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University College Cork, Ireland

Ospidéal Ollscoile Phort Láirge
University Hospital Waterford
Regional Cancer Centre South East

RCSI

GRAND ROUNDS TEACHING
OCTOBER 21 2022

ADULT & PAEDIATRIC EPISTAXIS

Liam Skinner

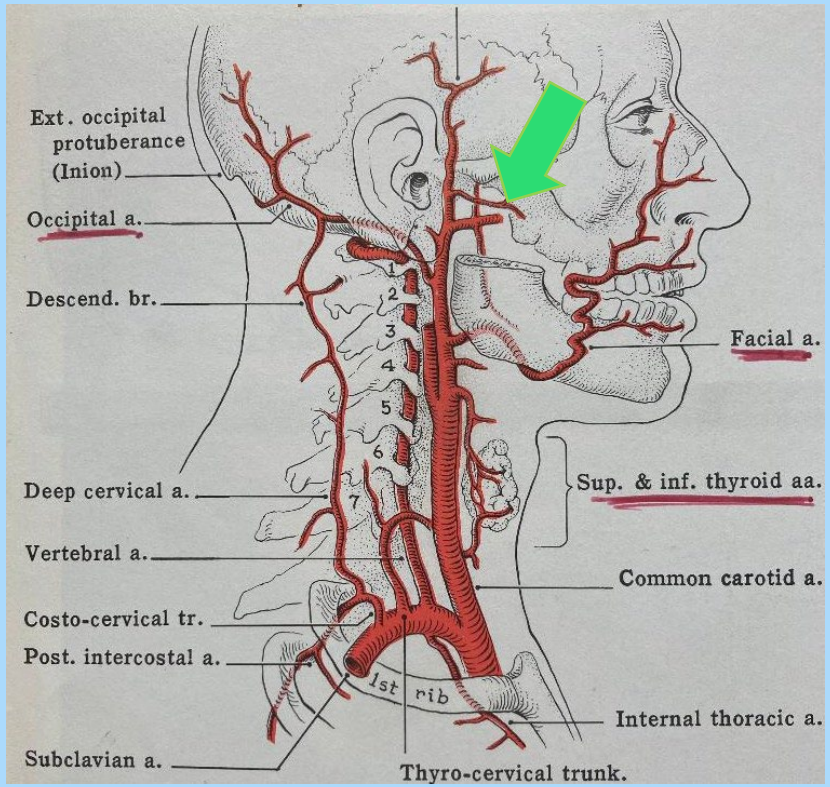
LEARNING OBJECTIVES

1. BLOOD SUPPLY & AETIOLOGY & A QUICK NOD TO HYPERTENSION
2. SPRINGBOARD TO ANSWER GENERAL OPENING QUESTION
3. WHAT'S IN IT AND HOW DOES IT WORK
4. BUT HOW DOES IT REALLY WORK
5. TRANSEXAMIC ACID
6. SURGICAL LANDMARKS
7. HEREDITARY HAEMORRHAGIC TELANGIECTASIA
8. EMBOLISATION
9. JNA
10. PREGNANCY AND A FINAL WORD

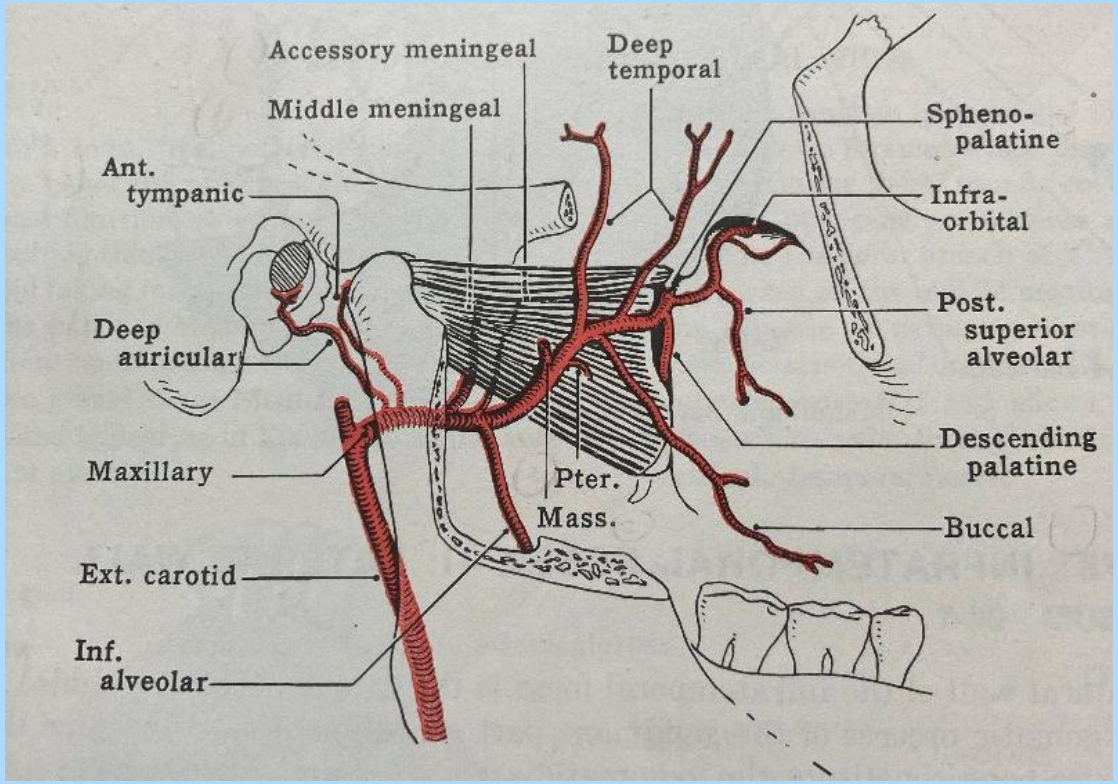
- **NOT AN EXHAUSTIVE LIST**

1. BLOOD SUPPLY & AETIOLOGY

Branches of External Carotid Artery

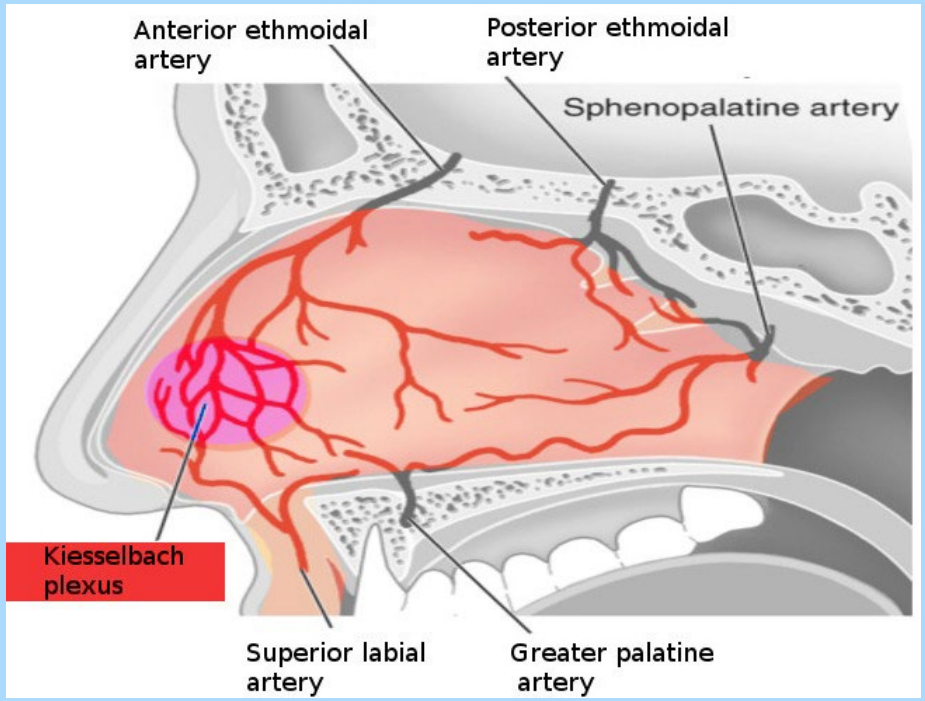


Maxillary Artery

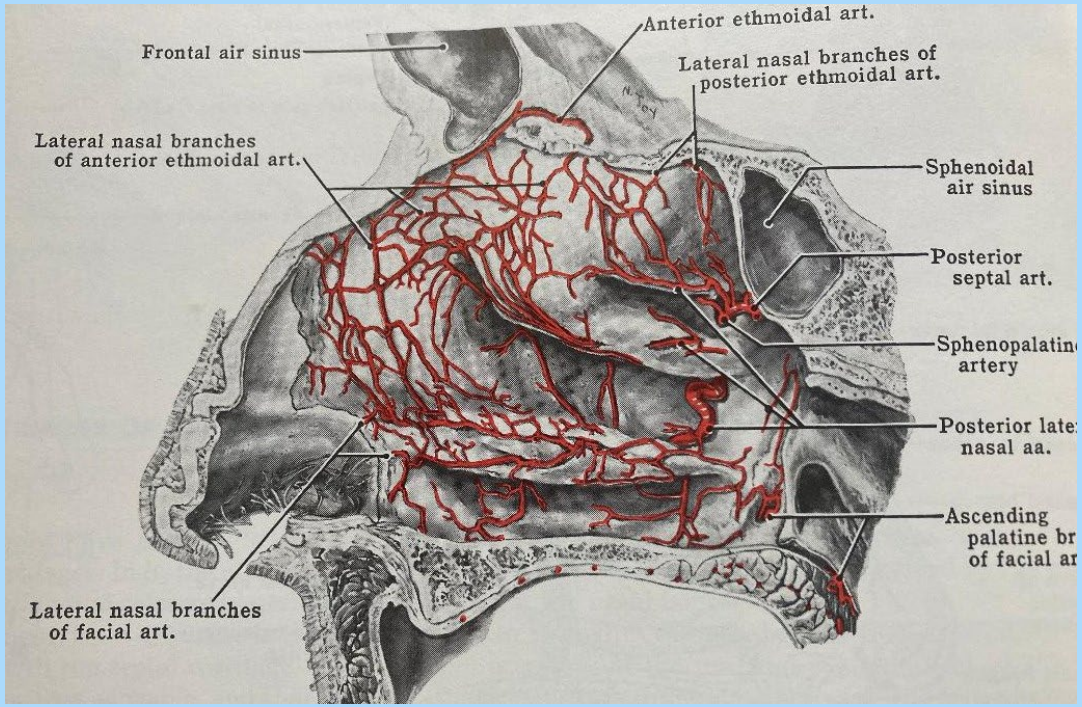


Maxillary artery divided into three parts by the lateral pterygoid muscle

Arteries to septum



Lateral nasal wall arterial supply



TRAUMA : nose-picking, foreign body, iatrogenic (surgery or sprays)

MUCOSAL IRRITATION : allergic rhinitis, dry air, URTI, inhaled irritants

TUMOURS : hamenagiomas, JNA, pyogenic granuloma, inverting papilloma, sinonasal tumours

ANATOMICAL : septal deviation

BLEEDING DISORDERS : platelet disorders, Von Willebrand's, haemophilia, inherited or acquired coagulation disorders, HHT

GRANULOMATOUS DISORDERS : GPA, sarcoidosis, tuberculosis

MEDICATIONS : NSA, anticoagulants, valproic acid

???????? HYPERTENSION

Review > Otolaryngol Head Neck Surg. 2017 Dec;157(6):921-927.
doi: 10.1177/0194599817721445. Epub 2017 Jul 25.

