Dr. Rahul Bagla ENT Textbook
Ultimate Guide – Makes You Best

Juvenile Nasopharyngeal Angiofibroma

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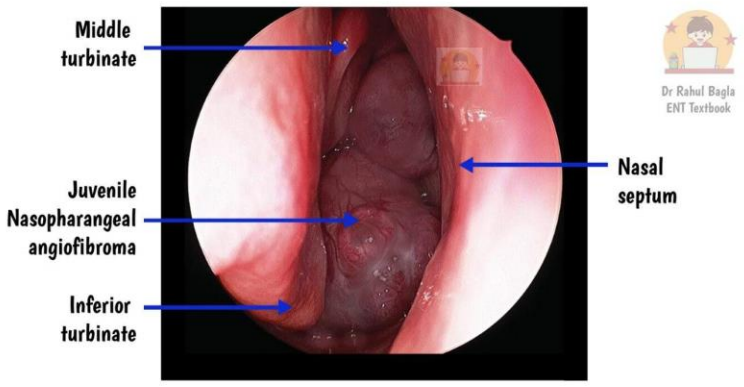
Juvenile Nasopharyngeal Angiofibroma is the most common benign tumour of the nasopharynx, almost exclusively affecting adolescent males, typically around 14 years (range 7–19 years). Although benign, it is highly aggressive and spreads to nearby structures through natural openings like foramina and fissures.



Diagnostic nasal endoscopy showing globular pink mass (JNA) in the posterior part of the nasal cavity, pushing septum to the opposite side.

Aetiology

The **exact cause is unknown**, but hormone receptors (androgen, estrogen, progesterone) have been found in the tumour. Two main theories explain its origin:

1. **Testosterone Dependency Theory**: This theory is supported by the tumour's occurrence in adolescent males during puberty. The presence of male sex hormones, particularly testosterone, is believed to **activate a pre-existing vascular hamartomatous nidus** in the nasopharynx, causing it to grow into a full-fledged tumour. Therefore, hormonal factors play a significant role in its development.
2. **Branchial Arch Artery Theory**: This theory suggests that JNA arises from the **incomplete regression of the first branchial arch artery** (maxillary artery), particularly in the region of the **sphenopalatine foramen** during embryonic development. This failure leaves behind a vascular remnant, a hamartomatous nidus, which later receives blood supply from the sphenopalatine and maxillary arteries and is stimulated by androgens at puberty. This theory explains the tumour's typical location and its primary blood supply.
   A primary aberration of the **pituitary-gonadal axis** is suggested but not proved.

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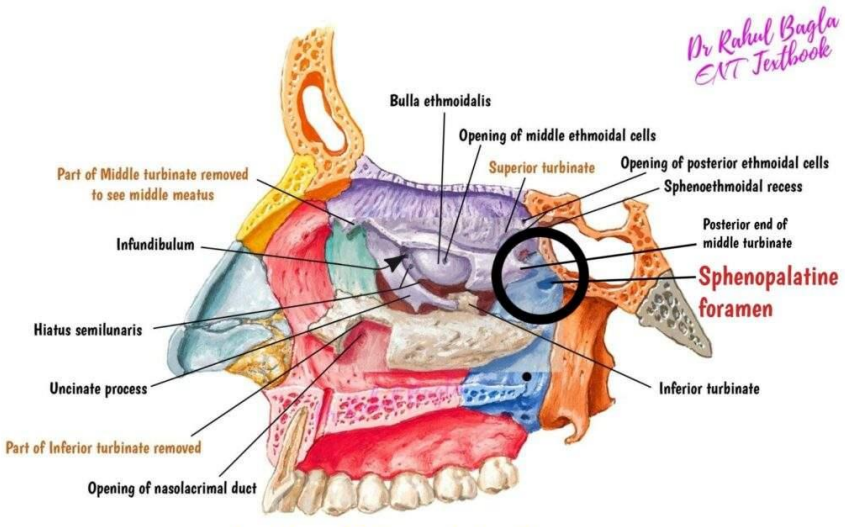
Angiofibromas: Composition and Surgical Considerations

Angiofibromas are **vascular malformations** that are **firm, non-encapsulated**, highly fibrovascular tumours made of **fibrous + vascular tissue**. There is no true capsule; instead, the epithelial lining may thicken to form a **pseudo-capsule**.

