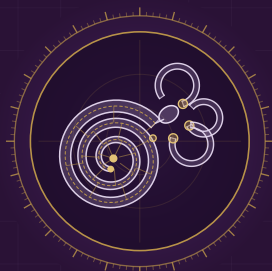
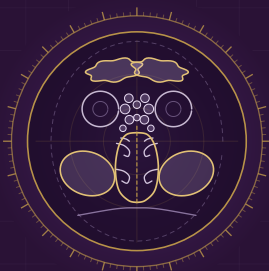




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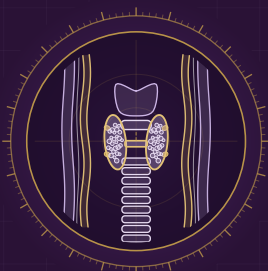
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DNB ENT

Based on Cummings Otolaryngology–Head and Neck Surgery (8th ed.), Scott-Brown's Otorhinolaryngology (9th ed.), Glasscock-Shambaugh's Surgery of the Ear (7th ed.) and Stell & Maran's Head and Neck Surgery and Oncology (6th ed.)

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- Volume 1** Part 1 · Anatomy, Embryology & Physiology of Ear: answers 1–6 and 9
Taken from the printed volume, pages 11–26 and 36–38
- Volume 2** Part 14 · Anatomy, Embryology & Physiology of Nose & PNS: answers 137–144
Taken from the printed volume, pages 10–27
- Volume 3** Parts 28–29 · Oral premalignant lesions and oral cavity cancer: answers 247–252
Taken from the printed volume, pages 11–29
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- **One answer, many questions.** Repeated or overlapping questions are answered once. The header lists every paper it was asked in ("ASKED n×") and the exact wording of each version.
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- Cummings Otolaryngology–Head and Neck Surgery, 8th edition
- Scott-Brown's Otorhinolaryngology and Head and Neck Surgery, 9th edition
- Glasscock-Shambaugh's Surgery of the Ear, 7th edition
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1. Middle ear mucosal folds and spaces, with labelled diagrams

ASKED 1* • 5-mark answer

Asked in: Paper I • Dec 2024 • Q1(a)

Q: Describe with the help of labelled diagrams, the various middle ear mucosal folds and spaces. [5]

SOURCE

- Cummings Otolaryngology (8e, Vol 2) — ch. 124 Anatomy of the Temporal Bone, External Ear, and Middle Ear — §Middle Ear — pp. 1950–1951; Fig. 124.10, p. 1951
- Cummings Otolaryngology (8e, Vol 2) — ch. 143 Middle Ear Endoscopic Surgery — §Endoscopic Ear Anatomy: Middle Ear Spaces; §Epitympanum — pp. 2233–2235; Fig. 143.3, p. 2234
- Scott-Brown's Otorhinolaryngology (9e, Vol 1) — ch. 18 Anatomy and embryology of the external and middle ear — §Tympanic cavity – lateral wall; – posterior wall — pp. 198–201; Fig. 18.6, p. 200
- Scott-Brown's Otorhinolaryngology (9e, Vol 1) — ch. 1 Physiology of hearing — §The middle ear mucosal folds — p. 12
- Scott-Brown's Otorhinolaryngology (9e, Vol 1) — ch. 29 Squamous chronic otitis media — Fig. 29.2, p. 291
- Glasscock-Shambaugh Surgery of the Ear (7e) — ch. 3 Anatomy of the Temporal Bone and Skull Base with Surgical Implications — Fig. 3.12, p. 33

Overview: divisions of the middle ear

- Spaces are named by their relation to the **tympanic annulus**: **mesotympanum** within it, **protympanum** anterior, **epitympanum** superior (above the annulus and lateral process of malleus), **retrotympanum** posterior, **hypotympanum** inferior.
- The ossicles, their ligaments and **mucosal folds** almost completely wall off the epitympanum from the mesotympanum — the **epitympanic diaphragm**.
- Only small openings remain, anterior and posterior to the stapes: **isthmus tympani anticus** and **posticus**.

Mucosal folds

Table 1. Principal middle ear folds and ligaments

Fold	Attachment / course	Significance
Tensor fold	From tensor tympani canal and cochleariform process	Separates anterior epitympanic space from supratubal recess; complete in 73%, absent/incomplete in 27%
Lateral malleal fold	One of three malleal folds arising from the malleus head	Roof of Prussak's space; isolates it from rest of posterior epitympanum
Anterior and posterior malleal folds	Lateral process of malleus to ends of tympanic annulus	Demarcate pars flaccida from pars tensa; anterior and inferior limits of Prussak's space
Lateral incudomalleal fold	Short process of incus, between incus body and long process, to malleus head; aligns with posterior and lateral malleal folds	Splits lateral posterior epitympanum into superior and inferior lateral attic
Posterior incudal ligament	Short process of incus to fossa incudis	Part of diaphragm; isthmus passes medial to it
Others (Proctor)	Medial and superior incudal, interosseous, superior malleolar folds; plica stapedis; obturatoria stapedis	Complete the partition; medial incudal, interosseous and tensor folds close the attic floor

CUM ch. 124, p. 1951; CUM ch. 143, pp. 2234–2235; SB ch. 18, p. 199.

Spaces

- **Epitympanum** — divided by the **cog** (bony septum from the tegmen, anterior to the malleus head, vertical over the cochleariform process):
 - **Anterior epitympanic space**: tegmen above, root of zygoma in front, chorda and anterior tympanic rim lateral, bone over geniculate ganglion medial, tensor canal–cochleariform process–tensor fold below.
 - **Posterior epitympanum**: malleus head, incus body and short process; opens into antrum through the aditus.
- **Superior lateral attic**: tegmen above, lateral incudomalleal fold below, tympanic facial nerve medially; drains to mastoid via aditus.
- **Inferior lateral attic**: lateral incudomalleal fold above, incus medially, scutum laterally; opens directly into mesotympanum — reliable ventilation.
- **Prussak's space** (most lateral posterior epitympanic compartment): pars flaccida lateral, malleus neck medial, lateral malleal fold above, posterior malleal fold below, anterior malleal fold in front — site of pars flaccida cholesteatoma.
- **Pouches of von Trötsch**: anterior and posterior pouches beside the malleal folds; the **posterior pouch** is the commonest aeration route of Prussak's space.
- **Supratubal recess**: anterosuperior extension of mesotympanum near the ET; large when tensor fold is vertical, narrow when horizontal.
- **Mesotympanum**: medial to pars tensa, ET orifice to facial nerve; contains handle of malleus, long process of incus, stapes, oval and round windows, promontory.

Ventilation pathways (applied)

- **Tympanic isthmus**: ET — mesotympanum — medial to manubrium, long process of incus and lateral incudomalleal fold — between tensor tendon and posterior incudal ligament — superior lateral attic and mastoid.
- With a complete tensor fold the isthmus is the **sole** attic route; its blockage causes **selective attic dysventilation**, retraction and cholesteatoma.
- **Prussak's space** has a separate route between posterior and lateral malleal folds.
- At surgery: **open a complete tensor fold** and clear the isthmus.

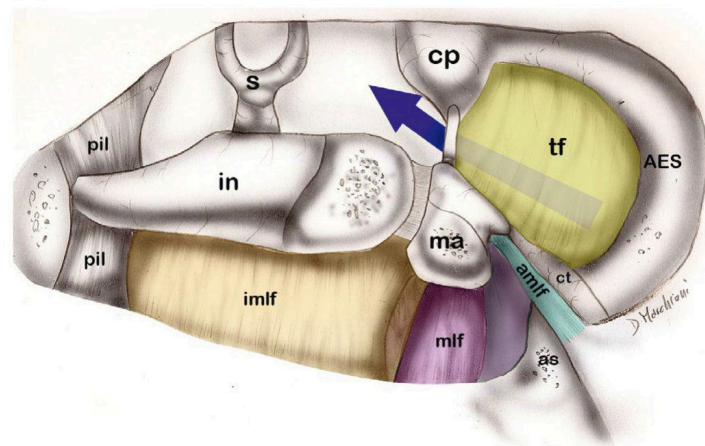
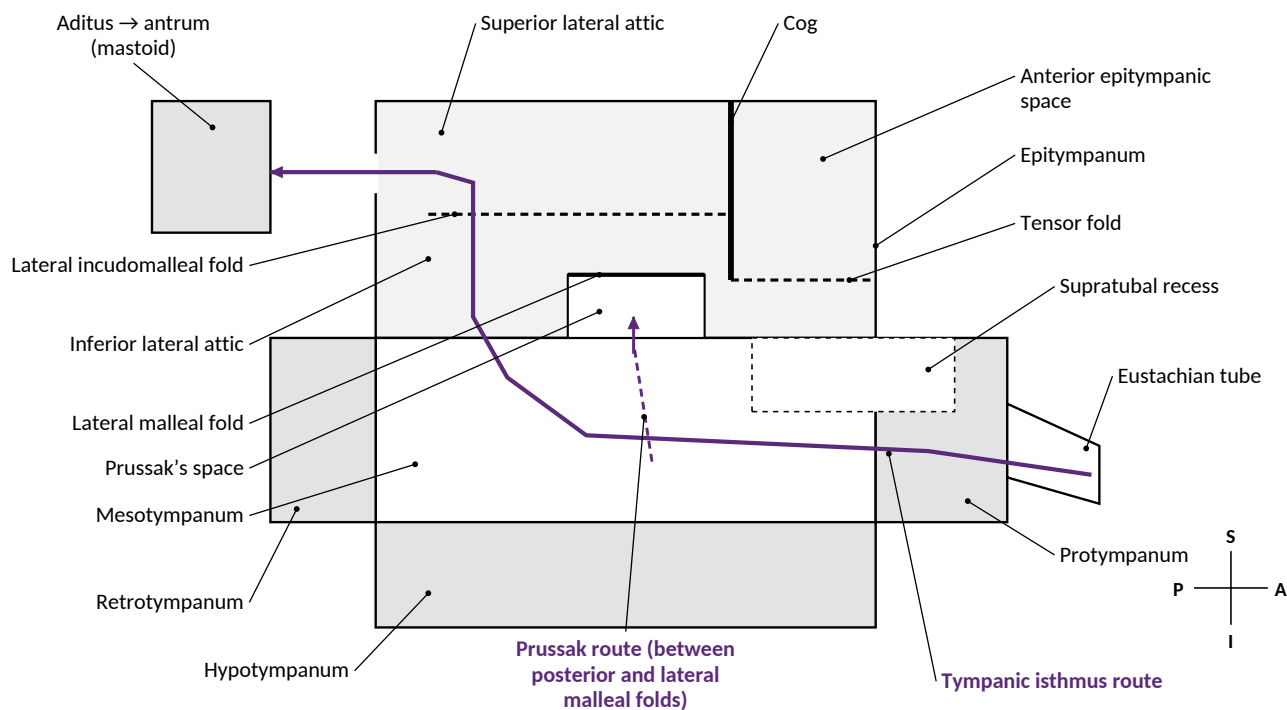


Fig. 143.3 Schematic drawing of the epitympanic diaphragm (right ear). Arrow shows aeration via the tympanic isthmus. AES, Anterior epitympanic space; amlf, anterior malleal ligament and fold; as, anterior spine; cp, cochleariform process; ct, chorda tympani; imlf, lateral incudomalleal fold; in, incus; ma, neck of the malleus; mlf, lateral malleal fold; pil, posterior incudal ligaments; s, stapes; tf, tensor fold.

Cummings (8e, Vol 2), ch. 143, Fig. 143.3, p. 2234.



Schematic (exam diagram): compartments, folds and ventilation routes of the right middle ear, lateral view (anterior to the right). Based on Cummings 8e Vol 2, Fig. 143.3, p. 2234; text pp. 2233–2235.

PEARLS

- Epitympanic diaphragm = ossicles + ligaments + folds (tensor, malleal, incudomalleal).
- **Prussak's space**: pars flaccida lateral, malleus neck medial, lateral malleal fold roof.
- **Tympanic isthmus** = main attic ventilation route; tensor fold complete in 73%.
- Cog divides anterior from posterior epitympanum.
- Draw lateral view: attic split by cog; isthmus arrow from ET.

2. Posterior mesotympanic (retrotympanic) spaces: enumeration and endoscopic anatomy of the retrotympanum

ASKED 2* · 4-mark answer

Asked in: Paper I · Dec 2021 · Q3(a) · Paper I · Dec 2022 · Q5(a)

Q: Enumerate the various posterior mesotympanic spaces. [4]

Q: Describe the endoscopic anatomy of retrotympanum with suitable diagrams. [4]

SOURCE

- Cummings Otolaryngology (8e, Vol 2) — ch. 143 Middle Ear Endoscopic Surgery — §Retrotympanum; §Hypotympanum — pp. 2235–2238; Fig. 143.7, p. 2236
- Cummings Otolaryngology (8e, Vol 2) — ch. 139 Chronic Otitis Media, Mastoiditis, and Petrositis — §Surgical Management — p. 2181
- Scott-Brown's Otorhinolaryngology (9e, Vol 1) — ch. 18 Anatomy and embryology of the external and middle ear — §Tympanic cavity – posterior wall — pp. 201–202; Fig. 18.7, p. 201
- Scott-Brown's Otorhinolaryngology (9e, Vol 1) — ch. 21 Endoscopic ear surgery — §Endoscopic anatomy and physiology of the middle ear; §Endoscope vs microscope — pp. 236–237

Definition and boundaries

- **Retrotympanum** = posterior part of the tympanic cavity, behind the tympanic annulus; a complex of bony **ridges and depressions**.
- **Boundaries:** anterosuperior — tympanic segment of facial nerve and posterior crus of stapes; anteroinferior — cochlear promontory.
- Hard to see without **angled endoscopes**; the **most frequent site of cholesteatoma recurrence**.

Bony landmarks (endoscopic view)

Table 1. Ridges and eminences of the retrotympanum

Landmark	Extent	Divides
Pyramidal eminence	Hollow cone below fossa incudis; stapedius tendon to stapes head	Marks second genu of facial nerve
Ponticulus	Promontory – pyramidal eminence; absent in ~20%	Posterior tympanic sinus (above) / sinus tympani (below)
Subiculum	Posterior pillar of round window niche – styloid eminence	Sinus tympani (above) / sinus subtympanicus (below)
Finiculus	Posterior hypotympanic rim – promontory at basal turn (SB: from anterior RW pillar towards jugular bulb)	Inferior retrotympanum / hypotympanum
Chordal ridge (chordiculus)	Pyramidal eminence – chordal eminence (chorda entry)	Facial sinus / lateral tympanic sinus
Styloid ridge	Chordal eminence – styloid eminence	—

CUM ch. 143, pp. 2235–2238; SB ch. 18, pp. 201–202.

Posterior mesotympanic spaces (enumeration)

- **1. Posterior tympanic sinus** (posterior sinus): posterior crus of stapes in front, tympanic facial nerve above, pyramidal eminence behind, ponticulus below, stapedial tendon laterally.
- **2. Sinus tympani** — the largest:
 - medial to the mastoid facial nerve, stapedial tendon and pyramid; lateral to vestibule and posterior SCC;
 - promontory in front, ponticulus above, subiculum below; may pass under the facial nerve.
- **3. Subpyramidal space:** medial and posterior to the pyramidal eminence; may join the posterior sinus or the sinus tympani.

- **4. Sinus subtypanicus** (subtypanic sinus, area concamerata): subiculum above, finiculus below, styloid eminence behind, round window niche and hypotympanic cells in front.
- **5. Facial sinus** and **6. lateral tympanic sinus**: lateral group, separated by the chordal ridge.
- **7. Hypotympanum**: below the finiculus and tympanic ring; contains the jugular bulb.

Endoscopic points (applied)

- **0°** scope shows most of the mesotympanum; **30–45°** scopes needed for the sinus tympani.
- Microscope fails to show the sinus tympani, even through a posterior tympanotomy.
- **Incomplete ponticulus** — sinus tympani confluent with posterior sinus; risk of stapes dislocation during dissection.
- Deep **subpyramidal space** — recurrence and stapes dislocation risk.
- **Sinus tympani** remains the commonest site of residual disease, endoscopic or microscopic.
- Subtypanic disease may track through **subcochlear canaliculi** to the petrous apex; a high jugular bulb restricts the hypotympanum.

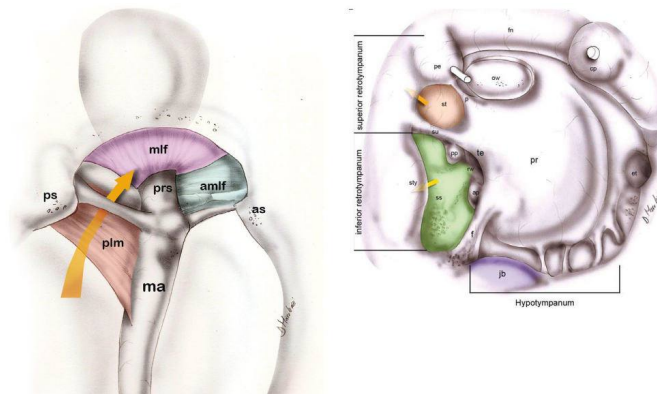
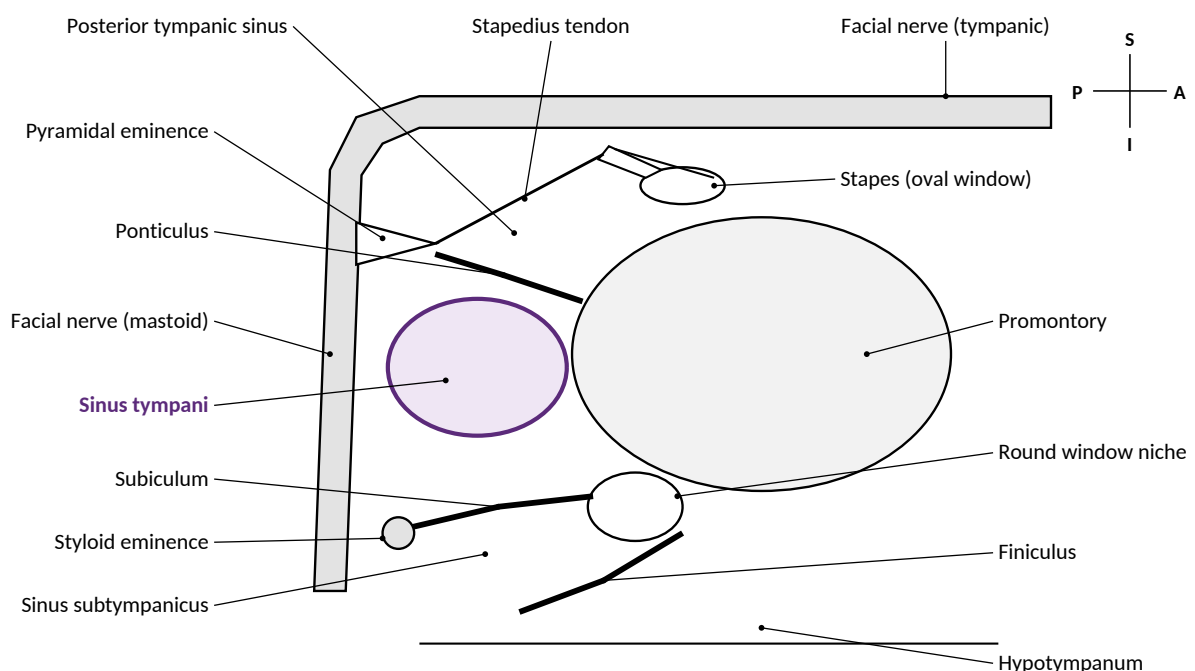


Fig. 143.7 Retrotympanum (right ear). ap, Anterior pillar; cp, cochleariform process; et, eustachian tube; f, finiculus; fn, facial nerve; jb, jugular bulb; ow, oval window; p, ponticulus; pe, pyramidal eminence; pp, posterior pillar; pr, promontory; rw, round window; st, sinus tympani; sty, styloid eminence; su, subiculum; ss, subtypanic sinus; te, round window tegmen.

Cummings (8e, Vol 2), ch. 143, Fig. 143.7, p. 2236.



Schematic (exam diagram): retrotympanum of the right ear, transcanal endoscopic view (posterior to the left). Based on Cummings 8e Vol 2, Fig. 143.7, p. 2236; text pp. 2235–2238; SB Fig. 18.7, p. 201.

PEARLS

- Three ridges: **ponticulus** (upper), **subiculum** (middle), **finiculus** (lower).
- Sinus tympani lies between ponticulus and subiculum, medial to facial nerve.
- Retrotympanum = commonest site of recurrent/residual cholesteatoma.
- Angled (30°/45°) endoscope is the tool for this region.

3. Types and grades of sinus tympani, with labelled diagrams

ASKED 1* · 6-mark answer

Asked in: Paper I · Dec 2021 · Q3(b)

Q: Describe the various types and grades of sinus tympani with labelled diagrams. [6]

SOURCE

- Cummings Otolaryngology (8e, Vol 2) — ch. 143 Middle Ear Endoscopic Surgery — §Retrotympanum — pp. 2235–2237; Fig. 143.8, p. 2237
- Cummings Otolaryngology (8e, Vol 2) — ch. 124 Anatomy of the Temporal Bone, External Ear, and Middle Ear — §Middle Ear — pp. 1950–1951
- Cummings Otolaryngology (8e, Vol 2) — ch. 139 Chronic Otitis Media, Mastoiditis, and Petrositis — §Surgical Management — p. 2181
- Scott-Brown's Otorhinolaryngology (9e, Vol 1) — ch. 18 Anatomy and embryology of the external and middle ear — §Tympanic cavity – posterior wall — pp. 201–202
- Scott-Brown's Otorhinolaryngology (9e, Vol 1) — ch. 21 Endoscopic ear surgery — §Endoscopic anatomy and physiology of the middle ear — pp. 236–238; Fig. 21.7, p. 238
- Glasscock-Shambaugh Surgery of the Ear (7e) — ch. 3 Anatomy of the Temporal Bone and Skull Base with Surgical Implications — Figs. 3.21, 3.22, p. 37

Definition and boundaries

- **Sinus tympani:** the largest retrotympanic sinus — a recess of the posterior mesotympanum behind the oval and round windows, **medial to the mastoid (vertical) facial nerve**, stapedial tendon and pyramidal eminence.
- **Lateral** to the vestibule and posterior semicircular canal.
- **Limits:** promontory anteriorly, **ponticulus** superiorly, **subiculum** (posterior pillar of round window niche → styloid eminence) inferiorly.
- May extend under the facial nerve; harbours **occult cholesteatoma**.

Types – morphology (Marchioni)

- Based on the shape of the **ponticulus**, as seen at endoscopic cholesteatoma surgery.
- **Classical:** limited by the ponticulus above and the subiculum below; lies medial to the facial nerve and pyramidal eminence.
- **Confluent:** ponticulus absent or incomplete — sinus tympani is continuous with the **posterior tympanic sinus**.
- **Partitioned:** a third bony ridge between ponticulus and subiculum, running from the vertical facial nerve to the promontory, divides it into **superior and inferior** parts.
- **Restricted:** a **high jugular bulb** reduces its inferior extent.

Grades – depth on axial CT (Marchioni)

Table 2. Depth classification of sinus tympani and surgical access

Grade	Definition (relation to facial nerve)	Access for cholesteatoma
Type A — small (limited)	Anterior edge of the vertical facial nerve is its medial and posterior boundary	Endoscopic, facial recess or wide canaloplasty
Type B — deep	Medial limit lies medial to the facial nerve; no extension beyond its posterior border	Endoscopic with angled instruments, or facial recess with skeletonised facial nerve
Type C — deep with posterior extension	Posterior and medial limits lie posterior to the facial nerve; very large and deep	Retrofacial (transmastoid) approach for full exposure; may not be accessible from the middle ear

CUM ch. 143, pp. 2236–2237; SB ch. 21, pp. 236, 238.

Ponticulus variants (Nogueira)

- **Classical:** complete ridge from pyramidal eminence to promontory; separates sinus tympani from posterior tympanic sinus.
- **Incomplete:** ponticulus absent — confluence of the two sinuses; higher risk of inadvertent **stapes mobilisation/dislocation**; dissect under direct vision.
- **Communicating:** only a small bony bridge — disease passes beneath it to the posterior crus and **subpyramidal space**; remove the bridge for exposure.
- Ponticulus is absent in about 20% of ears (SB).
- Depth is a continuum — shallow, medium and deep sinuses are described (GS); historically a frequent site of residual cholesteatoma.

Clinical significance

- Assess depth on **preoperative axial CT** to plan the approach.
- Complex or deep sinus → higher recurrence; sinus tympani is the **commonest site of residual disease**, endoscopic or microscopic.
- Microscope cannot see it, even through a posterior tympanotomy; a **30–45°** endoscope can.
- Type A can be cleared through the canal or facial recess; type B needs angled instruments or a skeletonised facial nerve; type C cannot be reached from the middle ear.
- A deep **subpyramidal space** may open into the sinus tympani — adds recurrence risk and risk to the stapes.
- Deep disease needs endoscopic transcanal or transmastoid retrofacial removal to avoid a dehiscent facial nerve or high jugular bulb.

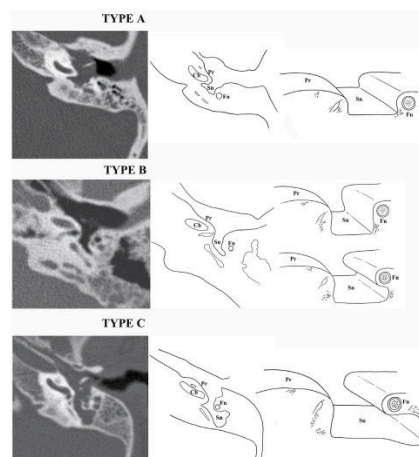
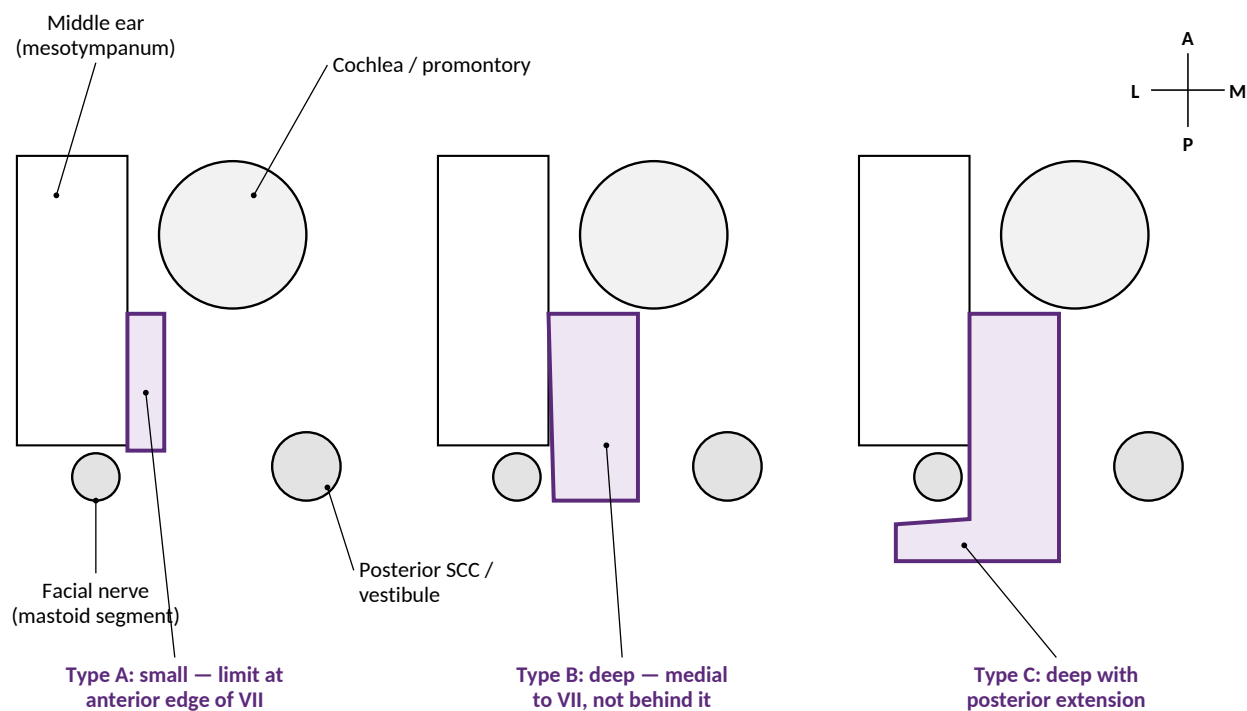


Fig. 143.8 Sinus tympani depth classification. Type A, small sinus tympani where the anterior edge of the vertical segment of the facial nerve is the medial and posterior boundary of the sinus tympani. Type B, deep sinus tympani where the medial limit of the sinus tympani lies medial to the facial nerve. Type C, deep sinus tympani with posterior extension where the posterior and medial boundaries of the sinus tympani lie posterior to the facial nerve. Ch, Cochlea; Fn, facial nerve; Pr, promontory; Sn, sinus tympani.

Cummings (8e, Vol 2), ch. 143, Fig. 143.8, p. 2237.



Schematic (exam diagram): depth grades of the sinus tympani on axial section — type A, B and C relative to the mastoid facial nerve. Based on Cummings 8e Vol 2, Fig. 143.8, p. 2237; text pp. 2236–2237; SB Fig. 21.7, p. 238.

PEARLS

- **Types** (morphology): classical, confluent, partitioned, restricted.
- **Grades** (depth on CT): A small, B deep medial to VII, C deep posterior to VII.
- Type C — **retrofacial approach**.
- Limits: ponticulus above, subiculum below, promontory in front.
- Absent ponticulus — stapes at risk.

4. Position of the round window membrane and its relations (with measurements) to other landmarks

ASKED 1* · 6-mark answer

Asked in: Paper I · Dec 2022 · Q5(b)

Q: Discuss the relation (along with measurements) of the position of round window membrane with other landmarks.
[6]

SOURCE

- Cummings Otolaryngology (8e, Vol 3) — ch. 156 Pharmacologic and Molecular Therapies of the Cochlear and Vestibular Labyrinths — §Round Window Membrane: Anatomy; §Intratympanic delivery — pp. 2406–2408; Fig. 156.4, p. 2408
- Cummings Otolaryngology (8e, Vol 3) — ch. 159 Medical and Surgical Considerations in Cochlear Implantation — §Round Window Membrane Cochleostomy — p. 2453
- Cummings Otolaryngology (8e, Vol 3) — ch. 166 Surgery for Vestibular Disorders — §Singular Neurectomy — p. 2555
- Cummings Otolaryngology (8e, Vol 3) — ch. 195 Pediatric Otologic Surgery — §Cochleostomy Versus Round Window Insertion — p. 2992
- Cummings Otolaryngology (8e, Vol 2) — ch. 142 Mastoidectomy: Surgical Techniques — §The Facial Recess — p. 2223
- Scott-Brown's Otorhinolaryngology (9e, Vol 1) — ch. 18 Anatomy and embryology of the external and middle ear — §Tympanic cavity – medial wall — pp. 199–201
- Scott-Brown's Otorhinolaryngology (9e, Vol 1) — ch. 21 Endoscopic ear surgery — p. 237; Fig. 21.8, p. 239
- Glasscock-Shambaugh Surgery of the Ear (7e) — ch. 21 Inner Ear Pathology for the Cochlear Implant Surgeon — §The Round Window Region — pp. 323–324
- Glasscock-Shambaugh Surgery of the Ear (7e) — ch. 20 Cochlear Implants in Adults — p. 307; ch. 54 Benign Paroxysmal Positional Vertigo — p. 788; ch. 50 Sudden Sensorineural Hearing Loss — p. 736

Position and orientation

- Round window niche** (fossula fenestrae cochleae) lies **just posteroinferior to the promontory**; the RWM closes the basal end of the **scala tympani**.
- Medial wall, superior → inferior: lateral SCC prominence, tympanic facial nerve, oval window, round window.
- Rim of the RWM lies roughly at **right angles** to that of the stapes footplate; membrane is **concave** as seen from the tympanic cavity.
- RWM is angled **27°–65° inferior to the sagittal plane**; >45° (about 10%) makes it look smaller than a 1-mm burr and an electrode tends to hit the modiolus.
- Membrane is usually partly hidden by the bony overhang (**RW tegmen**), mostly the posterior pillar — drill to see it.

Relations with measurements

Table 1. Round window: relations and measurements

Landmark	Relation	Measurement
Umbo (through intact TM)	RW niche posteroinferior to umbo	3.44 mm (±0.68) from umbo
Handle of malleus	Angle between handle and umbo–RW line	113.2° (±9.8°)
Oval window / stapes	RW lies inferior and posterior to OW	~2 mm
Promontory	RW niche lies just posteroinferior to it	—

CUM ch. 156, pp. 2406–2408; GS ch. 20, p. 307.

Relations medial to the membrane (inner ear)

- **Osseous spiral lamina and basilar membrane** lie **0.5 mm** from the centre of the RW, superior to it — insert the electrode with an **inferior trajectory**, parallel to them.
- **Ductus reuniens** lies close to the **posterior** margin of the RWM; RW insertion avoids it.
- **Cochlear aqueduct** and **inferior cochlear vein** lie close to the **inferior** margin; the aqueduct arises from the scala tympani at the inferior basal turn and is bone-occluded in 7%.
- **Singular nerve**: drill about **0.7 mm posteroinferior** to the posteromedial RWM margin, depth **1.5 mm** (another series ≥ 0.7 mm from the edge at 1.3 mm); GS — 1–2 mm deep to the inferior RWM in the posterior third of the niche.
- Posterior canal ampulla, cochlear aqueduct and inferior cochlear vein all lie within **2 mm** of that drilling point.
- **Spiral ligament**: very close posterosuperiorly, farthest anteroinferiorly — so drill the RW tegmen from anteroinferior to posterosuperior.
- **Cochleostomy**: anterior and inferior to the RWM, 0.8–1.2 mm; if the RW is obliterated, drill 1.5 mm inferior to the pyramidal process or stapes.

Bony framework of the niche

- **Posterior pillar** → **subiculum** → styloid eminence: sinus tympani above, sinus subtympanicus below.
- **Funiculus** from the niche region to the hypotympanum; **fustis** forms the floor of the RW chamber and points to the membrane.
- **Promontory** (basal turn) in front, with Jacobson's nerve on it.

Surgical corridors

- Seen through the **facial recess** (chorda laterally, facial nerve medially, fossa incudis above), with promontory and incudostapedial joint.
- RW is relatively **posterior in infants**; facial recess–RW orientation differs in children — an extended RW approach may be needed.
- Round window is the **0°** reference point for angular insertion depth of cochlear implant electrodes.

Membrane structure (relevant numbers)

- Three layers: outer epithelium (middle ear mucosa), middle connective tissue, inner epithelium (scala tympani); about **70 μ m** thick.
- **False membrane** in 21%; fibrous or fat plug in 11% — obstructs drug delivery and RW insertion.

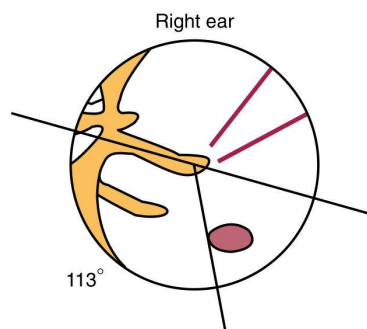
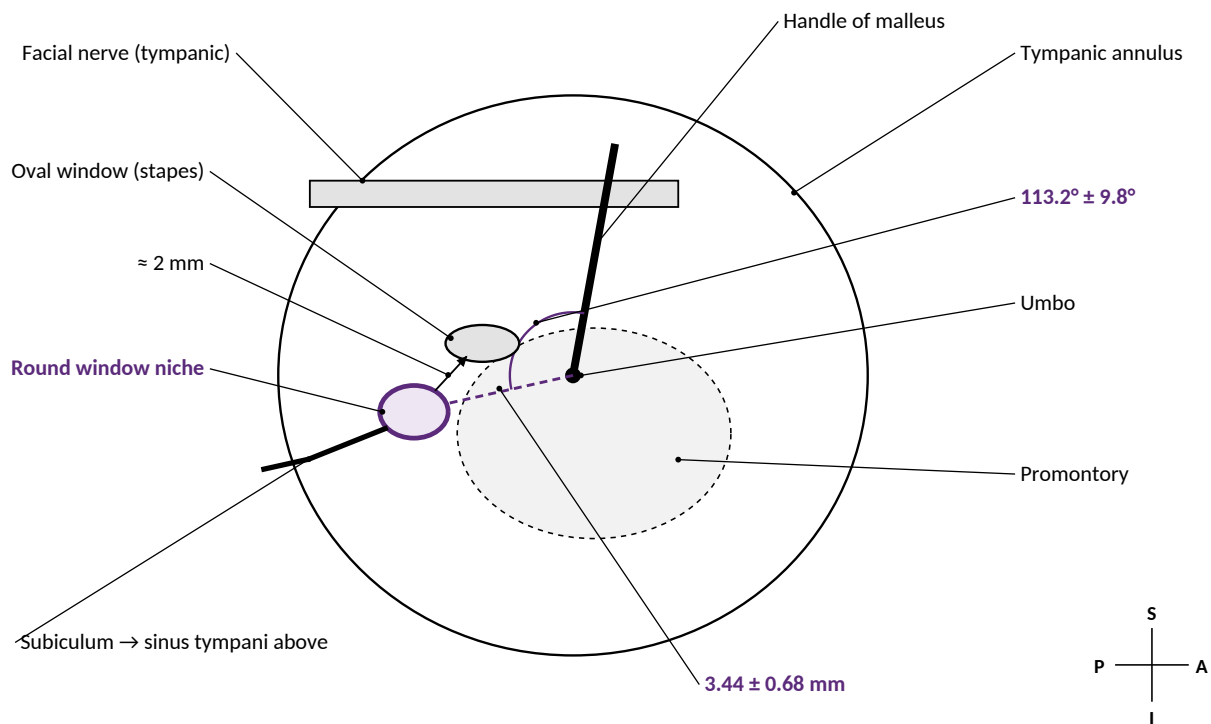


Fig. 156.4 Illustration showing how the angle between the handle of the malleus and the round window (shown in the supine operative position) is calculated.