Association between Hypertension and Epistaxis: Systematic Review and Meta-analysis

Hyun Jin Min [1], Hyun Kang [2], Geun Joo Choi [2], Kyung Soo Kim [1]

2768 unique studies screened

10 selected for this meta-analysis

DID NOT SUPPORT A CAUSAL RELATIONSHIP

2. SPRINGBOARD TO ANSWER

Application of ATLS assessment protocols
IV access and FBC, clotting studies and blood for group & hold / cross-match
Locate area of bleeding / bleeding points
Pressure
Local cautery
Anterior nasal packing
Posterior nasal packing

Endoscopic sphenopalatine artery ligation
Ligation of Maxillary artery
Anterior ethmoidal artery ligation
External carotid artery ligation
Embolisation

Practice Guideline › Otolaryngol Head Neck Surg. 2020 Jan;162(1_suppl):S1-S38.
doi: 10.1177/0194599819890327.

Clinical Practice Guideline: Nosebleed (Epistaxis)

David E Tunkel [1], Samantha Anne [2], Spencer C Payne [3], Stacey L Ishman [4], Richard M Rosenfeld [5], Peter J Abramson [6], Jacqueline D Alikhaani [7], Margo McKenna Benoit [8], Rachel S Bercovitz [9], Michael D Brown [10], Boris Chernobilsky [11], David A Feldstein [12], Jesse M Hackell [13], Eric H Holbrook [14], Sarah M Holdsworth [15], Kenneth W Lin [16], Meredith Merz Lind [17], David M Poetker [18], Charles A Riley [19], John S Schneider [20], Michael D Seidman [21] [22] [23], Venu Vadlamudi [24], Tulio A Valdez [25], Lorraine C Nnacheta [26], Taskin M Monjur [26]

2. SPRINGBOARD TO ANSWER

J Laryngol Otol. 2017 Dec;131(12):1142-1156. doi: 10.1017/S0022215117002018.

The British Rhinological Society multidisciplinary consensus recommendations on the hospital management of epistaxis

National ENT Trainee Research Network

INTEGRATE

National multi-centre audit of patients with epistaxis over November 2016

834 patients included

Cautery at first specialist review can reduce hospital treatment times

Observational Study > Rhinology. 2019 Jun 1;57(3):180-189. doi: 10.4193/Rhin18.239.

National prospective observational study of inpatient management of adults with epistaxis – a National Trainee Research Collaborative delivered investigation

INTEGRATE (UK National ENT research trainee network) on its behalf:; Nishchay Mehta [1], Kara Stevens [2], Matthew E Smith [3], Richard J Williams [4], Matthew Ellis [5], John C Hardman [6], Claire Hopkins [7]

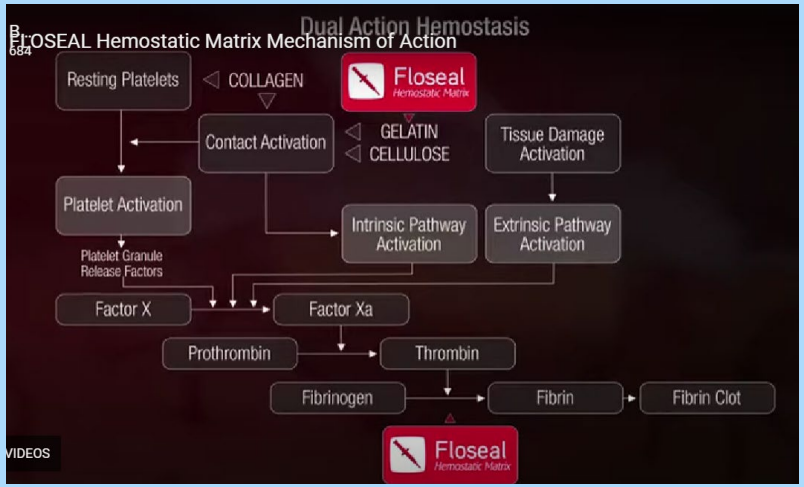
3. WHAT'S IN IT AND HOW DOES IT WORK

Silver Nitrate Cautery

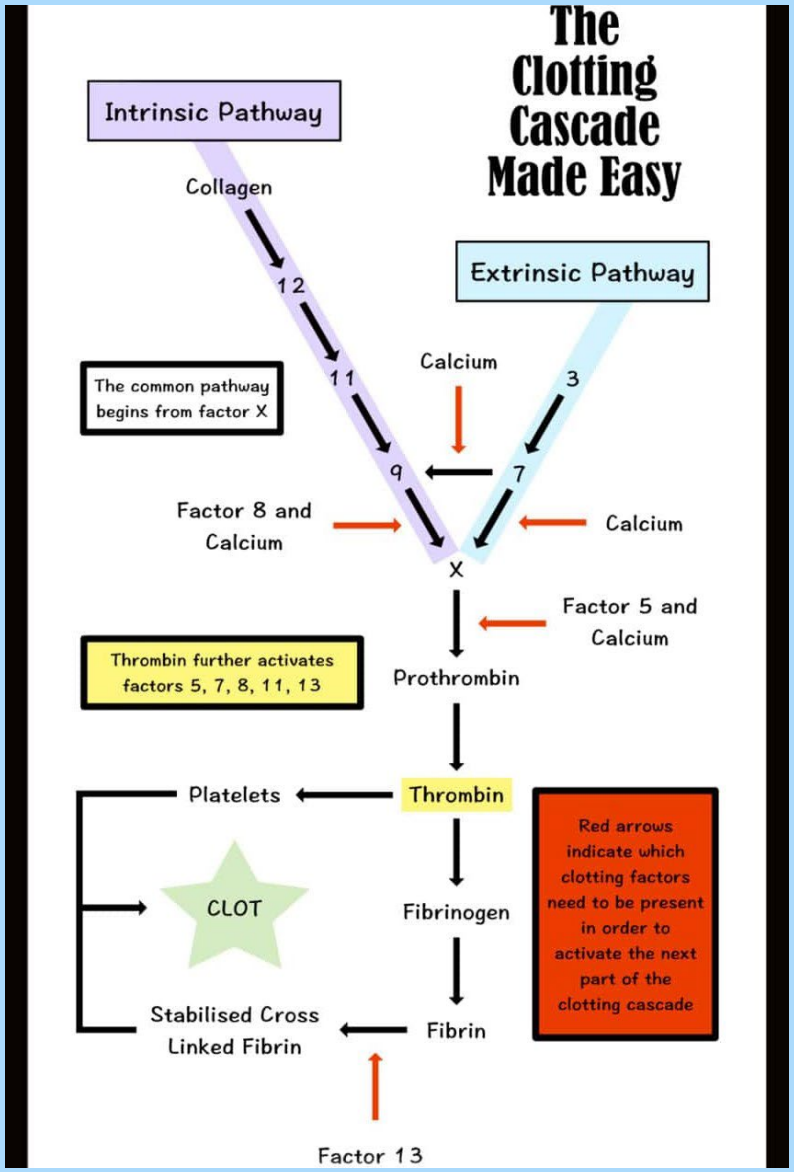
$$AgNO3 + HOH \rightarrow AgOH + HNO3$$

FloSeal

Human thrombin-impregnated
Bovine gelatin matrix



4. BUT HOW DOES IT REALLY WORK



Vascular Spasm

Formation of a platelet plug

Clotting cascade

INTRINSIC - **I**NJURY

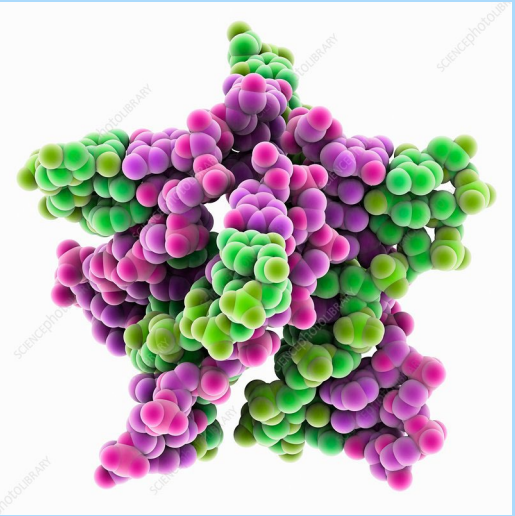
12 → 11 → 9 → 10

EXTRINSIC - **E**VERYTHING ELSE

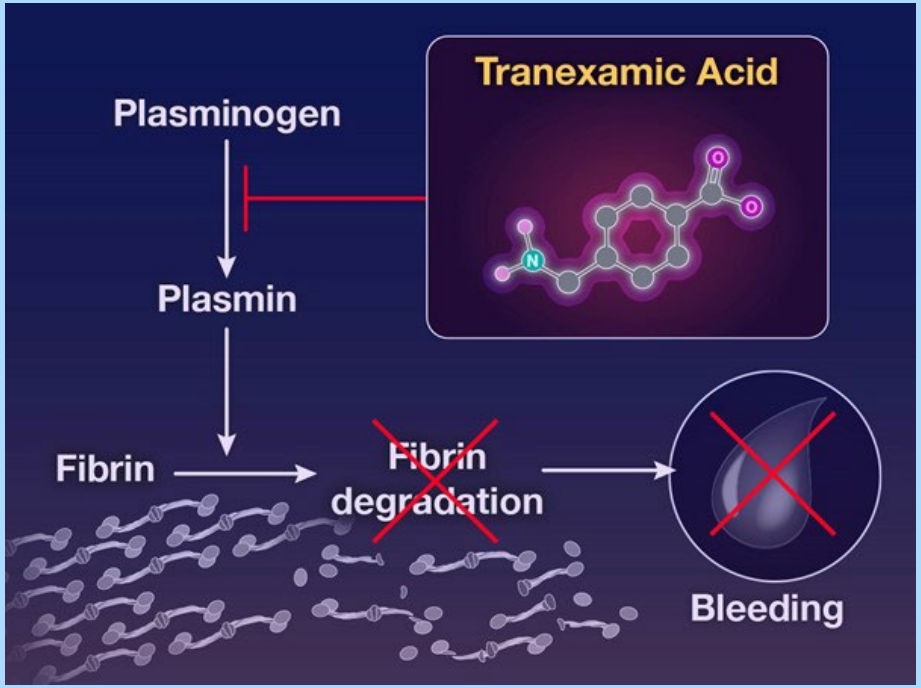
3 → 7 → 10

OCTAPLEX - PROTHROMBIN COMPLEX CONCENTRATE

Initial INR	2-2.5	2.5-3	3-3.5	>3.5
Approximate dose* (ml Octaplex/kg body weight)	0.9-1.3	1.3-1.6	1.6-1.9	>1.9
*The single dose should not exceed 3.000 IU (120 ml Octaplex).				