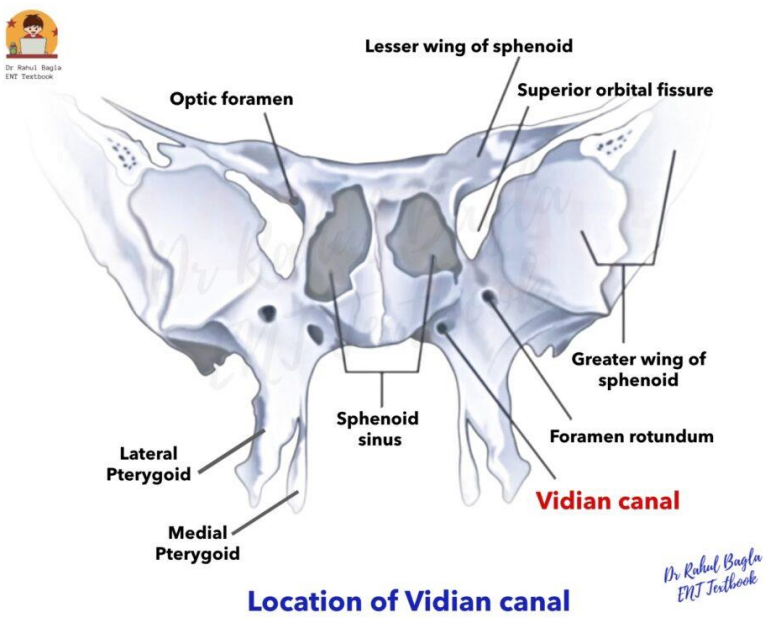
1. **Components:** **Angiomatous (vascular) part** – more in younger patients. **Fibrous part** – increases with age.
2. **Blood vessel structure:** The tumour's blood vessels **lack a muscular layer**, so they are incapable of contracting, which makes them prone to severe bleeding during surgical dissection
3. **Surgical challenge:** Prone to **severe bleeding** during surgery. Bleeding **cannot be controlled with adrenaline**. The best approach is to **dissect along the pseudo-capsule** to minimise bleeding.

Site of origin and growth

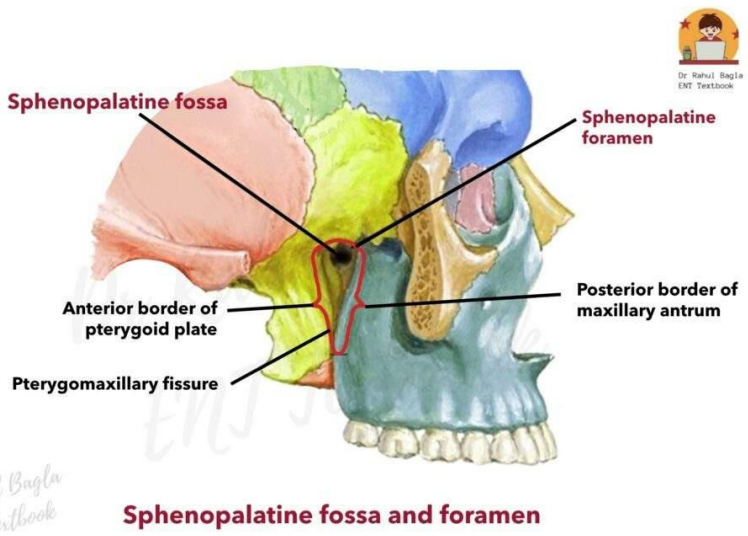
JNA is believed to originate from the posterior part of the lateral wall of the nasal cavity, from the superior margin of the **sphenopalatine foramen and the vidian canal**. The sphenopalatine foramen is present 1 cm behind the posterior end of the middle turbinate. From this starting point, the tumour grows aggressively into the nasopharynx, which is why it is often called a "nasopharyngeal angiofibroma."