Cummings (8e, Vol 3), ch. 156, Fig. 156.4, p. 2408.



Schematic (exam diagram): transcanal landmarks of the right round window — distance and angle from umbo and malleus handle, and its relation to the oval window. Based on Cummings 8e Vol 3, Fig. 156.4, p. 2408; text pp. 2406–2408; GS p. 307.

PEARLS

- RW niche: **3.44 mm from umbo at 113°** to malleus handle — intratympanic injection target.
- RW **≈ 2 mm inferior and posterior** to oval window.
- Basilar membrane/OSL **0.5 mm** above RW centre — aim inferiorly.
- Singular nerve: posteroinferior, 1–2 mm deep.
- False membrane in 21%.

5. Congenital anomalies of the middle ear; the facial recess

ASKED 1* · 5-mark answer

Asked in: Paper I · Jun 2022 · Q3(b)

Q: Describe various congenital anomalies of middle ear. Describe facial recess. [5]

SOURCE

- Scott-Brown's Otorhinolaryngology (9e, Vol 2) — ch. 127 Congenital middle ear abnormalities and microtia — §Classification of atresia; §Classification of congenital ossicular malformations; §Congenital stapes fixation; §Isolated non-stapes middle ear anomalies; §Congenital oval window atresia — pp. 1368–1374; Tables 127.1, p. 1369, 127.2, p. 1373
- Glasscock-Shambaugh Surgery of the Ear (7e) — ch. 33 Surgery for Congenital Aural Atresia and Stenosis — p. 478; ch. 3 Anatomy of the Temporal Bone and Skull Base — Figs. 3.17, 3.21, pp. 35–37; ch. 19 Pediatric Cochlear Implantation — p. 289
- Cummings Otolaryngology (8e, Vol 3) — ch. 151 Tinnitus and Hyperacusis — p. 2359; ch. 175 Temporal Bone Neoplasms and Lateral Cranial Base Surgery — p. 2714; ch. 196 Congenital Malformations of the Inner Ear — p. 3009
- Cummings Otolaryngology (8e, Vol 2) — ch. 134 Neuroradiology of the Temporal Bone and Skull Base — §Carotid Artery — p. 2094
- Scott-Brown's Otorhinolaryngology (9e, Vol 1) — ch. 18 Anatomy and embryology of the external and middle ear — §Tympanic cavity – anterior wall; – floor; – nerves and blood vessels — pp. 199, 202–203
- Glasscock-Shambaugh Surgery of the Ear (7e) — ch. 20 Cochlear Implants in Adults — §Incision; §Facial Recess — pp. 305–307
- Cummings Otolaryngology (8e, Vol 2) — ch. 124 Anatomy of the Temporal Bone, External Ear, and Middle Ear — §Facial Nerve — pp. 1951–1953
- Cummings Otolaryngology (8e, Vol 2) — ch. 142 Mastoidectomy: Surgical Techniques — §The Facial Recess — pp. 2223–2224; Fig. 142.5, p. 2223
- Scott-Brown's Otorhinolaryngology (9e, Vol 1) — ch. 39 Middle-ear implants — p. 412

Congenital anomalies of the middle ear

- **Major** malformation = aural atresia: absent canal and drum with an underdeveloped middle-ear cleft; **minor** = normal canal and drum (Bellucci).
- **Minor** anomalies: congenital stapes fixation, absent long process of incus, malleus bar, absent oval window, single stapes crus.
- Present as congenital **conductive loss** (≈95% of microtia-atresia; a few have SNHL, sometimes profound); may pass OAE screening; **CT** is recommended; often more than one ossicle is abnormal.
- Atresia is graded **complete, partial or stenosis**; stenosis can develop cholesteatoma but suits hearing-restoration surgery best.
- **Oval window atresia** is under-represented in surgical series because it is usually diagnosed on CT without exploration.

Table 1. Cremers' classification of minor ossicular anomalies (modified by Tos; 144 operated ears)

Class	Main anomaly	%
1	Isolated congenital stapes ankylosis — footplate fixation (normal, monopodial or monocrucial arch) or suprastructure fixation (long pyramid; bony bars to pyramid, facial canal or promontory)	30.6
2	Stapes ankylosis plus another ossicular anomaly (incus/malleus deformity, absent long process of incus, bony malleus/incus fixation)	38.2
3	Ossicular anomaly with mobile footplate — discontinuity (aplastic/dysplastic long process of incus); epitympanic or tympanic fixation	15.3 + 6.3
4	Aplasia or severe dysplasia of oval or round window ; crossing (prolapsed) facial nerve; persistent stapedia artery	6.9; 2.1; 0.7

SB ch. 127, Table 127.1, p. 1369.

Table 2. Jahrsdoerfer grading for atresia surgery (10 points)

Structure	Score	Structure	Score
Stapes present	2	Mastoid pneumatisation	1
Oval window patent	1	Incus-stapes connection	1
Middle ear space	1	Round window	1
Facial nerve position	1	External ear	1
Malleus-incus complex	1	Total	10

SB ch. 127, Table 127.2, p. 1373.

- **Congenital stapes fixation** (Shambaugh, 1952):
 - annular ligament fails to differentiate from the **lamina stapedia** — continuous ossification from otic capsule to footplate; footplate margins are hard to see, unlike otosclerosis;
 - other mechanisms: ossified stapedia tendon (cartilaginous like the pyramid precursor), persistent contact with **Reichert's cartilage**;
 - CT first — dilated IAM fundus, **IP1** or **IP3** (X-linked) — **perilymph/CSF gusher**, SNHL, meningitis risk;
 - surgery as for otosclerosis but expect concomitant malleus-incus fixation, thick crura (KTP laser), odd ossicle-footplate distances; ABG ≤20 dB in >70% — inferior to otosclerosis.
- **Isolated non-stapes anomalies**: attic fixation (needs atticotomy; incus removal + PORP), bony bar (laser, drill, curette), malleus handle fixed to an atretic plate, absent long process of incus (interposition prosthesis).
- **Oval window atresia**: common; crura poorly formed, facial nerve often runs over the atretic window — hearing aid or implant rather than surgery.
- **Persistent stapedia artery** (0.02–0.5%): through the stapes obturator foramen, over promontory, exits near geniculate ganglion; CT — absent foramen spinosum, enlarged geniculate facial canal.
- **Aberrant ICA**: enters via an enlarged inferior tympanic canaliculus; pulsatile red mass — a hazard before biopsy of any middle-ear mass.
- **Facial nerve**: tympanic segment dehiscent above the oval window in **55%**; may prolapse onto the stapes arch and mimic fixation; anomalous over an atretic oval window.
- **High or dehiscent jugular bulb**: above the annulus — hazard at grommet insertion and flap elevation.
- Others: congenital perilymph fistula, inner-ear malformation, vestibulocochlear nerve hypoplasia (SB).

Facial recess

- **Definition**: triangular posterior tympanic space between the **mastoid facial nerve** and the **chorda tympani** — the route of a **posterior tympanotomy** from mastoid to middle ear.
- **Boundaries** (Fig. 1):
 - lateral — **chorda tympani** (GS: anterior);
 - medial — **facial nerve** (GS: posterior);
 - superior — **fossa incudis / incudal buttress**.
- Formed by the **chordofacial angle** — chorda leaves the mastoid facial nerve at a variable point, at about **23°** on average; it enters the middle ear through the iter chordae posterior.

- Size varies with chorda course and pneumatization; width similar in children and adults (orientations differ); **≥3 mm** needed to pass a floating mass transducer.
- **Opening it** (cochlear implant technique):
 - landmarks: short process of incus, lateral SCC dome, thinned posterior canal wall; skeletonise the mastoid facial nerve in its middle two-thirds;
 - enter at the **widest point just below the incus buttress**; enlarge anterior and parallel to the facial nerve with progressively smaller burrs under continuous facial nerve monitoring, never resting the drill shaft on the nerve;
 - the round window lies about 2 mm inferior and posterior to the oval window.
- **Seen through it**: promontory, round window niche, incudostapedial joint, cochleariform process, pyramidal process, medial drum, ET orifice.
- **Extended**: widened up and down; sacrificing the chorda exposes the hypotympanum (lateral limit = annulus); removing the fossa incudis joins it to the aditus.
- **Uses**: canal-wall-up mastoidectomy (mesotympanum, sinus tympani), cochlear implant, middle-ear implants, glomus tympanicum (extended).
- Lies **lateral** to the facial nerve; the sinus tympani lies **medial** to it.

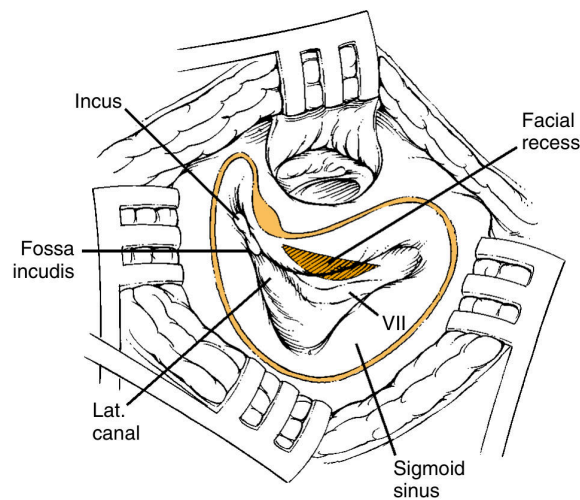


Fig. 142.5 The facial recess is shown as the triangle.
Cummings (8e, Vol 2), ch. 142, Fig. 142.5, p. 2223.

PEARLS

- Minor anomaly = normal canal and drum; commonest is **stapes fixation** (Cremers classes 1–2).
- CT before congenital stapes surgery — IP3 means gusher.
- Facial recess: chorda lateral, VII medial, incus buttress above.
- Facial recess lateral, sinus tympani medial to VII.

6. Microstructure of the cochlea, with labelled diagrams of the cochlea and cochlear duct

ASKED 2* · 5-mark answer

Asked in: Paper I · Jun 2020 · Q3(a) · Paper I · Jun 2022 · Q3(a)

Q: Describe the microstructure of Cochlea. [5]

Q: Draw labelled diagram of cochlea & cochlear duct. What is auditory pathway? [5]

SOURCE

- Cummings Otolaryngology (8e, Vol 2) — ch. 125 Neuroanatomy of the Auditory System — §Cochlear Anatomy: Osteology; Membranous Labyrinth and Inner Ear Fluids; Hair Cells; Innervation — pp. 1955–1958; Fig. 125.1, p. 1956
- Cummings Otolaryngology (8e, Vol 2) — ch. 126 Principles of Applied Auditory Physiology — §Inner Ear Physiology — p. 1965
- Scott-Brown's Otorhinolaryngology (9e, Vol 1) — ch. 19 Anatomy of the cochlea and vestibular system — §General characteristics of hair cells; §The cochlea; §Organ of Corti; §Ion-transporting epithelia; §Reissner's membrane — pp. 209–222
- Scott-Brown's Otorhinolaryngology (9e, Vol 1) — ch. 1 Physiology of hearing — §Cochlear fluid — p. 15

Bony cochlea

- Snail-shaped coil of about **2½ turns** around a porous central core, the **modiolus**, which carries the cochlear nerve fibres and the cochlear artery and vein.
- **Osseous spiral lamina** projects from the modiolus; it is **wider at the base**, while the basilar membrane is **narrower and thicker at the base**, wider and thinner at the apex — basis of **tonotopy** (high frequencies basal, low apical).
- Cochlear duct length 28–40 mm, average about 33–34 mm (CUM); 27.6–33.4 mm, mean 30.7 mm (SB).
- **Three scalae**: **scala vestibuli** (perilymph, from the vestibule/oval window), **scala media** (endolymph), **scala tympani** (perilymph, ends at the round window); vestibuli and tympani meet at the **helicotrema**.

Cochlear duct (scala media) – triangular in section

- **Roof — Reissner's membrane**: two cell layers; tight junctions keep endolymph and perilymph apart; bulges in hydrops.
- **Floor — basilar membrane** (osseous spiral lamina to spiral ligament; radial collagen IV fibrils) carrying the **organ of Corti**.
- **Lateral wall — stria vascularis** on the **spiral ligament**:
 - **marginal** cells (face endolymph, secrete K^+), **intermediate** cells (melanocytes; generate the endocochlear potential), **basal** cells (tight-junction seal);
 - intrastrial capillaries form a blood–strial barrier.
- **Medial — spiral limbus** on the osseous spiral lamina: anchors Reissner's membrane and gives off the **tectorial membrane**; inner spiral sulcus beside it.
- **Endolymph**: K^+ ~140 mM, Na^+ ~1 mM, endocochlear potential about **+80 mV**; perilymph is high Na^+ , low K^+ .

Organ of Corti

Table 1. Inner versus outer hair cells

Feature	Inner hair cells	Outer hair cells
Number, rows	≈3500 (3000 in ch. 126), one row	≈12,000, three rows
Shape, position	Flask; modiolar side of tunnel of Corti, over rigid bony lip	Cylindrical; strial side, on most flexible basilar membrane
Stereocilia	Shallow U-shaped; do not touch tectorial membrane	V/W-shaped; tallest embedded in tectorial membrane
Afferents	Type I (90–95%), ~20 fibres per cell; one fibre – one IHC	Type II (5–10%), one fibre – many OHCs
Efferents	Lateral olivocochlear, onto afferent terminals	Medial olivocochlear, direct (~80% of efferents)
Role	Sensory transducer — sends signal to brain	Cochlear amplifier (prestin); source of OAEs

CUM ch. 125, pp. 1957–1958; SB ch. 19, pp. 218–221.

- **Supporting cells:** inner and outer **pillar cells** (arch = **tunnel of Corti**); **Deiters' cells** cup each OHC base; inner phalangeal and border cells round the IHC; Hensen, Claudius and Boettcher cells laterally; gap junctions (Cx26, Cx30) recycle K^+ .
- **Reticular lamina:** apical junctions of hair and supporting cells — the real endolymph–perilymph barrier; tunnel of Corti, space of Nuel and outer tunnel contain **perilymph**.
- **Hair bundle:** actin stereocilia in graded rows; **tip links** (cadherin 23, protocadherin 15) open MET channels; kinocilium persists only as a basal body.
- **Innervation:** ~30,000 bipolar neurons in the **spiral ganglion** (Rosenthal's canal); fibres reach hair cells through the **habenula perforata**.
- **Blood supply:** spiral modiolar artery – vestibulocochlear artery – AICA — an **end artery**.

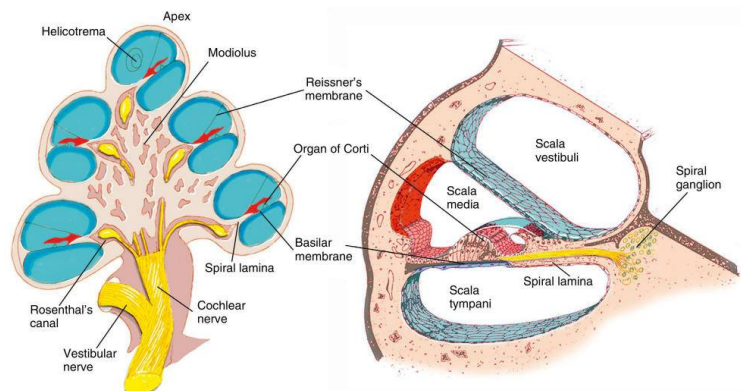


Fig. 125.1 Cross section of the cochlea showing the passage of the cochlear nerve through the modiolus to the organ of Corti (left). A higher-power view shows the osseous cochlear duct and membranous compartments within the cochlea (right).
Cummings (8e, Vol 2), ch. 125, Fig. 125.1, p. 1956.

9. Homeostasis of the intracochlear fluids

ASKED 1* · 5-mark answer

Asked in: Paper I · Jun 2020 · Q3(b)

Q: Discuss the homeostasis of intracochlear fluids. [5]

SOURCE

- Cummings Otolaryngology (8e, Vol 3) — ch. 147 Cochlear Transduction and Peripheral Auditory Pathology — §Stria Vascularis, Perilymphatic-Endolymphatic Barrier, and Endolymph Homeostasis — pp. 2283, 2287–2290; Fig. 147.9, p. 2290
- Cummings Otolaryngology (8e, Vol 2) — ch. 125 Neuroanatomy of the Auditory System — §Membranous Labyrinth and Inner Ear Fluids — pp. 1955–1956; ch. 126 Principles of Applied Auditory Physiology — pp. 1965, 1967; Fig. 126.4, p. 1967
- Cummings Otolaryngology (8e, Vol 3) — ch. 156 Pharmacologic and Molecular Therapies of the Cochlear and Vestibular Labyrinths — §Cerebrospinal Fluid Communication; Table 156.1 — p. 2406
- Scott-Brown's Otorhinolaryngology (9e, Vol 1) — ch. 19 Anatomy of the cochlea and vestibular system — §Introduction; §Supporting cells; §Ion-transporting epithelia; §Vascular supply; §Reissner's membrane — pp. 207–222
- Scott-Brown's Otorhinolaryngology (9e, Vol 1) — ch. 1 Physiology of hearing — §Cochlear fluid — p. 15; ch. 10 Ménière's disease — p. 122; ch. 34 Ototoxicity — p. 350
- Glasscock-Shambaugh Surgery of the Ear (7e) — ch. 5 Auditory Physiology: Inner Ear — §Organ of Corti and Inner Ear Fluids — p. 71; ch. 21 — p. 324; ch. 51 Ménière's Disease — §Pathophysiology — pp. 743–744
- Cummings Otolaryngology (8e, Vol 3) — ch. 197 Enlarged Vestibular Aqueduct Syndrome — p. 3017; ch. 156 — §Round Window Membrane: Physiology — p. 2407

Fluid compartments

Table 1. Intracochlear fluid compartments

Compartment	Site	Composition / potential	Source and drainage
Perilymph	Scala vestibuli, scala tympani, spaces of organ of Corti	High Na^+ , low K^+ and Ca^{2+} (CSF-like)	Joins CSF through the cochlear aqueduct (patency variable; bone-occluded in 7%)
Endolymph	Scala media (continuous with vestibular endolymph, endolymphatic duct and sac)	$\text{K}^+ \sim 140 \text{ mM}$, $\text{Na}^+ \sim 1 \text{ mM}$, little Ca^{2+} ; endocochlear potential +80 mV (+60 to +100)	Secreted by stria vascularis ; absorbed in the endolymphatic sac
Intrastrial fluid	Between marginal and intermediate cells	Low K^+ ; high positive potential	Sealed by basal-cell tight junctions; fed by capillaries

SB ch. 19, pp. 207, 221–222; SB ch. 1, p. 15; CUM ch. 125, p. 1956; CUM ch. 147, p. 2290; GS ch. 5, p. 71.

- Origin of perilymph — books differ:** an ultrafiltrate of plasma and CSF (SB ch. 1, ch. 10); neither a simple ultrafiltrate nor CSF but **locally produced** behind a blood–perilymph barrier, differing between the two scalae (SB ch. 19, ch. 34).
- CSF–perilymph oscillations across the aqueduct follow respiratory pressure changes (CUM).

Barriers that keep the fluids apart

- Tight junctions** lining the scala media — Reissner's membrane, reticular lamina of the organ of Corti, spiral limbus, sulcus cells and stria marginal cells — stop paracellular leak of water and ions.
- Reticular lamina:** hair-cell stereocilia sit in endolymph, cell bodies in perilymph; the basilar membrane is freely permeable.
- Blood–labyrinth (blood–stria) barrier:** endothelium, pericytes and perivascular macrophage-type melanocytes control entry from blood.

Potassium recycling – the core of homeostasis

Flowchart 1. Cochlear K^+ cycle

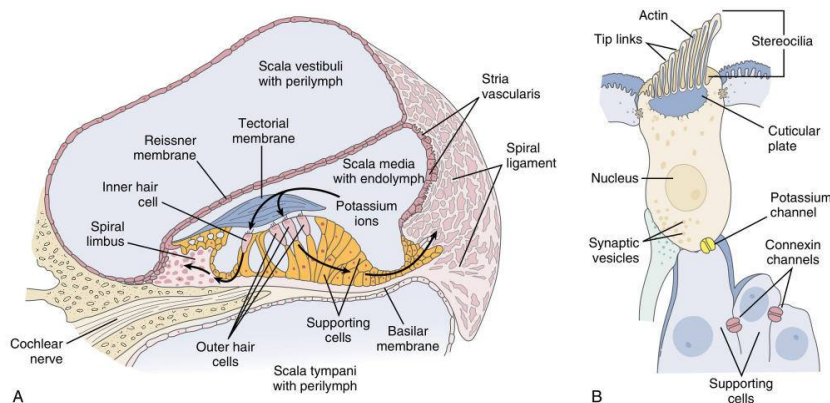
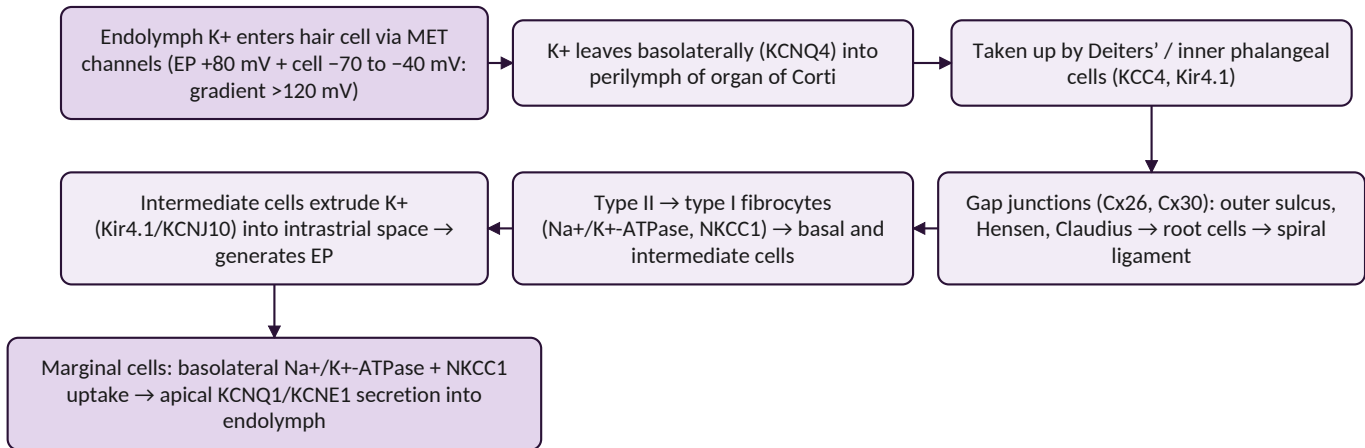


Fig. 126.4 Mechanoelectrical transduction of the auditory signal depends on the recycling of potassium ions in the organ of Corti. (A) Schematic cross-sectional view of the human cochlea. The scala media (cochlear duct) is filled with endolymph, and the scala vestibuli and tympani are filled with perilymph. The endolymph of the scala media bathes the organ of Corti, located between the basilar and tectorial membranes and containing the inner and outer hair cells. A relatively high concentration of potassium in the endolymph of the scala media relative to the hair cell creates a cation gradient maintained by the activity of the epithelial supporting cells, spiral ligament, and stria vascularis. (B) Cells contain stereocilia along their apical surface and are connected by tip links. The potassium gradient is essential to enable depolarization of the hair cell after influx of potassium ions in response to mechanical vibration of the basilar membrane, deflection of stereocilia, displacement of tip links, and opening of gated potassium channels. Depolarization results in calcium influx through channels along the basolateral membrane of the hair cell, which causes degranulation of neurotransmitter vesicles into the synaptic terminal and propagates an action potential along the auditory nerve. Gap junction proteins between the hair cells (potassium channel, yellow) and epithelial supporting cells (connexin channels, red) allow for the flow of potassium ions back to the stria vascula

Cummings (8e, Vol 2), ch. 126, Fig. 126.4, p. 1967.

- **Stria vascularis** has the highest oxidative metabolism in the body; marginal cells keep endolymph K^+ high, intermediate cells (neural-crest melanocytes) generate the EP, basal cells insulate it.
- Basal cells, intermediate cells and fibrocytes form one **gap-junction syncytium**; marginal cells stand apart.
- **K^+ secretion and EP are separate**: in development endolymph K^+ is high and marginal-cell Na^+/K^+ -ATPase active before any EP; the EP appears only when intermediate cells, capillaries and the basal-cell seal form; without intermediate cells (neural-crest defect) no EP is generated.
- Supporting-cell gap junctions pass ions and metabolites up to 1.2 kDa; hair cells have none, so they stay electrically isolated.
- **Vestibular dark cells** (utricle, canals; none in saccule):
 - no basement-membrane barrier — basolateral surface bathed in perilymph;
 - Na^+/K^+ -ATPase (2 K^+ in, 3 Na^+ out) and NKCC1 take up K^+ ; apical K^+ channels release it into endolymph.

Endolymph volume regulation

- **Longitudinal flow** is very slow (0.004–0.007 mm/min): stria → scala media → ductus reuniens → saccule → **endolymphatic sac**, the end-point of circulation and absorption.
- The **valve of Bast** regulates flow from the utricle into the endolymphatic duct.
- **Endolymphatic sac**: proximal part (lined like the duct), intermediate part (cuboidal epithelium, partly in the aqueduct and dura) and distal part in the dura.
- **Books differ on flow**: GS ch. 5 describes slow longitudinal flow in the normal ear; GS ch. 51 (citing Salt) says normal endolymph has no true flow — longitudinal flow to the sac appears only when fluid is in excess.
- The **round window membrane** may also absorb perilymph (tracer passage shown).
- Reissner's membrane stretches with excess endolymph (**hydrops**) before it ruptures.
- **Blood supply**: spiral modiolar artery (from vestibulocochlear artery, AICA) — an **end artery**; microcirculation autoregulated by lactate, NO, K^+ , pericytes and fibrocytes.
- **Strial capillaries** run longitudinally, fed by cochlear-artery branches over the roof of the scala vestibuli; they drain beneath the scala tympani to the cochlear vein in the modiolus.

Clinical correlation

- **GJB2** (Cx26) mutation — commonest non-syndromic hereditary deafness; **KCNQ1/KCNE1** — Jervell–Lange–Nielsen (long QT).
- **Loop diuretics** block NKCC1 in marginal cells → strial oedema, acute ototoxicity.
- Loss of EP when barriers break (rupture of Reissner's membrane); noise depresses the K^+ cycle.
- **Ménière's disease**: hydrops from excess production or poor absorption — Paparella: sac/duct obstruction alters longitudinal flow; Schuknecht: membrane rupture leaks K^+ -rich endolymph into perilymph (attack), healing ends it.
- **Pendred syndrome / EVA** (SLC26A4): mouse models show fluctuating hearing with fluctuating EP and strial degeneration; mitochondria-rich cells of the sac absorb Na^+ , Cl^- and water during development.

PEARLS

- Endolymph: high K^+ (~140 mM), +80 mV — made by stria vascularis.
- Perilymph: high Na^+ ; connects to CSF via cochlear aqueduct.
- K^+ cycle: hair cell → supporting cells → gap junctions → fibrocytes → stria → endolymph.
- Intermediate cells (Kir4.1) make the EP; marginal cells (KCNQ1/KCNE1) secrete K^+ .
- Sac absorbs endolymph; obstruction → hydrops.

137. Embryological development of the nose and paranasal sinuses

ASKED 1* • 5-mark answer

Asked in: Paper II • Jun 2023 • Q1(a)

Q: Embryological development of nose and paranasal sinuses. [5]

SOURCE

- Cummings Otolaryngology (8e, Vol 1) — ch. 29 Management of the Nasal Septum — §Embryology and Anatomy of the Nose — pp. 462–463
- Cummings Otolaryngology (8e, Vol 3) — ch. 186 Cleft Lip and Palate — §Embryology — p. 2893
- Cummings Otolaryngology (8e, Vol 3) — ch. 189 Congenital and Acquired Malformations of the Nose and Nasopharynx — §Developmental Errors of the Anterior Neuropore; §Central Midface; §Nasobuccal Membrane — pp. 2925, 2929–2930, 2933; Fig. 189.8, p. 2930
- Cummings Otolaryngology (8e, Vol 3) — ch. 190 Pediatric Facial Fractures — Table 190.1 Summary of Paranasal Sinus Development — p. 2938
- Scott-Brown's Otorhinolaryngology (9e, Vol 1) — ch. 58 Anatomy of the nose and paranasal sinuses — §Development of the Nose and Paranasal Sinuses — pp. 611–613; Fig. 58.1, p. 612
- Scott-Brown's Otorhinolaryngology (9e, Vol 1) — ch. 59 Physiology of the nose and paranasal sinuses — §The Role of Paranasal Sinuses — p. 625

External nose and nasal cavity

- **Timing:** nasal development begins in the **4th week** and occurs between weeks 4 and 12; neural crest cells migrate from the dorsal neural folds to form the facial prominences around the **stomodeum** — frontonasal above, maxillary laterally, mandibular below.
- **Nasal placodes:** paired ectodermal thickenings on the frontonasal process (neural crest proliferation) appear in weeks 3–4.
- **Nasal pits – nasal sacs:** the placodes sink (5th week) into nasal pits, which deepen into nasal sacs; the surrounding ridge forms the **medial and lateral nasal prominences**.
- **Separation of nostrils:** maxillary processes grow medially (weeks 6–7) to fuse with the medial nasal prominences and frontonasal process, closing off the nasal pits into two nasal cavities.
- **Bucconasal (nasobuccal) membrane:** separates nasal sac from mouth; it thins as the sacs extend backwards and **ruptures by the 10th week** to form the **choanae**.
- **Nasolacrimal duct:** ectoderm buried between the lateral nasal prominence and maxillary process canalises (from above downwards, completed postnatally).

Table 1. Derivatives of the facial prominences

Prominence	Derivatives
Frontonasal process (with fused medial nasal prominences)	Nasal bones, frontal bones, cartilaginous nose, ethmoid, central incisors, hard palate
Medial nasal prominences	Philtrum, columella, medial crura of lower lateral cartilages
Lateral nasal prominences	Nasal alae; nasal bones, upper lateral cartilages, lateral crura of lower lateral cartilages (SB)
Maxillary processes	Lateral two-thirds of upper lip, superior alveolar ridges, palatal shelves

CUM ch. 29, p. 462; CUM ch. 189, p. 2930; SB ch. 58, p. 611.

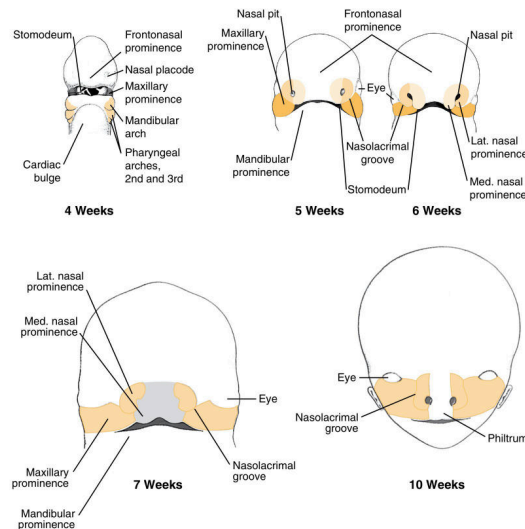


Fig. 189.8 Embryo at weeks 4, 5, 6, 7, and 10, showing the developing nasal structures.

Cummings (8e, Vol 3), ch. 189, Fig. 189.8, p. 2930.

Palate and nasal septum

- **Septum:** a midline downward extension of the merged medial nasal processes and nasofrontal process (ridge from the posterior frontonasal process in the oral roof, extending back to Rathke's pouch).
- **Palatal shelves:** vertical beside the tongue (20 mm fetus); become horizontal and fuse **anterior** → **posterior** (48 mm fetus); septum–palate fusion begins in the **9th week**, complete posteriorly by the **12th week**; a midline gap remains at the incisive foramen.
- **Incisive foramen** divides **primary palate** (premaxilla, lip, nasal tip, columella) from **secondary palate**.
- **Ossification:** septum entirely cartilaginous at birth; upper part ossifies to **perpendicular plate of ethmoid**, posteroinferior part to **vomer**.
- **Growth:** spurts in the first 2 years and at puberty; **sphenospinal** and **sphenodorsal** cartilage zones drive nasal and maxillary growth — early trauma may cause later deviation or spurs.

Paranasal sinuses

- **Origin:** outgrowths (evaginations) of the nasal cavity, so nasal disease involves the sinuses too.
- **Ethmoid (weeks 9–10):** folds on the lateral wall of the nasal capsule — **ethmoturbinals** — fuse into crests forming all ethmoid structures; the inferior fold forms the **inferior turbinate (maxilloturbinal)**, a separate bone.
- **First ethmoturbinal:**
 - ascending part → **agger nasi**; descending part → **uncinate process**;
 - bulla present by week 12; primordial infundibulum between uncinate and bulla by week 14.
- **Ethmoturbinals** → **surgical lamellae** (stepwise dissection to sphenoid face):
 - 1st: agger nasi and uncinate; 2nd: ethmoid bulla;
 - 3rd: **basal (ground) lamella** of middle turbinate; 4th: superior turbinate; 5th: supreme turbinate if present.
- **Maxillary (weeks 7–10):** expands from the ethmoidal infundibulum into the maxilla; small at birth; rapid growth to 7 years, then slow.
- **Sphenoid (week 12):** evagination of the **sphenoethmoidal recess**; enlarges from age 3; reaches the sella floor by about 7 years.
- **Frontal (week 16):** regarded as an **anterior ethmoid cell**; superior projection by 5 years, largely formed by 12, may grow to 18 years.

Table 2. Paranasal sinus development

Sinus	First appears	At birth	Pneumatisation complete
Maxillary	Weeks 7–10	Present (small)	15 years (CUM); final size ~17 years (SB)
Ethmoid	Weeks 9–10	Present	12 years
Sphenoid	Week 12	Absent (CUM); small (SB)	14 years; reaches sella floor ~7 years
Frontal	Week 16	Absent	Postpubertal; largely by 12, up to 18 years

CUM Table 190.1, p. 2938; SB ch. 58, pp. 612–613.

Applied embryology

- **Choanal atresia:** failure of the nasobuccal membrane to rupture (weeks 5–6) or abnormal neural crest migration.
- **Midline nasal masses:** dura extends through the foramen caecum across the **prenasal space** (or via the **fonticulus frontalis**, patent until week 8); failed regression → dermoid sinus or cyst, glioma, encephalocele.
- **Arhinia:** abnormal neural crest migration, failed fusion of nasal processes or non-resorption of nasal epithelial plugs; **proboscis lateralis:** lateral nasal process sequestered as a tube.
- **Maxillary hypoplasia** (up to 10%): type 1 mild with normal uncinate; type 2 hypoplastic uncinate; type 3 cleft-like sinus, uncinate nearly absent.
- **Frontal sinus** may be aplastic (SB Fig. 58.5) — identify before surgery.

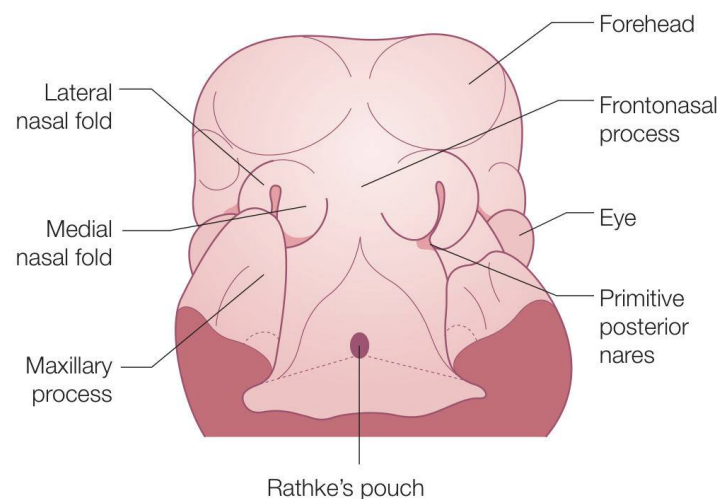


Figure 58.1 Embryological development of the primitive nose and palate during fusion of the maxillary process to the lateral and medial nasal prominences.