5. TRANSEXAMIC ACID

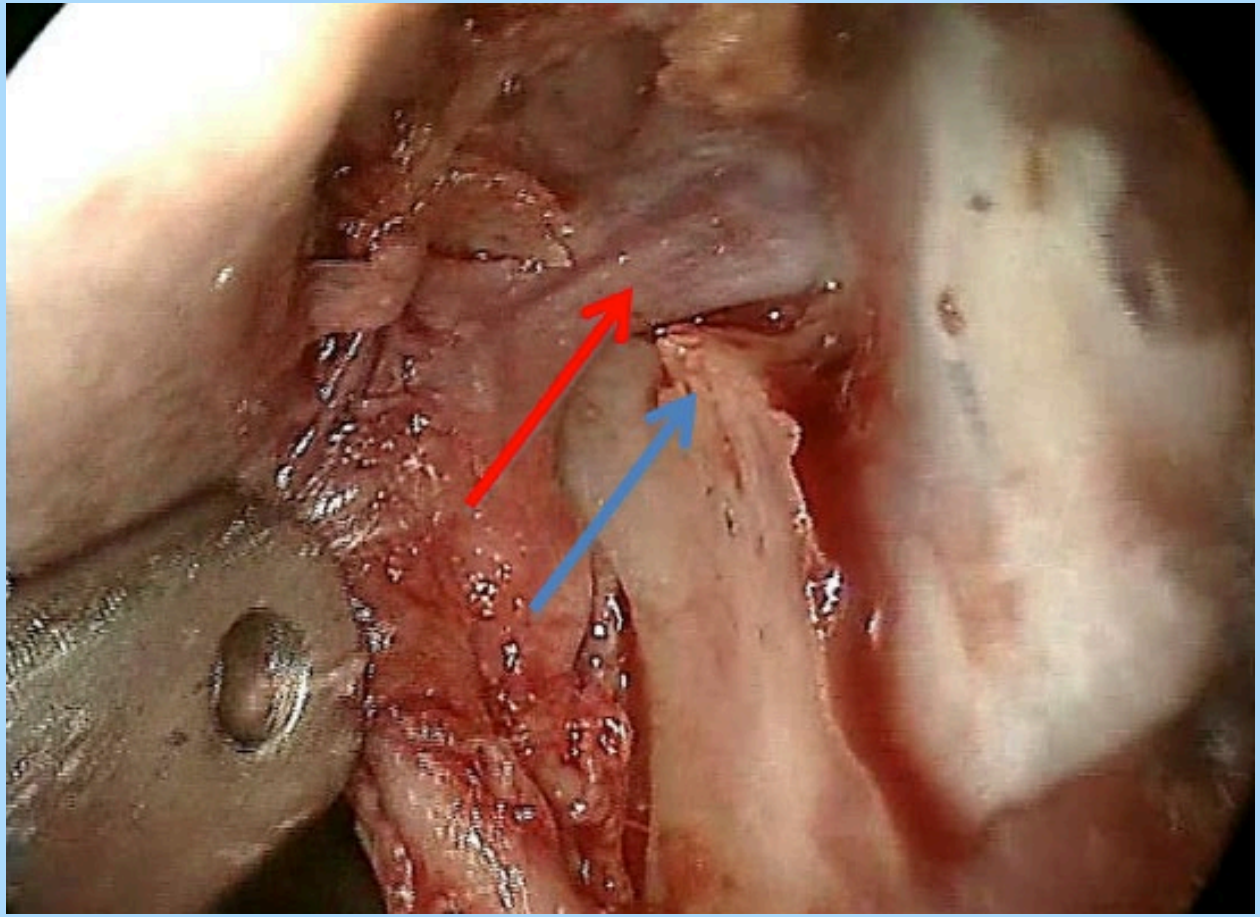


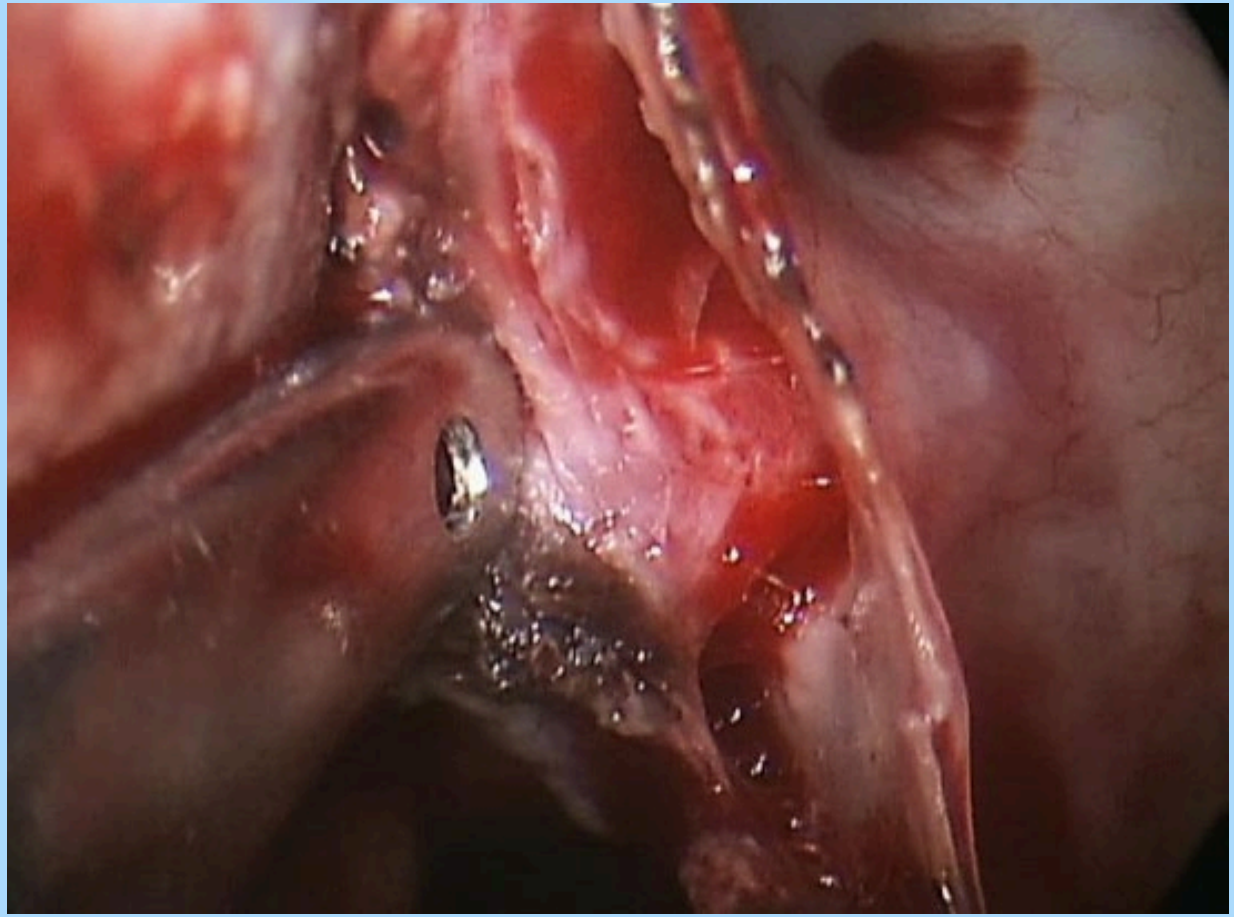
Synthetic analogue of the amino acid lysine

Serves as an antifibrinolytic agent

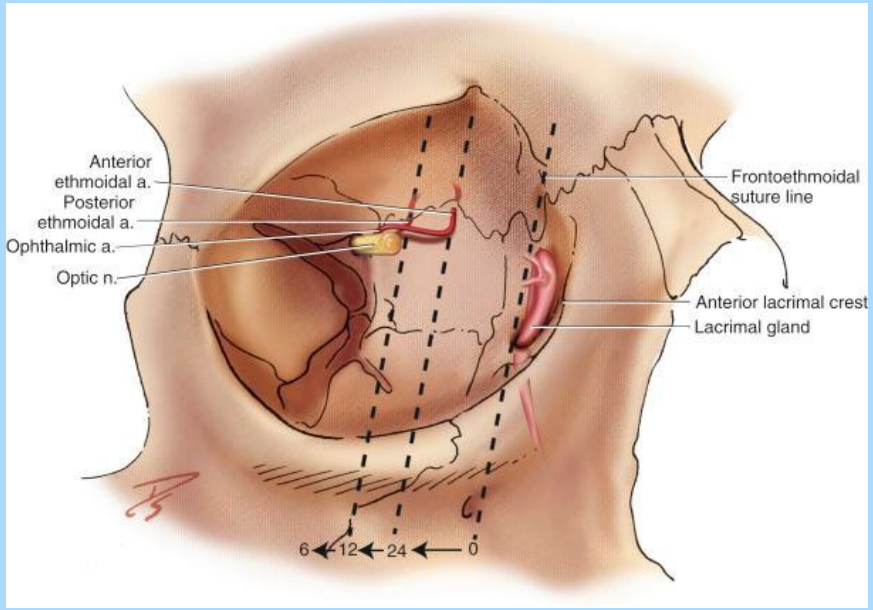
Reversibly binds four to five lysine receptor sites on plasminogen