Location of Sphenopalatine foramen



Location of Vidian canal



Sphenopalatine fossa and foramen

Relevant anatomy of the Sphenopalatine foramen

The **sphenopalatine foramen** is a key anatomical structure in the lateral wall of the nasal cavity, acting as a communication pathway between the **pterygopalatine fossa** and the **nasal cavity**. It's situated in the posterolateral wall of the nasal cavity and is clinically significant because it's the most common site of origin for **Juvenile Nasopharyngeal Angiofibroma (JNA)**. Several important neurovascular structures pass through the sphenopalatine foramen to supply the nasal cavity and nasopharynx. These include:

- **Sphenopalatine artery**: This is a terminal branch of the **internal maxillary artery** and is the main artery of the nasal cavity.
- **Posterior superior and inferior nasal nerves**: These branches of the **maxillary nerve (V2)** supply sensory innervation to the nasal cavity and nasopharynx.
- **Sphenopalatine ganglion**: This parasympathetic ganglion is also known as the Meckel's ganglion. It sends secretomotor fibres to the nasal and palatine glands.

Sphenopalatine Fossa Boundaries

- **Anteriorly:** The posterior wall of the **maxillary antrum** (or maxillary sinus) forms the anterior boundary.
- **Posteriorly:** The anterior surface of the **pterygoid plate** defines the posterior boundary.
- **Laterally:** The **infratemporal fossa** lies lateral to this region.
- **Medially:** The **lateral wall of the nasopharynx** constitutes the medial boundary.

This fossa serves as a crucial anatomical crossroads, housing the **sphenopalatine ganglion**, branches of the **maxillary nerve**, and the **terminal branches of the maxillary artery**. Its location and connections are highly relevant in conditions like Juvenile Nasopharyngeal Angiofibroma.

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Blood Supply of Nasopharyngeal Fibroma

- **External carotid artery (majority)** – Internal maxillary artery, ascending pharyngeal artery, palatine arteries
- **Internal carotid artery (less common)**, usually in larger tumours – Sphenoidal branches, ophthalmic artery.

Blood Supply of Nasopharyngeal Fibroma according to the site of the extension

- Nasopharyngeal fibromas receive their blood supply primarily from the internal maxillary artery and its branches, including the sphenopalatine and pterygovaginal arteries. These vessels provide blood to the tumour at its origin in the anterior nasopharynx and posterior nasal cavity.
- As the tumour grows larger and extends into areas such as the sphenoid sinus, infratemporal fossa, or parapharyngeal space, it acquires additional blood supply from other branches of the ECA, such as the accessory meningeal, ascending pharyngeal, and ascending palatine arteries.
- In advanced stages, the tumour's blood supply becomes more complex, with contributions from the internal carotid arteries (ICAs) and, in some cases, the vertebral arteries. This bilateral blood supply is a characteristic of more advanced tumours, especially large juvenile angiofibromas.

Spread of Nasopharyngeal Fibroma

Nasopharyngeal fibroma, while benign, is a locally invasive tumour that tends to spread through anatomical spaces and foraminae, destroying adjoining structures. The tumour may extend into various areas, resulting in distinct symptoms and complications:

Medial spread from the sphenopalatine foramen

- **Anteriorly into the nasal cavity and paranasal sinuses**: When the tumour extends into the nasal cavity, it can cause nasal obstruction, epistaxis (nosebleeds), and nasal discharge. From there, the tumour can invade the maxillary, sphenoid, and ethmoid sinuses, contributing to further complications and obstruction.
- **Posteriorly into the nasopharynx.**

Lateral spread from the sphenopalatine foramen

- **Laterally into the sphenopalatine and Infratemporal Fossae**: The tumour may spread laterally through the sphenopalatine foramen into the sphenopalatine fossa, and from there through the pterygomaxillary fissure into the infratemporal fossa and cheek. When the tumour is in the infratemporal fossa, it causes anterior bowing of the posterior wall of the maxillary sinus (*antral sign or* ***Holman-Miller sign*** *seen on radiology*) is pathognomonic of angiofibroma. From the infratemporal fossa, it can erode the greater wing of the sphenoid to reach the middle cranial fossa.