Scott-Brown's (9e, Vol 1), ch. 58, Fig. 58.1, p. 612.

PEARLS

- Nose: 4th–12th week; placode → pit → sac; choanae when the **bucconasal membrane ruptures (10th week)**.
- Medial nasal prominence → philtrum, columella, medial crura; lateral → alae.
- Septum–palate fusion 9th–12th week, anterior to posterior.
- First ethmoturbinal → agger nasi + uncinate; lamellae guide ESS.
- Maxillary and ethmoid present at birth; frontal is an anterior ethmoid cell.

138. Surgical anatomy of the lateral wall of the nose

ASKED 1* · 5-mark answer

Asked in: Paper II · Jun 2023 · Q1(b)

Q: Describe briefly surgical anatomy of lateral wall of nose. [5]

SOURCE

- Cummings Otolaryngology (8e, Vol 1) — ch. 43 Primary Sinus Surgery — \$Anatomy: Ostiomeatal Complex; Middle Turbinate; Ethmoidal Complex; Maxillary Sinus; Sphenoid Sinus; Frontal Sinus — pp. 687–692, 703; Fig. 43.3, p. 689
- Cummings Otolaryngology (8e, Vol 1) — ch. 29 Management of the Nasal Septum — \$Lymphatics — p. 464
- Cummings Otolaryngology (8e, Vol 1) — ch. 37 Imaging of the Nose and Sinuses — \$Imaging of Normal Anatomy and Physiology — pp. 615–617
- Cummings Otolaryngology (8e, Vol 1) — ch. 44 Causes of Failure, Revision Surgery for Rhinosinusitis — \$Nasolacrimal Duct Injury — p. 726
- Cummings Otolaryngology (8e, Vol 1) — ch. 46 Epistaxis — \$Endoscopic Sphenopalatine Artery Ligation — p. 756
- Cummings Otolaryngology (8e, Vol 3) — ch. 173 Transnasal Endoscopic-Assisted Surgery of the Anterior Skull Base — \$Anatomy — pp. 2663–2664
- Scott-Brown's Otorhinolaryngology (9e, Vol 1) — ch. 58 Anatomy of the nose and paranasal sinuses — \$Nasal Cavity; \$Lateral Nasal Wall; \$Paranasal Sinuses — pp. 616–620
- Scott-Brown's Otorhinolaryngology (9e, Vol 1) — ch. 70 The frontal sinus — \$Frontal recess — p. 747; Fig. 70.2, p. 747

Overview and bony framework

- Lateral wall carries three medially projecting **turbinates (conchae)** — superior, middle, inferior — each roofing a **meatus** lateral to it.
- Upper half:** frontal process of maxilla, lacrimal bone and lamina papyracea of the ethmoid; contains the ethmoid air cells separating nose from orbit.
- Lower half:** medial wall of the maxillary sinus — maxilla anteriorly, **perpendicular plate of palatine** posteriorly; the middle turbinate base attaches near the orbit–maxillary sinus junction.
- Posterior limit:** choana, bounded laterally by the **medial pterygoid plate**.

Table 1. Turbinates and meati

Meatus	Drains	Surgical points
Inferior (longest)	Nasolacrimal duct — Hasner valve ~1 cm behind the IT head	IT sinusoids contribute greatly to nasal resistance and drive the nasal cycle; NLD must be protected in pre-lacrimal approaches
Middle	Frontal, maxillary and anterior ethmoid sinuses	Site of the ostiomeatal complex ; key to ESS
Superior	Posterior ethmoid cells	Supreme turbinate in about two-thirds
Sphenoethmoidal recess	Sphenoid sinus	Between septum and superior turbinate

SB ch. 58, p. 618; CUM ch. 37, pp. 615–616.

Middle meatus — ostiomeatal complex (OMC)

- OMC:** a functional concept — final common pathway of the anterior ethmoid, maxillary and frontal sinuses, between medial orbital wall and middle turbinate.
- Uncinate process** — first structure seen on medialising the MT:
 - sickle-shaped, sagittal plane, runs anterosuperior → posteroinferior;
 - anteriorly meets the lacrimal bone (**anterior maxillary line**); inferiorly attaches to the inferior turbinate; superiorly to lamina papyracea, skull base or MT;
 - forms the medial wall of the **ethmoidal infundibulum**.
- Hiatus semilunaris:** 2-D slit between the free uncinate edge and the bulla; leads into the 3-D **infundibulum**.

- **Maxillary ostium:** elliptical, opens into the floor of the infundibulum at **45°**, lateral to the lower uncinata; seen only after uncinectomy; lies in the inferior third of the infundibulum in 65%.
- **Fontanelles:** bone-free areas anterior and posterior to the uncinata; round **accessory ostia** ($\geq 10\%$) — mucus always flows to the natural ostium.
- **Bulla ethmoidalis:** largest anterior ethmoid cell; suprabullar/retrobullar recesses above and behind it.
- **Agger nasi:** most anterior ethmoid cell (98.5% on CT), at the MT attachment, just behind the lacrimal sac — anterior boundary of the frontal recess.

Table 2. Middle turbinate basal lamella — three parts

Part	Plane	Attachment
1. Anterior vertical	Sagittal	Agger nasi region, then lateral lamella of cribriform plate
2. Middle oblique	Coronal	Lamina papyracea; separates anterior from posterior ethmoids; only part that can be sacrificed
3. Posterior horizontal	Axial	Lamina papyracea, maxilla, perpendicular plate of palatine (crista ethmoidalis)

CUM ch. 43, p. 689; SB ch. 58, p. 618.

Posterior lateral wall

- **Sphenoid ostium** in the sphenoethmoidal recess, medial to the superior turbinate, about 1.5 cm above the choana, lower than the maxillary sinus roof.
- **Sphenopalatine foramen** just behind the **crista ethmoidalis** (palatine–sphenoid ridge), above the bony tail of the MT; within 1 mm of the crista in 95%.

Blood, nerve and lymphatic supply

- **Arteries:** bulk from the **sphenopalatine artery** (posterior lateral nasal branches to turbinates and meati); facial artery anteriorly; greater palatine inferiorly; anterior and posterior ethmoidal arteries superiorly.
- **Nerves:** sensory V1 (ethmoidal nerves) and V2 (posterolateral nasal nerves) via the sphenopalatine ganglion; parasympathetic (vidian nerve) secretomotor, sympathetic vasoconstrictor tone.
- **Lymph:** anterior part to upper-lip lymphatics; posterior part to retropharyngeal and deep cervical nodes.

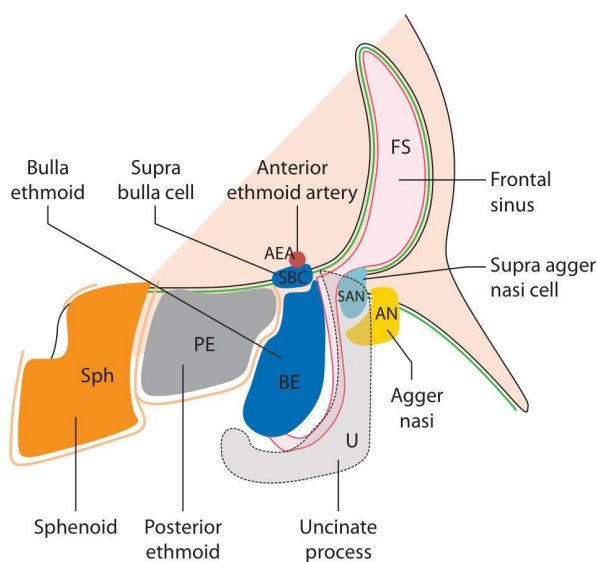
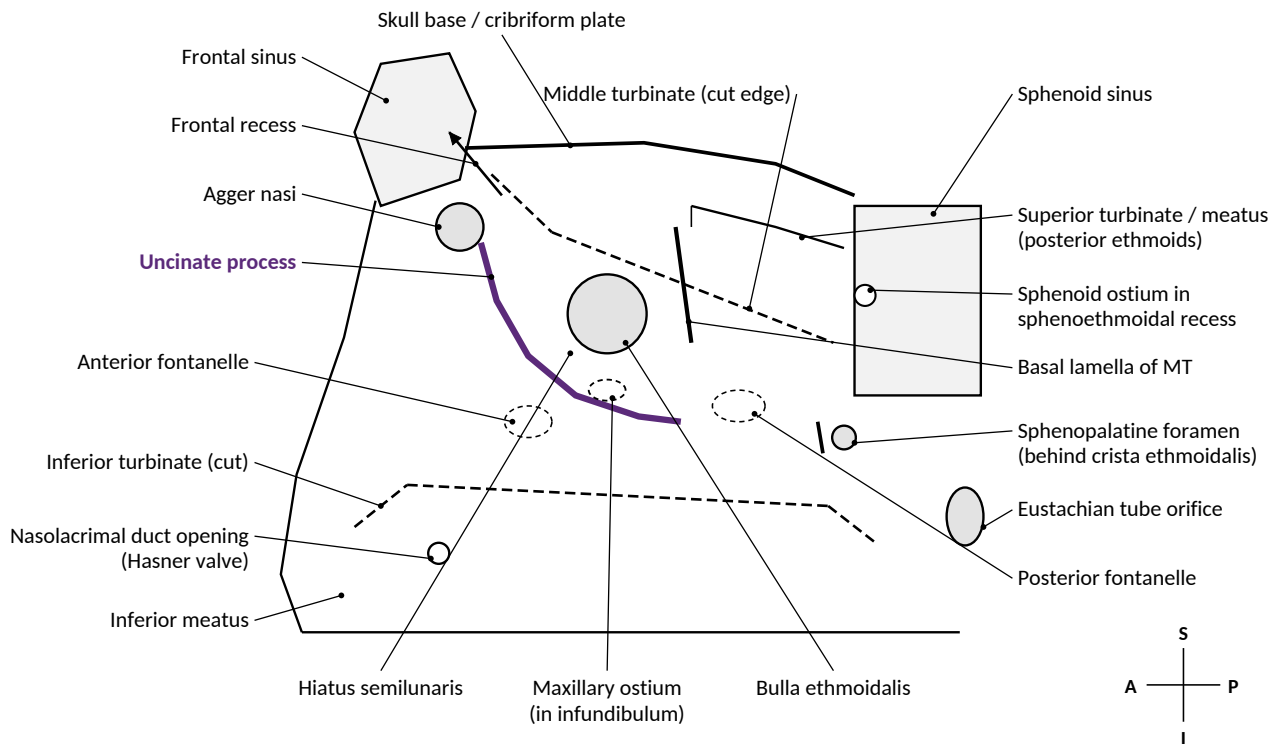


Figure 70.2 The lateral nasal wall. The uncinate process is outlined in a black dotted line. Note its relationship with the agger nasi (AN).

Scott-Brown's (9e, Vol 1), ch. 70, Fig. 70.2, p. 747.



Schematic (exam diagram): right lateral nasal wall with turbinates cut away, medial view (anterior to the left). Based on Scott-Brown's 9e Vol 1, Fig. 70.2, p. 747; text CUM 8e Vol 1, pp. 687–692 and SB pp. 616–620.

Applied surgical anatomy

- **Uncinectomy:** complete removal (including the inferior horizontal part) is needed to find the natural ostium; incomplete removal + posterior fontanelle antrostomy → **missed ostium** and recirculation.
- **Nasolacrimal duct** lies in front of the uncinate — over-aggressive anterior/backbiting removal injures it.
- **Middle turbinate:** preserve vertical and horizontal attachments — injury lateralises the MT and scars the middle meatus; medial polyps lie on the thin cribriform plate.
- **Ground lamella** is entered parallel to the palate at maxillary-roof height to reach the sphenoid safely.
- **Infraorbital (Haller) cell** may narrow the infundibulum; **Onodi cell** exposes optic nerve and ICA.

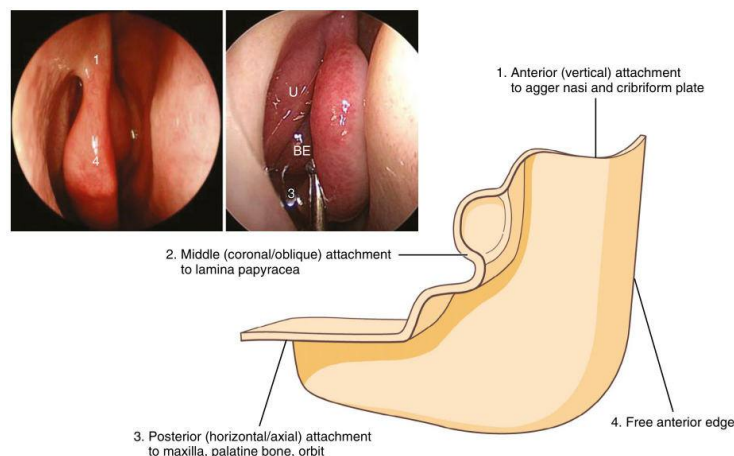


Fig. 43.3 Schematic view of the right middle turbinate viewed from the lateral aspect illustrates the anterior vertical (1), middle oblique (2), and posterior horizontal (3) attachments. Inset, Endoscopic views of the right middle turbinate show the free anterior edge (4) and the anterior (1) and posterior (3) attachments. BE, Bulla ethmoidalis; U, uncinate.

Cummings (8e, Vol 1), ch. 43, Fig. 43.3, p. 689.

PEARLS

- Middle meatus = OMC: uncinat, hiatus, infundibulum, bulla, ostia.
- Maxillary ostium: infundibulum floor at 45°, hidden by uncinat.
- NLD opens 1 cm behind IT head (Hasner valve).
- MT basal lamella: vertical (cribriform), oblique (lamina), horizontal (crista).
- SPF just behind the crista ethmoidalis.

139. Attachments of the uncinat process

ASKED 1* · 3-mark answer

Asked in: Paper II · Dec 2025 · Q2(b)

Q: Briefly discuss the attachments of uncinat process. [3]

SOURCE

- Cummings Otolaryngology (8e, Vol 1) — ch. 43 Primary Sinus Surgery — §Ostiomeatal Complex; §Endoscopic Sinus Surgery — pp. 687–688, 692, 701, 703; Fig. 43.2, p. 688
- Cummings Otolaryngology (8e, Vol 1) — ch. 37 Imaging of the Nose and Sinuses — §Variations in the Uncinat Process — pp. 617–619
- Cummings Otolaryngology (8e, Vol 1) — ch. 44 Causes of Failure — §Nasolacrimal Duct Injury — p. 726; ch. 45 Management of the Frontal Sinuses — p. 731; ch. 48 Sino-Orbital Interface — p. 777
- Scott-Brown's Otorhinolaryngology (9e, Vol 1) — ch. 58 Anatomy of the nose and paranasal sinuses — §Anterior ethmoid; §Superior uncinat process — pp. 619–620, 623
- Scott-Brown's Otorhinolaryngology (9e, Vol 1) — ch. 70 The frontal sinus — §Frontal recess — p. 747

The uncinat process

- Sickle-shaped bone of the ethmoid in the sagittal plane, running anterosuperior → posteroinferior; **free posterior edge** faces the bulla (hiatus semilunaris); forms the medial wall of the ethmoidal infundibulum.

Attachments

Table 1. Attachments of the uncinat process

Border	Attached to	Note
Anterior	Lacrimal bone — the “lacrimal line” / anterior maxillary line; fuses with posteromedial walls of agger nasi cell and nasolacrimal duct	Harder bone here; penetration injures the NLD
Inferior / posteroinferior	Inferior turbinate; medial maxilla near the posterior NLD	Horizontal part overlies the natural maxillary ostium
Superior (variable)	Lamina papyracea, skull base, or middle turbinate — often several	Decides frontal sinus drainage
Posterior	Free edge	Hiatus semilunaris

CUM ch. 43, pp. 687, 701, 703; CUM ch. 37, p. 617; CUM ch. 44, p. 726; SB ch. 58, p. 620; SB ch. 70, p. 747.

Superior attachment and frontal drainage

- **Lamina papyracea** (or bulla): forms a blind **recessus terminalis**; frontal sinus drains **medial** to the uncinat into the middle meatus — access is medial to the “vertical bar”.
- **Skull base** or **middle turbinate**: frontal sinus drains **into the infundibulum**, lateral to the uncinat.
- Variants: atelectatic uncinat on the orbital floor (hypoplastic sinus, silent sinus); pneumatized or bifid uncinat.

Table 2. Superior attachment — frequencies by book (examinable disagreement)

Cummings	Scott-Brown ch. 58	Scott-Brown ch. 70
Lamina papyracea “more commonly”	Medial orbital wall 85%; skull base or MT less common	Lamina 33%; skull base or MT 10%; combination 57%

CUM ch. 43, p. 687; SB pp. 623, 747.

Surgical relevance

- **Uncinectomy** starts with a ball probe behind the free edge or an incision along the anterior (lacrimal) attachment; the superior third may be left initially to avoid frontal recess scarring.
- The **inferior horizontal part** is often missed — residue causes antrostomy stenosis and a missed natural ostium.

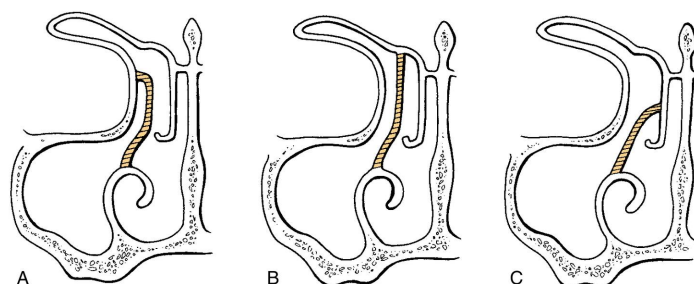


Fig. 43.2 Coronal schematic view of the ostiomeatal complex showing the superior attachments of the uncinate process to the lamina papyracea (A), the roof of the ethmoidal complex (B), or the middle turbinate (C). If the uncinate process attaches to the roof of the ethmoid or to the middle turbinate, the frontal sinus drains into the infundibulum. If the uncinate attaches to the lamina papyracea, the frontal sinus drains medially, next to the middle turbinate.

Cummings (8e, Vol 1), ch. 43, Fig. 43.2, p. 688.

PEARLS

- Anterior — lacrimal bone; inferior — inferior turbinate; superior — lamina, skull base or MT; posterior — free.
- Lamina attachment — recessus terminalis — frontal drainage medial to uncinate.
- Review superior attachment on CT before frontal recess surgery.

140. Haller cell and Onodi cell — definition and clinical relevance

ASKED 1* · 3-mark answer

Asked in: Paper II · Dec 2025 · Q2(a)

Q: Define Haller cell and Onodi cell and write about their clinical relevance. [3]

SOURCE

- Cummings Otolaryngology (8e, Vol 1) — ch. 43 Primary Sinus Surgery — §Ethmoidal Complex; §Maxillary antrostomy — pp. 690–691, 704; Fig. 43.5, p. 690
- Cummings Otolaryngology (8e, Vol 1) — ch. 37 Imaging of the Nose and Sinuses — §Anatomic Variations — pp. 617, 619–620
- Cummings Otolaryngology (8e, Vol 1) — ch. 44 Causes of Failure, Revision Surgery for Rhinosinusitis — p. 725; ch. 48 Sino-Orbital Interface — §Pertinent Anatomy — pp. 785–786
- Cummings Otolaryngology (8e, Vol 3) — ch. 173 Transnasal Endoscopic-Assisted Surgery of the Anterior Skull Base — §Paranasal Sinuses — p. 2664
- Scott-Brown's Otorhinolaryngology (9e, Vol 1) — ch. 58 Anatomy of the nose and paranasal sinuses — §Anterior ethmoid; §Maxillary sinus; §Posterior ethmoid cells — pp. 619–621

Definitions

Table 1. Haller and Onodi cells

	Haller cell	Onodi cell
Current name	Infraorbital ethmoidal cell (IOC)	Sphenoethmoidal cell (SEC)
Origin	Anterior ethmoid cell	Posterior ethmoid cell
Position	Pneumatizes the orbital floor / maxillary sinus roof beneath the bulla, above the maxillary ostium; may reach the infraorbital canal	Lateral and superior (posterior) to the sphenoid sinus, into the sphenoid body; sphenoid lies inferomedial to it
Structures at risk	Maxillary ostium, infraorbital nerve	Optic nerve, internal carotid artery, skull base

CUM ch. 43, pp. 690–691; CUM ch. 37, p. 619; SB ch. 58, pp. 619–621.

Clinical relevance — Haller cell

- Narrows the **inferior infundibulum** and maxillary ostium; oedema of its common wall obstructs maxillary drainage.
- Lateral wall may be attached to the **infraorbital nerve canal** — remove carefully.
- Marsupialise at middle meatal antrostomy, after locating the infraorbital nerve; remnants impair clearance through the natural ostium — a cause of ESS failure.

Clinical relevance — Onodi cell

- **Optic nerve and ICA** may bulge into, or be dehiscent within, its lateral wall — the optic prominence lies in the Onodi cell, not the sphenoid.
- May be mistaken for the sphenoid; dissection is directed towards the **orbital apex** — risk of blindness, carotid injury and intracranial entry.
- Part of the **CLOSE** preoperative CT checklist (Cribriform, Lamina, Onodi, Sphenoid, Ethmoid artery); best seen on coronal plus sagittal CT.
- In optic nerve decompression the partition between SEC and sphenoid is removed to expose the canal.

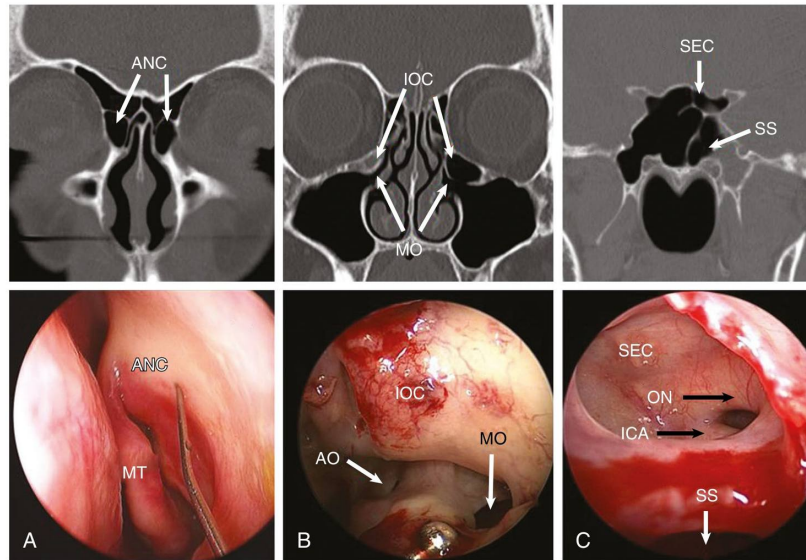


Fig. 43.5 Ethmoidal cells. Top row shows CT scan with corresponding endoscopic views below. (A) The agger nasi cell (ANC) is the most anterior cell seen on a coronal CT scan and anterior to the middle turbinate (MT). Endoscopically it is seen as a bulge on the MT attachment and may narrow the superior ethmoidal infundibulum. (B) Coronal CT section shows bilateral infraorbital ethmoidal cell (IOC; Haller cell) narrowing the inferior ethmoidal infundibulum and attaching laterally to the infraorbital canal. The maxillary sinus opens into the inferior part of the infundibulum at a 45-degree angle. Endoscopic view of the left infundibulum after uncinectomy shows the IOC narrowing the inferior infundibulum and potentially obstructing drainage of the natural maxillary ostium (MO). The natural maxillary ostium is elliptically shaped and opens into the floor of the infundibulum at a 45-degree angle, not directly into the lateral wall. Accessory ostia (AO) are usually circular and are present here in the posterior fontanelle. (C) The sphenothmoidal cell (SEC), or Onodi cell, is a posterior ethmoidal cell that is lateral and superior to the sphenoid sinus (SS), which is usually smaller, pushed medially and inferiorly. The figures show arrows pointing to a left SEC on coronal and sagittal CT cuts. The endoscopic image demonstrates the relationship of the SEC to the SS and shows the optic nerve (ON) and internal carotid artery (ICA) lying in relation to the SEC lateral wall. Cummings (8e, Vol 1), ch. 43, Fig. 43.5, p. 690.

PEARLS

- Haller = infraorbital ethmoid cell – maxillary ostium narrowing.
- Onodi = sphenothmoidal cell – optic nerve/ICA at risk.
- Identify both on preoperative CT (CLOSE).

141. Boundaries of the frontal recess

ASKED 1x · 2-mark answer

Asked in: Paper II · Dec 2025 · Q5(c)

Q: Enumerate the boundaries of frontal recess. [2]

SOURCE

- Cummings Otolaryngology (8e, Vol 1) — ch. 43 Primary Sinus Surgery — §Ostiomeatal Complex; §Ethmoidal Complex; §Frontal Sinus — pp. 687, 690, 692–693; Fig. 43.8, p. 693
- Cummings Otolaryngology (8e, Vol 1) — ch. 45 Management of the Frontal Sinuses — pp. 731–732; Fig. 45.1, p. 732
- Cummings Otolaryngology (8e, Vol 1) — ch. 37 Imaging of the Nose and Sinuses — pp. 616–617
- Scott-Brown's Otorhinolaryngology (9e, Vol 1) — ch. 70 The frontal sinus — §Frontal ostium; §Frontal recess — pp. 746–747
- Scott-Brown's Otorhinolaryngology (9e, Vol 1) — ch. 58 Anatomy of the nose and paranasal sinuses — Box 58.5 — p. 622

Frontal recess

- Inferior part of the **hourglass-shaped** frontal sinus drainage pathway, below the **frontal ostium** (the waist); opens into the middle meatus (commonly) or the upper ethmoidal infundibulum.
- Not a duct — “nasofrontal duct” is a misnomer.

Boundaries

Table 1. Boundaries of the frontal recess (simplest configuration)

Boundary	Formed by
Anterior	Posterior wall of agger nasi cell and nasal (frontal) beak — nasal process of frontal bone; supra agger cells when present
Posterior	Bulla ethmoidalis and bulla lamella (upward continuation of the bulla face); a suprabullar space if the lamella is deficient
Posterosuperior	Anterior skull base / ethmoid roof (fovea ethmoidalis), crossed by the anterior ethmoidal artery
Medial	Anterior (vertical) part of the middle turbinate and lateral lamella of the cribriform plate
Lateral	Lamina papyracea (medial orbital wall) and/or agger nasi cells
Superior	Frontal ostium — frontal sinus
Inferior	Opens into middle meatus or ethmoidal infundibulum (by uncinate attachment)

CUM ch. 43, pp. 692–693; CUM ch. 45, p. 732; SB ch. 70, p. 747.

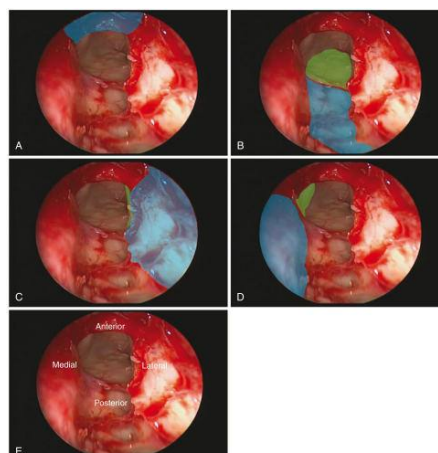
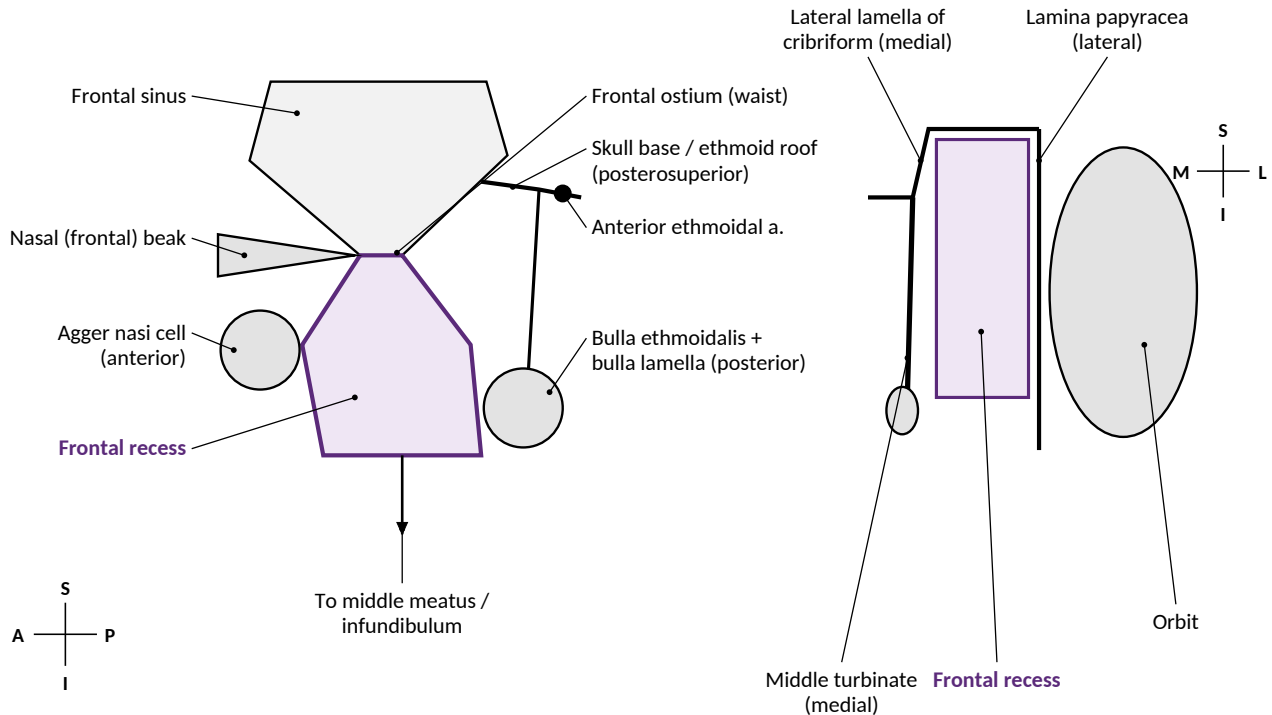


Fig. 45.1 The boundaries of the frontal recess can be defined by the front wall of the agger nasi or nasofrontal beak anteriorly (blue) (A); posterior to the frontal recess lies the ethmoid roof (blue), with the anterior ethmoid artery running across it, and the posterior wall (green) (B). The lateral wall of the frontal recess is formed by the medial orbital wall/lamina papyracea (blue) and orbital roof (green) (C), and the medial wall of the frontal recess is formed by the middle turbinate/lateral lamella (blue) and intersinus septum (green) (D), whose height is determined by the level of the cribriform plate. The boundaries of the frontal recess should be seen at the end of Draf IIa (E).

Cummings (8e, Vol 1), ch. 45, Fig. 45.1, p. 732.



Schematic (exam diagram): frontal recess boundaries in parasagittal (left, anterior to the left) and coronal (right) views. Based on Cummings 8e Vol 1, Fig. 45.1, p. 732 and Fig. 43.8, p. 693; text SB p. 747.

Surgical significance of the boundaries

- **Agger nasi:** its pneumatization sets beak thickness and recess width; a retained cap (dome) of the cell scars the recess.
- **Lateral lamella:** thinnest skull base (Keros depth varies) — medial dissection risks CSF leak.
- **Anterior ethmoidal artery:** a few millimetres behind the frontal ostium; exposed if the bulla lamella is absent, and in a mesentery with supraorbital ethmoid cells.
- **Uncinate:** lamina papyracea attachment — recess drains medial to it; skull base/MT attachment — into the infundibulum.
- Frontoethmoidal cells (IFAC) alter the boundaries: anterior cells push the pathway medially/posteriorly, posterior cells anteriorly, frontal septal cells laterally.

PEARLS

- Anterior — agger nasi + beak; posterior — bulla lamella + skull base (AEA).
- Medial — MT + lateral lamella; lateral — lamina papyracea.
- Frontal ostium (waist): beak in front, skull base behind, lamina lateral, MT lamella and lateral lamella medial.

142. Labelled diagram: neurovascular relations of the sphenoid sinus

ASKED 1* · 4-mark answer

Asked in: Paper II · Dec 2025 · Q5(a)

Q: Draw a labelled diagram showing neurovascular relations of sphenoid sinus. [4]

SOURCE

- Cummings Otolaryngology (8e, Vol 3) — ch. 172 Surgical approaches to the cranial base — Fig. 172.37, p. 2657
- Cummings Otolaryngology (8e, Vol 3) — ch. 173 Transnasal Endoscopic-Assisted Surgery of the Anterior Skull Base — §Paranasal Sinuses — pp. 2664–2666; Fig. 173.9, p. 2666
- Cummings Otolaryngology (8e, Vol 1) — ch. 43 Primary Sinus Surgery — §Sphenoid Sinus — p. 692; ch. 37 Imaging — §Extensive Pneumatization of the Sphenoid Sinus — pp. 619–621; ch. 48 Sino-Orbital Interface — p. 785
- Scott-Brown's Otorhinolaryngology (9e, Vol 1) — ch. 58 Anatomy of the nose and paranasal sinuses — §Pterygopalatine fossa; §Sphenoid sinus — pp. 620–622
- Scott-Brown's Otorhinolaryngology (9e, Vol 1) — ch. 98 Nasopharyngeal endoscopic resection — §Surgical anatomy — p. 1074
- Scott-Brown's Otorhinolaryngology (9e, Vol 1) — ch. 93 Pituitary and parasellar lesions — p. 1028
- Scott-Brown's Otorhinolaryngology (9e, Vol 1) — ch. 84 Imaging of the anterior skull base — §Anatomy; §Pneumatized optic strut — pp. 904–905

Diagram

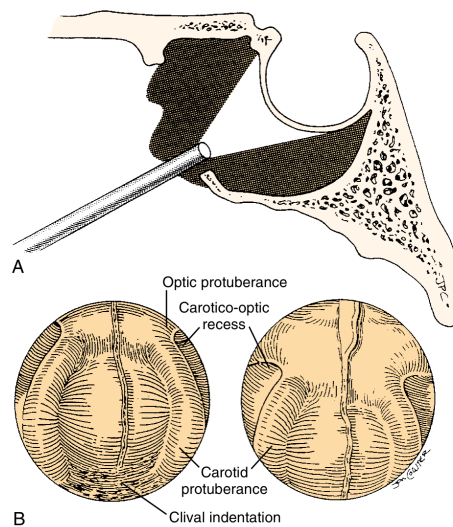
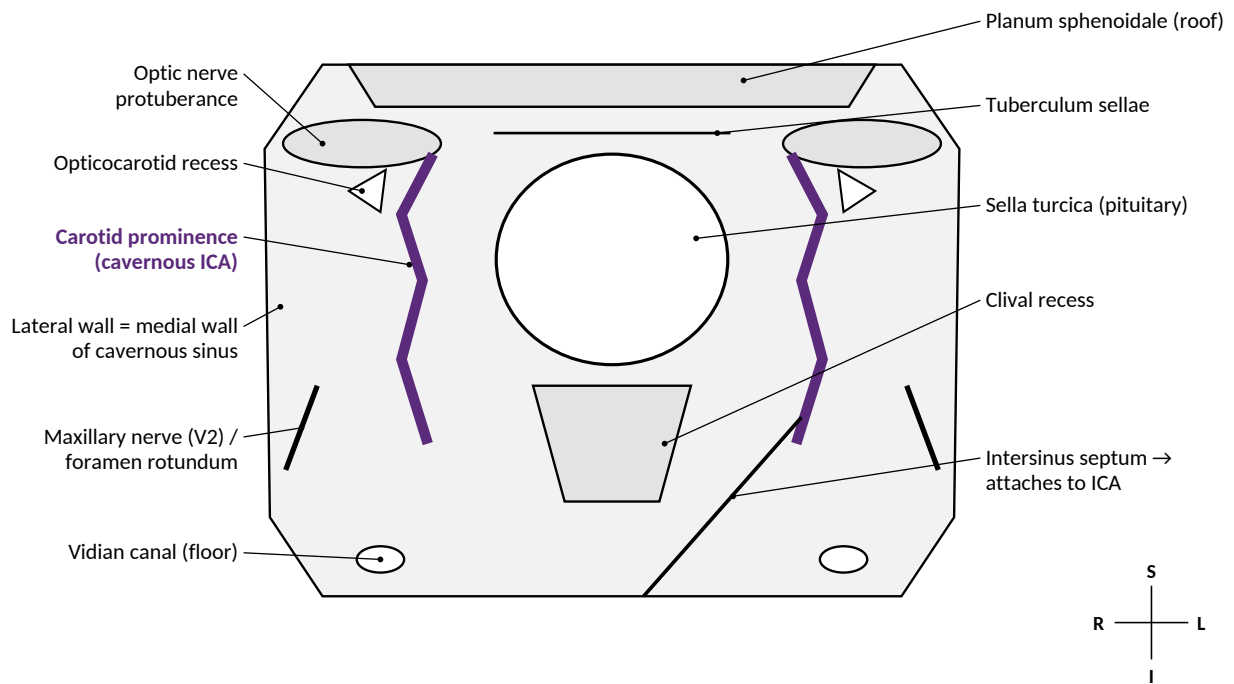


Fig. 172.37 (A) Endoscopic view of the sphenoid sinus after the completion of anterior sphenoidotomy and resection of the sphenoidal septum. (B) Left: View with a zero-degree endoscope reveals the caroticoptic recesses, carotid protuberances, and clival indentation to the anterior wall of the sella. Right: A 30-degree endoscope provides a better panoramic view of the optic protuberances, the caroticoptic recesses, the carotid protuberances, and the upper portion of the anterior wall of the sella.