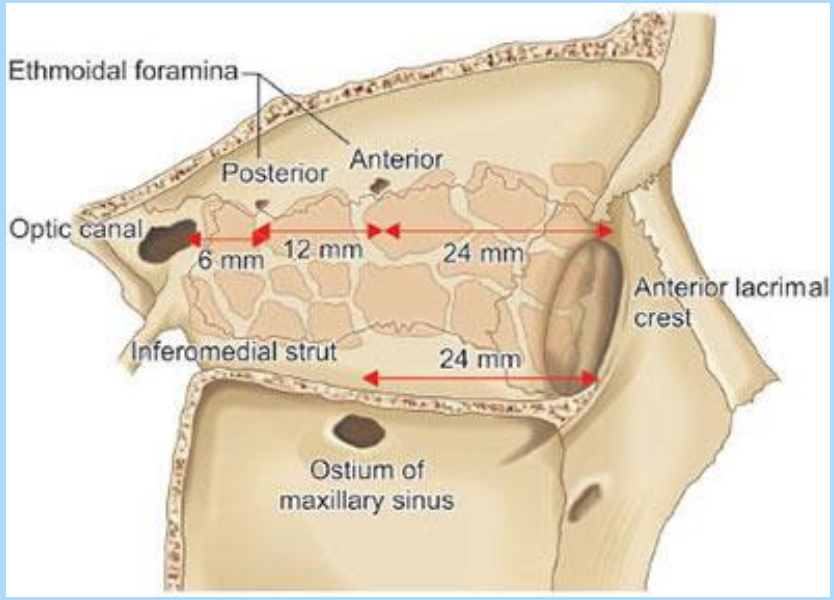
6. SURGICAL LANDMARKS





6. SURGICAL LANDMARKS

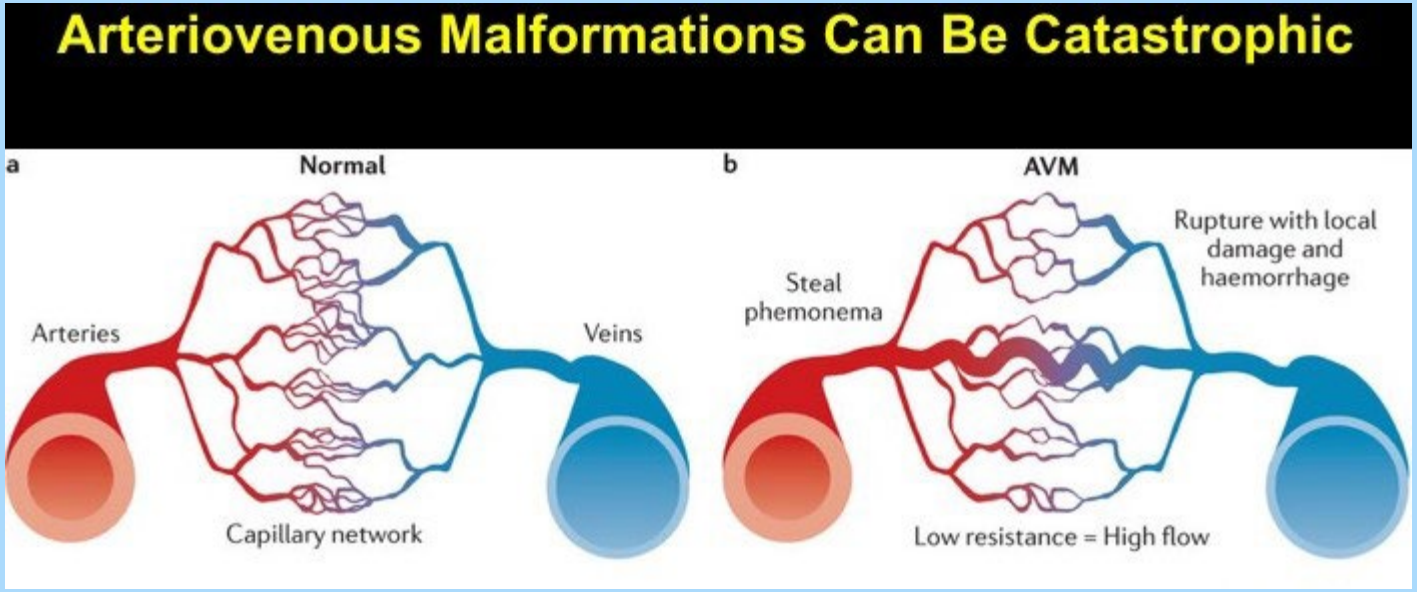




MEDIAL ORBITAL WALL 24 – 12 – 6 RULE

24 mm from lacrimal crest to AEA
12 mm from AEA to PEA
6 mm from PEA to optic canal ring

7. HEREDITARY HAEMORRHAGIC TELANGIECTASIA

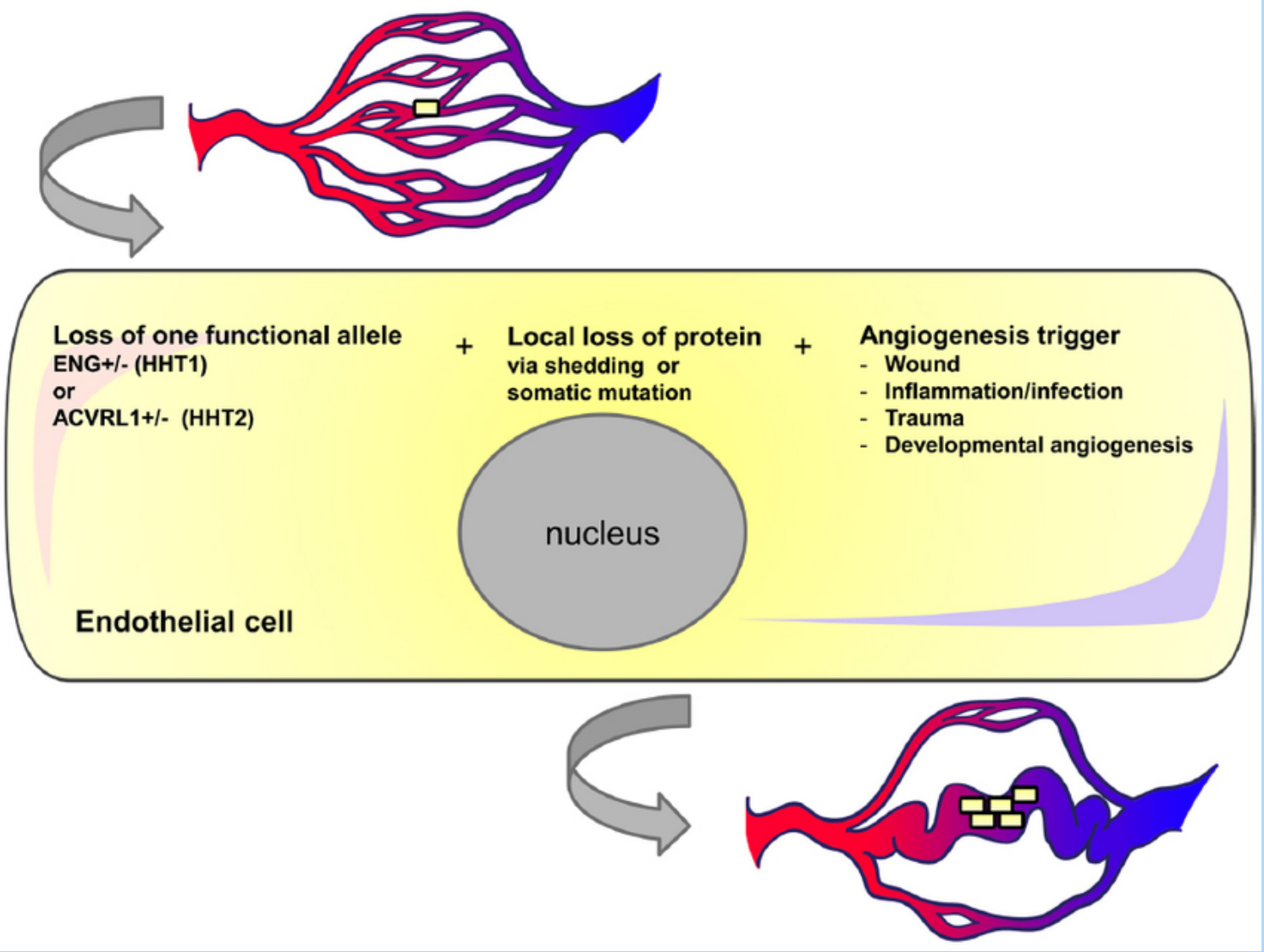


Causative mutation in one of three genes

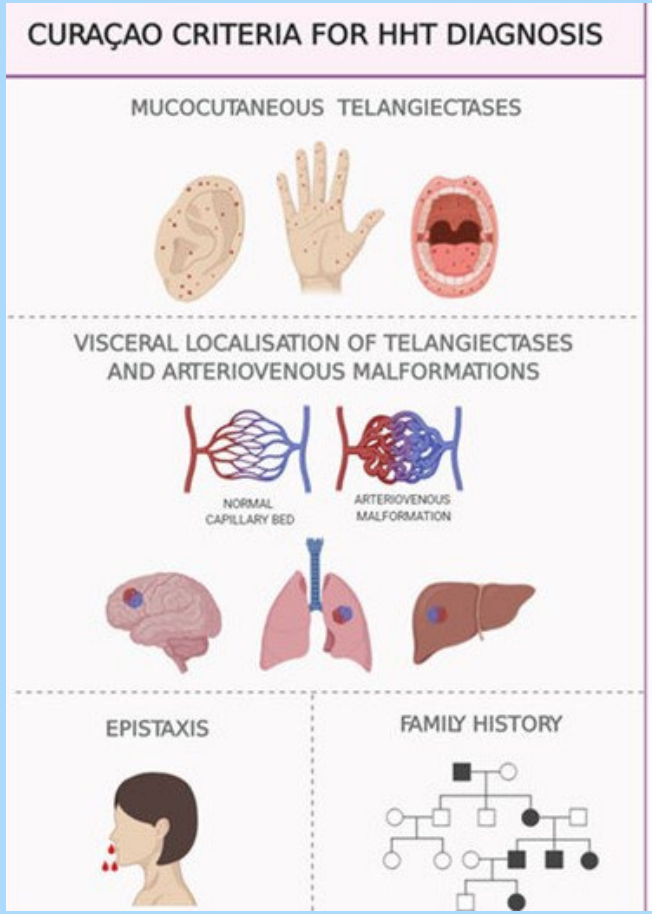
1. Endoglin - HHT, type 1
2. Activin receptor-like kinase 1 - HHT, type 2
3. Smad 4 - HHT, type 3

