pressure atrophy of contiguous structures by the enlarging mass. So far as we know, there is no well authenticated instance of malignant transformation of this tumor. In one case of the present series, the patient developed numerous recurrences, one of which showed on microscopic examination unusual cellularity and localized areas of malignant transformation. Seven subsequent recurrences were examined histologically, however, and none of these revealed any unsual changes. During the three years that have elapsed since the suspected malignant recurrence was noted, the tumor has not shown any evidence clinically of malignant propensities. Although Shaheen<sup>26</sup> stated that some of his cases underwent "carcinomatous and sarcomatous" changes, as mentioned earlier in this discussion, his series was not critically selected and in our opinion his conclusions are therefore unacceptable. We suspect that Shaheen's cases of "malignant transformation" were actually malignant nasopharvngeal cancers and not nasopharvngeal fibromas in the beginning. Two isolated case reports of malignant nasopharyngeal fibroma appeared in the literature in 1904 and 191214, 5 but here again the presented evidence is entirely unconvincing. Some of these errors undoubtedly arose from a mistaken morphologic interpretation of a highly vascular and highly cellular tumor as "angiosarcoma." Although the tumor in Wirth's patient28 in the beginning simulated nasopharyngeal angiofibroma in some respects, the predominant

picture was that of chondrosarcoma, and it metastasized as such; since this case is complex and at complete variance with the accepted criteria necessary for a diagnosis of juvenile nasopharyngeal angiofibroma, it would hardly be reasonable to classify it as such.

In brief, the prognosis in a case of juvenile nasopharyngeal fibroma properly managed is excellent so far as the question of life is concerned. The greatest hazard both as regards life and permanent disability lies in injudicious treatment either by radiation therapy or surgery. As we have pointed out, the growth is practically incurable from the standpoint of its complete eradication and prevention of recurrences before sexual maturity is attained. After sexual maturity has been reached, however, the growth will disappear spontaneously in most instances.

#### END-RESULTS

Practically all patients with nasopharyngeal fibroma should recover and become symptom free when sexual maturity is reached. In our series there were two deaths due to brain abscess, resulting from over-dosage with interstitial radiation. A third patient succumbed to acute rheumatic fever just after the onset of treatment for nasopharyngeal fibroma.

#### SUMMARY

The thesis has been advanced that juvenile nasopharyngeal fibroma occurs only in pubescent males. For other reasons, namely its spontaneous or readily induced regression with the appearance of full sexual development, a sex-endocrine relationship for this tumor probably exists. Although its histogenesis has not been definitely established, a vascular origin is proposed in this report. This proposal is based on specific involutional changes which can be induced with male sex hormone therapy and irradiation. The induction of vascular changes by hormone administration has considerable experimental support.

Even though nasopharyngeal fibroma is essentially benign, it frequently produces serious and disabling symptoms because of its progressive growth and tendency to profuse hemorrhage. The indications, methods, and hazards of both radiation and surgical treatment in combating these symptoms are discussed. The trend on the Head and Neck Service at Memorial Hospital has been to employ one or more of these methods of treatment in an effort to control the growth since, in most cases, spontaneous regression can be expected after sexual maturity. Aggressive measures either by irradiation or surgery will never completely and permanently eradicate the neoplasm and will involve considerable risk of ultimate disability or even death.

### REFERENCES

- Allen, Edgar: Sex and Internal Secretions. A Survey of Recent Research, ed. 2, Baltimore, Williams & Wilkins, 1939.
- <sup>2</sup> Bensch, H.: Beitrage zur Beurtheilung der Chirurgischen Behandlung der Nasenrachenopolypen, Breslau, E. Morgenstern, 1878.