Cummings (8e, Vol 3), ch. 172, Fig. 172.37, p. 2657.



Schematic (exam diagram): sphenoid sinus posterior and lateral walls, endoscopic view after septum removal (patient's right on the viewer's left). Based on Cummings 8e Vol 3, Fig. 172.37, p. 2657 and Fig. 173.9, p. 2666; text pp. 2664–2665; SB pp. 621–622.

Relations by wall

Table 1. Neurovascular relations of the sphenoid sinus

Wall	Relations
Roof	Planum sphenoidale and tuberculum sellae; optic chiasm above and behind the chiasmatic sulcus
Posterior	Sella turcica (pituitary gland) above; clivus below; intercavernous sinus at the sellar face
Lateral	Medial wall of the cavernous sinus with intracavernous ICA ; optic canal superolaterally; opticocarotid recess between them; Meckel cave and V2 (foramen rotundum) inferolaterally
Floor	Rostrum with the vidian (pterygoid) canal ; nasopharynx below
Anterior	Sphenoethmoidal recess and natural ostium; posterior ethmoid cells (Onodi cell may lie superolateral)

SB ch. 58, p. 621; SB ch. 84, p. 904; CUM ch. 173, pp. 2664–2666.

Labelled points

- **Carotid prominence:** serpiginous ridge of the intracavernous ICA — **presellar** (anterior vertical segment and bend), **infraselar** (horizontal) and **retrosellar** segments; horizontal segment prominent in 67%, its bony cover dehiscent in 6%.
- **Optic canal:** bony bulge superoanterior on the lateral wall; bulges into the sinus in 57%, dehiscent in 6%, no bony canal in 1%; carries optic nerve and ophthalmic artery.
- **Opticocarotid recess (OCR):** depression between optic canal and presellar carotid; extends into the optic strut — a pneumatised strut gives access to the anterior clinoid.
- **V2:** prominent in 48%, dehiscent in 5%; **vidian nerve** prominent in 18%.
- **Intercarotid distance:** 13.9 mm (10–17) just below the tuberculum — narrowest point; about 20 mm at the sellar face, 17.4 mm at the clivus.
- **Intersinus septum:** eccentric, often inserts on the carotid canal — avoid twisting it.
- **Lateral recess** pneumatisation beyond the foramen rotundum–vidian line, and anterior clinoid pneumatisation, expose V2, optic nerve and ICA further.

Applied relevance

- **Safe entry:** natural ostium in the sphenoethmoidal recess, medial to the lower superior turbinate, below the maxillary sinus roof, ~7.1 cm from the nasal spine at 30–34° — open inferomedially, away from optic nerve and ICA.
- **Optic nerve:** lies 3–7 mm behind the posterior ethmoidal foramen; in an Onodi cell its prominence is in the posterior ethmoid.
- **Transsphenoidal exposure** is complete when planum and tuberculum (above), both OCRs (laterally) and clivus and floor (below) are seen.
- **Dehiscent ICA/optic canal** or >50% of the nerve surrounded by air on CT = high risk of carotid haemorrhage or blindness — check preoperatively (CLOSE).

PEARLS

- Lateral wall = medial wall of cavernous sinus: ICA below, optic nerve above, OCR between.
- Roof planum, back sella over clivus, floor vidian canal, inferolateral V2.
- Never twist septa attached to the carotid.
- Onodi cell shifts the optic prominence into the posterior ethmoid.

143. Pneumatisation patterns of the sphenoid sinus

ASKED 1* · 4-mark answer

Asked in: Paper II · Dec 2025 · Q5(b)

Q: Briefly discuss the various pneumatization patterns of sphenoid sinus. [4]

SOURCE

- Scott-Brown's Otorhinolaryngology (9e, Vol 1) — ch. 58 Anatomy of the nose and paranasal sinuses — §Sphenoid (development); §Sphenoid sinus — pp. 612–613, 621; Fig. 58.4, p. 613
- Scott-Brown's Otorhinolaryngology (9e, Vol 1) — ch. 94 Endoscopic approach and management of the clivus and posterior fossa — p. 1039; ch. 93 Pituitary and parasellar lesions — p. 1027
- Scott-Brown's Otorhinolaryngology (9e, Vol 1) — ch. 91 Juvenile nasopharyngeal angiofibroma — p. 1003; ch. 84 Imaging of the anterior skull base — p. 905; ch. 60 Radiological investigations used in rhinology — p. 635
- Cummings Otolaryngology (8e, Vol 1) — ch. 37 Imaging of the Nose and Sinuses — §Extensive Pneumatization of the Sphenoid Sinus; §Arrested Pneumatization — pp. 616, 619–621; Fig. 37.8, p. 620
- Cummings Otolaryngology (8e, Vol 3) — ch. 173 Transnasal Endoscopic-Assisted Surgery of the Anterior Skull Base — §Paranasal Sinuses — pp. 2664–2665

Development

- Recognised from the **12th week** as an evagination of the sphenoethmoidal recess; small at birth, enlarges from age 3, reaches the sella floor by about 7 years.
- Pneumatisation is highly variable and often **asymmetric**, with an eccentric intersinus septum.

Antero-posterior (sagittal) patterns — relation to the sella

Table 1. Sphenoid pneumatisation patterns on midline sagittal CT

Pattern	Extent of air	Frequency	Surgical meaning
Sellar (type III)	Behind the sella turcica; sella and clival recess contours clear	90%	Sellar floor visible — easiest transsphenoidal access
Presellar (type II)	Up to the anterior wall of the sella; clival recess not aerated	9%	Sellar bulge not seen — drilling needed
Conchal (type I)	Shallow bowl; trabecular bone separates sinus from sella — almost no air	1%	Landmarks absent — drilling and navigation (CT/MRI) needed

SB ch. 58, p. 613; SB ch. 94, p. 1039; SB ch. 93, p. 1027.

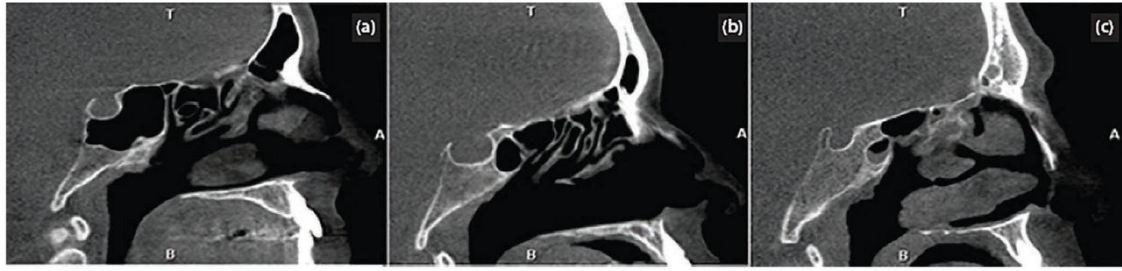


Figure 58.4 Sphenoid sinus pneumatization patterns. Midline sagittal CT indicating the (a) sellar (b) pre-sellar and (c) conchal types of sphenoid sinus pneumatization patterns.

Scott-Brown's (9e, Vol 1), ch. 58, Fig. 58.4, p. 613.

Lateral and accessory extensions

- **Lateral recess:** pneumatization into the pterygoid root beyond a line joining foramen rotundum and vidian canal; present in >50%; reached by transpterygoid (pterygoid wedge drilling), expanded endonasal or transorbital routes.
- **Anterior clinoid / optic strut:** air may surround the optic nerve; a pneumatized strut opens the lateral optiocarotid recess; >50% of the nerve surrounded by air raises injury risk.
- **Clival (posterior) extension:** sinus embedded in the clivus behind the sella.
- **Prominences into the sinus (Seibert):** horizontal ICA 67%, optic nerve 57%, V2 48%, vidian 18%; dehiscence of ICA 6%, V2 5%.
- **Arrested pneumatization (2%):** non-aerated, septate, mildly expansile area of fatty marrow with sharply defined margins — a “don't touch” lesion, not tumour.
- **Onodi cell** pneumatizes above/lateral to the sphenoid, pushing it inferomedially.

Clinical significance

- Pattern determines exposure — and risk of injury — of the ICA, optic nerve and V2 when anatomy is not appreciated on preoperative imaging.
- **Preoperative CT** shows degree of pneumatization, ostium position, intersinus septum, and carotid or optic dehiscence and protrusion.
- In **presellar and conchal** types the sellar prominence is not seen — anticipate significant drilling.
- Wide lateral pneumatization places the carotid at risk; the eccentric intersinus septum often inserts on the carotid canal — never twist it.
- **Naming note:** SB ch. 94 numbers them type I (conchal, “postsellar”), II (presellar), III (sellar); SB ch. 58 gives the frequencies 1%, 9%, 90%.

PEARLS

- Sellar 90% > presellar 9% > conchal 1%.
- Conchal: no sellar landmarks — navigation essential.
- Lateral recess pneumatization in >50% — beyond foramen rotundum–vidian line.
- Arrested pneumatization = do not biopsy.

144. Sternberg's canal

ASKED 1* · 5-mark answer

Asked in: Paper II · Jun 2025 · Q9(a)

Q: Sternberg's canal. [5]

SOURCE

- Cummings Otolaryngology (8e, Vol 1) — ch. 47 Cerebrospinal Fluid Rhinorrhea — §Spontaneous CSF Leaks With Elevated Intracranial Pressure; §Congenital CSF Leaks; §Diagnosis; §Surgical Repair — pp. 763–765, 768, 771; Fig. 47.3, p. 768
- Cummings Otolaryngology (8e, Vol 1) — ch. 37 Imaging of the Nose and Sinuses — §Extensive Pneumatization of the Sphenoid Sinus; §Arrested Pneumatization — pp. 619–621; Fig. 37.8, p. 620
- Scott-Brown's Otorhinolaryngology (9e, Vol 1) — ch. 97 Transorbital approaches — pp. 1065–1066
- Scott-Brown's Otorhinolaryngology (9e, Vol 1) — ch. 58 Anatomy of the nose and paranasal sinuses — §Sphenoid — p. 613
- Scott-Brown's Otorhinolaryngology (9e, Vol 1) — ch. 89 CSF Rhinorrhoea — Fig. 89.6, p. 971; Table of approaches, p. 974

NOT COVERED IN SOURCE

NOT FULLY IN THE BOOKS. Searched the full text of CUM Vols 1–3, SB, GS and SM for “Sternberg”, “craniopharyngeal|Sternberg”, “lateral craniopharyngeal”, “persistent ... canal ... sphenoid” and “lateral (sphenoid|recess) ... (leak|encephalocele|defect)” (with spelling expansion); the SB index (pdf pp. 2836–2874: only “Sternberg canal defects 1065”), the GS and SM indexes (no entry), and the likely chapters (CUM ch. 37, 47; SB ch. 58, 84, 89, 97). The books give only its name, its site (medial to foramen rotundum) and its disputed role in lateral sphenoid CSF leaks. Its embryological origin, exact course, dimensions and incidence are not described in CUM, SB, GS or SM. Related book material follows, labelled as such.

What the books state

- Sternberg's canal = lateral craniopharyngeal canal (CUM).**
- It and the adjacent area have been implicated in the pathogenesis of **lateral sphenoid CSF leaks and meningoencephaloceles**.
- Site:** if present, it lies **medial to the foramen rotundum**.
- Controversy (CUM, SB):** many reports wrongly attribute spontaneous, high-pressure **sphenoid lateral recess leaks** to the canal — these defects lie **lateral to the foramen rotundum**.

Table 1. Sternberg canal defect vs lateral recess defect (book statements)

Feature	Sternberg canal defect	Lateral recess (pterygoid recess) defect
Position	Medial to foramen rotundum	Lateral to foramen rotundum and vidian canal
Mechanism	Congenital canal (implicated)	Pneumatized pterygoid process + thin roof + raised ICP → middle cranial fossa defect, temporal lobe herniation
Repair route	Not specified in books	Extended transpterygoid (medial pterygomaxillary space), transmaxillary/infraorbital, or transorbital lateral portal

CUM ch. 47, pp. 763, 765, 771; SB ch. 97, p. 1065; SB ch. 89, p. 974.

Related book material — lateral sphenoid recess

- Lateral pneumatisation** into the pterygoid root forms the lateral sphenoid recess; seen in **>50%** on CT, often beyond a line joining foramen rotundum and vidian canal.
- Hyperpneumatization of the lateral recess beyond the foramen rotundum–vidian line and of the anterior clinoid is seen on coronal CT (CUM Fig. 37.8).
- Arrested pneumatisation** (2%) of the sphenoid is a non-aerated fatty marrow area — a “don't touch” variant, not a defect.

Related book material — congenital sphenoid encephaloceles

- **Intrasphenoidal:** extends into the sphenoid sinus but is confined by its floor.
- **True transsphenoidal:** traverses the sinus floor into the nasal cavity or nasopharynx; corresponds to the **median cleft face syndrome**, with possible face, optic and brain anomalies and hypothalamic–pituitary dysfunction.

Related book material — spontaneous lateral sphenoid CSF leaks

- **Cause:** most spontaneous leaks are a variant of **idiopathic intracranial hypertension**; CSF pressure 24.3–36 cm H₂O vs normal 10–15 cm H₂O.
- **Patients:** obese middle-aged women — 88.2% female, mean age 52 years, mean BMI 37.3 kg/m² (222 patients); up to a third have multiple defects.
- **Imaging:**
 - intervene only with a CT defect and/or chemical marker (β 2-transferrin or β -trace protein); MR cisternography sensitivity 0.87, specificity 0.57;
 - thin-cut coronal CT — eroded roof of the pterygoid recess (CUM Fig. 47.3);
 - MRI — meningocele filling the sinus; **empty sella** (up to 90%), dilated optic nerve sheaths and Meckel caves;
 - CT may show pneumocephalus with a lateral recess defect and encephalocele (SB Fig. 89.6).
- **Repair:**
 - central sphenoid defects — transseptal approach with posterior septectomy;
 - **lateral defects — extended transpterygoid approach**; ipsilateral SPA and vidian nerve often sacrificed;
 - transorbital lateral portal reaches defects lateral to foramen rotundum without endonasal dissection.

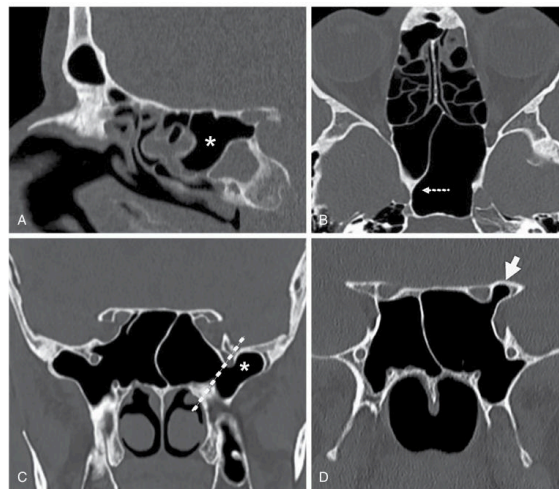


Fig. 37.8 Sphenoid sinus variants. (A) Sagittal CT demonstrates an intrasphenoid ethmoid air cell or Onodi cell (asterisk) divided from the true sphenoid sinus by a complete bony shelf posteroinferiorly. (B) Axial CT shows the intersphenoid sinus septum asymmetrically attaching to the right carotid canal (dashed arrow). When not properly identified in presurgical planning, this can result in injury to the carotid artery. (C and D) Coronal CT images depict variant hyperpneumatization patterns in the lateral sphenoid recess (asterisk) extending beyond a plane from the foramen rotundum and vidian canal (dashed line), and pneumatization of the anterior clinoid process (thick arrow). The relationship of the optic nerve to the sphenoid sinus and variants is important to minimize cranial nerve injury. When more than 50% of the nerve is surrounded by air, an increased risk of optic nerve damage during functional endoscopic sinus surgery is present. Areas of bony dehiscence (not shown) increase risk of nerve injury and should be evaluated for presurgical planning. Cummings (8e, Vol 1), ch. 37, Fig. 37.8, p. 620.

247. Oral premalignant (potentially malignant) lesions and conditions: enumeration and management

ASKED 2* • 5-mark answer

Asked in: Paper II • Jun 2020 • Q7(a) • Paper II • Dec 2020 • Q6(a)

Q: Oral premalignant lesions and their management. [5]

Q: Enumerate various premalignant conditions of oral cavity. [3]

SOURCE

- Cummings Otolaryngology (8e, Vol 2) — ch. 88 Oral Mucosal Lesions — §Oral Leukoplakia; §Histopathologic Features; §Treatment; §Oral Lichen Planus; §Relationship to Oral Squamous Cell Carcinoma; §Submucous Fibrosis; §Candidiasis — pp. 1296–1305; Fig. 88.5, p. 1298
- Cummings Otolaryngology (8e, Vol 2) — ch. 92 Malignant Neoplasms of the Oral Cavity — §Etiology; §Premalignant Lesions; §Diagnostic Evaluation; §Photodynamic Therapy; §Chemoprevention — pp. 1357, 1361–1363, 1380
- Cummings Otolaryngology (8e, Vol 1) — ch. 11 Upper Aerodigestive Manifestations of Systemic Disease — p. 193; ch. 58 Laser Surgery — Table, p. 895
- Stell & Maran's Head and Neck Surgery and Oncology (6e) — ch. 6 Pathology — §Potentially malignant disorders; §Epithelial dysplasia; Table 6.5 — pp. 106–108
- Stell & Maran's Head and Neck Surgery and Oncology (6e) — ch. 23 Lip and oral cavity — §Premalignant disorders — p. 395; ch. 2 Epidemiology and prevention — §Prevention — p. 18; ch. 14 Systemic therapy — §Chemoprevention — p. 238
- Scott-Brown's Otorhinolaryngology (9e, Vol 2) — ch. 184 Tumour biology — p. 1954; ch. 191 Oral cavity tumours — §Floor of mouth — p. 2025; ch. 226 Benign oral and dental disease — §Fungal infections; Table 226.8 — pp. 2483–2484
- W1 • Warnakulasuriya S et al. — Oral potentially malignant disorders: a consensus report from an international seminar on nomenclature and classification, convened by the WHO Collaborating Centre for Oral Cancer, Oral Diseases (doi:10.1111/odi.13704) — 2021

Definition

- **Oral potentially malignant disorders (OPMDs)** — WHO 2017: “clinical presentations that carry a risk of cancer development in the oral cavity, whether in a clinically definable precursor lesion or clinically normal mucosa”; preferred over “premalignant” (SM).
- **Premalignant lesion:** morphologically altered tissue in which cancer is more likely than in its normal counterpart (CUM).
- **Lesions vs conditions:** leukoplakia and erythroplakia are the key lesions; the “other OPMDs” were formerly called potentially malignant **conditions** (SM).
- Global prevalence of OPMDs **4.47%**, higher in Asians and males; risk factors — smoked and smokeless **tobacco**, excess **alcohol**, **betel quid with areca nut**; HPV role controversial (SM).
- **Field cancerisation** (Slaughter 1953): cancer arises in a field of genetically altered epithelium — risk persists after removal (SB).

Enumeration

Table 1. Oral premalignant lesions and conditions

Group	Entity	Key point · malignant transformation (MT)
Lesions	Leukoplakia — homogeneous / non-homogeneous (speckled, nodular, verrucous)	White patch not scraped off and not any other disease; commonest; dysplasia in 3.7–28.7%; 6% → SCC (Bánóczy); floor of mouth 1–2.9%/year (SB)
	Erythroplakia; erythroleukoplakia	Red plaque, no mechanical cause; 91% dysplasia or CIS (Shafer–Waldron) — highest risk
	Proliferative verrucous leukoplakia	Females without risk habits; multifocal, gingiva/palate; SCC in up to 74%
	Actinic (solar) cheilitis	Lower-lip leukoplakia from sun exposure (CUM, SM)
Conditions	Oral submucous fibrosis	Areca nut; MT 7.6% over 17 years
	Oral lichen planus / lichenoid lesions	<1% to ~5%; erosive/atrophic > reticular
	Discoid lupus erythematosus; dyskeratosis congenita	Listed OPMDs (SM)
	Chronic hyperplastic candidiasis	Considered potentially malignant; link now less clear (SB)
	Plummer–Vinson syndrome; chronic syphilis; immunosuppression, HIV, GVHD	Associated with oral carcinoma (CUM ch. 92, ch. 11)

CUM ch. 88, pp. 1296–1303; ch. 92, pp. 1357, 1361; SM ch. 6, p. 106; SB pp. 2025, 2484.

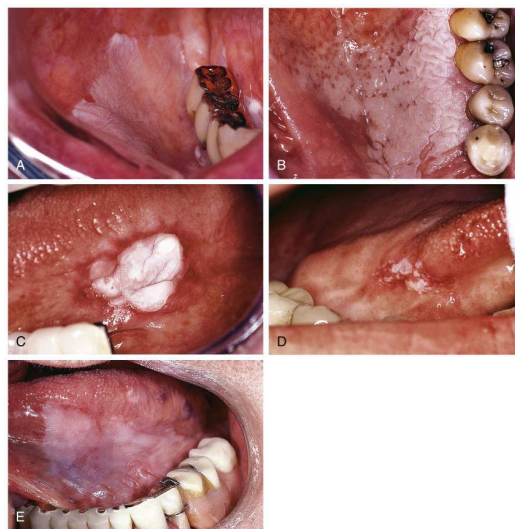


Fig. 88.5 Leukoplakia. (A) A homogeneous, slightly opaque alteration is well marginated superiorly but merges with the gingival mucosa inferiorly. (B) Hard palatal leukoplakia with a minimally elevated surface crossing the palatal midline. (C) A thick, sharply marginated focal leukoplakia of the ventral/lateral tongue with a uniform erythematous periphery. (D) Speckled or heterogeneous leukoplakia, where the leukoplakic element is set on an erythroplakia. (E) A diffuse, thin leukoplakia of the ventral tongue surface with very homogeneous qualities and slightly diffuse peripheral margins.

Cummings (8e, Vol 2), ch. 88, Fig. 88.5, p. 1298.

Markers of high risk

- **Site:** floor of mouth, ventrolateral tongue, retromolar trigone/soft-palate complex (CUM, SM).
- **Appearance:** change from homogeneous to speckled/nodular → **mandatory rebiopsy** (CUM).
- **Dysplasia:** raises MT sevenfold; leukoplakia in non-smokers paradoxically riskier (CUM ch. 92).
- **Molecular:** LOH at 3p and 9p → 3.8-fold risk; added 4p, 8p, 11q or 17p loss → 33-fold (CUM); aneuploidy (SM).
- **Dysplasia features:** drop-shaped rete ridges, basal cell hyperplasia, irregular stratification, abnormal mitoses, premature keratinisation, pleomorphism, raised N:C ratio, lost cohesion and basal polarity (CUM); “differentiated dysplasia” and HPV 16/18-associated dysplasia also carry risk — p16 is not a reliable surrogate (SM).

- **Behaviour:** nodular or mass-forming dysplastic lesions progress more often; surveillance of a lesion stable beyond 5 years showed no added benefit (CUM).

Table 2. Grading of oral epithelial dysplasia (WHO 2022)

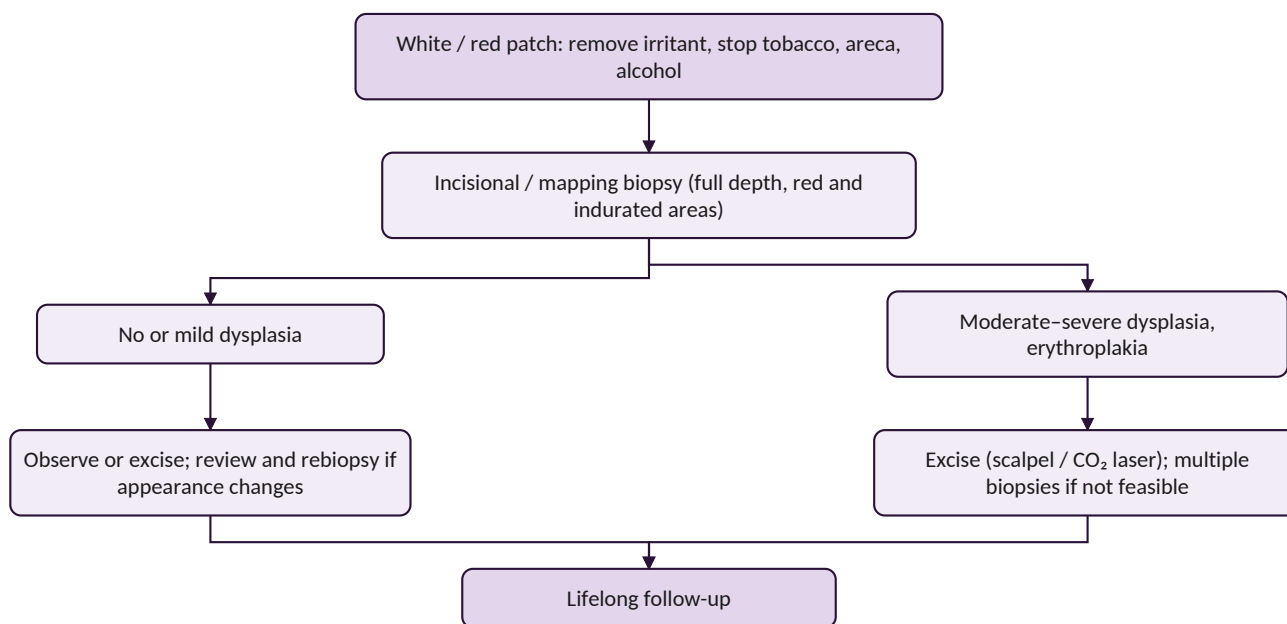
Grade	Extent of atypia	Action
Mild	Atypia confined to the lower epithelial strata	Observe or excise
Moderate	Several layers; upper half still matures normally	Remove
Severe (includes CIS)	Near full-thickness atypia, no invasion	Remove

CUM ch. 88, pp. 1298–1299, Fig. 88.7; SM ch. 6, p. 106, Table 6.5.

Management

- **1. Remove the cause**
 - stop tobacco, areca/betel quid and alcohol; behavioural intervention cut OPMD incidence in Indian quitters (SM);
 - frictional keratosis reverses once trauma stops — not true leukoplakia (CUM).
- **2. Establish histology**
 - **incisional biopsy** — lesional + paralesional tissue, full depth (SM);
 - **mapping biopsies** of extensive lesions, sampling red, granular, ulcerated, indurated areas (CUM);
 - adjuncts (brush cytology, tissue reflectance, fluorescence, methylene blue) are not better than examination and never replace biopsy (CUM);
 - chronic hyperplastic candidiasis with dysplasia: **systemic antifungal, then rebiopsy** (SB).
- **3. Treat by risk**
 - benign or mild dysplasia — observation or elective excision;
 - **moderate dysplasia or worse — remove** (CUM);
 - **erythroplakia, erythroleukoplakia, leukoplakia with moderate/severe dysplasia — excise**; multiple biopsies if complete excision is not feasible (SM).
- **4. Methods of removal**
 - scalpel excision (narrow-band-imaging assisted), **CO₂ laser** excision/vaporisation (large areas), electrocautery, cryoablation (CUM);
 - **photodynamic therapy** for widespread lesions — Photofrin activated by 620-nm light; skin photosensitivity up to 6 weeks (CUM).
- **5. Chemoprevention** — none proven
 - retinoids (isotretinoin), COX-2 inhibitors, antioxidants, PPAR agonists; vitamin E/β-carotene failed in smokers (CUM);
 - isotretinoin cut second primaries at 1 year but not at 4.5 years; erlotinib + celecoxib promising (phase I) (SM).
- **6. Condition-specific**
 - **OLP:** topical moderate–ultrapotent steroids or tacrolimus; intralesional triamcinolone 10–40 mg/mL; follow erosive forms (CUM);
 - **OSMF:** stop areca; see S1_02.
- **7. Lifelong surveillance:** excision lowers but does not remove risk; median time to MT of dysplasia 436 days (CUM, SM).

Flowchart 1. Management of an oral white or red patch



PEARLS

- OPMD = WHO 2017 term; leukoplakia commonest, erythroplakia riskiest (91% dysplasia).
- PVL: non-smoking women, multifocal, SCC up to 74%.
- High-risk sites: floor of mouth, ventrolateral tongue, soft-palate complex.
- Moderate dysplasia or worse = excise; biopsy is never replaced by adjuncts.
- No chemoprevention is proven; follow up for life (field cancerisation).

CURRENT GUIDELINE

- **W1** · WHO Collaborating Centre for Oral Cancer consensus (Warnakulasuriya et al., Oral Dis 2021; workshop 2020).
- The classification is mainly clinical and keeps the established OPMDs: **leukoplakia, proliferative verrucous leukoplakia, erythroplakia, oral submucous fibrosis, oral lichen planus, palatal lesions in reverse smokers, lupus erythematosus, dyskeratosis congenita**. Some definitions were revised slightly.
- **Newly added:** oral lichenoid lesions; oral manifestations of chronic graft-versus-host disease.
- **Not added** (insufficient evidence): chronic hyperplastic candidosis, oral exophytic verrucous hyperplasia. **Epidermolysis bullosa** moved to the limited-evidence group.

248. Oral submucous fibrosis: aetiopathogenesis and medical and surgical management

ASKED 2* · 10-mark answer

Asked in: Paper III · Jun 2025 · Q8 · Paper II · Dec 2020 · Q6(b)

Q: Describe the aetiopathogenesis of oral submucous fibrosis. Discuss the medical and surgical management of oral submucous fibrosis. [10]

Q: Etiopathogenesis and management of oral submucous fibrosis. [7]

SOURCE

- Cummings Otolaryngology (8e, Vol 2) — ch. 88 Oral Mucosal Lesions — §Submucous Fibrosis: Definition; Etiology and Pathogenesis; Clinical Features; Histologic and Diagnostic Features; Treatment — pp. 1295–1296, 1303; references 47–53, pp. 1319.e1–e2
- Cummings Otolaryngology (8e, Vol 2) — ch. 92 Malignant Neoplasms of the Oral Cavity — §Etiology; §Molecular Biology; §Premalignant Lesions — pp. 1357–1358, 1361–1362
- Cummings Otolaryngology (8e, Vol 2) — ch. 79 Biology of Head and Neck Cancers (NF-κB) — p. 1146; ch. 94 Prosthetic Management of Head and Neck Defects — §Osteoradionecrosis (pentoxifylline/tocopherol) — pp. 1402–1403
- Scott-Brown's Otorhinolaryngology (9e, Vol 2) — ch. 183 Aetiology and epidemiology — p. 1948; ch. 191 Oral cavity tumours — §Buccal mucosa — p. 2024; ch. 196 Hypopharyngeal cancer — p. 2102; ch. 223 Maxillofacial prosthodontics — p. 2453
- Stell & Maran's Head and Neck Surgery and Oncology (6e) — ch. 2 Epidemiology and prevention — p. 18; ch. 6 Pathology — p. 106; ch. 12 Reconstructive surgery — §Buccal mucosa defects — p. 208; ch. 17 Emergencies and complications — p. 295; ch. 22 Pain management and palliative care — §Trismus — pp. 380–381
- Stell & Maran's Head and Neck Surgery and Oncology (6e) — ch. 23 Lip and oral cavity — §Buccal mucosa; §Surgical access; §Early rehabilitation — pp. 404–405, 421, 425; Fig. 23.14, p. 405

Definition

- Oral submucous fibrosis (OSMF)** — a **multifactorial**, chronic, progressive fibrosis of the oral submucosa and lamina propria whose chief cause is the **habitual use of areca (betel) nut** products (CUM).
- A **chronic inflammatory reaction** to betel nut / betel quid; presents with **burning** of the buccal mucosa and progresses to severe **trismus** (CUM ch. 92).
- An accepted **oral potentially malignant disorder** (formerly “potentially malignant condition”) (SM, CUM).

Aetiology

Table 1. Aetiological factors in OSMF

Factor	Evidence from the books
Areca nut — chief agent	Main aetiological agent of OSMF and itself carcinogenic — IARC group 1 carcinogen (SB, SM); betel nut and its derivatives are chewed by about 10% of the world population (CUM)
Form and frequency of use	Chewing; a quid (paan masala) parked in the buccal or labial sulcus several times a day; packaged powdered gutkha ; used over many years (CUM)
Betel quid ingredients	Piper betel leaf, slaked lime, spices, tobacco and areca nut (SB, SM); absorption of the red juice gives short-term cholinergic stimulation and long-term carcinogenesis (SB)
Dose-response	Clear dose-response relationship with habitual use (CUM)
Tobacco	Its presence or absence in the mixture does not alter the carcinogenic potential of areca; adding tobacco does not significantly raise carcinogenicity (CUM)
Carcinogenic load	Betel quid raises oral cancer risk in an exposure-dependent way: meta-RR 2.56 without and 7.74 with tobacco (India), 24.84 without tobacco (Taiwan); the side habitually chewed is the side of tumour (SM, SB); attributable risk of regular betel quid ≈50% (SM ch. 2)
Associated local factors	Poor oral hygiene and advanced periodontitis (CUM)
Geography	India, South and South-East Asia, where betel use is socially embedded (CUM, SB, SM)

CUM ch. 88, p. 1303; ch. 92, pp. 1357, 1361; SB pp. 1948, 2024; SM ch. 23, p. 404.

Pathogenesis

- **Step 1 — mucosal injury and inflammation**
 - repeated contact of areca constituents with the buccal and labial mucosa;
 - early **erythema ± vesiculation**, attributed to increased **inducible nitric oxide synthase**;
 - infiltrate of lymphocytes and plasma cells (CUM).
- **Step 2 — oxidative stress**
 - areca generates **reactive oxygen species**;
 - ROS raise **collagen synthesis**, damage microenvironmental fibroblasts and alter DNA (CUM).
- **Step 3 — failure of collagen remodelling**
 - basic defect: failed remodelling with altered **epithelial-mesenchymal and microenvironment interactions**;
 - diminished **functional collagenase** → collagen accumulates instead of being degraded;
 - collagenous **bands and aggregates** form in the submucosa and lamina propria (CUM).
- **Step 4 — hypovascularity and hypoxia**
 - reduced **endothelial cell proliferation** → hypovascularity → tissue **hypoxia** (CUM);
 - overlying epithelium becomes **atrophic**; inflammation recedes, mucosa turns **pale** (CUM).
- **Step 5 — hyalinisation and contracture**
 - loose delicate collagen → progressive **hyalinisation** → complete hyalinisation;
 - scar bands deep in the buccal soft tissues → **reduced mouth opening and tongue mobility**; buccal mucosa thick and fibrotic (CUM).
- **Step 6 — malignant transformation**
 - areca carcinogens (with tobacco smoke) activate **NF-κB** by degrading IκB → IL-8 (angiogenesis), Bcl-xL (anti-apoptosis), cyclin D1 (proliferation), IL-6/IL-1α (CUM ch. 79);
 - **TIMP3 rs9862** polymorphism linked with betel-related oral cancer (CUM);
 - atrophic, dysplastic epithelium thickens and becomes **hyperplastic to verrucous** as SCC develops (CUM).