Superior spread from the sphenopalatine foramen

- **Orbit**: The tumour can reach the orbit via the inferior orbital fissure, leading to proptosis (bulging of the eye) and/or optic nerve compression, which can cause visual disturbances. And then through the superior orbital fissure, it enters the middle cranial fossa.
- **Superiorly into the cranial Cavity**: The tumour can extend into the cranial cavity in several ways:
  – Anterior Cranial Fossa: Through the roof of the ethmoids or the cribriform plate.
  – Middle Cranial Fossa: By eroding the floor of the middle cranial fossa or indirectly by invading the sphenoid sinus and sella turcica. In the former case, the tumour lies lateral to the internal carotid artery; in the latter case, medial to the artery.

Posterior spread from the sphenopalatine foramen

- **Through the pterygoid plates.** The spread will be through natural openings in the pterygoid plates (foramen rotundum and vidian canal). The maxillary nerve comes from the brain into the sphenopalatine fossa.
  In cases of intracranial tumour growth, juvenile angiofibromas are primarily located in the extradural space. Dural infiltration or brain involvement is rare but can occur.

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Spread Pathways of Nasopharyngeal Fibroma

Direction of Spread	Route of spread	Structures Involved	Clinical Features
Medial Spread	From Sphenopalatine Foramen → Anterior Nasal Cavity	Nasal cavity	Nasal obstruction, epistaxis, nasal discharge
	From Sphenopalatine Foramen → Posterior Nasopharynx	Nasopharynx	Postnasal drip, nasal speech
	Extension to Paranasal Sinuses	Maxillary, sphenoid, ethmoid sinuses	Sinusitis symptoms, obstruction
Lateral Spread	Sphenopalatine Foramen → Sphenopalatine Fossa → Pterygomaxillary Fissure → Infratemporal Fossa	Infratemporal fossa, cheek	Cheek swelling, facial pain
Superior Spread	Inferior Orbital Fissure	Orbit	Proptosis, cheek swelling, frog-face deformity, optic nerve compression
	Superior Orbital Fissure	Orbit	Ophthalmoplegia, visual disturbance
	Ethmoid Roof / Cribriform Plate	Anterior cranial fossa	CSF leak, headache
	Erosion of Middle Cranial Fossa Floor	Middle cranial fossa	Temporal lobe compression, seizures
	Via Sphenoid Sinus & Sella Turcica	Pituitary region	Endocrine disturbances
Posterior Spread	Through Pterygoid Plates (Foramen Rotundum & Vidian Canal)	Pterygopalatine fossa, base of skull	Trigeminal nerve symptoms (facial numbness/pain)
	Intracranial (Extradural, rarely intradural)	Cavernous sinus region	Cranial nerve palsies, severe headache

Clinical Features

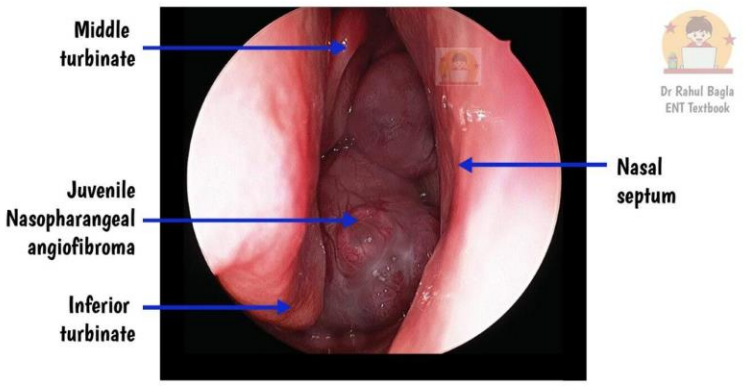
The patient usually presents with nasal obstruction (80%) but also epistaxis (50%), headache (25%) and facial swelling (15%). He can also have eye symptoms and signs (diplopia, proptosis) and unilateral otological symptoms (OME).