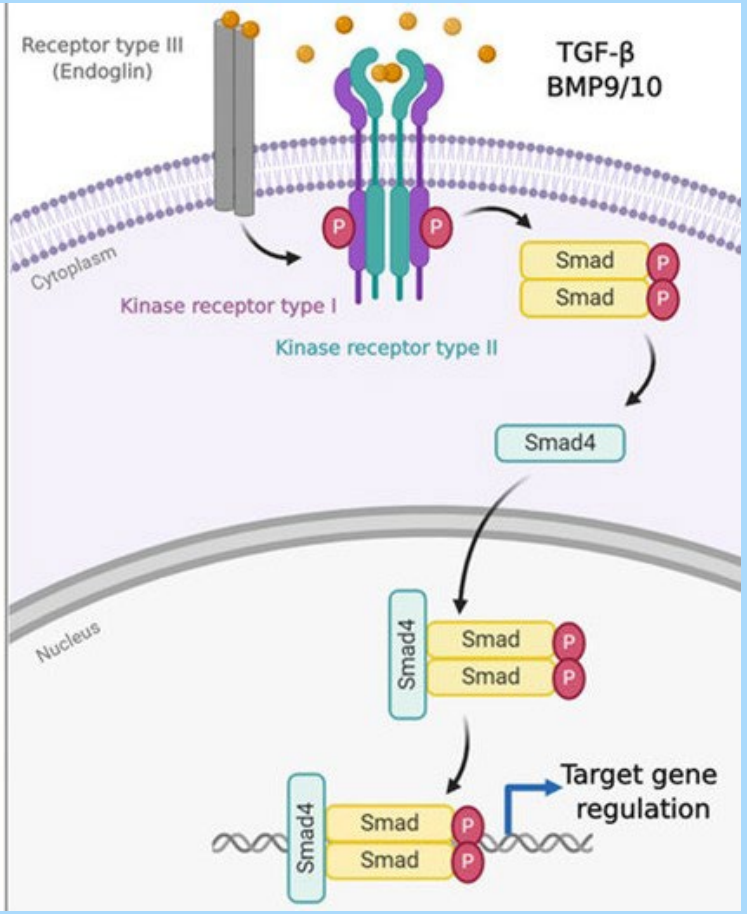
7. HEREDITARY HAEMORRHAGIC TELANGIECTASIA

3 event hypothesis
For AVM formation
In HHT



7. HEREDITARY HAEMORRHAGIC TELANGIECTASIA

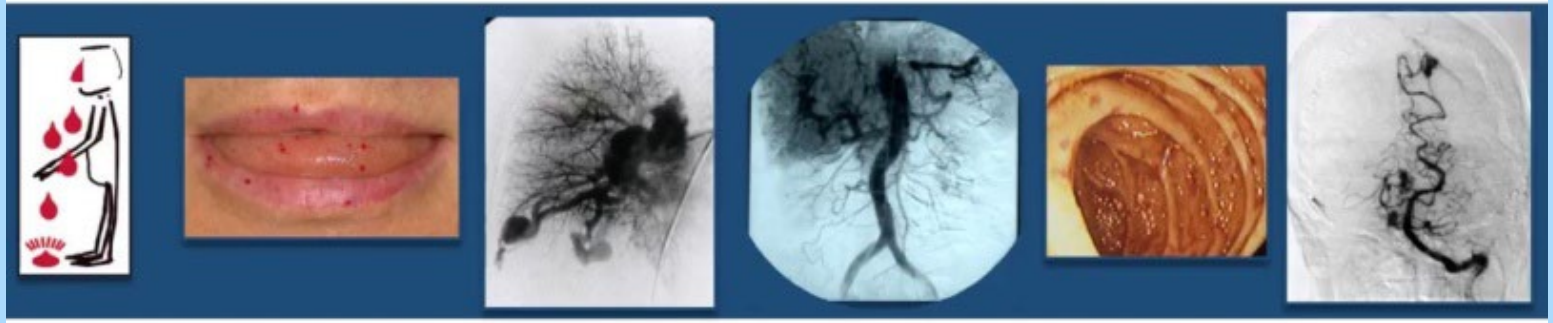




90%+	Nose bleeds
80%	Skin, lips, mouth telangiectasic
30%	Pulmonary AVMs
<30%	Hepatic AVMs
15%	Gastrointestinal bleeds
10%	Cerebral AVMs
1%	Spinal AVMs

7. HEREDITARY HAEMORRHAGIC TELANGIECTASIA

HHT: An inherited condition resulting in arteriovenous malformations (AVMs) and smaller telangiectasia in multiple vascular beds:



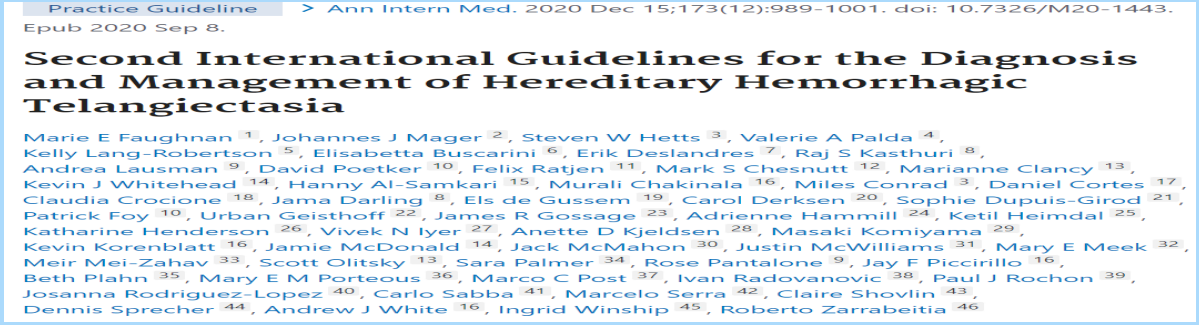
Frequency of abnormal HHT vessels :

>95%	Nose (→ nosebleeds)
>90%	Skin (telangiectasia
50%	Lungs (pulmonary AVMs)
50%	Liver (hepatic AVMs)
20%	Gastrointestinal tract

Compared to general population, more frequent:

- Iron deficiency anemia
- Strokes (ischaemic and haemorrhagic)
- Brain (and other deep-seated) abscesses
- Migraines
- Venous thromboemboli (VTE)
- Pulmonary hypertension

VEGF



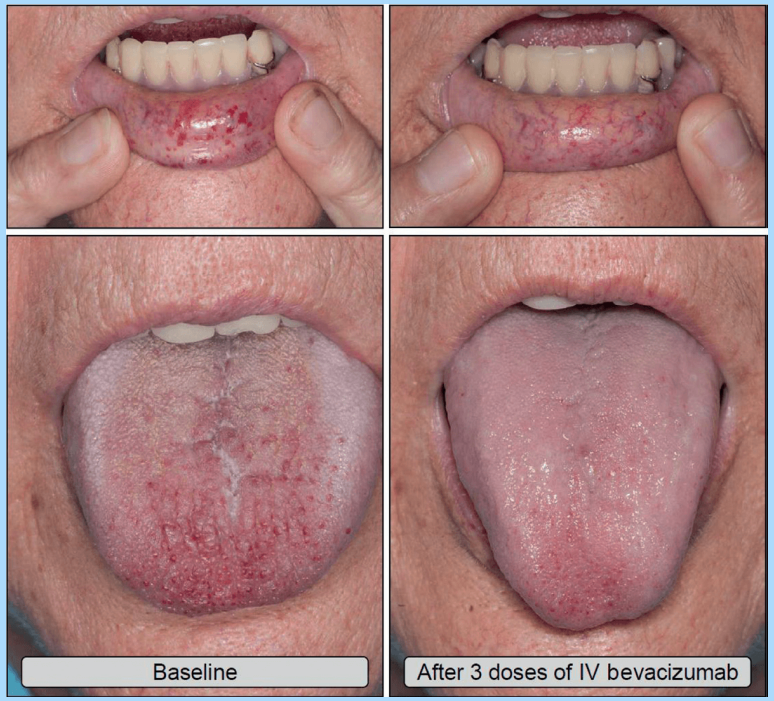
Practice Guideline > Ann Intern Med. 2020 Dec 15;173(12):989-1001. doi: 10.7326/M20-1443. Epub 2020 Sep 8.

Second International Guidelines for the Diagnosis and Management of Hereditary Hemorrhagic Telangiectasia

Marie E Faughnan [1], Johannes J Mager [2], Steven W Hetts [3], Valerie A Palda [4], Kelly Lang-Robertson [5], Elisabetta Buscarini [6], Erik Deslandres [7], Raj S Kasthuri [8], Andrea Lausman [9], David Poetker [10], Felix Ratjen [11], Mark S Chesnutt [12], Marianne Clancy [13], Kevin J Whitehead [14], Hanny Al-Samkari [15], Murali Chakinala [16], Miles Conrad [3], Daniel Cortes [17], Claudia Crocione [18], Jama Darling [8], Els de Gussem [19], Carol Derksen [20], Sophie Dupuis-Girod [21], Patrick Foy [10], Urban Geisthoff [22], James R Gossage [23], Adrienne Hammill [24], Ketil Heimdal [25], Katharine Henderson [26], Vivek N Iyer [27], Anette D Kjeldsen [28], Masaki Komiyama [29], Kevin Korenblatt [16], Jamie McDonald [14], Jack McMahon [30], Justin McWilliams [31], Mary E Meek [32], Meir Mei-Zahav [33], Scott Olitsky [13], Sara Palmer [34], Rose Pantalone [9], Jay F Piccirillo [16], Beth Plahn [35], Mary E M Porteous [36], Marco C Post [37], Ivan Radovanovic [38], Paul J Rochon [39], Josanna Rodriguez-Lopez [40], Carlo Sabba [41], Marcelo Serra [42], Claire Shovlin [43], Dennis Sprecher [44], Andrew J White [16], Ingrid Winship [45], Roberto Zarrabeitia [46]

1. Patients with HHT-related epistaxis should use moisturising topical therapies that humidify the nasal mucosa to reduce epistaxis
2. Clinicians should consider the use of oral transexamic acid for the management of epistaxis that does not respond to moisturising topical therapies
3. Clinicians should consider ablative therapies for nasal telangiectasias, including laser treatment , radiofrequency ablation., electrosurgery and sclerotherapy, in patients that have failed to respond to moisturising topical therapies
4. **Clinicians should consider the use of systemic anti-angiogenic agents for the management of epistaxis that has failed to respond to mosturising topical therapies, ablative therapies and / or transexamic acid**
5. Clinicians should consider a septodermoplasty for patients whose epistaxis has failed to respond sufficiently to moisturising topical therapies, ablative therapies, and / or transexamic acid
6. Clinicians should consider a nasal closure for patients whose epistaxis has failed to respond sufficiently to moisturising topical therapies, ablative therapies, and / or transexamic acid

STAGE	EPISTAXIS				GASTROINTESTINAL BLEEDING
Initial Management	Moisturizing topical therapies				Argon Plasma Coagulation of actively bleeding lesions (at initial diagnosis only)
Step 1 Treatment Options	Oral tranexamic acid	Local ablative therapies			Oral tranexamic acid (mild bleeding)
Step 2 Treatment Options	Systemic antiangiogenic agents	Septodermoplasty	Nasal closure		Systemic antiangiogenic agents (moderate to severe bleeding)
SPECIFIC TREATMENT CHOICES	Local ablative therapies for epistaxis:	<u>Stronger Evidence</u> Laser treatment Sclerotherapy	<u>Less Evidence</u> Electrosurgery Radiofrequency ablation	Antiangiogenic agents:	<u>Multiple Studies to Support</u> Bevacizumab Thalidomide	<u>Primarily Investigational</u> Pomalidomide Pazopanib Nintedanib Doxycycline Others



Multicenter Study > Haematologica. 2021 Aug 1;106(8):2161-2169.
doi: 10.3324/haematol.2020.261859.