Flowchart 1. Pathogenesis of oral submucous fibrosis

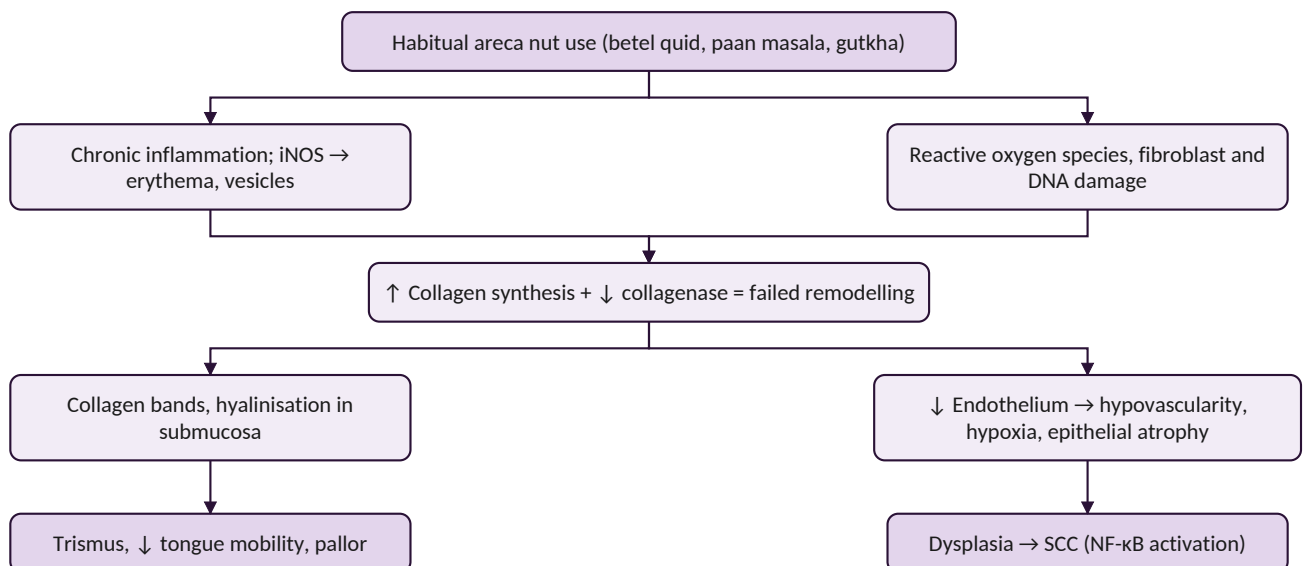


Table 2. Histopathology and its clinical result

Stage / feature	Histology	Clinical result
Early	Delicate, loosely arranged collagen; chronic inflammation (lymphocytes, plasma cells)	Burning, erythema ± vesicles
Progressive	Increasing hyalinisation beneath atrophic epithelium	Pallor; falling mouth opening and tongue mobility
Late	Complete hyalinisation of supporting connective tissue	Deep buccal scar bands; severe trismus
Dysplasia	Mild 46%, moderate 52%, severe 2% (Chennai series); dysplasia in 2.5% of cases in another series	Epithelial thickening, verrucous change = suspect SCC
Malignant transformation	Up to 7.6% over 17 years (India); >5% in other reports	Lifelong surveillance

CUM ch. 88, p. 1303; ch. 92, p. 1357.

Assessment before treatment

- **Mouth opening:** measure maximal inter-incisal opening; trismus is defined as opening **<35 mm**; its causes may be extra- or intra-articular (masticatory muscles vs temporomandibular joint) and it impairs speech, chewing and swallowing (SM).
- **Tongue mobility** and the extent of pale, band-like mucosa document disease progression (CUM).
- **Biopsy** any thickened, hyperplastic, verrucous, red or ulcerated area — erythroleukoplakia and SCC hide within OSMF (CUM, SB).
- **Recent-onset trismus** in an areca user suggests advanced buccal cancer (masticator space) — distinguish it from the **long-standing trismus of OSMF**; examination under anaesthesia may be needed (SM).

Medical management

- **Principle:** management is problematic, especially in advanced disease and when areca use continues (CUM).
- **1. Stop the habit** — first and essential
 - counsel to stop areca, betel quid, gutkha and tobacco;
 - behavioural intervention among betel quid and smokeless tobacco users reduced OPMD incidence among quitters (SM).
- **2. Pentoxifylline** — proposed adjunct (CUM)
 - causes vasodilation, ↓ platelet aggregation, ↑ erythrocyte flexibility — better blood flow to hypoxic tissue;
 - **anti-TNF action decreases fibrosis** (CUM ch. 94);
 - dose quoted for radiation fibrosis/ORN: pentoxifylline 400 mg + tocopherol 500 IU twice daily for ≥6 months; avoid with recent internal bleeding, caution in renal insufficiency (CUM ch. 94 — related use, not an OSMF regimen).
- **3. Collagenase** — proposed (CUM)
 - rationale: functional collagenase is deficient;
 - studied for its effect on **oral opening and eating function** (Lin and Lin, CUM ref. 49).
- **4. Mouth-opening physiotherapy** (trismus measures, SM — described for head and neck cancer)
 - start exercises as soon as the problem is identified;
 - active and passive jaw movement; jaw-opening devices — springs between the teeth, hydraulic bulbs, screws between central incisors;
 - **TheraBite** and **Dynasplint** passive-motion systems; muscle relaxants or botulinum toxin for spasm and pain.

NOT COVERED IN SOURCE

Searched Cummings 8e Vols 1–3, Scott-Brown 9e, Glasscock-Shambaugh 7e and Stell & Maran 6e full text for “submucous fibrosis”, “submucosal fibrosis”, “OSMF”, “OSF”, “areca/arecoline/betel”, “hyaluronidase”, “intralesional steroid/triamcinolone/dexamethasone”, “placental extract”, “lycopene/curcumin”, “antioxidant + oral/fibrosis”, “iron deficiency + fibrosis”, “chilli/capsaicin”, “interincisal/mouth opening mm”, “trismus grade/stage”, “band release/fibrotomy”, “temporalis myotomy”, “coronoidectomy”, “nasolabial flap”, “buccal fat pad”, plus the SB index (pp. 2836–2874; no OSMF entry), SM index (OSMF p. 106 only) and CUM ch. 88 and 92. The books give no clinical staging/grading of OSMF, no intralesional (steroid, hyaluronidase) or antioxidant regimen, and no OSMF-specific operation (band excision with interposition grafts, temporalis myotomy, coronoidectomy for OSMF). Closely related book material on trismus, buccal lining reconstruction and coronoidectomy follows, labelled as such.

Surgical management

- **Surgical release of scar bands has been only modestly successful**, results being poorest in advanced disease with continued areca use (CUM).
- **Release and resurfacing** — options for a buccal mucosal defect (SM, SB; described after buccal resection)
 - healing by secondary intention → postoperative **trismus unless vigorous mouth-opening exercises** are done;
 - **split-thickness skin graft** with silicone sheets to stabilise it — deep defects leave a thin cheek;
 - **buccal fat pad flap is NOT an option** in patients with trismus or **submucosal fibrosis** (SM ch. 12);
 - **radial forearm free flap** — thin, pliable, preferred for large mucosa-only defects and gives **better mouth opening** than skin graft or buccal fat pad; anterolateral thigh flap for bulk (SB, SM) (Fig. 1);
 - low threshold for free-flap lining to avoid trismus (SB).
- **Coronoidectomy** reduces trismus — listed as an adjunct during maxillectomy for obturator fitting (SB ch. 223; related use).
- **Postoperative:** jaw-stretching exercises begin early and continue; trismus is hard to treat once established (SM ch. 17, 23).

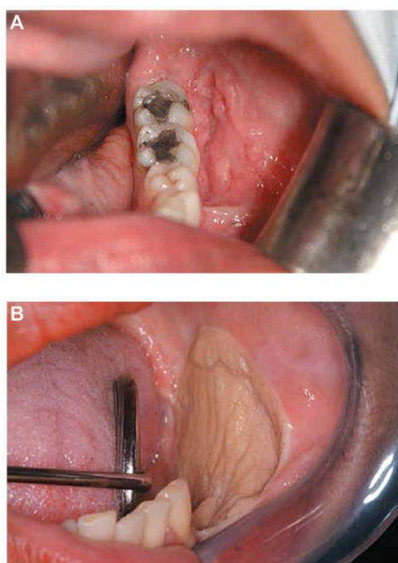


Figure 23.14 SCC buccal mucosa. (A) Preoperative photograph; (B) radial free forearm flap reconstruction.

Stell & Maran's (6e), ch. 23, Fig. 23.14, p. 405 — buccal lining reconstruction shown after SCC resection (related material).

Surveillance and OSMF with carcinoma

- **Coexisting OPMDs:** areca users also develop leukoplakia (up to 4.9% in India) and erythroleukoplakia alongside OSMF (CUM, SB) — biopsy and treat as in S1_01.
- **Lifelong follow-up:** betel chewers develop **multicentric** and second primary tumours — 34.6%, 8.6% and 2.3% second, third and fourth oral primaries over 10 years in an endemic region (CUM).
- **Site of betel-related cancer:** buccal mucosa, whereas tobacco–alcohol cancers favour the oral tongue and floor of mouth (SB); up to 40% of oral cancers in South-East Asia are buccal (SB, SM).

- **OSMF-associated SCC** (Chaturvedi, 112 of 371 patients): buccal mucosa >50%, then oral tongue; **younger males** (mean 45.11 years); lower regional metastasis and less extranodal spread (CUM).
- **Access:** trismus may prevent peroral excision and compromise margins even for early anterior tumours – facial access (lower-cheek flap, lip split) (SB, SM).
- **Reconstruction** in OSMF is complicated by wound breakdown (CUM); OSMF is a **contraindication to transoral** resection of hypopharyngeal cancer (SB).

Table 3. Management ladder in OSMF (book material)

Level	Measure	Source
All patients	Stop areca, betel quid, gutkha, tobacco; biopsy suspicious areas	CUM, SM
Medical	Pentoxifylline; collagenase (proposed agents)	CUM ch. 88
Physical	Jaw-opening exercises, devices (TheraBite, Dynasplint)	SM ch. 22
Surgical	Release of scar bands (modest success) + lining: skin graft or radial forearm/ALT free flap; no buccal fat pad	CUM, SM, SB
Follow-up	Lifelong — multicentric SCC, second primaries	CUM ch. 92

CUM pp. 1303, 1361–1362; SM pp. 18, 208, 380–381, 405; SB p. 2024.

PEARLS

- Areca nut (IARC group 1) is the chief cause; tobacco is not needed for its carcinogenicity.
- Core defect: ↓ collagen synthesis (ROS) + ↓ collagenase = failed remodelling → hyalinised bands.
- Hypovascularity → hypoxia → atrophic epithelium → dysplasia; MT up to 7.6% over 17 years.
- Stopping the habit is the first treatment; pentoxifylline and collagenase are proposed adjuncts.
- Band release alone is modestly successful — resurface (free flap gives the best mouth opening) and exercise.
- New trismus in an OSMF patient = exclude buccal/masticator-space cancer.

249. Risk factors for oral carcinomas

ASKED 1* • 3-mark answer

Asked in: Paper II • Dec 2025 • Q6(c)

Q: Enumerate the risk factors for oral carcinomas. [3]

SOURCE

- Cummings Otolaryngology (8e, Vol 2) — ch. 92 Malignant Neoplasms of the Oral Cavity — §Risk Factors; §Premalignant Lesions; §Squamous Cell Carcinoma Variants; §Hard Palate — pp. 1356–1357, 1361–1362, 1374
- Scott-Brown's Otorhinolaryngology (9e, Vol 2) — ch. 191 Oral cavity tumours — §Introduction — p. 2018; ch. 183 Aetiology and epidemiology — §Risk factors specific to oral cavity SCC — p. 1948
- Stell & Maran's Head and Neck Surgery and Oncology (6e) — ch. 2 Epidemiology and prevention of head and neck cancer — §Aetiology — p. 18; ch. 5 Imaging — §Oral cavity — p. 64; ch. 23 Lip and oral cavity — §Epidemiology and risk factors; §Premalignant disorders; §Buccal mucosa — pp. 393, 395, 404

A. Habits (major, preventable)

- **Tobacco smoking** — cigarettes, bidi, pipe, cigar:
 - RR $\approx$ 3.43 for cigarettes, OR 4.0 for bidi (SM); smokers 5–10 $\times$ risk (SB);
 - risk reaches non-smoker level only 10–20 yr after quitting (SB).
- **Smokeless tobacco** — gutka, khaini, snuff:
 - IARC: sufficient evidence of causation; nitrosamines NNN and NNK; 4-fold risk (CUM).
- **Betel quid / areca nut**:
 - areca = IARC group 1 carcinogen; $\approx$ 50% of oral cancer in India and Taiwan attributable (SM);
 - RR 2.56 without and 7.74 with added tobacco in the Indian subcontinent (SM).
- **Alcohol**:
 - heavy use 3–9 $\times$, even 1–2 drinks/day 1.5–2 $\times$ (SB);
 - **synergy** with tobacco — 2 packs + 4 units/day $\boxtimes$ 35 $\times$ risk (CUM).
- **Reverse smoking** — hard palate carcinoma (CUM).

B. Local and mucosal factors

- **Potentially malignant disorders**: leukoplakia (dysplasia $\boxtimes$ 7 $\times$ risk of progression), erythroplakia (91% show dysplasia or CIS), oral submucous fibrosis (MT >5%), erosive lichen planus (CUM).
- **Chronic trauma**: sharp or broken teeth, ill-fitting dentures; **poor oral hygiene** alters the oral microbiome (SB).
- **UV light**: lower-lip vermilion SCC (CUM).

C. Host factors

- **Immunosuppression**: HIV, transplant, chronic GVHD, prior haematological malignancy (CUM).
- **Genetic and systemic**: Fanconi anaemia, Plummer–Vinson syndrome, chronic syphilis (CUM).
- **Diet** lacking antioxidants (SM); **prior irradiation** — radiation-induced SCC, median latency 13 yr (CUM).

D. Uncertain

- **HPV**: role in oral cavity SCC controversial; no survival advantage, unlike oropharynx (CUM, SM).
- **E-cigarettes**: long-term risk unknown (CUM, SM).
- **Young non-smokers** with oral tongue cancer are rising without identifiable risk factors (CUM).

PEARLS

- Big three: tobacco (smoked or chewed), alcohol, betel quid — synergistic.
- Lip: sunlight; palate: reverse smoking.
- Tobacco signature in the tumour: TP53 mutation, LOH 3p, 4q, 11q13 (CUM).

250. Extrinsic muscles of the tongue and their actions

ASKED 1* · 4-mark answer

Asked in: Paper II · Dec 2025 · Q6(a)

Q: Enumerate the extrinsic muscles of tongue along with their actions. [4]

SOURCE

- Scott-Brown's Otorhinolaryngology (9e, Vol 2) — ch. 217 Anatomy of the mouth and teeth — \$Oropharynx; \$Muscles of the tongue; \$Motor supply; \$Arterial supply; \$Submandibular glands — pp. 2367, 2369–2370, 2372, 2375–2376, 2380; Fig. 217.8, p. 2369; ch. 170 Physiology of swallowing — p. 1825
- Cummings Otolaryngology (8e, Vol 2) — ch. 87 Physiology of the Oral Cavity — \$Lingual Muscles and Reflexes — p. 1284; ch. 92 Malignant Neoplasms of the Oral Cavity — \$Arteriovenous Anatomy; \$Oral Tongue; \$History and Physical Examination — pp. 1359–1360, 1363
- Stell & Maran's Head and Neck Surgery and Oncology (6e) — ch. 5 Imaging — p. 64; ch. 7 Staging — pp. 143–144; ch. 17 Management of emergencies and complications — Fig. 17.23, p. 292; ch. 23 Lip and oral cavity — \$Concept of compartment resection in tongue — p. 414

Extrinsic vs intrinsic

- **Extrinsic muscles** have one attachment to bone outside the tongue and alter the **position** of the whole tongue; intrinsic muscles lie wholly within it and alter its **shape** (SB).
- **Four bilateral pairs:** genioglossus, hyoglossus, styloglossus, palatoglossus; the halves are separated by the midline fibrous septum attached to the hyoid body (SB, CUM).
- **Combined action:** in protrusion genioglossus (with geniohyoid) drives the tongue forward while intrinsic vertical and transverse fibres lengthen it — hydrostatic model (CUM).

The four muscles

- **Genioglossus** — superior mental spine (above geniohyoid); fans out sagittally:
 - inferior fibres to the hyoid body, the rest into the tongue mucosa from root to apex;
 - **bilateral:** protrudes the tongue and creates a central gutter for the bolus; CUM adds depression;
 - **unilateral:** deviates the tongue to the opposite side;
 - holds the tongue forward, keeping the airway open; provides most of the tongue bulk (SB, CUM).
- **Hyoglossus** — greater cornu and body of hyoid; quadrilateral sheet into the side of the tongue:
 - **depresses and retracts;** lowers the sides of the tongue, not its centre (SB).
- **Styloglossus** — styloid process near its apex and stylomandibular ligament; passes below the superior constrictor:
 - interdigitates with hyoglossus; **retracts and elevates** the tongue (SB).
- **Palatoglossus** — oral surface of the palatine aponeurosis; descends in the anterior faucial pillar:
 - **elevates the tongue root** and approximates the palatoglossal arches, narrowing the oropharyngeal isthmus like a sphincter; depresses the soft palate (SB).

Table 1. Extrinsic tongue muscles — action, nerve and artery

Muscle	Main action	Nerve	Artery
Genioglossus	Protrusion (major protruder, CUM); contralateral deviation	Hypoglossal (XII)	Sublingual (lingual), submental (facial)
Hyoglossus	Depression, retraction	XII	Sublingual, submental
Styloglossus	Retraction, elevation	XII	Sublingual only
Palatoglossus	Elevates root; closes isthmus	Vagus via pharyngeal plexus	Ascending palatine, ascending pharyngeal

SB ch. 217, pp. 2369–2370, 2372; CUM ch. 87, p. 1284.

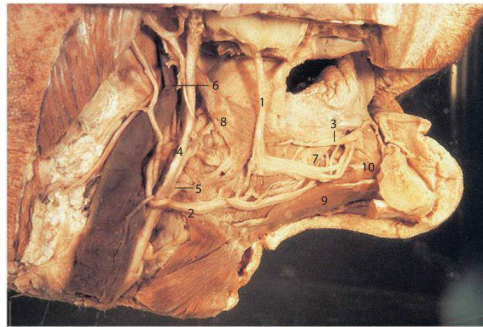


Figure 217.8 Muscles of the tongue and structures on the hyoglossus muscle in the floor of the mouth. 1: Lingual nerve; 2: Hypoglossal nerve; 3: Submandibular duct (cut); 4: External carotid artery; 5: Lingual artery; 6: Glossopharyngeal nerve (cut); 7: Hyoglossus muscle; 8: Styloglossus muscle; 9: Geniohyoid muscle; 10: Genioglossus muscle. (Reprinted from Ref 10 by permission from Elsevier.)

Scott-Brown's (9e, Vol 2), ch. 217, Fig. 217.8, p. 2369.

Applied points

- **Hyoglossus relations:** lingual nerve, submandibular duct and hypoglossal nerve lie on it; the lingual artery runs deep to it — divided to expose the artery (SB, CUM).
- **Hypoglossal palsy:** atrophy and deviation of the protruded tongue to the paralysed side (SM Fig. 17.23).
- **Tumour:** limited mobility and deviation signal deep muscle invasion (CUM).
- **AJCC 8th:** extrinsic muscle invasion removed from oral cavity T4a, replaced by depth of invasion (SM).
- **Compartment resection:** detaches genioglossus, hyoglossus and styloglossus from their bony origins (SM).

PEARLS

- GHSP = genioglossus, hyoglossus, styloglossus, palatoglossus.
- Protruder: genioglossus; retractors: hyoglossus, styloglossus.
- All XII except palatoglossus (vagus, pharyngeal plexus).

251. Differential causes of a non-healing ulcer over the hard palate

ASKED 1* · 4-mark answer

Asked in: Paper II · Jun 2020 · Q2(a)

Q: Enumerate the differential causes of non-healing ulcer over hard palate. [4]

SOURCE

- Cummings Otolaryngology (8e, Vol 2) — ch. 91 Benign Tumors and Tumor-like Lesions of the Oral Cavity — \$Key Points; \$Necrotizing Sialometaplasia — pp. 1350, 1352; ch. 92 Malignant Neoplasms of the Oral Cavity — \$Other Pathologies; \$Hard Palate — pp. 1362–1363, 1374; Fig. 92.28, p. 1374
- Cummings Otolaryngology (8e, Vol 1) — ch. 50 Systemic Disease of the Nose and Sinuses — \$Granulomatosis With Polyangiitis; \$Cocaine-Induced Midline Destructive Lesions; \$Extranodal NK/T-Cell Lymphoma; \$Rhinoscleroma — pp. 810, 812, 815
- Cummings Otolaryngology (8e, Vol 2) — ch. 114 Lymphomas Presenting in the Head and Neck — \$Extranodal NK/T-cell lymphoma — p. 1798
- Scott-Brown's Otorhinolaryngology (9e, Vol 2) — ch. 226 Benign oral and dental disease — \$Oral ulceration; \$Systemic diseases and the mouth; Tables 226.5, 226.7 — pp. 2479–2481, 2484; ch. 217 Anatomy of the mouth and teeth — \$Hard palate — p. 2366; ch. 191 Oral cavity tumours — \$Maxillary alveolus and hard palate — p. 2029; ch. 168 Pharyngitis — \$Syphilis — p. 1801
- Scott-Brown's Otorhinolaryngology (9e, Vol 1) — ch. 79 Granulomatous conditions of the nose — \$Cocaine; \$Extranodal NK/T-cell lymphoma — pp. 866–867
- Stell & Maran's Head and Neck Surgery and Oncology (6e) — ch. 23 Lip and oral cavity — \$Pathology; \$Hard palate and upper alveolus — pp. 395, 418–419

Basis

- Rule:** any oral ulcer persisting >2 weeks must be biopsied to exclude malignancy (SB, CUM).
- Site anatomy:** masticatory mucoperiosteum; the posterolateral submucosa holds the greater palatine bundle and minor salivary glands, most numerous at the hard-soft palate junction; 33% of palatal tumours are salivary (SB, SM).

A. Neoplastic

- Squamous cell carcinoma** — commonest palatal malignancy; elderly male smoker; **reverse smoking**; spreads to nasal floor and antrum and along the greater palatine nerve (CUM).
- Minor salivary gland carcinoma** — adenoid cystic, mucoepidermoid, adenocarcinoma, polymorphous low-grade adenocarcinoma; submucosal nodule at the hard-soft junction, ulceration uncommon (CUM).
- Mucosal melanoma** — pigmented plaque on palate or maxillary gingiva; poor prognosis (CUM, SM).
- Kaposi sarcoma** — palate is its commonest oral site; HIV (CUM).
- Extranodal NK/T-cell lymphoma** (“lethal midline granuloma”) — EBV-driven necrosis of nose, face and palate; CD56-positive; multiple biopsies often needed (CUM, SB).
- Maxillary sinus carcinoma** eroding the palate; **sarcomas** of the hard palate (SM, CUM).

B. Infective

- Mucormycosis** — antral disease with palatal ulceration in the immunocompromised, especially diabetics (SB).
- Aspergillosis** (rhinocerebral) — palatal necrosis; **histoplasmosis**, **blastomycosis** — oral ulcers (SB).
- Tertiary syphilis** — gumma, a nodule that breaks down into an ulcer, can arise in the hard palate (SB).
- Rhinoscleroma** — may progress to the palate (CUM).

C. Granulomatous and destructive

- Granulomatosis with polyangiitis** — septal and palatal perforation (CUM).
- Cocaine-induced midline destructive lesion** — hard and soft palate perforation, commoner than in GPA (CUM, SB).

D. Reactive, traumatic and immune

- **Necrotising sialometaplasia** — 77% palatal; painful butterfly-shaped ulcer <2 cm mimicking SCC; histology shows lobular necrosis with squamous metaplasia of ducts and acini, and pseudoepitheliomatous hyperplasia can be misread as carcinoma; heals in 3–6 weeks (CUM).
- **Denture or repetitive trauma** — inflammatory lesions that mimic malignancy (CUM).
- **Major aphthous ulcer** — >10 mm, lasts up to 3 months, keratinised mucosa possible, may scar (SB).
- **Erosive lichen planus, pemphigus, pemphigoid; mucositis** after chemoradiotherapy (SB).

Table 1. Bedside clues

Clue	Think of
Elderly smoker, indurated ulcer, reverse smoking	SCC
Smooth submucosal swelling at hard–soft junction	Minor salivary gland tumour
Pigmented lesion	Melanoma, Kaposi sarcoma
Diabetic or immunocompromised, rapid necrosis	Mucormycosis, aspergillosis
Perforation with nasal destruction	GPA, cocaine, NK/T-cell lymphoma, gumma
Butterfly ulcer healing in weeks	Necrotising sialometaplasia

CUM ch. 92, p. 1374; CUM ch. 50; SB ch. 226.



Fig. 92.28 A large, ulcerative carcinoma of the hard palate extends to the upper alveolar ridge. Margin control for this tumor would require an infrastructure maxillectomy, and retrograde spread along the greater palatine nerve could result in skull base extension.

Cummings (8e, Vol 2), ch. 92, Fig. 92.28, p. 1374.

PEARLS

- Biopsy every palatal ulcer >2 weeks.
- Commonest malignancy: SCC; next: minor salivary gland carcinoma.
- Necrotising sialometaplasia is the classic benign mimic.
- Diabetic with palatal necrosis = mucormycosis until proved otherwise.

252. AJCC 8th edition TNM staging of lip and oral cavity (oral tongue) cancer, its new inclusions, and the role of biomarkers

ASKED 3* · 10-mark answer

Asked in: Paper IV · Jun 2022 · Q4 · Paper II · Dec 2022 · Q8 · Paper II · Dec 2025 · Q6(b)

Q: Latest AJCC TNM staging system with modifications for oral cancer staging. Describe the role of biomarkers for oral cancer. [10]

Q: What are the new inclusions in 8th edition of AJCC for oral cavity malignancy? Discuss the management of T4aN1Mx lesion of oral tongue. [AJCC part answered here; management in the tongue answer] [10]

Q: Write the TNM classification for carcinoma tongue. [3]

SOURCE

- Cummings Otolaryngology (8e, Vol 2) — ch. 92 Malignant Neoplasms of the Oral Cavity — \$Molecular Biology; \$Pathology; \$Staging; \$Prognostic Metrics; \$Chemotherapy — pp. 1358, 1361, 1364–1365, 1379
- Cummings Otolaryngology (8e, Vol 2) — ch. 74 Biology of Head and Neck Cancers — \$DNA methylation; \$MicroRNAs — pp. 1099–1101; ch. 77 Chemotherapy and Targeted Biologic Agents — \$Recurrent/metastatic disease — p. 1147; ch. 88 Oral Mucosal Lesions — \$Oral Leukoplakia — p. 1297
- Scott-Brown's Otorhinolaryngology (9e, Vol 2) — ch. 185 Staging — \$Overall stage grouping; \$Regional lymph node staging; \$Lip and oral cavity; Tables 185.2, 185.5, 185.8 — pp. 1968–1970; ch. 191 Oral cavity tumours — \$Investigations; \$TNM staging; \$Sentinel lymph node biopsy; \$Horizon scanning — pp. 2019–2020, 2027, 2030
- Stell & Maran's Head and Neck Surgery and Oncology (6e) — ch. 7 Staging — \$TNM staging nomenclature; \$Major changes in the 8th edition; \$Pros and cons of the TNM staging system; Tables 7.4, 7.7, 7.8 — pp. 135–139, 143–146; Fig. 7.1, p. 143
- Stell & Maran's Head and Neck Surgery and Oncology (6e) — ch. 5 Imaging — \$Oral cavity; Tables 5.3, 5.4 — pp. 64–65; ch. 23 Lip and oral cavity — \$Premalignant disorders; \$Staging of disease; Tables 23.3–23.5 — pp. 395, 397–399
- Stell & Maran's Head and Neck Surgery and Oncology (6e) — ch. 3 Molecular biology of HNSCC — pp. 35, 37–39; ch. 6 Pathology — \$Emerging diagnostic and predictive markers — pp. 110–112; ch. 15 Genomics and targeted therapy — \$Genomic biomarkers for targeted treatment — pp. 252–253; ch. 51 Personalised approaches — \$Role of liquid biopsy — pp. 920–921
- W1· AJCC Cancer Staging Manual, 8th edition — oral cavity T categories (Radiopaedia staging summary) — 2017

A. Framework of the TNM system

- Joint UICC/AJCC 8th edition** (2016/2017): one staging for all head and neck sites; T = primary, N = regional nodes, M = distant spread (SM, SB).
- Time points:**
 - cTNM** — before treatment, from examination, imaging, biopsy; selects primary therapy;
 - pTNM** — after resection; guides adjuvant therapy and prognosis;
 - yc/ypTNM** after (neoadjuvant) therapy, **rTNM** at recurrence, **aTNM** at autopsy; residual tumour R0–R2 (SM).
- Rules:** carcinomas only, histologically confirmed; cN0 and cM0 may be assigned on clinical grounds alone; a selective neck dissection specimen should contain ≥10 nodes, a radical or modified radical ≥15; when in doubt choose the lower category; minor salivary carcinomas are staged by their site, e.g. lip (SM, SB).
- Sites (SB):**
 - lip** — upper and lower vermillion, commissures;
 - oral cavity** — from the wet lip mucosa (dry vermillion excluded) to the hard–soft palate junction and circumvallate papillae: buccal mucosa (labial, cheek, retromolar, bucco-alveolar sulci), upper and lower alveolus and gingiva, hard palate, **tongue** anterior to the vallate papillae (dorsum, lateral borders, ventral surface), floor of mouth.
- Carcinoma tongue** (oral, anterior two-thirds) uses the oral cavity scheme; base of tongue is staged as oropharynx (SB).

Table 1. T category — lip and oral cavity (AJCC 8th)

T	Definition
TX / Tis	Primary cannot be assessed / carcinoma in situ
T1	≤2 cm and DOI ≤5 mm
T2	≤2 cm with DOI >5 mm and ≤10 mm, or >2 cm but ≤4 cm with DOI ≤10 mm
T3	>4 cm or DOI >10 mm (see Table 4 for the updated wording)
T4a lip	Invades through cortical bone, or involves inferior alveolar nerve, floor of mouth or skin of face (chin or nose)
T4a oral cavity	Invades adjacent structures only — through cortical bone of mandible or maxilla, maxillary sinus, or skin of face. Superficial erosion of bone/tooth socket by a gingival primary alone is not T4
T4b	Masticator space, pterygoid plates, skull base, and/or encasement of internal carotid artery

CUM ch. 92, p. 1364; SB Table 185.8, p. 1970; SM Tables 5.3, 23.4, pp. 65, 398.

Flowchart 1. Assigning T for an oral cavity primary (AJCC 8th)

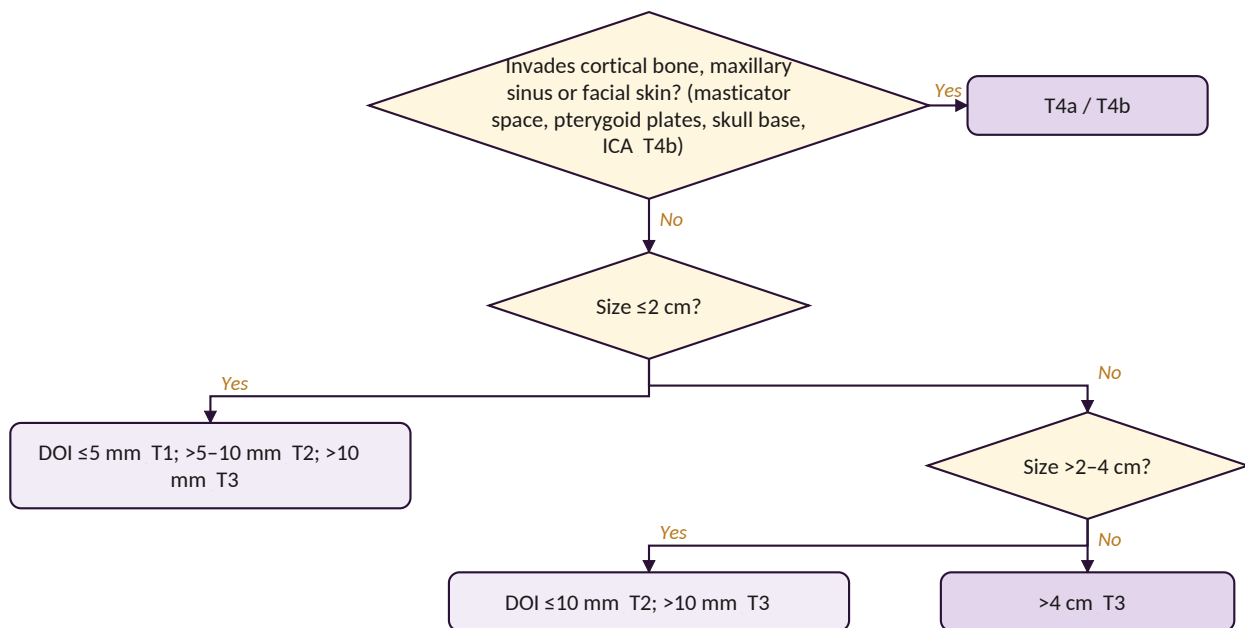


Table 2. N category — oral cavity and all HPV-negative HNSCC

N	Clinical (cN)	Pathological (pN)
N1	Single ipsilateral ≤3 cm, ENE(-)	Same
N2a	Single ipsilateral >3 to ≤6 cm, ENE(-)	Same, or single ipsilateral/contralateral ≤3 cm ENE(+)
N2b	Multiple ipsilateral, none >6 cm, ENE(-)	Same
N2c	Bilateral or contralateral, none >6 cm, ENE(-)	Same
N3a	Any node >6 cm, ENE(-)	Same
N3b	Any node(s) with clinically overt ENE	Single ipsilateral >3 cm ENE(+); multiple nodes ENE(+)

SM Table 7.7, p. 144; SM Table 23.5, p. 399; SB Table 185.5, p. 1969.

- **M:** M0 / M1; M1 may be qualified PUL, HEP, BRA; mediastinal and axillary nodes count as distant (SM).
- **Suffixes:** U or L for nodes above or below the lower border of the cricoid; ENE(-)/ENE(+); sentinel node (sn), e.g. pN1(sn); isolated tumour cells ≤0.2 mm = N0(i+) (SM).

Table 3. Prognostic stage groups (oral cavity, HPV-negative HNSCC)

Stage	T N M
0	Tis N0 M0
I	T1 N0 M0
II	T2 N0 M0
III	T3 N0 M0; T1–T3 N1 M0
IVA	T4a N0–N1 M0; T1–T4a N2 M0
IVB	Any T N3 M0; T4b any N M0
IVC	Any T any N M1

SM Table 7.8, p. 145; SB Table 185.2, p. 1968.

B. Modifications (new inclusions) in the 8th edition

- **1. Depth of invasion (DOI) in T1–T3** — replaces 7th-edition tumour thickness:
 - three bands ≤ 5 , >5 – ≤ 10 and >10 mm; each 5 mm step raises T by one level (SM, SB);
 - DOI predicts occult nodes and disease-specific survival better than thickness (SM, SB).
- **DOI measurement:**
 - **pathological** — perpendicular from the basement-membrane level of the closest adjacent normal mucosa to the deepest point of invasion (SM, SB);
 - **thickness $\neq$ DOI:** exophytic tumour — thickness $>$ DOI; ulcerated tumour — thickness $<$ DOI (Fig. 1);
 - **clinical** — bimanual palpation is sufficient (SM ch. 7), helped by imaging: MRI–histology correlation 0.869, CT 0.80; intraoral US overestimates by only 0.2 mm versus 2–3 mm for CT and MRI (SM).
- **2. Extrinsic tongue muscle invasion removed from T4a** — hard to assess clinically and pathologically; replaced by DOI (SM, SB ch. 191).
- **3. Extranodal extension (ENE) added to N:**
 - ENE = carcinoma extending from within a node through its capsule into surrounding tissue, regardless of stromal reaction (SM);
 - **clinical ENE** needs overt signs — skin involvement, deep fixation or tethering to muscle or adjacent structures, nerve involvement; imaging alone is insufficient $\boxtimes$ cN3b (SB);
 - **pathological ENE** — single ipsilateral node ≤ 3 cm $\boxtimes$ pN2a; all others $\boxtimes$ pN3b; minor (<2 mm) and major (>2 mm) ENE both count as ENE(+), recorded for data (SB, SM).
- **4. Separate cN and pN definitions; U/L level suffix (SM).**
- **5. T0 not used** for oral cavity — an exact site cannot be assigned; EBV-positive or HPV-positive unknown primaries are staged as nasopharynx or oropharynx (SB, SM).
- **6. Gingival note:** superficial bone or tooth-socket erosion is not T4 (SM).
- **Why DOI matters clinically:**
 - DOI ≥ 4 mm carries a 20–30% risk of occult nodes and guides elective neck dissection (SB); every 5 mm increase lowers disease-specific survival (SM ch. 5);
 - biopsy thickness >2 mm usually means final thickness >3.5 mm — a deep biopsy helps plan the neck (SB);
 - CT and MRI overestimate DOI (upstaging $>50\%$ in one series) because formalin shrinks the specimen (SM ch. 5).
- **Impact:** pT upstaged in 31% and pN in 14% of 167 patients, with better DSS discrimination (Tirelli); 25% of 244 upstaged versus 7th edition (Amit) (CUM).
- **Limitations of the current TNM (SM ch. 7):**
 - stage groups were built on presumed prognosis, without prospective multivariate analysis;
 - stage migration with new diagnostic tools; inter-observer and resource variation between centres;
 - static, not individualised; M is binary although oligometastatic disease does better;
 - non-anatomical factors — comorbidity, performance status, smoking, nutrition, biomarkers — are not yet included.