1. **Age and Sex**: This tumour predominantly affects males aged 10-20 years. It is rarely seen in older persons and females.
2. **Epistaxis**: Profuse, recurrent, and spontaneous nasal bleeding are the most common symptoms. Patients often become markedly anaemic due to repeated blood loss.
3. **Nasal Obstruction and Speech Changes**: Progressive nasal obstruction caused by the tumour mass in the postnasal space leads to hyponasal speech. There can be snoring and features of obstructive sleep apnoea.
4. **Hearing Loss and Otitis Media**: Conductive hearing loss and otitis media with effusion occur due to the obstruction of the eustachian tube by the tumour.
5. **Nasopharyngeal Mass**: The tumour appears as a sessile, lobulated, or smooth mass in the nasopharynx, obstructing one or both choanae. It is pink or purplish and has a firm consistency. Digital palpation should be avoided until the time of the operation.
6. **Frog facies.** Long-standing tumours may present with proptosis, swelling of the cheek, and broadening of the nose.
7. **Trismus:** May be seen in long-standing tumour in the infratemporal fossa.
8. **Other Clinical Features**: There may be involvement of the second, third, fourth, and sixth cranial nerves.

Diagnosis and Investigations of Nasopharyngeal Fibroma

The diagnosis of nasopharyngeal fibroma is primarily based on its typical clinical and radiological findings. Biopsy of the tumour is generally avoided due to the high risk of severe bleeding. If a biopsy is necessary to differentiate it from other tumours, it should be performed under general anaesthesia with all arrangements in place to control bleeding and provide blood transfusions if needed.

1. Nasal Endoscopy: This procedure reveals a sessile, lobulated, or smooth reddish mass in the nasal cavity.



Diagnostic nasal endoscopy showing globular pink mass (JNA) in the posterior part of the nasal cavity, pushing septum to the opposite side.

2. Contrast-Enhanced Computed Tomography (CT) Scan Nose & PNS: It is the investigation of choice, and it is essential for staging the tumour, which guides treatment planning. It has replaced the traditional X-rays. After a patient is injected with a contrast dye, the tumour shows up as a bright, enhanced mass. This helps the scan reveal its size, spread, and whether it has destroyed or displaced surrounding bones.

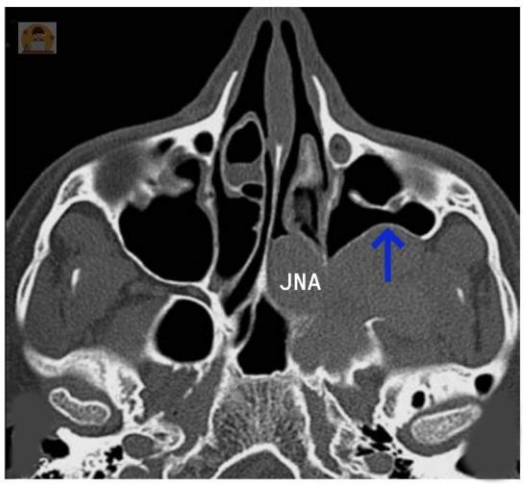
The tumour causes several key signs on the scan:

- Anterior bowing of the posterior wall of the maxillary sinus (also known as the antral sign or **Holman-Miller sign**) is a definite indicator of an angiofibroma.
- Posterior bowing of the pterygoid plates and erosion of the sphenoid sinus can be seen.
- The scan will also show a widening of the pterygomaxillary fissure, vidian canal, pterygopalatine fossa, and sphenopalatine foramen.
- The widening of the pterygoid wedge is called **Ramaharan's sign**.

During surgery, the surgeon drills the base of the pterygoid to remove all parts of the tumour and reduces the rate of recurrence of JNA. A post-surgery CT scan will then reveal the **"chopstick sign**," which is caused by the separation of the two pterygoid plates, resulting in parallel lines.

Radkowski Classification of Juvenile Angiofibroma.