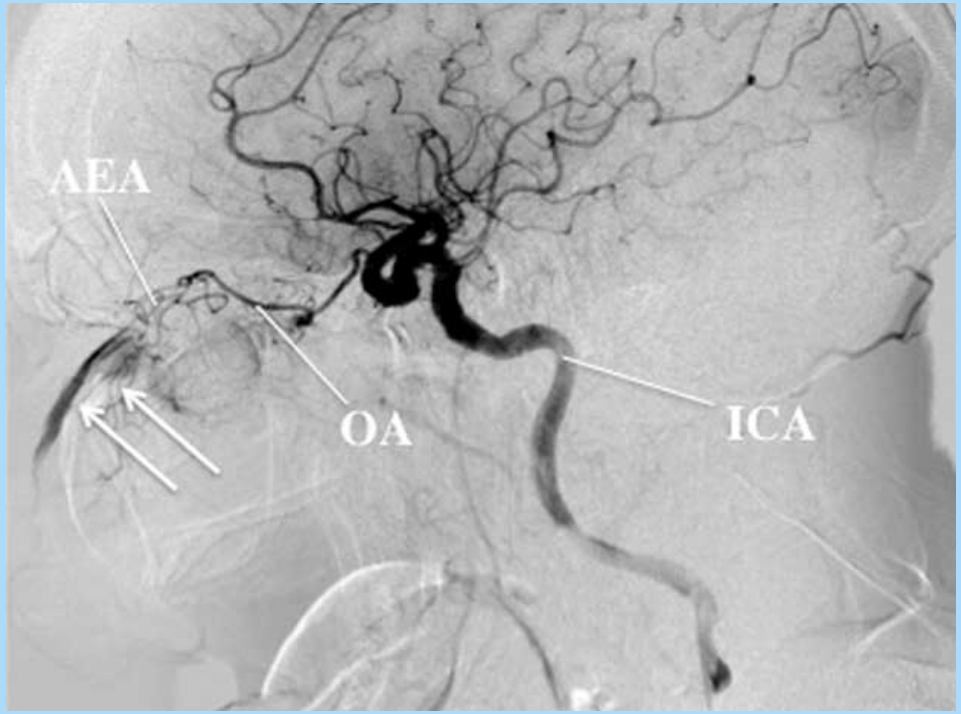
An international, multicenter study of intravenous bevacizumab for bleeding in hereditary hemorrhagic telangiectasia: the InHIBIT-Bleed study

Hanny Al-Samkari [1], Raj S Kasthuri [2], Joseph G Parambil [3], Hasan A Albitar [4], Yahya A Almodallal [5], Carolina Vázquez [6], Marcelo M Serra [6], Sophie Dupuis-Girod [7], Craig B Wilsen [8], Justin P McWilliams [8], Evan H Fountain [9], James R Gossage [9], Clifford R Weiss [10], Muhammad A Latif [10], Assaf Issachar [11], Meir Mei-Zahav [11], Mary E Meek [12], Miles Conrad [13], Josanna Rodriguez-Lopez [14], David J Kuter [15], Vivek N Iyer [16]

Retrospective study - 238 patients

Safe – VTE rate of 2% and no fatalities

8. EMBOLISATION



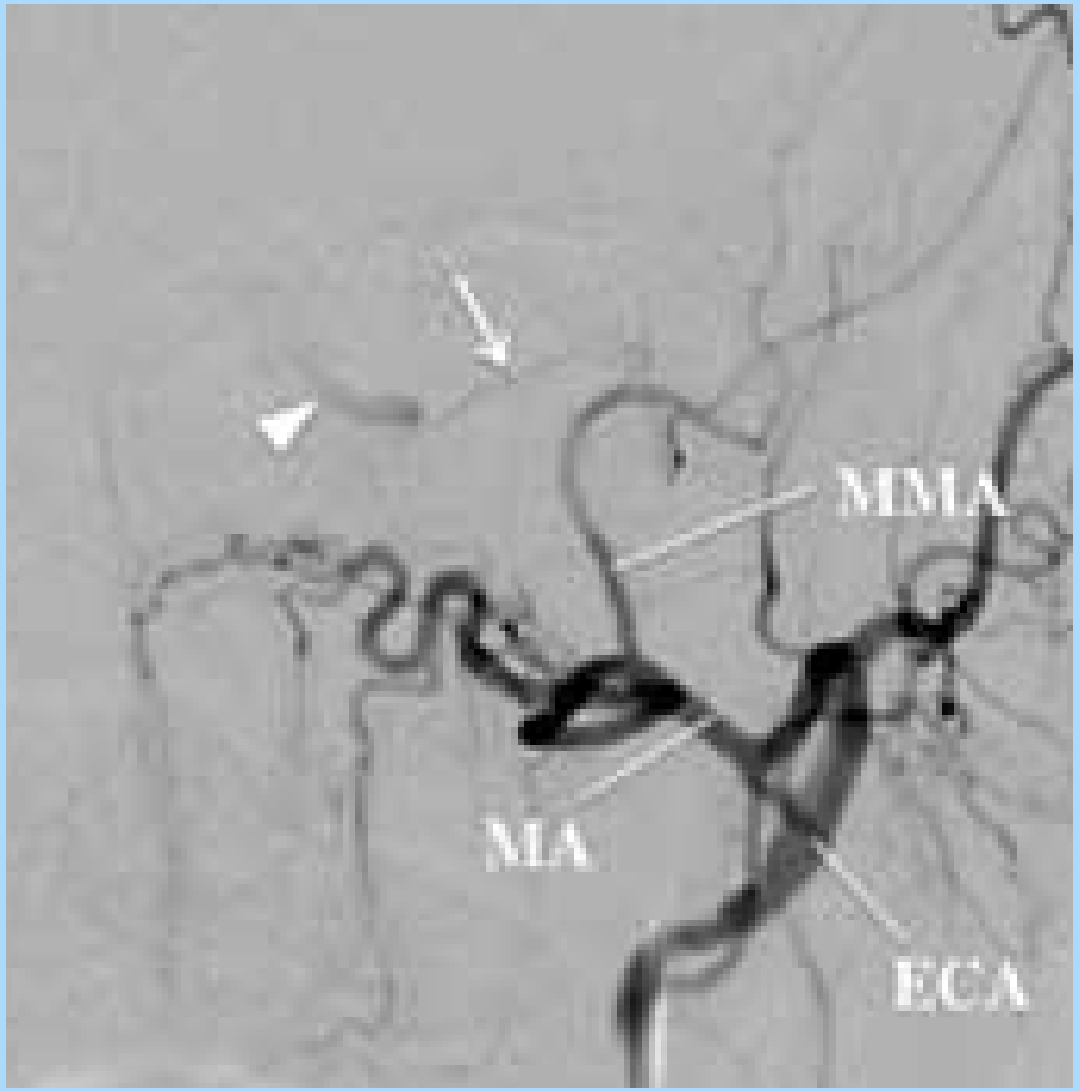
Severe, but low percentage rate, complications