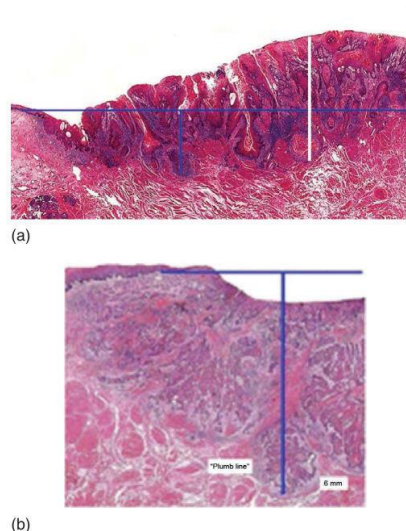


Figure 7.1 Prognostic importance of depth of invasion (DOI). The terms DOI and tumour thickness have often been used interchangeably, which is incorrect. (a) Shown here is an exophytic carcinoma. The white bar represents maximum tumour thickness, which is greater than the DOI, represented by the blue bar. The blue horizontal line is at the level of the closest adjacent normal mucosa. (b) DOI in an ulcerated carcinoma. The blue bar represents the DOI, measured from the blue horizontal line up to the deepest part of the tumour. Notice how tumour thickness would be deceptively thinner than DOI.¹

Stell & Maran's (6e), ch. 7, Fig. 7.1, p. 143.

Table 4. Examinable book disagreement — wording of the 8th edition

Item	Cummings; Scott-Brown; Stell & Maran ch. 5, 23	Stell & Maran ch. 7 (Table 7.4)
T3	>4 cm, or DOI >10 mm	>2–4 cm with DOI >10 mm, or >4 cm with DOI ≤10 mm
T4	Only by invasion of adjacent structures	Also >4 cm and DOI >10 mm
Extrinsic muscle	Removed from T4a (SB ch. 191, SM ch. 5, 7)	SB Table 185.8 still lists deep/extrinsic tongue muscle in T4a
U/L boundary	Lower border of cricoid (SM ch. 23)	Lower border of thyroid cartilage (SM ch. 7)

CUM p. 1364; SB pp. 1970, 2020; SM pp. 65, 139, 143, 398.

C. Role of biomarkers

- **Uses:** screening and early diagnosis, risk of malignant change in potentially malignant disorders, prognosis, prediction of response, and post-treatment surveillance (CUM, SM).
- **Status:** apart from HPV in oropharynx, no biomarker is yet routine in HNSCC; genomic data have not translated into practice as in lung or breast cancer (SM ch. 3).
- **1. Histological (routine prognostic):**
 - DOI, perineural and lymphovascular invasion — S100 and CD31 immunostaining reveal more PNI and LVI than H&E (CUM);
 - margin status, ENE, differentiation; cancer-associated fibroblasts (αSMA) — poor prognosis; tumour-infiltrating lymphocytes — prognostic, relevant to immunotherapy (SM ch. 6).
- **2. HPV / p16:**
 - p16 IHC (strong, >70% of cells) is the HPV surrogate for oropharynx (SM);
 - in oral cavity SCC HPV/p16 has no prognostic value and does not enter staging (CUM).
- **3. Genetic:**
 - **TP53** point mutations in up to 45% of HNSCC; key in >50% of smokers' cancers (CUM); loss of p53-mediated apoptosis may explain poorer results with radiation and cisplatin (SM);
 - **CDKN2A** (p16INK4A) loss and **CCND1** amplification abrogate the G1–S checkpoint (SM);
 - exome sequencing: TP53, CDKN2A, PIK3CA, HRAS, FBXW7, NOTCH1 — NOTCH1 a tumour suppressor (CUM);

- **LOH** at 3p and 9p → 3.8-fold cancer risk in premalignant lesions; with added 4p, 8p, 11q or 17p loss → 33-fold (CUM); aneuploid dysplasia → higher risk (SM).
- **Transcriptional subtypes:**
 - basal, mesenchymal, atypical and classical groups (TCGA 31%, 27%, 24%, 18%); a six-group meta-analysis found mesenchymal and hypoxia subgroups worst and HPV-like best — likely the future treatment classifier (SM ch. 3).
- **4. Predictive / targeted:**
 - **EGFR** overexpression → poor outcome; cetuximab with platinum/5-FU raised OS from 7.4 to 10.1 months in recurrent/metastatic disease, yet EGFR level did not predict benefit (CUM, SM);
 - **PIK3CA** mutation 10–20% (PI3K inhibitors in trials); **HRAS** mutation 4–8% → tipifarnib, response 55% of 20 patients (SM, CUM);
 - **PD-L1 combined positive score** selects pembrolizumab (KEYNOTE-048); tumour mutational burden is a candidate marker (SM); oral cavity responds worse to checkpoint inhibitors than other sites (CUM).
- **5. Saliva and blood (liquid biopsy):**
 - eight methylated genes in a 20 mL saline oral rinse — sensitivity 100%, specificity 87.5% for oral SCC (CUM); methylation is detectable early, even in normal-looking tissue, and in saliva/plasma (CUM ch. 74);
 - **microRNAs** — >260 abnormally expressed; salivary miR-31 rises in oral SCC and falls after resection — a surveillance candidate (CUM ch. 74);
 - circulating tumour DNA found at baseline in 66–86% of locally advanced HNSCC; persistence after surgery signals relapse — a minimal-residual-disease marker (SM ch. 51).
- **6. Host and miscellaneous:**
 - high neutrophil-lymphocyte ratio → worse OS but better chemotherapy response; low pretreatment neutrophils, monocytes, lymphocytes, haemoglobin and albumin (H-index) → worse survival (CUM);
 - drain-fluid MMP-1, MMP-3 and sFlt-1 lower in those who recur; perinodal MCT-4, APOE expression, TIMP3 polymorphism in betel users (CUM).
- **Limitations:** tumour heterogeneity, variable assays and cut-offs, small retrospective series; most await prospective validation before entering the TNM system (SM ch. 3, 7, 51).

PEARLS

- 8th edition = DOI in T, extrinsic muscle out of T4a, ENE in N.
- DOI bands 5 and 10 mm; size bands 2 and 4 cm.
- Clinical ENE → N3b; pathological ENE in a single ≤3 cm node → pN2a.
- HPV/p16 does not change oral cavity stage or prognosis.
- Predictive marker in clinical use: PD-L1 CPS for pembrolizumab; EGFR does not predict cetuximab benefit.

CURRENT GUIDELINE

- **W1 · AJCC 8th edition, oral cavity T category.** Depth of invasion (DOI) is added to size.
- **T1:** ≤2 cm, DOI ≤5 mm. **T2:** ≤2 cm with DOI >5–10 mm, or >2–4 cm with DOI ≤10 mm.
- **T3:** >4 cm with DOI ≤10 mm, or any tumour with DOI >10 mm.
- **T4a:** >4 cm with DOI >10 mm, **or** invasion of cortical bone of mandible/maxilla, maxillary sinus or facial skin. Superficial erosion of a tooth socket by a gingival primary is not T4. **T4b:** masticator space, pterygoid plates, skull base, or encasement of the ICA.
- This matches Stell & Maran Table 7.4 (T4a includes >4 cm with DOI >10 mm). Nodal staging places new emphasis on extranodal extension.

377. Thyroid Imaging Reporting and Data System (TI-RADS): classification and scoring of thyroid nodules

ASKED 1* • 5-mark answer

Asked in: Paper IV • Dec 2020 • Q3(a)

Q: What is the thyroid imaging reporting and data system (TI-RADS) classification and scoring system of thyroid nodules? [5]

SOURCE

- Cummings Otolaryngology (8e, Vol 1) — ch. 8 Overview of Diagnostic Imaging of the Head and Neck — \$Thyroid gland — p. 132
- Cummings Otolaryngology (8e, Vol 2) — ch. 112 Ultrasound Imaging of the Neck — \$Thyroid Ultrasound; Box 112.2; Box 112.3; Box 112.4 — pp. 1744–1748; Fig. 112.8, p. 1747
- Cummings Otolaryngology (8e, Vol 2) — ch. 120 Management of Thyroid Neoplasms — \$Fine-Needle Aspiration Cytology; \$Imaging — pp. 1889–1890
- Cummings Otolaryngology (8e, Vol 3) — ch. 205 Pediatric Thyroid Disease — \$Ultrasound — p. 3117
- Scott-Brown's Otorhinolaryngology (9e, Vol 2) — ch. 230 Assessment, investigation and imaging of the thyroid — \$Thyroid imaging; \$Thyroid nodules; \$Fine-needle aspiration; \$Computed tomography — pp. 2553–2556
- Stell & Maran's Head and Neck Surgery and Oncology (6e) — ch. 40 Surgical management of differential thyroid cancer — \$Radiology: Ultrasound — p. 764
- W1 • American College of Radiology — ACR TI-RADS: White Paper of the ACR TI-RADS Committee (Tessler FN et al., J Am Coll Radiol) — 2017

Definition and purpose

- **TI-RADS** (Thyroid Imaging Reporting and Data System): a standardised ultrasound (US) lexicon that grades each nodule's **risk of malignancy** and decides the need for **guided FNAC** or follow-up (SM).
- Basis: nodule management “boils down to” **biopsy versus serial US**; TIRADS studies since 2009 have improved US-based risk stratification (CUM).
- **ACR TI-RADS** differs from the other systems: it **assigns points to each sonographic feature** and classifies the nodule by the **total score** (CUM).
- Parallel systems in use: **Korean (K-TIRADS)**, **European (EU-TIRADS)**, **ATA sonographic patterns** and the **BTA “U” classification** (CUM, SB).
- **US** is the gold-standard imaging for nodules: sensitivity about 80% for carcinoma in experienced hands and the most accurate way to measure them (CUM).

Scoring: the five ultrasound feature categories

- Every nodule is scored on **five characteristics: composition, echogenicity, shape, margin and echogenic foci**; points are added to give one of five categories (SM).

Table 1. TI-RADS feature categories — reassuring versus suspicious findings

Category	Reassuring (few or no points)	Suspicious (more points)
Composition	Purely cystic (<1% malignancy); spongiform (<3%)	Solid ; a cystic part does not exclude cancer (cystic PTC ≈5%)
Echogenicity	Anechoic; iso- or hyperechoic (solid: 5–10%)	Hypoechoic (10–20%); very hypoechoic vs strap muscle (BTA U4)
Shape (transverse)	Wider than tall	Taller than wide
Margin	Smooth, well circumscribed; complete halo	Irregular / microlobulated ; absent halo; extrathyroidal extension
Echogenic foci	Comet-tail (ring-down) artefact of colloid; coarse or peripheral eggshell calcification	Punctate microcalcifications ; rim calcification with extrusive soft tissue; disrupted peripheral calcification

CUM ch. 112, pp. 1744–1746; CUM ch. 120, p. 1890; CUM ch. 205, p. 3117; SB ch. 230, p. 2554; SM ch. 40, p. 764.

- **Microcalcification**: high specificity but low sensitivity for malignancy (SM); **inspissated colloid** with comet-tail can be misread as microcalcification and is **not** a risk factor (CUM).
- Feature cluster with **70–90% risk**: microcalcification, intrinsic (central) vascularity, absent halo, extrathyroidal extension, taller-than-wide shape, irregular margin (CUM Box 112.4).
- **Colour Doppler** marked intranodular (type III) flow also favours malignancy (SM).

Classification: the five TI-RADS categories

Table 2. TI-RADS categories (SM) set beside the ATA sonographic patterns (CUM) in order of rising suspicion — the books do not formally equate the two

TI-RADS (SM)	Descriptor	ATA pattern · risk (CUM)	ATA FNA cut-off
TR1	Benign	Benign — pure cyst · <1%	Not required
TR2	Not suspicious	Very low — spongiform / partly cystic · <3%	Consider ≥2 cm
TR3	Mildly suspicious	Low — iso/hyperechoic solid, eccentric solid part · 5–10%	≥1.5 cm
TR4	Moderately suspicious	Intermediate — hypoechoic solid, smooth margin · 10–20%	≥1 cm
TR5	Highly suspicious	High — hypoechoic + microcalcification, irregular margin, taller-than-wide, ETE · >70–90%	≥1 cm

SM ch. 40, p. 764; CUM ch. 112, pp. 1747–1748, Figs 112.8–112.9; CUM ch. 120, p. 1890.

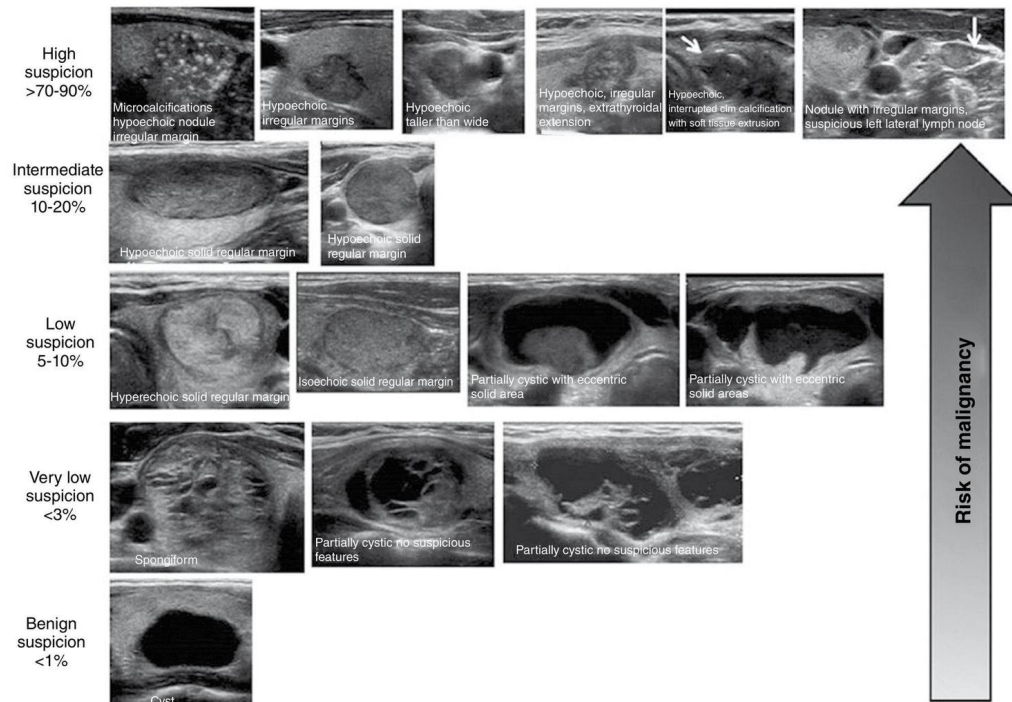


Fig. 112.8 American Thyroid Association nodule sonographic patterns and risk of malignancy. Cummings (8e, Vol 2), ch. 112, Fig. 112.8, p. 1747.

NOT COVERED IN SOURCE

Searched Cummings 8e V1-V3, Scott-Brown 9e, Glasscock 7e and Stell & Maran 6e full text for “TI-RADS/TIRADS”, “Thyroid Imaging Reporting”, “ACR”, “TR1-TR5”, “points/score” with echogenicity or echogenic foci, “mildly/moderately/highly suspicious”, plus the SB (pp. 2836-2874) and SM (pp. 956-977) indexes and CUM ch. 8, 112, 120, SB ch. 230 and SM ch. 40. The books give the five feature categories, the five TI-RADS names and the ATA patterns, but not the **ACR point value of each feature** (0-3 per category), the **point totals defining TR1-TR5** or the **ACR size thresholds for FNA versus follow-up**. The FNA column in Table 2 is the book’s ATA-pattern threshold, shown as the closest book material.

How the score is applied

- Assess and score **each nodule separately** — in a multinodular gland the largest is not necessarily the one to sample, unless all are very low risk (spongiform) (CUM).
- Report alongside each nodule: lobe dimensions, number, site and size of nodules, vascularity and **central and lateral neck nodes** (CUM Box 112.2).
- Suspicious nodes** (round, loss of fatty hilum, microcalcification, cystic change) are sampled regardless of the nodule score (CUM).
- FNAC result is then reported by **Bethesda**, which sets management (CUM Fig. 112.9).
- US guidance** improves FNAC accuracy and yield, especially for small, cystic or previously non-diagnostic nodules (CUM).
- Incidental nodules seen on CT, MRI or PET are characterised by US, as CT and MRI do not separate benign from malignant (CUM, SB).

British Thyroid Association “U” system (UK equivalent)

- U1** normal; **U2** benign (halo, iso/hyperechoic, spongiform, ring-down colloid, eggshell calcification, peripheral vascularity); **U3** indeterminate; **U4** suspicious; **U5** malignant (SB Fig. 230.1).
- Any **U3 or above** should be considered for sampling; it gives near 100% sensitivity in selecting malignant nodules (SB).

Limitations

- No single feature is pathognomonic; risk rests on the **combination** of features (CUM).
- Operator- and interpreter-dependent, especially in children (CUM, SB).
- Size cut-offs (e.g. 1 cm) for sampling remain controversial (SB).
- Clinical risk (age, radiation, family history, nodes) can override a low score (SB).

PEARLS

- TI-RADS = five features (composition, echogenicity, shape, margin, echogenic foci) – points – TR1–TR5.
- **Most specific single sign:** microcalcification; do not confuse with colloid comet-tail.
- **Highest-risk pattern:** solid hypoechoic, irregular, taller-than-wide, microcalcified (>70–90%).
- Spongiform and pure cystic nodules are near-benign — FNA usually unnecessary.
- Score every nodule in a multinodular goitre; always scan the neck nodes.

CURRENT GUIDELINE

- **W1 · ACR TI-RADS white paper (2017).** Points are summed; echogenic foci are additive.
- **Composition:** cystic/spongiform 0 · mixed 1 · solid 2. **Echogenicity:** anechoic 0 · hyper/iso 1 · hypo 2 · very hypo 3.
Shape: wider-than-tall 0 · taller-than-wide 3.
- **Margin:** smooth/ill-defined 0 · lobulated/irregular 2 · extrathyroidal extension 3. **Echogenic foci:** none/large comet-tail 0 · macrocalcification 1 · rim 2 · punctate 3.
- **Levels:** TR1 = 0 (benign) · TR2 = 2 (not suspicious) · TR3 = 3 (mildly) · TR4 = 4–6 (moderately) · TR5 ≥ 7 points (highly suspicious).
- **FNA / follow-up thresholds:** TR3 FNA ≥ 2.5 cm, follow ≥ 1.5 cm · TR4 FNA ≥ 1.5 cm, follow ≥ 1 cm · TR5 FNA ≥ 1 cm, follow ≥ 0.5 cm. TR1–TR2: no FNA.

378. Solitary thyroid nodule — colloid nodule and indeterminate (Bethesda III “follicular”) cytology: clinical features, investigations, treatment options and surgical technique of hemithyroidectomy

ASKED 2* · 10-mark answer

Asked in: Paper III · Jun 2020 · Q2 · Paper III · Jun 2023 · Q8

Q: Clinical features, investigations and treatment options and surgical technique of a case of colloid nodule of thyroid. [10]

Q: A 30-year-old lady has presented with solitary thyroid nodule of 1 year duration suggestive of follicular neoplasm (Bethesda category III). How will you manage such a case. [10]

SOURCE

- Cummings Otolaryngology (8e, Vol 2) — ch. 112 Ultrasound Imaging of the Neck — §Thyroid Ultrasound; Box 112.3 — pp. 1745–1748; Fig. 112.7, p. 1747
- Cummings Otolaryngology (8e, Vol 2) — ch. 119 Disorders of the Thyroid Gland — §Physical Examination; §TSH measurement — pp. 1870, 1874
- Cummings Otolaryngology (8e, Vol 2) — ch. 120 Management of Thyroid Neoplasms — §Clinical Assessment; §Thyroid Nodules—Initial Evaluation; §Thyroid Adenoma; §Thyroid Cyst; §Follicular Carcinoma; §Surgical Anatomy; §Approach to the Thyroid Gland; §Extent of Surgery; §Nonsurgical Treatment — pp. 1886–1890, 1892–1893, 1896, 1900–1904, 1908, 1910, 1912; Fig. 120.2, p. 1901
- Scott-Brown's Otorhinolaryngology (9e, Vol 2) — ch. 228 Thyroid and parathyroid gland pathology — §Fine-needle aspiration cytology; Table 228.1 — pp. 2500–2501
- Scott-Brown's Otorhinolaryngology (9e, Vol 2) — ch. 230 Assessment, investigation and imaging of the thyroid — §Fine-needle aspiration — p. 2554
- Scott-Brown's Otorhinolaryngology (9e, Vol 2) — ch. 232 Surgical approaches to the thyroid — §Indications; §Preoperative considerations; §Theatre setup; §Surgical technique: standard thyroidectomy; Table 232.1; §Postoperative care — pp. 2573–2580
- Scott-Brown's Otorhinolaryngology (9e, Vol 2) — ch. 235 Radioactive iodine for thyroid disease — p. 2609; ch. 244 Ablative technologies in the thyroid and parathyroids — §Types of ablative technology; §Patient selection — pp. 2681–2684
- Stell & Maran's Head and Neck Surgery and Oncology (6e) — ch. 38 Molecular biology and genetic testing — §Clinical gene panels; §Evidence surrounding avoiding diagnostic surgery — pp. 717–720
- Stell & Maran's Head and Neck Surgery and Oncology (6e) — ch. 39 Thyroid and parathyroid gland pathology and cytology — Table 39.1 — pp. 731, 733
- Stell & Maran's Head and Neck Surgery and Oncology (6e) — ch. 40 Surgical management of differential thyroid cancer — §The thyroid nodule; Box 40.2; §Cytology; Table 40.10; §Surgical management of the thyroid in FTC; §Surgical anatomy; §Surgical technique in DTC — pp. 760–763, 770–771, 775–779; Fig. 40.20, p. 778

A. Clinical features

- **Background:** palpable nodules in 4–7% of adults; only about 5% are malignant; benign causes are mainly **colloid (hyperplastic) nodules** and **follicular adenomas**, the commonest benign neoplasm (CUM, SM).
- **Typical benign nodule:** usually a woman, painless, mobile, **smooth** nodule that **moves with swallowing**, often found incidentally; usually **euthyroid**; smooth-contoured nodularity usually represents colloid goitre (CUM).
- **Sudden painful enlargement:** haemorrhage into a benign nodule or adenoma — pain is rarely due to carcinoma (CUM).
- **Pressure symptoms:** dysphagia, positional dyspnoea, globus, cosmetic swelling; retrosternal extension — check lower border and **Pemberton sign** (CUM, SB).
- **Red flags for malignancy** (CUM, SM Box 40.2):
 - age <20 years (20–50% malignant) or men >50 (20–40%);
 - childhood neck irradiation (50% risk); family history, Cowden, FAP, MEN 2;

- rapid growth; firm or fixed nodule; nodule >2 cm or solid;
- hoarseness, stridor, dysphagia; ipsilateral nodes.
- **Examine** from behind with swallowing; nodes from mandible to clavicle; **flexible laryngoscopy** for cord mobility; hyper- or hypothyroid signs (CUM).
- **Thyroid status:** most are euthyroid; toxic symptoms suggest an autonomous nodule; hypothyroidism suggests Hashimoto thyroiditis (CUM).
- **Pathology of the colloid nodule:** hyperplastic nodule of large colloid-filled macrofollicles, often with cystic change or old haemorrhage (SM).

B. Investigations

Table 1. Investigation of a solitary nodule

Test	Expected finding	Meaning
TSH (first test) ± FT4/T3	Normal in most	Low TSH → isotope scan for toxic (hot) nodule
High-resolution US of thyroid and neck	Colloid nodule: well circumscribed, spongiform , comet-tail artefact (Fig. 1)	Sets risk pattern and FNA cut-off (≥1 cm high/intermediate, ≥1.5 cm low, ≥2 cm very low)
US-guided FNAC — Bethesda (Table 2)	Colloid nodule: abundant thin colloid, sparse evenly spaced follicular cells	Benign = Bethesda II / Thy2; accuracy depends on aspirator and cytologist
Isotope scan (¹²³ I / ^{99m} Tc)	Cold nodules 3× more likely malignant than hot	Only if TSH low, or after indeterminate FNAC
Serum calcium , thyroid antibodies	Baseline	Exclude hyperparathyroidism; interpret TFTs
Calcitonin	Not routine	Only if MTC suspected or family history of MEN 2
Thyroglobulin	Not useful	Does not separate benign from malignant
CT / MRI neck–chest	Retrosternal extent, tracheal compression	Large goitre or suspected invasion only

CUM ch. 112, pp. 1745–1748; CUM ch. 120, pp. 1888–1890; SM ch. 40, pp. 762–764.

- **Non-diagnostic FNAC** (≈15%, from cystic, haemorrhagic or hypocellular colloid nodules) is not a negative result — repeat under US; after repeated non-diagnostic aspirates, cancer was found in 4% of women and 29% of men at surgery (CUM).
- With two or more nodules >1–1.5 cm, aspirate the most suspicious-looking nodule first (CUM).
- FNAC reduces surgery by about one-third and doubles the malignancy yield of thyroidectomies (SB).



Fig. 112.7 Transverse/axial image of a colloid nodule with comet-tail artifact.
Cummings (8e, Vol 2), ch. 112, Fig. 112.7, p. 1747.

Table 2. Bethesda categories and risk of malignancy — book disagreement on the figures

Bethesda (UK Thy)	CUM: 2023 update (NIFTP as cancer / excluded)	SM/SB: older tables	Usual action (SM)
I Non-diagnostic (Thy1)	13% / 12%	1–4% (SM)	Repeat US-guided FNA
II Benign (Thy2)	4% / 2%	0–3%	Clinical follow-up
III AUS (Thy3a)	22% / 16%	5–15%	Repeat FNA
IV Follicular neoplasm (Thy3f)	30% / 23%	15–30%	Diagnostic lobectomy
V Suspicious (Thy4)	74% / 65%	60–75%	Surgery
VI Malignant (Thy5)	97% / 94%	97–99%	Surgery

CUM ch. 120, p. 1889; SM ch. 39, Table 39.1, p. 731; SB ch. 228, Table 228.1, p. 2501.

- **2023 Bethesda** dropped the alternate names: III is now only “atypia of undetermined significance”, IV only “follicular neoplasm” (CUM).
- **Note on the stem:** “suggestive of follicular neoplasm” is **Bethesda IV** (Thy3f); **Bethesda III** is AUS (Thy3a). Both are **indeterminate** and are managed below (CUM, SM).

C. Treatment options — benign colloid nodule (Bethesda II)

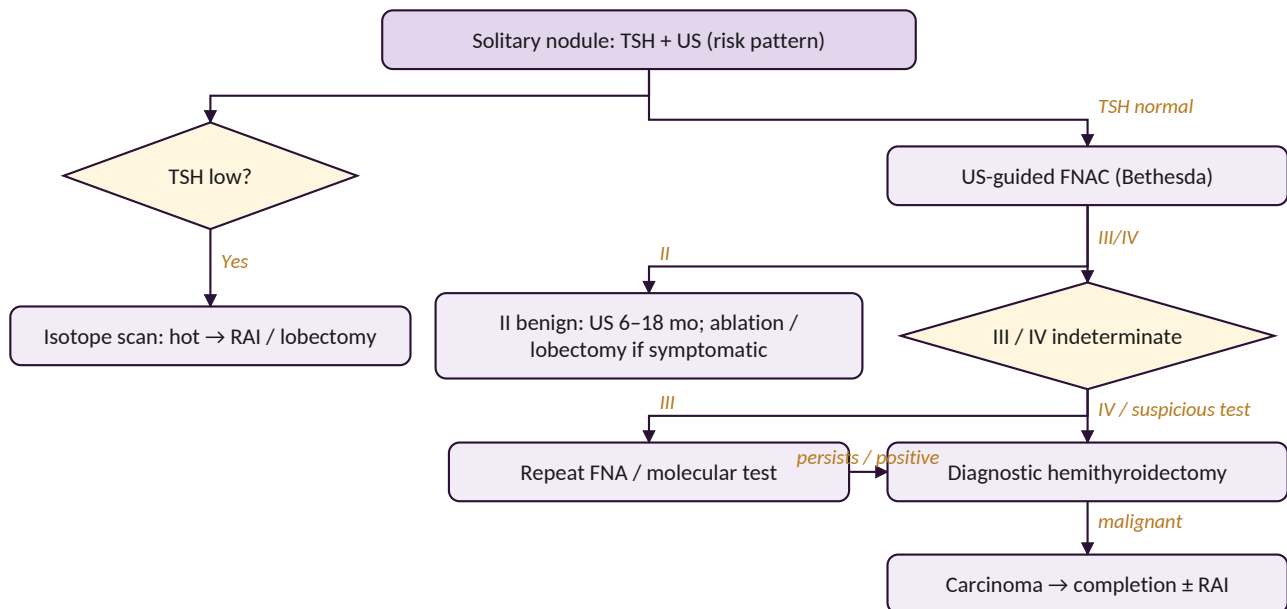
- **Observation** is the rule: easily palpable nodules — clinical review every 6–18 months; others — **US 6–18 months** after FNAC, then longer intervals if stable (CUM).
- **Repeat FNAC** (US-guided) if the nodule grows — growth alone is not proof of malignancy; FNAC false-negative rate ≈5% (CUM).
- **Levothyroxine suppression** for benign nodules: efficacy not agreed; generally not used (CUM).
- **Cystic colloid nodule:** complete aspiration; cure in most after 1–2 drainages; re-accumulation after 3 attempts or bloody fluid — excise (CUM). **Ethanol ablation** for cysts >80% cystic (SB).
- **Thermal ablation** (RFA, laser, microwave, HIFU) for **symptomatic or cosmetic** benign solid nodules with **two benign FNAs**; one session suffices for <15–20 mL; nodules <2 cm rarely need treatment; nerve injury risk 1–5%; indeterminate cytology is excluded (SB, CUM).
- **RAI** may shrink a non-toxic nodule by ~30% when surgery is not feasible (SB).
- **Autonomous (hot) nodule:** lobectomy (preferred <40 years) or RAI (CUM).
- **Hemithyroidectomy indications:**
 - compressive symptoms or poor cosmesis (SB);
 - suspicious US or cytology; solid nodule with repeatedly non-diagnostic FNAC (CUM);
 - patient preference (CUM).

D. Management of the indeterminate nodule (Bethesda III / IV) in a 30-year-old woman

- **Options** (CUM): observation, **repeat FNA**, core biopsy, **molecular testing** of the aspirate, or **diagnostic lobectomy** — chosen with US pattern and clinical risk.
- **Bethesda III (Thy3a):** repeat US-guided FNA and MDT review; ATA — molecular testing or repeat FNA in lieu of surgery or surveillance (SM).
- **Bethesda IV (Thy3f):** diagnostic **hemithyroidectomy** (BTA; PPV up to 40%) or molecular testing to supplement risk before surgery (ATA) (SM).
- **Molecular tests** (ThyroSeq v3: NPV 97%, sensitivity 94%; Afirma GSC: NPV 96%) — negative result allows surveillance; BRAF, RET/PTC or PAX8-PPARγ positive (>95% cancer) — surgery (SM, CUM).
- **¹²³I scan** after indeterminate FNAC: hot — observe; cold — surgery (CUM).
- **Why lobectomy:** it is the minimum operation for a possible cancer — nodulectomy or subtotal resection is unacceptable; a woman <55 years with a nodule <4 cm and no high-risk features is suited to lobectomy (CUM, SB, SM).
- **Oncocytic (Hürthle) cell aspirates:** about 20% malignant, so surgery is usually advised (CUM).
- **Frozen section is not helpful** — follicular carcinoma needs whole-capsule assessment for capsular or vascular invasion (CUM, SM).

- **Total thyroidectomy** instead: older patient with nodule >4 cm ($\approx 50\%$ cancer), family history of thyroid cancer, radiation exposure, patient preference (CUM).
- **After lobectomy**: benign or minimally invasive FTC — follow-up; widely invasive or angioinvasive FTC — **completion thyroidectomy** $\pm$ RAI (CUM, SM).
- **Counsel beforehand** that malignant histology may need a second operation; completion thyroidectomy, if required, is offered within 8 weeks of the histological diagnosis (SM).
- Overall, 70–80% of indeterminate nodules prove benign; surgery overtreats $\approx 60\%$ — the reason for molecular triage (SB, SM).

Flowchart 1. Management of the solitary nodule by cytology



E. Surgical technique — hemithyroidectomy (lobectomy + isthmusectomy)

- **Pre-op**: euthyroid state; review US and cytology; mark side; laryngoscopy if hoarse, large nodule or previous neck surgery; correct vitamin D; consent for voice change, bleeding, scar and hypothyroidism (up to 10–15% after lobectomy) (SB).
- **Anaesthesia/position**: GA with **nerve-monitoring (IONM) tube**, no long-acting relaxant; supine, **reverse Trendelenburg**, shoulder roll, head ring, neck extended (SB, CUM).
- **Incision**: symmetrical **Kocher collar incision** in a skin crease — ≈ 1 cm below cricoid (CUM), midway cricoid–sternal notch (SB) or 2–3 cm above the notch (SM); infiltrate LA with adrenaline (SB).
- **1. Flaps**: subplatysmal, up to thyroid notch and down to sternal notch; protect anterior jugular veins; self-retaining (Joll's) retractor (CUM, SB).
- **2. Midline**: open the investing fascia along the raphe between sternohyoids; separate sternothyroid from the gland; divide straps high (preserve ansa) only if needed; excise any invaded strap en bloc (CUM).
- **3. Lateral mobilisation**: sweep areolar tissue to the carotid; ligate **middle thyroid vein** to rotate the lobe medially (CUM, SB).
- **4. Superior pole**: downward-lateral traction opens **Joll's triangle**; ligate superior pole vessels **individually on the capsule** to spare the **EBSLN**; preserve posterior branches supplying the superior parathyroid (CUM, SM).
- **5. RLN**: find it in the tracheo-oesophageal groove — lateral approach via **Beahrs triangle** (CCA, inferior thyroid artery, RLN); inferior, superior (cricothyroid joint) or medial approaches when needed; beware right **non-recurrent nerve** ($\approx 2\%$); confirm with IONM (SB, SM, CUM).
- **6. Parathyroids**: capsular dissection keeps them on their pedicles; superior gland at cricoid level above the ITA, inferior gland near the lower pole/thyrothymic ligament; autotransplant a devascularised gland into SCM (CUM, SM, SB).
- **7. Inferior pole**: ligate inferior thyroid veins close to the gland; avoid paratracheal dissection (SM).

- **8. Berry ligament:** nerve seen and preserved, then sharp division off the trachea; control bleeding by pressure, not cautery near the nerve (CUM, SM).
- **9. Isthmus and pyramidal lobe:** divide isthmus at the contralateral side and transfix the edge; remove pyramidal lobe in continuity (CUM, SB).
- **10. Closure:** saline wash, Valsalva haemostasis, IONM check of nerve; straps approximated (gap left inferiorly), platysma, subcuticular skin; drain only in difficult cases (SB).

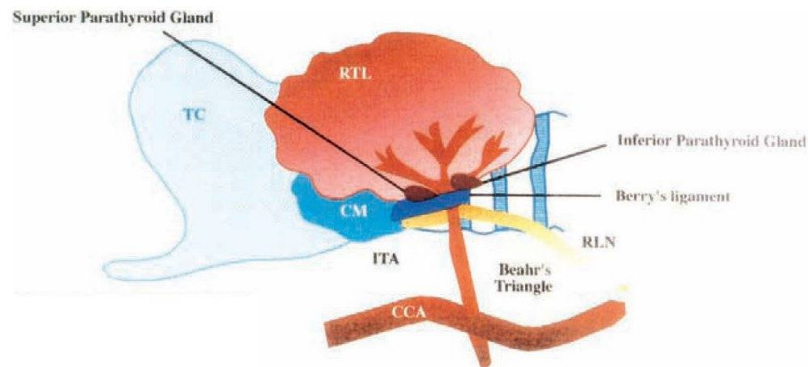


Figure 40.20 Beahr's triangle. Diagram to show the relationships of the recurrent laryngeal nerve. TC: Thyroid Cartilage; CM: Cricothyroid Muscle; RTL: Right Thyroid Lobe; CCA: Common Carotid Artery; ITA: Inferior Thyroid Artery; RLN: Recurrent Laryngeal Nerve. *Stell & Maran's (6e), ch. 40, Fig. 40.20, p. 778.*

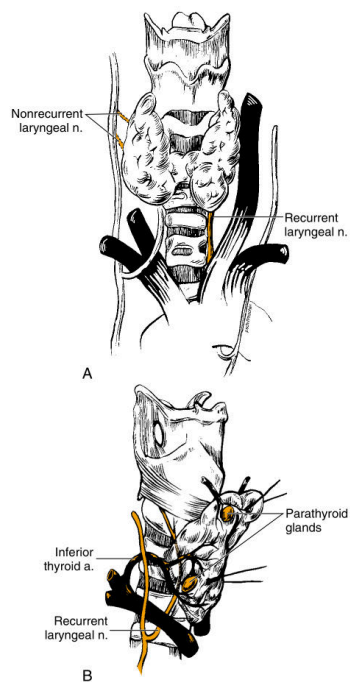


Fig. 120.2 (A-B) The thyroid gland is intimately associated with several important adjacent structures. In the lateral view, the gland has been mobilized medially to show the recurrent laryngeal nerve and its close relationship to the inferior thyroid artery. This relationship can vary between sides within a patient. The potential courses of the nonrecurrent laryngeal nerve are indicated (dashed lines).