Stage	Description	Direction of spread
1a	Tumour limited to nasal cavity & nasopharynx	Medial
1b	Tumour extends to one or more paranasal sinuses from nasal cavity.	Medial
2a	Minimal extension into pterygopalatine (sphenopalatine) fossa	Lateral
2b	Complete occupation of pterygopalatine fossa ± orbital involvement	Lateral
2c	Extension into infratemporal fossa ± cheek or pterygoid plate involvement	Lateral
3a	Minimal intracranial extension (skull base erosion, middle cranial fossa, or pterygoids)	Intracranial
3b	Extensive intracranial extension ± cavernous sinus involvement	Intracranial

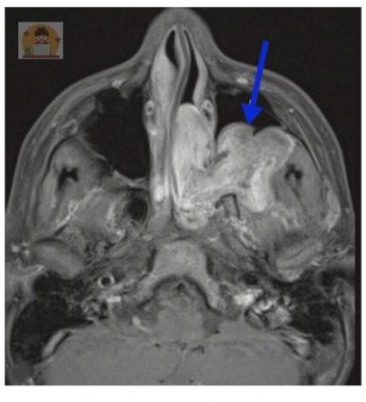


Axial CT bone windows showing massive juvenile nasopharyngeal angiofibroma within the widened left pterygopalatine fossa, laterally extending into the infratemporal fossa, anteriorly into the left nasal cavity and posteriorly along the medial pterygoid plates into the sphenoid sinus. The anterior bowing of the posterior wall of the maxillary sinus (antral sign or Holman-Miller sign, blue arrow) is pathognomonic of angiofibroma

3. Magnetic Resonance Imaging (MRI): MRI is superior for defining orbital and intracranial soft tissue extensions. An MRI is recommended in tumours with suspected intracranial extension, cavernous sinus involvement, orbital extension and carotid involvement. On a specific type of MRI scan called a T2 image, the tumour can have a **"salt-and-pepper" appearance**. This happens because:

- The fibrous parts of the tumour look white (salt).
- The blood vessels within the tumour show up as dark spots (pepper).

While this "salt-and-pepper" pattern is typically associated with another type of tumour called paragangliomas on T1 scans, it is more commonly seen in juvenile angiofibroma on T2 scans.



Axial T1-weighted magnetic resonance (MRI) image confirming relationships of the tumor. The solid arrow showing anterior bowing of the posterior wall of the maxillary sinus, also known as the antral sign or Holman-Miller sign.

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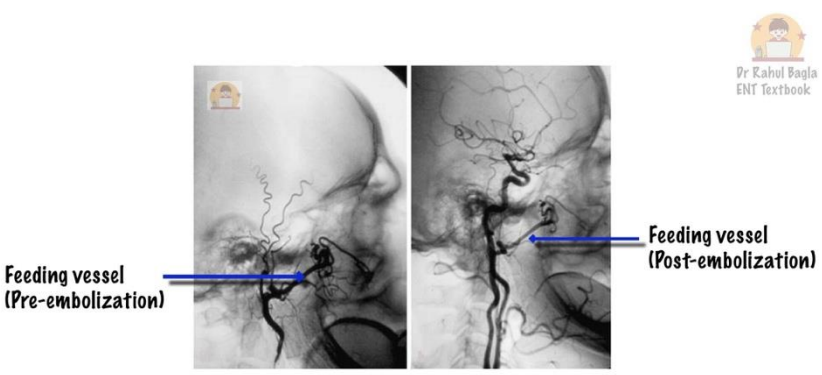
4. Carotid Angiography: Carotid Angiography is now standard for angiofibroma cases, particularly when embolisation is planned before surgery. The main arteries targeted for embolisation are the maxillary and ascending pharyngeal arteries.

What it shows:

- The size and spread of the tumour.
- How vascular the tumour is (how many blood vessels it has).
- The feeding blood vessels that feed the tumour usually come from the external carotid artery system.

Embolization is the process of blocking the tumour's blood supply. It is done 24-48 hours before surgery to **reduce bleeding** during the operation. Surgery must be performed within this 24-48-hour window to prevent revascularisation from the contralateral side. Using embolisation has significantly reduced blood loss during surgery. In the past, the average blood loss was about 2000 mL, but now it is less than 1000 mL. While angiography is used to identify and embolize the feeding vessels, some surgeons prefer to tie off these vessels during the actual surgery. This approach helps them avoid the risks associated with embolisation and allows them to spot any remaining tumour tissue by observing where bleeding occurs.