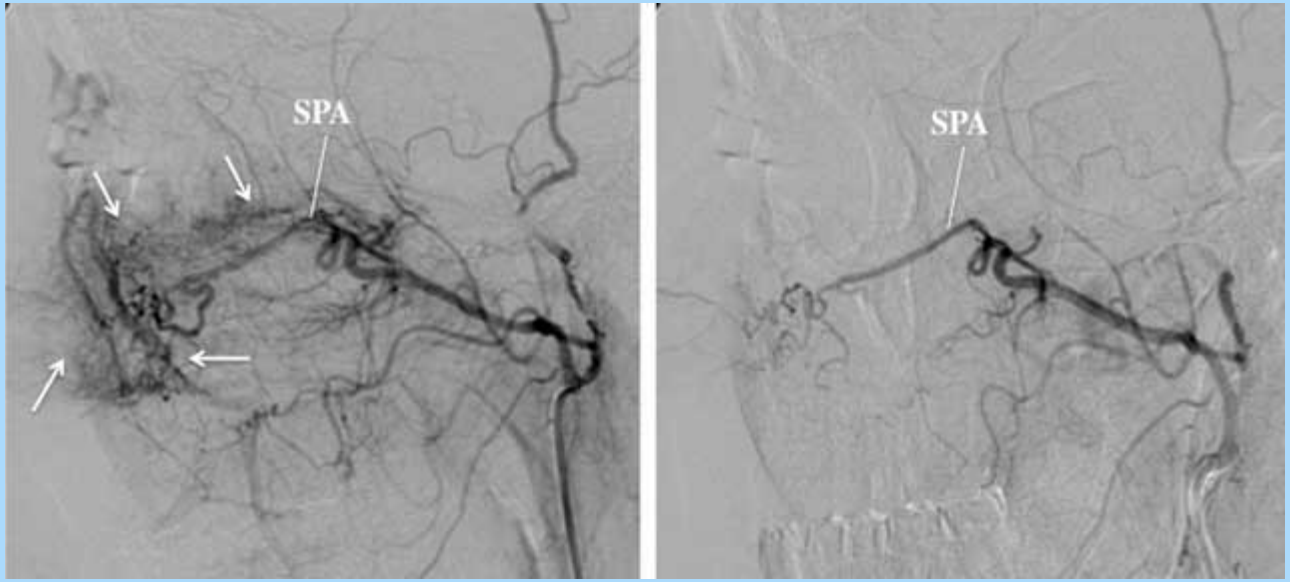
Cheaper and less invasive than surgery

Tortuous arteries
-thromboemboli
-wall dissection

Arrow – inferolateral trunk

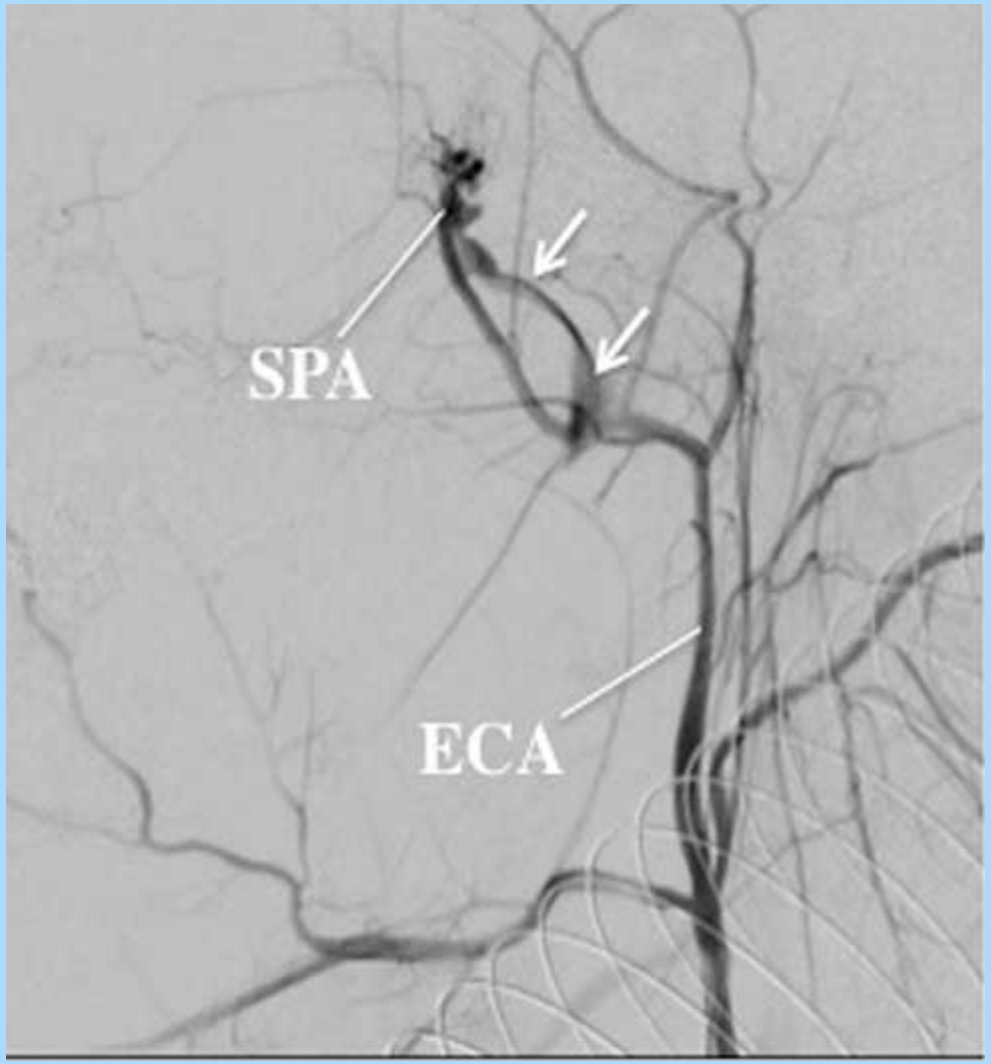
Arrowhead – petrous part of ICA connecting with middle meningeal artery



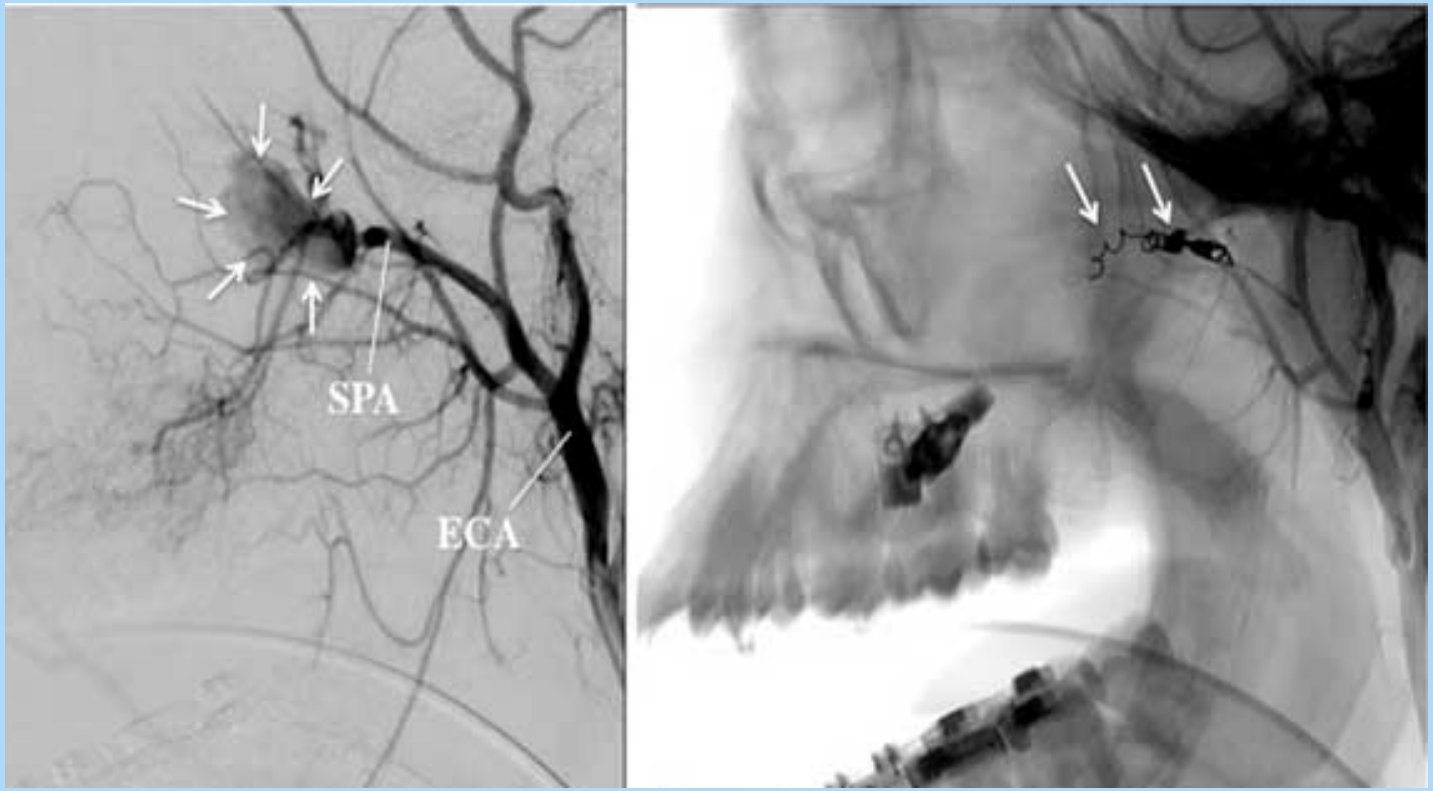


EMBOLIC AGENTS

Gelfoam
Micro-particles
Micro-coils



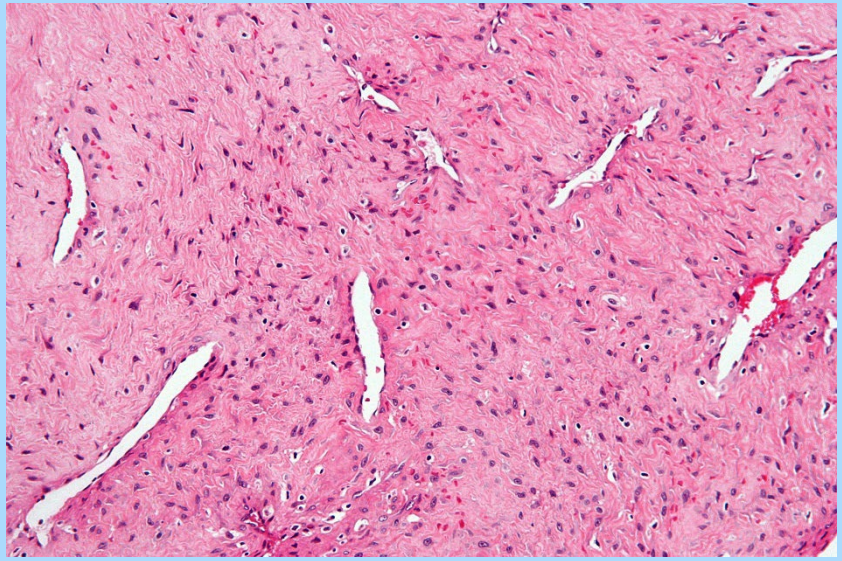
PSEUDO VEIN SIGN



PSEUDO ANEURYSM

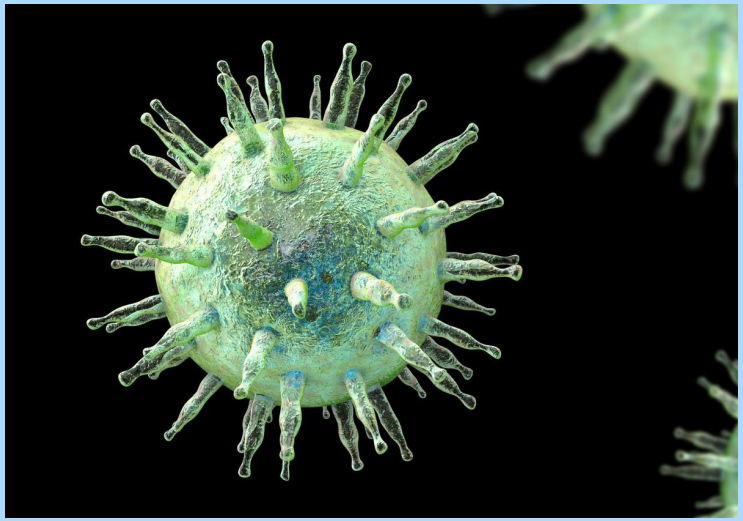
9. JNA

- Cellular, vascular, locally aggressive benign tumour
- Posterior nasal cavity – sphenoid base, sphenopalatine foramen
- Malignant transformation extremely rare (limited to case reports, RT related)
- Adolescent men (ages 9-19)
- Incidence: 1:150,000
- 0.05-0.5% H+N tumours



Aetiology - theories

- Hormonal
  - Adolescent boys
  - Tumours display oestrogen, progesterone, androgen receptors
  - Exogenous testosterone observed to stimulate tumour growth
  - However, no response to hormonal treatments
- Genetic
  - Genetic analysis of tumours identifying deletions in chromosome 17 (TP53 suppressor gene, HER-2/NEU oncogene
- Viral
  - Limited studies on HSV-8, EBV, HPV as possible aggravating factors for recurrence and variability in tumour behaviour.