Cummings (8e, Vol 2), ch. 120, Fig. 120.2, p. 1901.

- **Post-op:** head-up, analgesia; calcium monitoring not routinely needed after lobectomy; TFT at 6 weeks; histology decides completion surgery (CUM, SB).

PEARLS

- Colloid nodule: smooth, euthyroid, spongiform with comet-tail on US, Bethesda II — observe.
- Benign nodules: US at 6–18 months; repeat FNAC only if growing.
- Bethesda III = AUS; follicular neoplasm = Bethesda IV — both indeterminate.
- FNAC cannot diagnose follicular carcinoma; frozen section does not help — lobectomy gives the answer.
- Molecular testing (high NPV) can spare surgery in indeterminate nodules.
- Lobectomy keys: Joll's triangle (EBSLN), Beahrs triangle (RLN), capsular dissection (parathyroids), Berry ligament (danger point).

379. Role of molecular diagnostic tests in differentiated thyroid cancer

ASKED 1* · 5-mark answer

Asked in: Paper IV · Dec 2023 · Q7(b)

Q: Role of molecular diagnostic tests in differentiated thyroid cancers. [5]

SOURCE

- Cummings Otolaryngology (8e, Vol 2) — ch. 120 Management of Thyroid Neoplasms — §Molecular Alterations in Thyroid Pathology; Table 120.1; §Fine-Needle Aspiration Cytology; Box 120.1; §Papillary Carcinoma — pp. 1886–1887, 1890, 1892, 1895
- Scott-Brown's Otorhinolaryngology (9e, Vol 2) — ch. 229 The genetics of malignant thyroid disease and thyroid nodules — §Papillary thyroid cancer; §Follicular thyroid cancer; Table 229.1; Fig. 229.1 — pp. 2543–2545; Fig. 229.1, p. 2544
- Scott-Brown's Otorhinolaryngology (9e, Vol 2) — ch. 230 Assessment, investigation and imaging of the thyroid — §Fine-needle aspiration — pp. 2554–2555
- Scott-Brown's Otorhinolaryngology (9e, Vol 2) — ch. 236 Management of differentiated thyroid cancer — §Postoperative management; §Metastases detected on follow-up — pp. 2614, 2619; ch. 241 Management of advanced thyroid cancer — §Molecular pathology considerations; §Targeted therapies — pp. 2655, 2657–2658
- Stell & Maran's Head and Neck Surgery and Oncology (6e) — ch. 38 Molecular biology and genetic testing — §BRAF mutation; §RAS mutation; §TERT; §Clinical gene panels; §Somatic mutation panels; §Gene expression classifier; §Next-generation sequencing tests; §Evidence surrounding avoiding diagnostic surgery; §Augmenting RAI — pp. 709–712, 717–721
- Stell & Maran's Head and Neck Surgery and Oncology (6e) — ch. 40 Surgical management of differential thyroid cancer — §PAX8-PPAR γ — p. 767
- Stell & Maran's Head and Neck Surgery and Oncology (6e) — ch. 43 Non-surgical management of thyroid cancer — §Specific targeted therapies — p. 813

Basis

- FNAC is indeterminate (Bethesda III/IV, Thy3a/3f) in **20–30%** of nodules; diagnostic hemithyroidectomy then overtreats about **60%** (SM, SB).
- DTC is driven by alterations of the **MAPK and PI3K pathways**: **BRAF, RAS, RET/PTC** (mutually exclusive in PTC), **PAX8-PPAR γ** , NTRK; late events **TERT promoter, TP53** (SB Fig. 229.1, CUM).
- The Cancer Genome Atlas found a driver in **96.5%** of PTC: **BRAF-like** (classic, tall cell) and **RAS-like** (follicular variant) groups (CUM, SM).

Table 1. Key molecular alterations in DTC

Alteration	Frequency	Association / significance
BRAF V600E	≈45–60% PTC; 0% NIFTP	Classic/tall-cell PTC; nodes, recurrence, reduced RAI avidity; specificity 97.9%, PPV 99.9% for cancer
RAS (N/H/K)	≈10% PTC; 40–50% FTC; also adenomas	Follicular-patterned lesions; risk of cancer only 19–87% — benign, NIFTP or low-risk cancer
RET/PTC fusion	≈7–10% PTC	Radiation-induced and paediatric PTC
PAX8-PPARγ	≈35% FTC	FTC 53% vs adenoma 8%
TERT promoter	10% PTC, 20% FTC, 40% PDTC, 73% ATC	Not in benign tumours; with BRAF → aggressive, recurrent disease
TP53	Rare in DTC	Dedifferentiation to PDTC/ATC

CUM ch. 120, pp. 1886–1887; SB ch. 229, pp. 2544–2545; SM ch. 38, pp. 709–712, 718–720.

1. Diagnostic role — the indeterminate nodule

- **Rule-in tests** (high PPV): single **BRAF V600E**; **7-gene panel** (BRAF, N/H/KRAS, RET/PTC1, RET/PTC3, PAX8-PPAR γ) — specificity 97–99%, PPV 87–88%, but NPV only 86–94% (SM).
- **Rule-out test** (high NPV): **Afirma GEC**, mRNA of 167 genes — sensitivity 90%, NPV 94–95%, but PPV 37–38% (SM).
- **NGS tests** — both rule-in and rule-out: **Afirma GSC** (RNA; NPV 96%, specificity 68%, benign call 54%) and **ThyroSeq v3** (DNA-RNA, 112 genes, >120 fusions; sensitivity 94%, specificity 82%, NPV 97%, benign call 61%) (SM).
- Ideal NPV for rule-out and PPV for rule-in tests is **>95%**; both depend on local cancer prevalence (SM).
- **Practical points**: GEC needs a second dedicated FNA pass; its 25-gene screen first filters out MTC, parathyroid and metastatic lesions; GSC adds BRAF V600E, RET/PTC, Hürthle and MTC components (SM).
- **ATA/NCCN** support molecular testing in indeterminate cytology: Bethesda III — molecular test or repeat FNA instead of surgery or surveillance; Bethesda IV — molecular test before deciding on surgery (CUM, SM).

Table 2. How a molecular result changes management

Result	Action
Negative / benign on high-NPV test	Surveillance like a cytologically benign nodule (residual risk ≈3%)
BRAF, RET/PTC or PAX8-PPAR γ positive (>95% cancer)	Surgery; may convert two-stage to one-stage thyroidectomy
Isolated RAS positive	Hemithyroidectomy only, not radical resection (ETA)
7-gene panel negative	Does not exclude cancer — surgery still advised

SM ch. 38, pp. 718–720.

2. Prognostic role — risk stratification

- **BRAF V600E** enters the ATA recurrence risk table (e.g. intrathyroidal PTC <4 cm, BRAF-mutated ≈10%; PTC >1 cm with TERT ± BRAF ≈40%) (CUM Box 120.1).
- **BRAF + TERT** co-mutation predicts aggressive behaviour and relapse; absent BRAF in a small encapsulated tumour supports **NIFTP** (SB, SM).
- BRAF alone is not an independent prognostic factor in all studies and is **not recommended in microcarcinoma** (SB).
- **Isolated RAS**-positive DTC (mostly follicular variant) has an excellent prognosis and suits conservative treatment; its aggressive cases carry a co-existing TERT mutation (SM).
- **ThyroSeq cancer risk classifier** grades recurrence risk as low (RAS-like), intermediate (BRAF-like) or high (TERT, multiple mutations) (SM).

3. Therapeutic role — advanced and RAI-refractory disease

- About **40%** of thyroid cancers carry targetable alterations; test **RET** and **NTRK** fusions (ideally NGS) when advanced RAI-refractory disease is diagnosed; re-biopsy at late relapse (SB, SM).
- Targets: **RET** (selpercatinib, pralsetinib), **NTRK** (larotrectinib, entrectinib), **BRAF ± MEK** (dabrafenib ± trametinib) (SM, SB).

- **Predicting RAI response:** BRAF V600E lowers NIS expression and TERT mutation is linked to reduced radioiodine uptake in metastatic PTC (SM, SB).
- **Children:** RET and NTRK fusions are common in paediatric PTC; testing identifies targets for metastatic or unresectable disease (CUM).
- **Redifferentiation:** MAPK blockade restores NIS — selumetinib (best in NRAS) or dabrafenib before further RAI (SM).

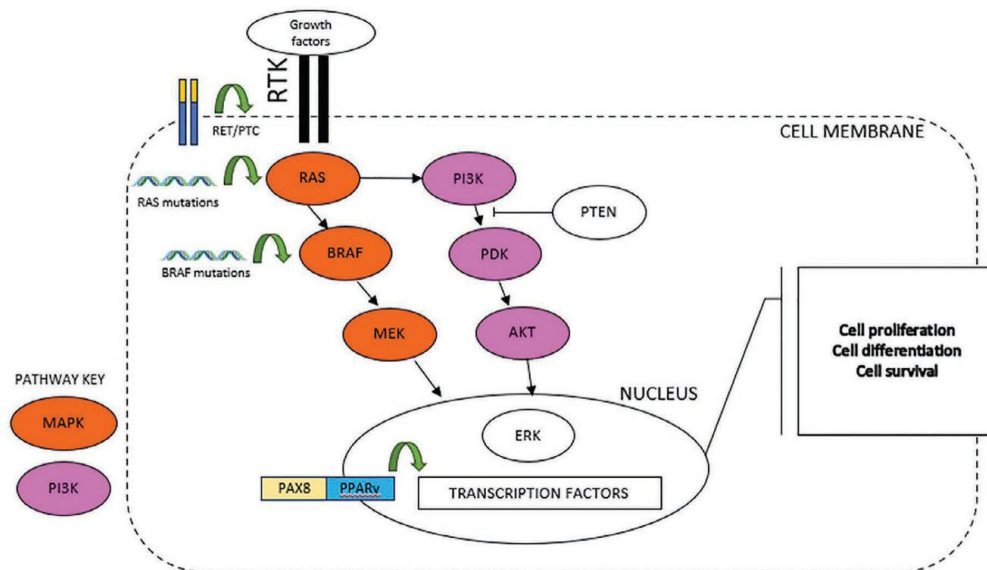


Figure 229.1 Simplified MAPK and PI3K pathway with the most significant genetic abnormalities. MAPK and PI3K are kinase cascade pathways that transmit signals from the cell membrane to the nucleus. They control functions such as cell proliferation, differentiation, motility and apoptosis. Growth factors activate the cascade via transmembrane receptor tyrosine kinase proteins. RET/PTC rearrangements promote this initial activation. RAS is a common protein for both pathways and the RAS family mutations promote the activation of subsequent kinases. BRAF mutations equally activate the downstream cascade. PPAR γ is a tumour suppressor gene and its fusion with PAX8 is thought to either negate PPAR γ tumour suppressor activity, or as a novel transcription factor with its own protooncogene capabilities. PTEN is a negative regulator of the PI3K pathway. Mutations or deletions of PTEN subsequently allow unregulated activity of the PI3K pathway.

Scott-Brown's (9e, Vol 2), ch. 229, Fig. 229.1, p. 2544.

Limitations

- Mostly US-validated, costly, need central laboratories; little long-term outcome data after avoided surgery; oncocytic lesions perform poorly (CUM, SB, SM).
- **Liquid biopsy** (ctDNA BRAF, circulating miRNA) is still investigational (SB).

PEARLS

- Molecular tests mainly triage **indeterminate (Bethesda III/IV)** nodules.
- Rule-in = mutation panels (high PPV); rule-out = Afirma (high NPV); NGS (ThyroSeq v3, Afirma GSC) does both.
- BRAF V600E: commonest PTC driver; absent in NIFTP.
- BRAF + TERT = aggressive PTC; TERT/TP53 = dedifferentiation.
- RET/NTRK/BRAF testing selects targeted drugs in RAI-refractory disease.

380. Indications for total thyroidectomy (ATA); methods of identifying the parathyroid glands during thyroidectomy; management of post-thyroidectomy hypocalcaemia

ASKED 1* · 10-mark answer

Asked in: Paper III · Jun 2024 · Q1

Q: Describe indications of total thyroidectomy according to ATA guideline. What are various methods of identification of parathyroids during thyroidectomy? Describe management of post thyroidectomy hypocalcaemia. [10]

SOURCE

- Cummings Otolaryngology (8e, Vol 2) — ch. 120 Management of Thyroid Neoplasms — \$Papillary Carcinoma; \$Follicular Carcinoma; \$Oncocytic Cell Tumor; \$Medullary Thyroid Carcinoma; \$Surgical Anatomy; \$Approach to the Thyroid Gland; \$Extent of Surgery; \$Children; \$Hypocalcemia — pp. 1894, 1896–1898, 1902–1904, 1907–1910; Fig. 120.6, p. 1902
- Cummings Otolaryngology (8e, Vol 2) — ch. 121 Management of Parathyroid Disorders — \$Parathyroid autofluorescence — p. 1920
- Scott-Brown's Otorhinolaryngology (9e, Vol 2) — ch. 232 Surgical approaches to the thyroid — \$Indications; \$Parathyroid glands; \$Autofluorescence; \$Postoperative care — pp. 2573, 2576–2577, 2580
- Scott-Brown's Otorhinolaryngology (9e, Vol 2) — ch. 233 Surgical management of the compressive thyroid goitre — Table 233.3 — p. 2589; ch. 234 Surgical management of hyperthyroidism — \$Surgery for Graves' disease — p. 2602; ch. 235 Radioactive iodine for thyroid disease — \$Future in radioactive iodine therapy — p. 2611
- Scott-Brown's Otorhinolaryngology (9e, Vol 2) — ch. 241 Management of advanced thyroid cancer — \$Thyroid cancer recurrence risk stratification — p. 2654; ch. 242 Management of paediatric thyroid cancers — p. 2667
- Scott-Brown's Otorhinolaryngology (9e, Vol 2) — ch. 245 Parathyroid preservation in thyroid surgery — \$Post-surgical hypoparathyroidism; Table 245.2; \$Strategies to aid parathyroid preservation; \$Intraoperative techniques; \$Role of intraoperative technologies; \$Postoperative management — pp. 2689–2695; Fig. 245.4, p. 2692
- Scott-Brown's Otorhinolaryngology (9e, Vol 2) — ch. 249 Redo parathyroid surgery — Table 249.4 — p. 2724; ch. 251 Complications of thyroid and parathyroid surgery — \$Hypoparathyroidism — p. 2737
- Stell & Maran's Head and Neck Surgery and Oncology (6e) — ch. 17 Management of emergencies and complications — \$Hypoparathyroidism — p. 297
- Stell & Maran's Head and Neck Surgery and Oncology (6e) — ch. 40 Surgical management of differential thyroid cancer — Table 40.8; \$Treatment of DTC; \$Surgical management of the thyroid gland in PTC and FTC; \$Surgical anatomy; \$Thyroidectomy; \$Central neck dissection — pp. 767–768, 770–771, 775–778, 780
- Stell & Maran's Head and Neck Surgery and Oncology (6e) — ch. 41 Medullary thyroid cancer — \$Extent of thyroidectomy — p. 793
- W1 · American Thyroid Association — 2025 management guidelines for adult patients with differentiated thyroid cancer (Ringel MD et al., Thyroid 35(8):841–985) — 2025

A. Indications for total thyroidectomy

- **Total thyroidectomy (TT):** removal of both lobes, isthmus and pyramidal lobe; subtotal operations are not acceptable for cancer (SM, CUM).
- **ATA principle (2015):** treatment is risk-adapted; a unifocal cancer <4 cm without extrathyroidal extension or nodes is so low-risk that the extent of surgery does not change outcome — hence lobectomy is acceptable for most (>80%) (SB, CUM).

Table 1. Indications for total thyroidectomy as given in the books (ATA-based)

Setting	Total thyroidectomy indicated when	Lobectomy acceptable when
PTC	Tumour >4 cm ; gross extrathyroidal extension ; clinical nodal or distant metastasis ; multifocal or familial disease; prior head–neck radiation	>1 cm and <4 cm, no ETE, cN0, M0 (SM: age <55); microcarcinoma ≤1 cm
FTC / oncocytic	>4 cm; widely invasive or ≥4 foci of vascular invasion ; invasive oncocytic carcinoma	Minimally invasive, <4 cm, low-risk woman <55
Follicular neoplasm (Bethesda IV)	Older patient with nodule >4 cm (≈50% cancer); family history; radiation; patient preference	Default: diagnostic lobectomy
Completion after lobectomy	Lymphovascular invasion, macroscopic multifocality, poor differentiation, positive margin, >4 cm, angioinvasive FTC	—
MTC	All MTC (with bilateral central dissection); all RET carriers / MEN 2 (prophylactic)	Rare unilateral sporadic MTC with undetectable post-op calcitonin
Children with DTC	Usually TT (bilateral and multifocal disease)	—
Benign	Graves' disease needing surgery; bilateral goitre with compression; sternotomy needed; troublesome Hashimoto (high antibody titre)	Unilateral goitre or dominant nodule; RLN palsy; comorbidity

CUM ch. 120, pp. 1894, 1896, 1898, 1907–1909; SB ch. 232, p. 2573; SB ch. 233, p. 2589; SB ch. 234, p. 2602; SB ch. 241, p. 2654; SM ch. 40, pp. 768, 771.

- **Why TT in higher-risk cancer:** allows RAI ablation and whole-body scanning, makes **thyroglobulin** a reliable marker, removes contralateral foci (30–70%) and lowers recurrence (SM Table 40.8, CUM).
- **Price:** bilateral surgery exposes both RLNs and all four parathyroids; lifelong thyroxine (SB, CUM).
- **Shift in practice:** a decade ago tumours >1 cm went to TT/completion and RAI; ATA 2015 and BTA 2014 now favour observation of the remaining lobe for low-risk 1–4 cm tumours without adverse features (SB).
- **NCCN criteria for lobectomy** (CUM): no prior radiation, no distant or nodal metastasis, no extrathyroidal extension, tumour <4 cm.
- Decision is shared with the patient, especially in low-risk DTC — patient values (e.g. professional voice use, wish to avoid hypoparathyroidism and lifelong thyroxine) weigh in (SB).

B. Methods of identifying the parathyroid glands

1. Anatomical and visual identification (the basis)

- **Superior gland:** constant position — at the level of the **cricoid**, near the cricothyroid joint and RLN, posterosuperior and **cephalad to the inferior thyroid artery (ITA)**, medial to the RLN–ITA crossing; the ITA is the best initial marker (CUM, SM, SB).
- **Inferior gland:** variable — caudal to the RLN–ITA crossing at the apex of Beahrs triangle; about half at or around the **lower pole**, a quarter near or in the **thymus/thyrothymic ligament**; ectopic, intrathyroidal (≈1%) or supernumerary glands occur (SM, SB).
- **Appearance:** **caramel / tan-yellow**, oval, 30–70 mg (just under 1 cm³), distinguished from paler yellow fat; becomes mahogany when bruised; colour lightens with age as fat content rises (CUM, SM).
- **Symmetry:** glands lie in the same position on both sides in about 80% — use the first side to find the second (SB, CUM).
- **Follow the vessels:** trace the ITA and its inferior branches to the thyrothymic ligament and inferior gland; slinging the ITA helps; feeding vessels often run on the thyroid capsule (SB).

2. Operative strategy that exposes the glands

- Adequate (not minimal) incision; mobilise the lobe laterally to the carotid sheath and open the plane to the prevertebral fascia — the posterolateral lobe where glands lie comes into view early (SB).
- **“Medial-to-lateral” lobectomy:** divide isthmus and poles first, leaving lateral attachments (and parathyroid vessels) until last (SB).
- **Intercapsular dissection** between true and false capsules and ligation of vessels on the capsule (CUM, SB).

- Look for glands throughout the operation rather than “hunting them down”; identifying more glands protects against hypocalcaemia (SB).

3. Adjunct technologies and confirmatory tests

Table 2. Adjuncts for parathyroid identification

Method	Principle / use	Limitation
Magnification loupes	Show glands and feeding vessels	Benefit not conclusively proven
Near-infrared autofluorescence — image-based (e.g. Fluobeam)	Parathyroid fluoresces more than thyroid; wide field, no contact; finds ectopic glands and glands on the specimen (Fig. 1)	Theatre lights off; operator-dependent
Autofluorescence — probe-based (e.g. PTeye)	Contact probe, quantitative audible signal, lights on	Calibration needed; contact only
ICG fluorescence	Maps feeding vessels; judges viability in situ	Hinders later autofluorescence; vasospasm mimics ischaemia
Saline float test	Fat floats, parathyroid sinks	Not 100% reliable
Frozen section of a tiny piece	Confirms doubtful tissue before autotransplantation	Needs pathologist; time
Specimen inspection	Detects inadvertently removed glands	—
Experimental	Electrical impedance spectroscopy, carbon nanoparticles, 3D exoscope	Limited evaluation

CUM ch. 120, pp. 1902–1904; CUM ch. 121, p. 1920; SB ch. 232, pp. 2576–2577; SB ch. 245, pp. 2691–2694; SM ch. 40, pp. 775–776.

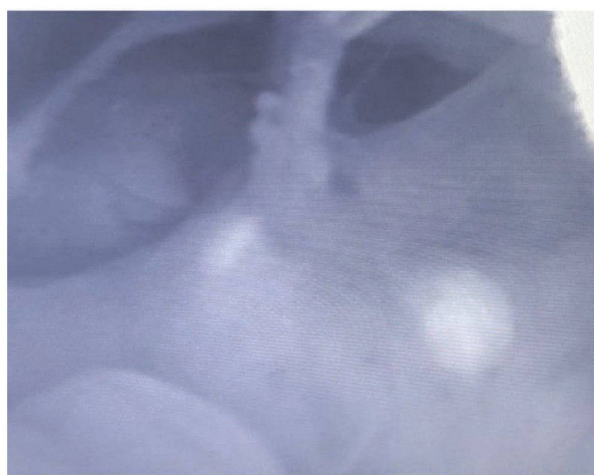


Figure 245.4 Detection of autofluorescence using near-infrared fluorescence imaging confirming the location of the two parathyroid glands.

Scott-Brown's (9e, Vol 2), ch. 245, Fig. 245.4, p. 2692.

- **Preservation after identification:** ligate vessels on the capsule; leave superior gland on its posterior superior-thyroid branches; in central dissection lateralise inferior glands on their pedicles (CUM, SM).
- **Viability check:** dusky gland — nick it to see bleeding or use ICG; non-viable or removed gland → minced into 1 mm³ pieces and **autotransplanted** into SCM (or forearm), pocket marked with clip or permanent suture (CUM, SB).
- False-positive fluorescence: brown fat, colloid nodules; vasospasm may mimic non-perfusion (SB).

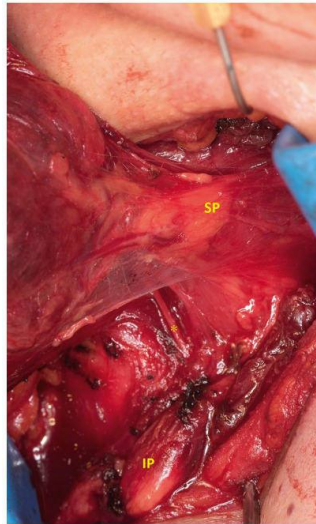


Fig. 120.6 Intraoperative view of the superior parathyroid gland (SP), inferior parathyroid gland (IP), and their relation to the recurrent laryngeal nerve (asterisk) which is traveling in the tracheoesophageal groove.

Cummings (8e, Vol 2), ch. 120, Fig. 120.6, p. 1902.

C. Management of post-thyroidectomy hypocalcaemia

Incidence, causes and risk factors

- **Incidence:** transient 7–25%, permanent 0.4–14% (CUM); temporary 10–15%, permanent 1–3% (SB, SM); higher in Graves' disease (temporary 14–60%) (SB).
- **Causes:**
 - **hypoparathyroidism** — gland removal, devascularisation, trauma (commonest);
 - **hungry bone syndrome** — normal/high PTH, low Mg and phosphate, after thyrotoxicosis;
 - dilutional/protein-binding change — usually asymptomatic (CUM, SB).
- **Risk factors** (SB Table 245.2): female sex, vitamin D deficiency, malabsorption/bariatric surgery; Graves', extensive cancer, nodes, large retrosternal goitre; central neck dissection, reoperation, concomitant parathyroid surgery.

Prevention

- Lobectomy instead of TT where safe; unilateral rather than bilateral central dissection (SB).
- Correct **vitamin D** pre-operatively; IV **dexamethasone** at induction modestly reduces hypocalcaemia (SB).
- Identify and preserve glands; autotransplant devascularised glands (CUM, SB).
- **Consider routine autotransplantation** when risk is high: TT with central neck dissection, en bloc resections taking parathyroids, reoperation after thyroid or parathyroid surgery (CUM).

Recognition and monitoring

- **Symptoms:** perioral and fingertip paraesthesia, cramps, tetany; severe — bronchospasm, laryngospasm/stridor, confusion, seizures, arrhythmia with **prolonged QT** (CUM, SB).
- **Signs:** Chvostek and Trousseau signs once calcium falls below about 8 mg/dL (CUM).
- **Tests after TT/completion:** adjusted calcium and **PTH at about 6 hours**, and next morning; low PTH predicts a later fall — calcium may lag 24–36 hours; discharge only with stable or rising calcium; lobectomy needs no routine calcium check (CUM, SB).
- Worrying pattern: **low calcium, high phosphate**, metabolic alkalosis; check magnesium (CUM, SB).

Treatment

- **Start treatment** if symptomatic or calcium <7.5 mg/dL; consider cardiac monitoring (CUM).
- **Acute/severe (tetany): 10 mL of 10% calcium gluconate IV** over about 10 minutes (in 5% dextrose, titrated to symptoms) — 10–30 mL over 10–15 min in the SB algorithm; careful cannula siting to avoid extravasation; repeat calcium levels (CUM, SB).

- **Oral calcium:** calcium carbonate 2–3 g/day (CUM) — e.g. 1 g two or three times daily (SB).
- **Active vitamin D:** calcitriol or 1-alfacalcidol (1 µg od to tds in the SB algorithm) when oral calcium alone is inadequate (CUM, SB, SM).
- Check magnesium (low in hungry bone syndrome) and treat any vitamin D deficiency promptly after surgery (SB).

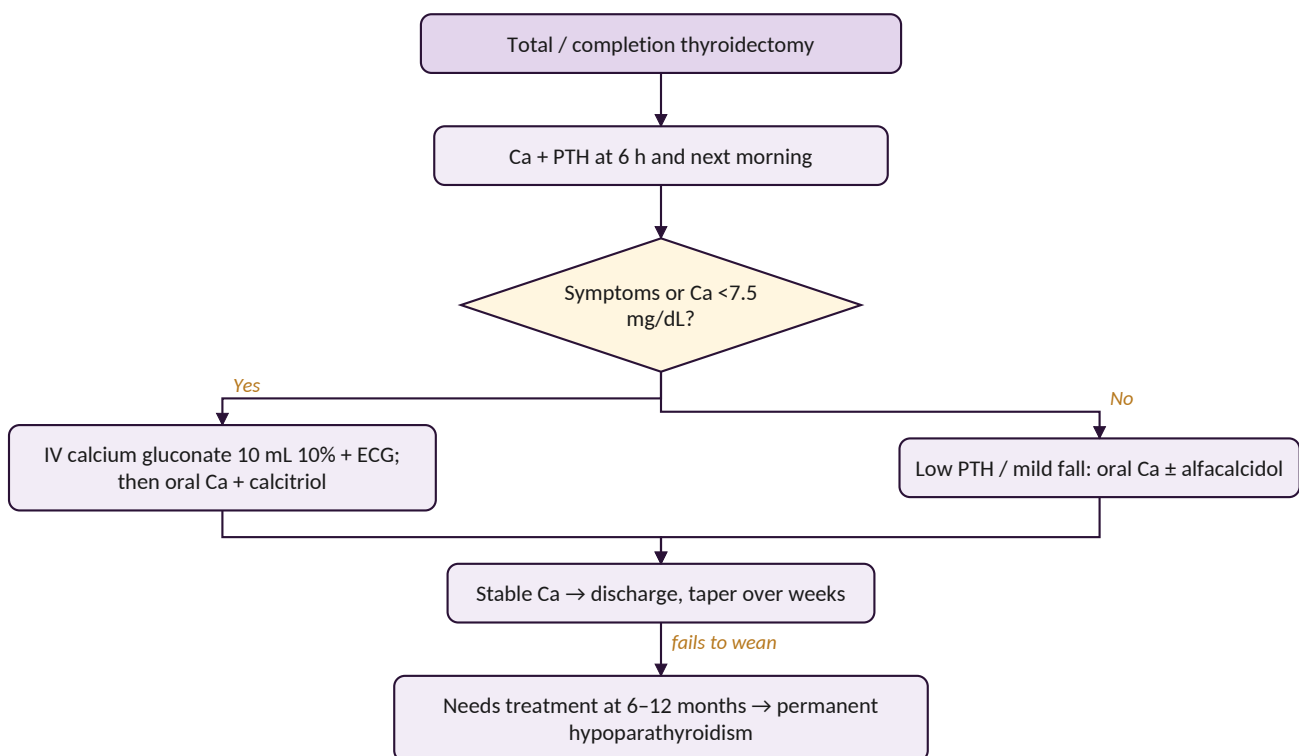
Table 3. Tiered algorithm for hypocalcaemia (SB Table 249.4)

Corrected Ca, mmol/L (mg/dL)	Symptomatic	Asymptomatic
>2.15 (8.6)	Milk	Nil
2.00–2.15 (8.0–8.5)	Calcium carbonate 1 g bd	Nil
1.90–2.00	Calcium 1 g tds + alfacalcidol 1 µg od	Calcium 1 g tds
1.80–1.90 (7.2–7.5)	Calcium 1 g tds + alfacalcidol 1 µg bd	Calcium 1 g tds + alfacalcidol 1 µg bd
<1.80 (<7.2)	Tetany: 10–30 mL IV calcium gluconate over 10–15 min	Calcium 1 g tds + alfacalcidol 1 µg tds

SB ch. 249, Table 249.4, p. 2724.

- **Follow-up:** most recover within 2 weeks if glands were preserved; outpatient taper with symptom education; calcium weekly, then every 6–8 weeks; wean supplements whenever possible (CUM, SB).
- **Strategies debated:** “stimulating” (allow mild hypocalcaemia to drive recovery) versus “splinting” (full replacement) (SB).
- **Permanent hypoparathyroidism:** still needing calcium ± vitamin D at **6–12 months**; monitor calcium, PTH, magnesium, phosphate and renal function; avoid hypercalcaemia — risks renal and brain calcification, CKD, poorer quality of life (SB, SM).

Flowchart 1. Post-thyroidectomy calcium pathway



PEARLS

- ATA: TT for >4 cm, gross ETE, clinical N1 or M1; lobectomy is acceptable for low-risk 1–4 cm DTC.
- TT for all MTC and RET carriers; for Graves' when surgery is chosen.
- Superior parathyroid is constant (cricoid level, above ITA); inferior is variable (thyrothymic ligament).
- Autofluorescence and ICG are adjuncts — anatomy and capsular dissection remain the key.
- Check PTH early: low PTH predicts hypocalcaemia before calcium falls.
- Tetany: 10 mL 10% calcium gluconate IV slowly; then oral calcium + calcitriol/alfacalcidol; permanent if still needed at 6–12 months.

CURRENT GUIDELINE

- **W1 · ATA DTC guideline (2025)** — extent of initial surgery; replaces the 2015 version used by the textbooks.
- **≤ 2 cm, intrathyroidal, cN0:** lobectomy is the recommended operation.
- **> 2 to ≤ 4 cm, intrathyroidal, cN0:** lobectomy or total thyroidectomy, chosen by tumour features, contralateral nodules and patient preference. Counsel about ~20% chance of conversion or completion thyroidectomy.
- **> 4 cm, extrathyroidal extension, nodal or distant spread:** total thyroidectomy with resection of all concerning neck nodes.
- Change from 2015: lobectomy is now the **recommended** choice (not just an option) for low-risk unilateral cancer; final choice by shared decision-making.

PEARLS

- Most constant RLN landmark: entry behind the cricothyroid joint; most dangerous point: Berry's ligament.
- Beahrs triangle (carotid–inferior thyroid artery–RLN) finds the nerve in the lateral approach.
- Expect a non-recurrent nerve on the right with arteria lusoria — the inferior approach will miss it.
- IONM loss of signal on side one — stage side two.
- Unilateral palsy: wait 3–6 months with therapy, inject if aspirating, then medialise or reinnervate.
- Bilateral palsy: airway first, wait 9–12 months, then widen the posterior glottis.

CURRENT GUIDELINE

- **W1 · INMSG guideline 2018 Part I** — defines adverse electrophysiological events, chiefly **loss of signal (LOS)**, and builds them into operative strategy. **W2 · Gür et al. 2019** — applies the INMSG algorithm.
- **LOS (as applied in W2):** RLN amplitude < 100 µV after an initial (R1) amplitude > 100 µV, persisting **after the troubleshooting algorithm** has excluded technical causes.
- **LOS on the first side, nerve intact: staged thyroidectomy** is the logical option (function often recovers). Nerve divided: reassess the need for the contralateral side; proceed only with expert input and continuous vagal monitoring.
- **LOS on the second side:** complete the resection, manage expectantly.
- **Laryngoscopy:** routine pre-operative vocal-cord examination; post-operative laryngoscopy (on table or day 1) in all monitored patients (W2). In W2, LOS with intact nerve had PPV 86.4% and NPV 100% for cord palsy.

392. Semon's law and the Wagner and Grossman theory

ASKED 1* · 2-mark answer

Asked in: Paper III · Dec 2025 · Q6(b)

Q: What are Semon's law and Wagner's and Grossman theory? [2]

SOURCE

- Scott-Brown's Otorhinolaryngology (9e, Vol 2) — ch. 161 Paralysis of the larynx — §Pathophysiology and natural history; References — pp. 1726–1727, 1735
- Scott-Brown's Otorhinolaryngology (9e, Vol 2) — ch. 251 Complications of thyroid and parathyroid surgery — §Recurrent laryngeal nerve — p. 2736
- Cummings Otolaryngology (8e, Vol 1) — ch. 55 Neurologic Disorders of the Larynx — p. 862; ch. 52 Laryngeal and Pharyngeal Function — p. 824; ch. 56 Laryngeal Paralysis — p. 872; ch. 63 Laryngeal Reinnervation — p. 959; ch. 62 References — p. 956.e1
- Cummings Otolaryngology (8e, Vol 2) — ch. 120 Management of Thyroid Neoplasms — §Recurrent Laryngeal Nerve Injury — p. 1910

NOT COVERED IN SOURCE

Searched Cummings 8e V1–V3, Scott-Brown 9e, Glasscock 7e and Stell & Maran 6e full text for “Semon”, “Semon's law”, “Wagner”, “Grossman”, “Rosenbach”, “abductor ... vulnerable/susceptible/first”, “position of the paralysed fold”, “cadaveric”, “paramedian/intermediate position” and “cricothyroid ... adduct/paramedian”; checked the SB (pp. 2836–2874), GS and SM indexes and CUM ch. 52, 55, 56, 63 and SB ch. 161, 251. No book states Semon's law or the Wagner–Grossman theory; “Semon's law” appears only as the title of a cited paper (Blitzer et al., “Semon's law revisited: an electromyographic analysis of laryngeal synkinesis”, CUM ch. 62 ref. 21; SB ch. 161 ref. 2). Closely related book material on the position of the paralysed vocal fold follows, labelled as such.

Related book material: position of the paralysed vocal fold

- **Old belief invalidated:** for most of the last century fold position was thought to reveal the **site or type of lesion**; careful clinical and laboratory work has disproved this (SB).
- The variable position reflects differing **degrees and patterns of denervation and reinnervation** (SB).
- Terms **intermediate**, **paramedian** and **cadaveric** do not describe glottic configuration; distance from the midline is **not a reliable indicator of lesion site** (CUM).
- The **cricothyroid** does not appreciably change the spatial orientation of the fold or glottis (CUM).