Angiography of a juvenile angiofibroma.

: Note the reduced blood supply after embolisation of the feeding vessel

Treatment of Juvenile Nasopharyngeal Angiofibroma.

Surgical excision is the treatment of choice, though radiotherapy and chemotherapy singly or in combination have also been used.

1. Surgery

Surgical excision is the primary **treatment of choice** for juvenile nasopharyngeal angiofibroma. Spontaneous regression of the tumour does not occur, and no wait-and-watch policy should be adopted. Various surgical approaches have been described:

1. Nasal endoscopy approach.
2. Trans palatal approaches: Transpalatal approach or Transpalatal with sublabial extension (Sardana's approach)
3. Trans maxillary approaches: Lateral rhinotomy/medial maxillectomy or Midfacial degloving or Le-Fort I osteotomy approach or Maxillary swing/facial translocation approach, or Wei's operation
4. Lateral skull base approaches: Preauricular subtemporal infra-temporal approach or Infratemporal approach type C.
5. Combination of approaches.

The specific approach depends on the tumour size, extension, surgeon experience and familiarity with the approach. Endoscopic resection has become the preferred technique for most juvenile angiofibromas in the hands of experienced surgeons specialising in sinonasal care. Before surgery for JNA, 2–3 units of cross-matched blood should be reserved, as bleeding can still occur despite embolisation. Blood loss can be reduced by head elevation, hypotensive anaesthesia, and modern instruments like LASER, coblation, or harmonic scalpel. The surgeon first frees all extensions, ligates the maxillary artery, and then removes the tumour. Finally, drilling the vidian canal and pterygoid base helps prevent recurrence.

Extent of juvenile nasopharyngeal angiofibroma and surgical approach

Location	Approach
A. Nose and nasopharynx	Transpalatal or endoscopic
B. Nose, nasopharynx maxillary antrum and pterygopalatine fossa	Lateral rhinotomy with medial maxillectomy OR Endoscopic OR Le Fort I
C. As in B + Infratemporal fossa	Extended lateral rhinotomy OR Infratemporal fossa approach OR Maxillary swing approach
D. As in C + Cheek extension	Extended lateral rhinotomy
E. As in B + C + Intracranial	Combined intracranial and extracranial approach (craniotomy + one of the extracranial approaches) OR Radiation if intracranial part is inaccessible
F. Residual or recurrent disease (extracranial)	Observation OR repeat surgery or radiation if inaccessible
G. Intracranial residual or recurrent	Stereotactic radiation (X or gamma knife)

2. Radiotherapy

Radiotherapy has been used as a primary treatment or for recurrent or surgically inaccessible tumours. A dose of 3000 to 3500 cGy in 15–18 fractions is delivered over 3–3.5 weeks. The tumour regresses slowly over about a year. Radiotherapy is also used for intracranial extension when the tumour derives its blood supply from the internal carotid system. The use of radiotherapy is controversial. Some reserve it for large tumours with intracranial extension or recurrent inoperable tumours, while others believe it should be avoided due to the risk of malignancy development in the young nasopharynx.

3. Hormonal Therapy

Since juvenile nasopharyngeal angiofibroma occurs in young males at puberty due to activation of male hormones (testosterone),

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oestrogen (diethylstilbestrol) therapy was once used to reduce the size and vascularity of the tumour. However, it was stopped because it caused feminine changes in boys. Adjuvant oral flutamide (an androgen blocker) in post-pubertal patients can sometimes shrink the tumour if given for 6 weeks before surgery, but overall results remain limited.

4. Chemotherapy

Very aggressive recurrent tumours and residual lesions have been treated with chemotherapy, using combinations of doxorubicin, vincristine and dacarbazine. Chemotherapy can arrest growth and cause some regression, but does not achieve complete tumour eradication. Recurrence of juvenile nasopharyngeal angiofibroma is not uncommon, occurring in up to 35% of cases. Management options for recurrence include observation, revision surgery, radiotherapy, hormonal therapy, and chemotherapy.

——— End of the chapter ———