Clinical features

- Symptoms often present 6-12 months pre-diagnosis
- Common:
  - Recurrent, profuse unilateral epistaxis (60%)
  - Unilateral nasal obstruction (80%)
  - Headache (25%) – often related to sinonasal obstruction
- Less common:
  - Conductive hearing loss (Eustachian tube obstruction)
- Symptoms of advanced disease:
  - Facial swelling
  - Visual / neurological symptoms (direct pressure to skull base, orbit, intracranial structures)

Diagnosis

- Clinical – red, lobulated mass in posterior nasal cavity
- Radiological
  - Arise from sphenopalatine foramen
  - CT:
    - features of bony remodelling more prominent than destruction
    - Widened sphenopalatine foramen
    - Base of pterygopalatine plate erosion
  - MRI:
    - T1: intermediate signal
    - T2: heterogeneous signal: flow voids appear dark
    - T1 C+ (Gd): shows prominent enhancement
    - “Salt and pepper” appearance due to flow voids (also commonly seen for paragangliomas)
  - Angiography: useful for defining feeding vessels to help target ebolization

- Biopsy not advised due to risk of torrential haemorrhage

UPMC (Snyderman et al 2010)

Table 2. University of Pittsburgh Medical Center (UPMC) Staging System for Angiofibroma

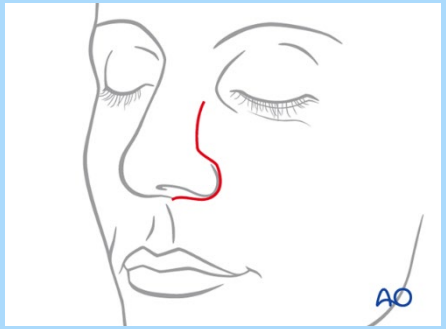
Stage	UPMC Staging System
I	Nasal cavity, medial pterygopalatine fossa
II	Paranasal sinuses, lateral pterygopalatine fossa; no residual vascularity
III	Skull base erosion, orbit, infratemporal fossa; no residual vascularity
IV	Skull base erosion, orbit, infratemporal fossa; residual vascularity
V	Intracranial extension, residual vascularity; M, medial extension; L, lateral extension

Management: *Surgery*

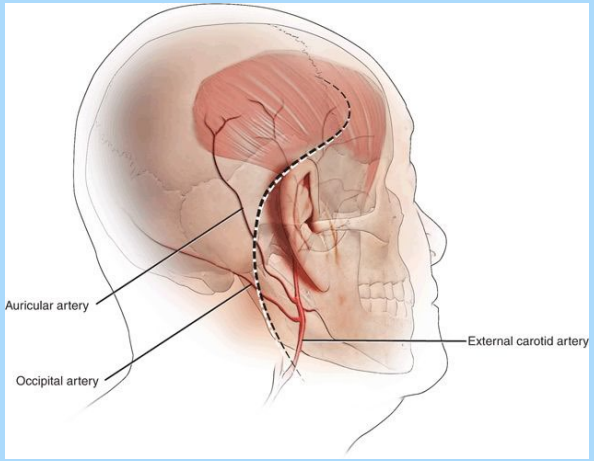
- Surgery = treatment of choice (case series, expert opinion)
- Primary aims:
  - Access to routes of tumour extension
  - Access to control of vascular supply
  - Avoidance of need for radiotherapy
- Secondary aims:
  - Avoidance of blood loss, cranial nerve injury, disruption of growth centres, cosmetic deformity, soft tissue/intracranial injury

Surgery: *Open approaches*

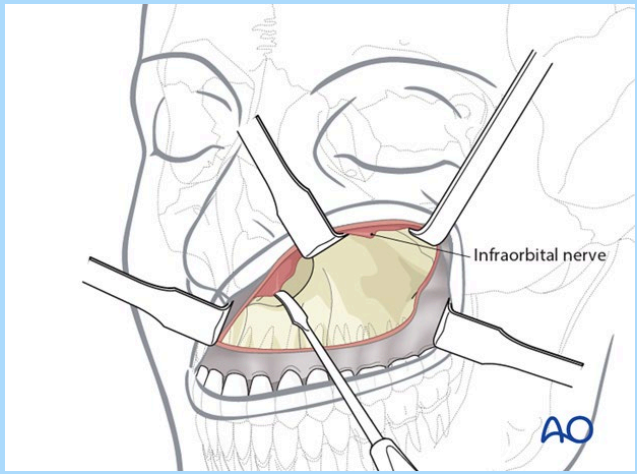
- Extensive tumours
- Significant intracranial or infratemporal/temporal involvement
- Optic nerve/ICA entrapment
- ICA supply



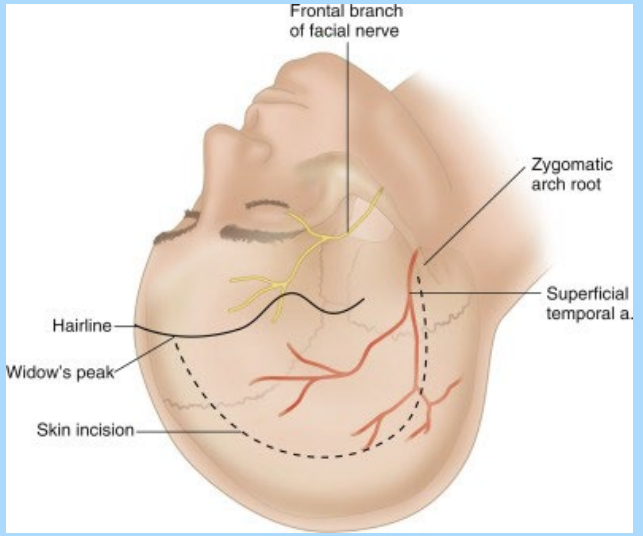
Lateral rhinotomy



Infratemporal fossa approach



Midface degloving



Frontotemporal craniotomy

Surgery: *Endoscopic approach*

- Advocated for all early stage tumours
- Can also be used for advanced tumours
- En-bloc resection not always necessary
- Relative contraindications include:
  - Supply from internal carotid artery (lack of embolization)
  - Extensive intracranial involvement

Management: *Adjuvant therapies?*

- Radiotherapy
  - Generally avoided – long term radiation side effects, sarcoma development
  - IMRT has been trialled for incompletely resectable advanced tumours or high resection risk e.g. carotid encasement, significant intracranial extension
- Chemotherapy
  - Little evidence, generally not recommended
- Hormonal/other therapies
  - Flutamide (androgen receptor antagonist) - limited, mixed low level evidence
  - Bevacuzimab (VEGF inhibitor) – limited data

Follow up

- Recurrences of 18-45% depending on stage
- Early detection can improve outcomes
- Most occur within 1-year

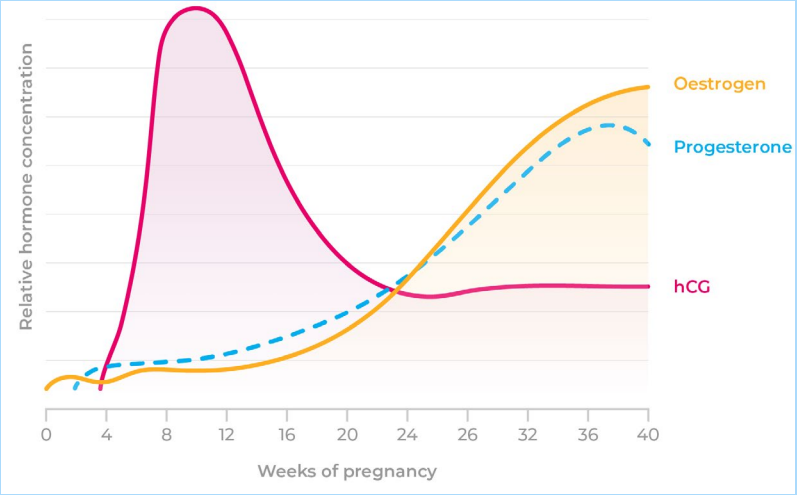
- Minimum of 3 years
- Clinical / endoscopic surveillance
- Imaging:
  - Variability in the literature
  - MRI preferred
  - Performed ~1 month postop, ~4 months after
  - Further depending on symptoms/clinical review

10. PREGNANCY & A FINAL WORD

Review > Otolaryngol Head Neck Surg. 2011 Aug;145(2):188-98.
doi: 10.1177/0194599811407572. Epub 2011 May 9.

Ear, nose, and throat manifestations during pregnancy

Rohit Kumar [1], Kathryn L Hayhurst, Andrew K Robson



Oestrogen - indirect effect on vascular wall by regulating signalling pathways involved by VEGF & VEGFR-2

Progesterone - provokes an increase in blood volume

Placenta Growth Hormone - causes vasodilatation

Immunological Changes - leads to nasal hypersensitivity

Other Issues - HELLP (haemolysis, elevated liver enzymes, low platelets) etc

NHS
South West Yorkshire
Area Prescribing Committee

Medicines Safety Sub-Group

Medicines Safety Bulletin

This bulletin places peanut allergy under the spotlight.

The Medicines and Healthcare Products Regulatory Agency (MHRA) has recommended that patients known to be allergic to peanuts should not use medicines containing arachis oil.

Although the BNF states that refined arachis oil (Arachis Oil BP) is unlikely to cause an allergic reaction, this relies upon the oil being adequately refined so that all peanut protein is removed. The manufacturers of the majority of pharmaceutical products which contain arachis oil advise that the products **should not** be used by patients with peanut allergy.

Due to potential cross-sensitivity between allergy to peanut and soya, some manufacturers advise that patients with soya allergy should also avoid their products that contain arachis oil. Substantial cross-sensitivity is also known to exist between peanuts, tree nuts and sesame, and patients with such allergies may consequently be advised to avoid each group

www.mhra.gov.uk

www.medicines.org.uk

Naseptin® Nasal Cream

chlorhexidine dihydrochloride 0.1%w/w,
neomycin sulfate 0.5% w/w, 3250 IU/g

Clinical Trial › BMJ. 1997 Apr 12;314(7087):1084-8. doi: 10.1136/bmj.314.7087.1084.

Randomised, double blind, crossover challenge study of allergenicity of peanut oils in subjects allergic to peanuts

J O Hourihane [1], S J Bedwani, T P Dean, J O Warner

60 pts with documented allergy to peanuts

NO REACTIONS TO REFINED OIL

VISIT WATERFORD