- S Chaveau, C.: Histoire des Maladies du Pharynx, Paris. J. B. Bailliere et Fils, vol. 5, 1006.
- 4 Chelius, J. M.: System of Surgery, vol. 2 (translated by John F. South). London, Henry Renshaw, 1847.
- Dabney, V.: Fibroma of the Nose and Nasopharynx with Sudden Malignant Degeneration. Laryngoscope, 22: 960-964, 1912.
- <sup>6</sup> Delevan, D. B.: The Effect of Radioactivity upon Nasopharyngeal Fibromas. Med. Rec., 1915.
- <sup>7</sup> Edwards, E. A., J. B. Hamilton, S. Q. Duntley, and G. Hubert: Cutaneous Vascular and Pigmentary Changes in Castrate and Eunnuchoid Men. Endocr., 28: 119-128, 1941.
- 8 Ewing, J.: Neoplastic Diseases, ed. 4, Philadelphia, W. B. Saunders Co., 1941.
- 9 Figi, F.: Fibromas of Nasopharynx. J. A. M. A., 115: 665-671, 1940.
- <sup>10</sup> Goldsmith, P. G.: Nasopharyngeal Fibroma; a Clinical and Pathological Study. J. Laryngol. & Otol., 38: 565-574, 1923.
- 11 Gosselin, Paul: Clinique Chirurgicale de l'hôpital de la Charité, ed. 2, Paris, 1876.
- <sup>12</sup> Hamilton, J. B.: Changes in Nasal Mucosa of Monkeys (Macaca rhesi) and Humans by Male Hormone Substances. Proc. Soc. Exper. Biol. & Med., 37: 366-369, 1937.
- <sup>13</sup> Hippocrates: Oeuvres Completes, Traduction Nouvelle par E. Littre, Paris, J. B. Bailliere, 1839-1861, 10v.
- 14 Jackson, C. D.: Fibroma of the Nasopharynx, Tracheotomy, External Carotid Ligation, Extirpation, Laryngoscope, 14: 267-270, 1904.
- 15 Jackson, C., and G. M. Coates: The Nose and Throat and Ear and Their Diseases. Philadelphia, W. B. Saunders Co., 1930.
- <sup>16</sup> Langenbeck, C. J. M.: Nosologie und Therapie der Chirurgischen Krankheiten, Göttingen, vol. 5, 1834.
- <sup>17</sup> Legouest, C.: Proceedings of Surgical Society of Paris, 1865.
- 18 McGrath, E. J., and L. G. Herrmann: Influence of Estrogens on the Peripheral Vasomotor Mechanism. Ann. Surg., 120: 607-615, 1944.
- <sup>19</sup> Mortimer, H., R. P. Wright and J. B. Collip: Effect of Administration of Oestrogenic Hormones on Nasal Mucosa of Monkey (Macaca mulatta). Canad. M. A. J., 35: 503-513, 1936.
- <sup>20</sup> Idem: Effect of Oestrogenic Hormones on Nasal Mucosa; Their Role in Naso-Sexual Relationship; and Their Significance in Clinical Rhinology. Canad. M. A. J., 335: 615-621, 1936.
- <sup>21</sup> New, G. B., and F. A. Figi: Treatment of Fibromas of the Nasopharynx: Report of 32 Cases. Am. J. Roentgenol., 122: 340-343, 1924.
- <sup>22</sup> Ollier Quoted by Nicholas Senn: The Pathology and Surgical Treatment of Tumours, ed. 2, Philadelphia, W. B. Saunders & Company, 1900.
- <sup>23</sup> Reynolds, S. R. M., and F. I. Foster: Specific Differences in Cholinergic Action of Estrogen. Am. J. Physiol., 131: 200-202, 1940.
- <sup>24</sup> Reynolds, S. R. M., J. B. Hamilton, J. R. DiPalma, and G. Hubert: Dermovascular Actions of Certain Steroid Hormones in Castrate, Eunnuchoid and Normal Men. J. Clin. Endocr., 2: 228-236, 1942.
- <sup>25</sup> Rouge: Quoted by Nicholas Senn: The Pathology and Surgical Treatment of Tumours, ed. 2, Philadelphia, W. B. Saunders & Company, 1900.
- <sup>26</sup> Shaheen, H. B.: Nasopharyngeal Fibroma. J. Laryng. and Otol., 45: 259-264, 1930.
- <sup>27</sup> Soskin, S., and L. B. Bernheimer: Mechanism of the Estrogen Effect on the Nasal Mucosa in Atrophic Rhinitis. Proc. Soc. Exper. Biol. & Med., 42: 223-224, 1939.
- <sup>28</sup> Wirth, J. E., and M. B. Shimkin: Chondrosarcoma of the Nasopharynx Simulating Juvenile Nasopharyngeal Fibroma. Arch. Path., 36: 85-88, 1943.
- <sup>29</sup> Verneuil: Quoted by H. Bensch: Beitrage zur Beurtheilung der Chirurgischen Behandlung der Nasenrachenpolypen. Breslau, E. Morgenstern, 1878.