491. Types of research studies — classification, each with an example; comparison of RCT with case-control study

ASKED 3* • 10-mark answer

Asked in: Paper I • Jun 2023 • Q6 • Paper I • Jun 2024 • Q1(a) • Paper I • Jun 2022 • Q1(b)

Q: What are the various types of Research studies? Explain each with example. [10]

Q: Classify various research study design. [3]

Q: What are various types of research studies? Compare RCT with Case-control study. [5]

SOURCE

- Cummings Otolaryngology (8e, Vol 1) — ch. 1 Outcomes Research — \$Introduction; \$Bias and Confounding; \$Control Groups; \$Fundamentals of Study Design; \$Other Study Designs — pp. 1–4; Table 1.1, p. 3
- Cummings Otolaryngology (8e, Vol 1) — ch. 2 Interpreting Medical Data — \$Habit 1: Check Quality Before Quantity; \$Habit 2; \$Habit 4 (qualitative research); \$Habit 6; \$Habit 7: View Science as a Cumulative Process; \$Surgical Satisfaction Swindle; \$Powerless Equalities; \$Understanding Sample Size — pp. 9–14, 17, 19–20, 22–25; Tables 2.2, 2.3, 2.5, 2.6, 2.8, 2.14
- Cummings Otolaryngology (8e, Vol 1) — ch. 10 Head and Neck Manifestations in the Immunocompromised Host — p. 178; ch. 12 Otolaryngology in Older Adults — p. 199
- Scott-Brown's Otorhinolaryngology (9e, Vol 1) — ch. 5 Age-related sensorineural hearing impairment — p. 65; ch. 45 Vestibular schwannoma presentation and natural history — p. 466
- Scott-Brown's Otorhinolaryngology (9e, Vol 2) — ch. 130 Acute otitis media — \$Epidemiology — p. 1392
- Stell & Maran's Head and Neck Surgery and Oncology (6e) — ch. 2 Epidemiology and prevention of head and neck cancer — \$Aetiology; \$Prevention — p. 18; ch. 47 Becoming a clinical trialist: How and why? — Boxes 47.1, 47.4, 47.6, 47.7 — pp. 861, 863–865

Basis of classification

- A study design is classified by **four questions** (CUM Table 2.2): how the data were collected; is it **experimental or observational**; is there a **control/comparison group**; what is the **direction of inquiry** (prospective, retrospective, cross-sectional).
- **Experimental**: conditions under direct control of the investigator — low potential for bias, reduced further by randomisation and masking.
- **Observational**: investigator is a bystander who only records, classifies and analyses the natural course of care — high potential for bias in selection, treatment assignment and measurement.
- **Controlled (analytic) vs uncontrolled (descriptive)**: a comparison group permits statements on efficacy, effectiveness and association; without one, only descriptive statements are possible (natural history, placebo effect).
- **Direction of inquiry**:
 - **prospective** — subjects identified before the outcome, future events recorded — measures **incidence** and causality;
 - **retrospective** — subjects identified after the outcome, past histories examined — measures prevalence (and causality if controlled);
 - **cross-sectional** — single time point — measures prevalence and **association**, not causality.

Flowchart 1. Classification of research study designs (CUM ch. 1-2)

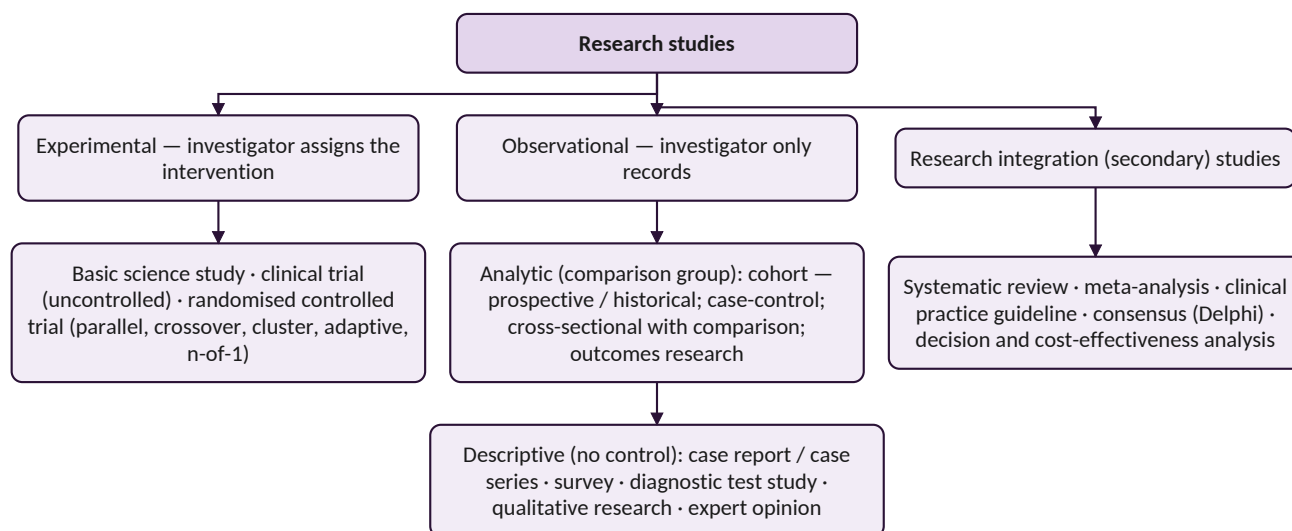


Table 1. Relationship of study type to study methodology

Study type	Data originally collected for	Control group	Direction of inquiry
Experimental			
Basic science study	Research	Yes or no	Prospective or cross-sectional
Clinical trial	Research	Yes or no	Prospective or cross-sectional
Randomised trial	Research	Yes	Prospective
Observational			
Cohort study	Clinical care or research	Yes or no	Prospective
Historical cohort (retrospective, non-concurrent)	Clinical care	Yes	Prospective
Outcomes research	Clinical care or research	Yes or no	Prospective
Case-control study	Clinical care	Yes	Retrospective
Case series	Clinical care	Yes or no	Retrospective or prospective
Survey study	Clinical care or research	Yes or no	Cross-sectional
Diagnostic test study	Clinical care or research	Yes or no	Cross-sectional

CUM ch. 2, Table 2.5, p. 12.

Experimental studies, with examples

- **Basic science study:** experimental, data collected for research; prospective or cross-sectional; control group optional. Example: animal experiments, where sample size is limited by cost, animal welfare and laboratory space — “why experiment on 200 chinchillas when only 100 are adequate?” (CUM).
- **Clinical trial** (uncontrolled or controlled): data collected for research by an a priori protocol (CUM).
 - **Example:** phase II window-of-opportunity trial of the PI3-kinase inhibitor AMG319 given for about 4 weeks between biopsy and surgery (SM Box 47.1);
 - **Example:** phase III ARTDECO trial failed to confirm the benefit of dose-escalated RT seen in phase II — practice should not change on early-phase data alone (SM Box 47.7).
- **Randomised controlled trial (RCT):** subjects randomly allocated to intervention or control and followed forward for the outcome.
 - only design that **proves causation**; randomisation balances known and unknown confounders; Level 1 if high quality, Level 2 if low quality (CUM Table 1.1);
 - **Example:** elective vs therapeutic neck dissection in node-negative early (T1/T2) oral cancer — about 500 patients randomised, primary end point overall survival; one death prevented for every **8** treated by elective neck dissection (SM Box 47.4);
 - **Example:** amoxicillin vs placebo in non-severe AOM — success 96% vs 92% ($P = .009$), NNT 25 (CUM);

- **Variants:** parallel-group, crossover, cluster-randomised and adaptive designs; superiority, equivalence or **non-inferiority** trials — the last needs a prespecified non-inferiority margin, a much larger sample, and both intention-to-treat and per-protocol analysis (CUM).
- **Efficacy vs effectiveness:** RCTs in controlled academic settings measure **efficacy**; outcomes research measures **effectiveness** in real-world, non-randomised populations (CUM).

Observational analytic studies, with examples

- **Cohort study:** patients identified at baseline before treatment or **exposure**, followed forward; measures incidence.
 - inclusion criteria less stringent, treatment assigned in routine care; challenge is a suitable control group; Level 2 with a control group, Level 4 without (CUM);
 - **Example:** COVIDSurg-HN — international prospective observational cohort of 1137 patients from 133 hospitals in 26 countries; primary outcome serious respiratory complications of COVID-19 within 30 days of surgery (SM Box 47.6);
 - **Example:** a US cohort study found the attributable fraction of oral cancer for tobacco and/or alcohol was 67% (SM);
 - **Inception cohort:** individuals identified at an early, uniform point in the course of the condition, or before it develops — best design for prognosis (CUM Table 2.14).
- **Historical (retrospective) cohort:** cohort assembled from past records (e.g. subjects with prior tonsillectomy and a comparison group with intact tonsils examined later for baldness); still measures incidence and can assess causality after adjustment for confounders (CUM Table 2.6).
- **Case-control study:** starts from the **outcome** — subjects with disease (cases) and without (controls) are compared for past exposure; opposite temporal direction; efficient for rare disease or long latency; Level 3 (CUM).
 - **Example:** cigarette smoking and oral cancer — $RR \approx 3.43$ (95% CI 2.37–4.94) from a pooled analysis of 12 case-control studies (SM);
 - **Example:** retrospective case-control study of 28 regressing sporadic vestibular schwannomas vs growing controls (SB);
 - **Example:** family-based case-control study in the Framingham Heart Study cohorts — hearing thresholds compared in spouse pairs vs sibling or parent–child pairs to estimate the genetic share of age-related hearing loss (SB).
- **Cross-sectional study:** exposure and outcome measured at one time point; measures **prevalence** and association; includes surveys, screening programmes and diagnostic test evaluation (CUM).
 - **Example:** a large cross-sectional study found facial lipoatrophy in 54% of adults on ART for >12 months (CUM);
 - **Example:** cross-sectional population surveys of otitis media — reported prevalence 0–11% in children (SB).
- **Outcomes research (clinical epidemiology):** study of treatment effectiveness from observational data, including large administrative databases and real-world data; needs special design and statistics (e.g. propensity score matching) to reduce bias (CUM).

Descriptive studies, with examples

- **Case report / case series:** least sophisticated; no control group, so no causal link between treatment and outcome; Level 4. Can show feasibility, technical detail and predictive factors. Example: only 4 of 35 endoscopic sinus surgery reports used a control group (CUM).
- **Best case series:** consecutive sample; full description of sample and interventions; all participants accounted for; adequate follow-up. A case series may be prospective or retrospective and should not be called a “retrospective review” (CUM).
- **Survey study:** cross-sectional questionnaire; valid only with a validated instrument and reported response rate. Example: “85% satisfied” surgical surveys — almost any survey achieves $\geq 80\%$ satisfaction (CUM).
- **Diagnostic test study:** cross-sectional; predictive value depends on prevalence — a middle-ear effusion test with PPV 90% in a referral population (prevalence 50%) gave PPV 50% in kindergarten screening (prevalence 10%) (CUM).
- **Qualitative research:** verbal data from observation or interviews, analysed by consensual, phenomenological, grounded-theory, case-study, photovoice or content-analysis methods (CUM).
- **Expert opinion:** used when even case series are unavailable — Level 5 (CUM).

Research integration (secondary) studies

- **Systematic review:** explicit, reproducible criteria to locate, appraise and synthesise articles with minimal bias; **meta-analysis** adds statistical pooling with heterogeneity assessment. Example: meta-analysis of 10 studies — bidi smoking and oral cancer OR 4.0 (SM).
- **Clinical practice guidelines** build on systematic reviews; **consensus statements / Delphi method** (8–20 experts) when evidence is weak (CUM).
- **Systematic review reporting:** flow diagram of articles through identification, screening, eligibility and inclusion; forest plots, funnel plots (publication bias) and network displays (CUM).
- **Real-world data (RWD) studies:** electronic health records, claims databases, population health surveys and registries — useful for drug safety and effectiveness and to create case-control studies, but prone to “garbage in, garbage out” (CUM).
- **Other designs:** decision analysis, cost-identification and cost-effectiveness studies, secondary analysis of administrative databases, machine-learning prognostic analyses (CUM).

Table 2. Same question, different designs — “Does tonsillectomy cause baldness?” (in order of increasing ability to prove causation)

Design	Execution	What it can show
Retrospective case series	Bald subjects asked about prior tonsillectomy	Prevalence only; no association or causality
Prospective case series	Tonsillectomy patients examined later for baldness	Incidence only; no association or causality
Cross-sectional	Baldness and tonsils examined at the same time	Prevalence and association; no causality
Case-control	Bald and non-bald subjects asked about prior tonsillectomy	Association; limited causal inference
Historical cohort	Prior tonsillectomy vs intact tonsils, examined later	Incidence, association; causality if confounders adjusted
Prospective cohort	Non-bald subjects with and without tonsillectomy followed	Incidence, association; causality if adjusted
RCT	Non-bald subjects randomised to tonsillectomy or observation	Causality despite baseline confounders

CUM ch. 2, Table 2.6, p. 12.

Comparison: RCT vs case-control study

Table 3. Randomised controlled trial versus case-control study

Feature	RCT	Case-control study
Type	Experimental, controlled	Observational, controlled (analytic)
Starting point	Subjects free of outcome, before exposure (intervention)	Subjects already with (cases) and without (controls) the outcome
Direction	Prospective — exposure → outcome	Retrospective — outcome → past exposure
Exposure allocation	Random assignment by investigator	Natural; clinician/patient choice; recorded from past
Data	Collected for research by a priori protocol	Clinical care records, recall
Control of bias	Randomisation balances known and unknown confounders; masking	Must rely on retrospective data — selection, recall and confounding bias
Measure of effect	Incidence; relative risk, rate difference, NNT	Prevalence and association; odds ratio
Causation	Only design that proves causation	Temporal sequence unclear — no firm causal judgement
Rare / long-latency disease	Impractical — huge numbers, decades	Efficient — ideal design
Cost	Expensive and complex	Cheaper than a cohort study
Selection criteria, generalisability	Restrictive; generalisability potentially low	Broad (patients seen); potentially high
Level of evidence	1 (high quality) or 2	3 (CUM ch. 1); 4 for treatment benefit (OCEBM, CUM ch. 2)

CUM ch. 1, Table 1.1, pp. 3–4; ch. 2, Tables 2.3, 2.5, 2.8, pp. 10–14.

- **Key line:** the RCT is the only design that can prove a **cause–effect** relationship; the case-control study is the quickest analytic route to an **association** when the outcome is rare or delayed (e.g. asbestos and laryngeal cancer, which a prospective study would need decades and huge numbers to answer) (CUM).
- **Odds ratio vs relative risk:** a case-control study reports OR (bald subjects 1.6 times more likely to have had tonsillectomy); a prospective study reports RR; the two are similar only when the event is rare (CUM).

PEARLS

- Classify by 4 questions: **data source · experimental/observational · control group · direction.**
- Prospective → incidence; retrospective and cross-sectional → prevalence.
- Only controlled studies measure **association**; only controlled studies with a time-span component assess **causality**.
- Case series and case reports are purely **descriptive** — no control group.
- RCT = causation, OR/RR; case-control = rare disease, OR, quick and cheap but recall and selection bias.
- Highest evidence = systematic review / meta-analysis of RCTs.

492. The terms “exposure” and “outcome variable” in a study

ASKED 1* · 3-mark answer

Asked in: Paper I · Jun 2024 · Q1(b)

Q: Describe the terms “exposure” and “outcome variable” in a study. [3]

SOURCE

- Cummings Otolaryngology (8e, Vol 1) — ch. 1 Outcomes Research — \$Key Terms and Concepts; \$Bias and Confounding; \$Cohort Study; \$Case-Control Study — pp. 2, 4
- Cummings Otolaryngology (8e, Vol 1) — ch. 2 Interpreting Medical Data — \$Habit 1; \$Habit 2: Describe Before You Analyze; \$Habit 4 — pp. 11, 13–14, 16; Tables 2.4, 2.8, 2.10

Exposure

- The **baseline factor** whose effect is studied — a treatment, a pathogen or a risk factor (e.g. carcinogen) that a subject has or receives **before** the outcome (CUM).
- Equivalent to the **predictor / independent variable**; the analysis is planned around the chosen independent and dependent variables (CUM).
- In a **cohort study or RCT**, subjects are identified before exposure and followed forward (e.g. tonsillectomy vs intact tonsils).
- In a **case-control study**, past exposure is compared between cases and controls (e.g. asbestos exposure in patients with and without laryngeal cancer).

Outcome variable

- The **end result** measured after exposure — the dependent variable (e.g. survival, recurrence, baldness, hearing level, quality-of-life score) (CUM).
- In risk-factor research the **disease itself is the outcome** (CUM).
- Its **measurement scale** — dichotomous, nominal, ordinal, numeric or censored — decides the summary statistic and test (e.g. dichotomous → OR/RR; censored → survival analysis).

Linked concepts

- **Information bias**: systematic differences in how exposures or outcomes are measured — reduced by blinded and prospective data collection.
- **Confounder**: a variable associated with both exposure and outcome (smoking for stained teeth and laryngeal cancer) that distorts the apparent effect.

PEARLS

- Exposure → **independent/predictor**; outcome → **dependent** variable.
- Cohort/RCT: exposure → outcome; case-control: outcome → past exposure.
- Information bias = errors in measuring exposure or outcome; confounder = linked to both.

493. Randomised controlled trial — description and flowchart

ASKED 1* · 10-mark answer

Asked in: Paper I · Dec 2020 · Q2

Q: Describe Randomized Controlled Trial. Give a flow chart depicting a Randomized Controlled Trial. [10]

SOURCE

- Cummings Otolaryngology (8e, Vol 1) — ch. 1 Outcomes Research — \$Introduction; \$Bias and Confounding; \$Efficacy; \$Effectiveness; \$Randomized Trial — pp. 1–3; Table 1.1, p. 3
- Cummings Otolaryngology (8e, Vol 1) — ch. 2 Interpreting Medical Data — \$Habit 1; \$Habit 4; \$Habit 5; \$Habit 6; \$Habit 7; \$Adverse Event Optimism; \$Powerless Equalities; \$Understanding Sample Size — pp. 9–12, 15, 17, 19–20, 24–25; Tables 2.2–2.6, 2.14
- Cummings Otolaryngology (8e, Vol 2) — ch. 103 Malignant Tumors of the Larynx — \$Nonsurgical Treatment of Advanced Laryngeal Cancer (Organ Preservation) — pp. 1590–1591; Figs. 103.10–103.11, p. 1590
- Stell & Maran's Head and Neck Surgery and Oncology (6e) — ch. 47 Becoming a clinical trialist: How and why? — \$Challenges in surgical trial delivery; \$Characteristics of successful surgical trials; \$Role of the surgeon; Boxes 47.1–47.7 — pp. 859–865; Fig. 47.2, p. 863

Definition

- An **experimental, prospective, controlled** study in which subjects free of the outcome are **randomly allocated** by the investigator to an intervention or a control (placebo / standard) group and followed forward to compare outcomes (CUM Tables 2.5–2.6).
- Only design that can **prove causation** — the controlled, experimental nature links treatment to outcome; random allocation distributes baseline variables without bias and minimises confounding (CUM).
- **High-quality RCT** (well-defined inclusion criteria, double-blinded treatment and assessment, low losses to follow-up, high statistical power) = **Level 1**; lower-quality RCT = Level 2; systematic review of RCTs = Level 1 (CUM Tables 1.1, 2.14).
- **Efficacy** — whether an intervention, in a controlled environment, does better than placebo; RCTs usually test efficacy. **Effectiveness** — whether the benefit holds in usual clinical care (CUM).

Essential components

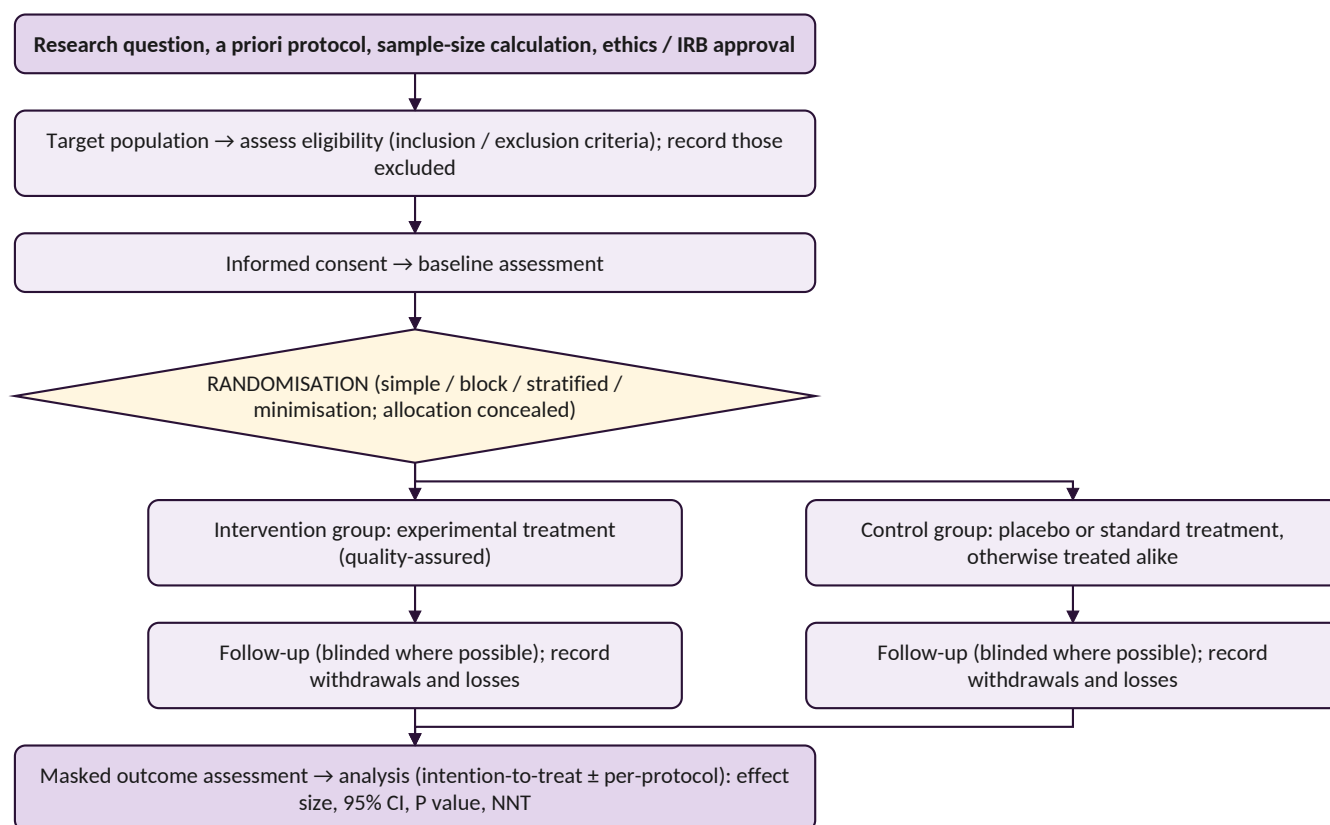
- **Control group** — separates a true treatment effect from other causes of change:
 - chance, natural history, regression to the mean;
 - placebo effect (needs a placebo control);
 - halo and Hawthorne effects (control group treated similarly) (CUM Table 2.4).
- **Randomisation** — balances **known and unknown** prognostic factors (severity, comorbidity); reduces allocation and selection bias; adds validity to probability theory.
 - methods: **simple, block, adaptive** (including minimisation) and response-adaptive randomisation (CUM);
 - **stratification** before randomisation by key prognostic factors — RTOG 91-11 stratified by site, T and N stage (Fig. 1);
 - post hoc **propensity-score matching** in non-randomised studies adjusts only for known, measured factors — randomisation also balances unknown ones (CUM).
- **Allocation concealment** — randomised allocation hidden from patients and investigators; failure causes performance, detection, expectation and attrition bias (CUM).
- **Blinding (masking)** — **single**: participants do not know their group; **double**: staff who collect and/or interpret data also do not know (CUM).
 - when sham treatment is impractical (e.g. hyperbaric oxygen), rigour comes from **blinded end-point assessment** by an external panel (SM, HOPON).
- **Equipoise** (tolerated clinical uncertainty) — in surgical trials it must be established for the individual, not only amongst a cohort of surgeons (SM).

- **Sample size and power** calculated before the study (see below).

Steps in conducting an RCT

- **1. Research question** with a conceptual biological basis and a clear, measurable primary end point (SM).
- **2. A priori protocol** — hypothesis, selection criteria, interventions, primary and supporting secondary end points, sample size, analysis plan (CUM Table 2.2; SM PARSPORT).
- **3. Ethics committee / institutional review board approval** with balanced trial information for patients (SM).
- **4. Eligibility, recruitment and informed consent**; a run-in period may be used (HOPON: 4-week run-in for eligibility, information and consent) (SM Fig. 2).
- **5. Baseline assessment** of every participant.
- **6. Randomisation** (e.g. 1:1), stratified and concealed.
- **7. Intervention vs control** delivered under **quality assurance** — e.g. credentialling of radiotherapy plans (PARSPORT); a pre-set number of procedures or a rolling negative-margin rate for surgical centres (SM).
- **8. Follow-up** at fixed intervals; record withdrawals and losses.
- **9. Outcome assessment**, masked where possible.
- **10. Interim analysis** — may reveal false assumptions (HOPON: expected ORN $\approx 30\%$, observed 6.4% vs 5.7%) (SM).
- **11. Analysis** — **intention-to-treat** (all randomised subjects analysed in the group assigned) plus per-protocol for non-inferiority trials; report P value, effect size, 95% CI, NNT and fragility index (CUM, SM).
- **12. Reporting and implementation** — PARSPORT result was rolled out from 8 centres to 35 cancer networks (SM).

Flowchart 1. Conduct of a randomised controlled trial (parallel two-arm design)



LARYNGEAL PRESERVATION STUDY

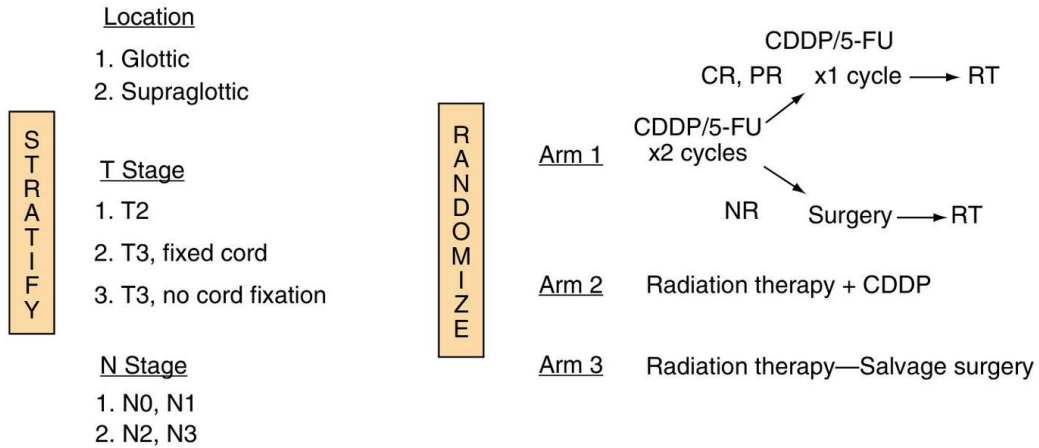


Fig. 103.11 Schematic of the study protocol of the Radiation Therapy Oncology Group and the Head and Neck Intergroup Laryngeal Cancer Study (RTOG 91-11) (2003). 5-FU, 5-Fluorouracil; CDDP, cisplatin; CR, complete response; NR, no response; PR, partial response; RT, radiation therapy.

Cummings (8e, Vol 2), ch. 103, Fig. 103.11, p. 1590.

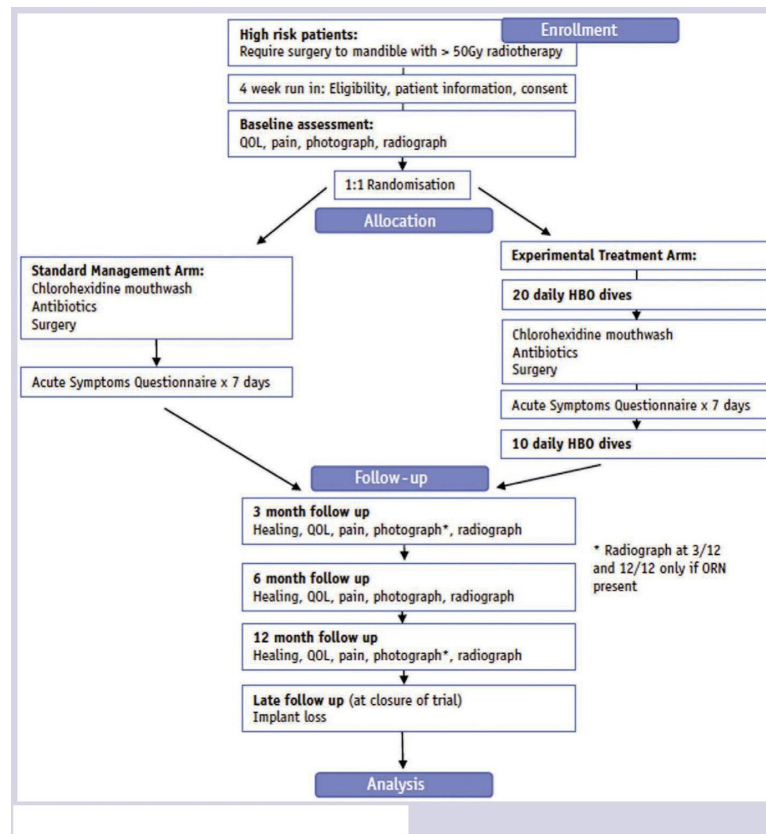


Figure 47.2 Trial schematic for HOPON trial.

Stell & Maran's (6e), ch. 47, Fig. 47.2, p. 863.

Sample size

- Inputs: (1) **minimal clinically important difference**; (2) confidence that a detected difference is not chance — usually **95%** (type I error 5%); (3) **power** — usually **80–90%** (type II error 10–20%); (4) variance for numeric outcomes (CUM).
- Sample size rises when the difference is small, the variance high and the error tolerance low; a two-tailed test needs more subjects and should be used unless a one-tailed test was chosen a priori (CUM).
- Detecting a 10% improvement in tumour control typically needs >300 patients and many centres (SM ARTDECO).

Analysis and reporting of results

- **Intention-to-treat (ITT):** every randomised participant analysed in the group originally assigned, regardless of treatment received — integral to RCT methodology to avoid bias (SM).
- **Per-protocol:** only subjects who completed the intervention; non-inferiority trials must report both, since ITT alone can make an inferior treatment look non-inferior when adherence is poor (CUM).
- **P value** = probability of type I error ($P < .05$ significant); a “negative” trial is judged by its **power**, not its P value (CUM).
- **Effect size** with **95% CI** — e.g. rate difference 30% (95% CI 10–50%) or relative risk 1.6 (95% CI 1.1–2.3); scrutinise the lower CI limit of a “significant” result and the upper limit of a “non-significant” one (CUM).
- **Number needed to treat** = $100 / \text{rate difference (\%)}$ — 4% difference in AOM gives NNT 25; a tiny P value from >1000 episodes may reflect a trivial clinical effect (CUM).
- **Fragility index** — minimum number of patients who would need to switch groups (intervention vs control) for the result to lose statistical significance; only 2–5 in many surgical trials (CUM).
- **Adverse events:** trials are powered for benefit, not harm — absence of evidence is not evidence of absence (CUM).

Features of successful trials

- A **conceptual biological basis** for the hypothesis, not just a new technology or individual skill (SM).
- A **common presentation** so the sample is achievable, low extra cost, sustainable follow-up and a powerful primary objective such as overall survival (SM Box 47.4).
- Robust, accepted primary end point backed by supporting secondary end points and pre-trial modelling for the sample size (SM PARSPORT).
- **National collaborative trial groups**, quality assurance of every centre and **public and patient involvement** in design and conduct (SM).
- Negative phase III trials are as important as positive ones — they chart future progress (SM ARTDECO).

Types of RCT

Table 1. Designs of randomised trials

Design	Feature
Parallel-group	Two or more concurrent (independent) groups — the traditional design, with crossover
Adaptive, cluster-randomised, complex randomisation	Newer, more diverse designs — bias must be assessed carefully
Superiority / equivalence / non-inferiority	Non-inferiority needs a prespecified margin (e.g. new drug ≥80% as effective) and a larger sample
Placebo-controlled, double-blind	Easiest for drugs; sham surgery has methodological and ethical problems
n-of-1 trials	Systematic review of n-of-1 trials is Level 1 evidence for treatment benefit
Phase II window-of-opportunity	Drug given between biopsy and surgery; tissue sampled either side (AMG319)
Phase III confirmatory	Large multicentre trial needed before practice changes (PARSPORT, ARTDECO)

CUM ch. 2, pp. 12, 20, 24; SM ch. 47, pp. 860–865.

Bias in RCTs

Table 2. Bias that can still affect an RCT

Bias	Cause	Prevention
Allocation (susceptibility)	Less severe or better-prognosis subjects allotted to treatment	Randomisation; comorbidity analysis
Performance	Systematic differences between groups beyond the primary intervention	Full allocation concealment; control group treated similarly
Detection (ascertainment)	Outcomes measured differently, favouring the treated group	Masked (blinded) outcome assessment
Expectation	Participants able to discern their study group	Concealment; placebo control
Attrition	Unequal dropouts or loss to follow-up	Account for all randomised subjects; intention-to-treat

CUM ch. 2, Table 2.4, p. 11; p. 12; SM ch. 47, p. 859.

Advantages and limitations

Table 3. RCT — advantages and limitations

Advantages	Limitations
Only design that proves causation	Expensive and complex; phase III trials take years
Unbiased distribution of known and unknown confounders	Restrictive selection — generalisability potentially low
High investigator control; objective, masked end points	Targets efficacy more than effectiveness
Analysis by comparison of groups (observational studies need multivariate regression)	Underpowered for adverse events; harms under-reported
Highest level of evidence (with meta-analysis)	Surgical trials: consent to randomisation, learning curve, blinding, quality assurance difficult

CUM ch. 1, Table 1.1, p. 3; ch. 2, Table 2.3, p. 10, p. 24; SM ch. 47, pp. 859–860.

- **Internal vs external validity:** the Paradise trial of prompt vs delayed tympanostomy tubes was internally valid but excluded children with syndromes or developmental delay and had few bilateral continuous effusions (18%), so it is not generalisable to typical tube candidates (CUM).
- **Surgical trial challenges (SM):**
 - consent to randomise to a procedure is harder than to a drug;
 - variation in delivery and the learning curve confound results;
 - blinding and sham surgery are difficult;
 - with intention-to-treat, complications in patients who never had surgery may sit in the non-surgical arm;
 - new procedures need no regulatory approval — hence the need for trials.

Examples from head and neck practice

- **VA Laryngeal Cancer Study (1991):** 332 stage III–IV laryngeal SCC randomised to induction chemotherapy + RT vs laryngectomy + RT; larynx preserved in 64%, 2-year survival 68% in both arms (CUM).
- **RTOG 91-11:** 518 patients, three arms; larynx preservation 84% (concurrent CRT) vs 72% and 67%; 5-year overall survival similar, 54–58% (CUM, Fig. 1).
- **Elective vs therapeutic neck dissection, NO early oral cancer:** ~500 patients; primary end point overall survival; NNT 8 to prevent one death (SM).
- **PARSPORT:** phase III RCT — parotid-sparing IMRT reduced xerostomia and became the global standard (SM).

PEARLS

- RCT = experimental + prospective + **random allocation** + control group.
- Randomisation balances **unknown** confounders — propensity scores cannot.
- Concealment prevents selection bias; blinding prevents performance and detection bias.
- Analyse by **intention-to-treat**; report effect size with 95% CI, not P alone.
- Power 80–90%, α 5%, MCID and variance set the sample size.
- High-quality RCT = Level 1; meta-analysis of RCTs is the top of the hierarchy.

494. Components of the research protocol of a randomised controlled trial

ASKED 1* · 4-mark answer

Asked in: Paper I · Dec 2022 · Q7(c)

Q: Discuss the components of research protocol of a randomised control trial of an epidemiological study. [4]

SOURCE

- Cummings Otolaryngology (8e, Vol 1) — ch. 1 Outcomes Research — \$Bias and Confounding; \$Psychometric Validation — pp. 2, 4–5
- Cummings Otolaryngology (8e, Vol 1) — ch. 2 Interpreting Medical Data — \$Habit 1; \$Habit 4; \$Habit 5; \$Habit 6: Seek the Sample Source; \$Adverse Event Optimism; \$Post Hoc P Values; \$Powerless Equalities; \$Understanding Sample Size — pp. 10–12, 15, 17–18, 20, 24–25; Tables 2.2, 2.4, 2.9, 2.12, 2.15
- Stell & Maran's Head and Neck Surgery and Oncology (6e) — ch. 47 Becoming a clinical trialist: How and why? — \$Role of the surgeon in clinical trial delivery; Boxes 47.2, 47.5 — pp. 860, 862–864; Fig. 47.2, p. 863

- A protocol is written **a priori**; data collected to it are of research quality, and hypotheses framed after seeing the data make P values invalid (CUM).

Components

- **1. Title, background and rationale** — the clinical problem and a conceptual biological basis for the hypothesis (SM).
- **2. Research question and hypothesis** — focused PICO question (patient, intervention, comparator, outcome); testable hypothesis inverted to a null hypothesis, both fixed in advance (CUM).
- **3. Objectives and end points** — one robust, accepted **primary end point** (e.g. patient-reported xerostomia in PARSPORT) with supporting **secondary end points**; each rigorously defined (HOPON had to define ORN and “minor bony spicules <20 mm²”) (SM).
- **4. Design** — parallel or other design; superiority or non-inferiority (prespecified margin); allocation ratio (e.g. 1:1) (CUM, SM).
- **5. Study population** — target and accessible population, sampling method, **inclusion and exclusion criteria** (CUM Table 2.12).
- **6. Sample size** — minimal clinically important difference, α (usually 5%), power (80–90%), variance for numeric data (CUM).
- **7. Recruitment and consent** — patient information, informed consent, run-in period, baseline assessment (SM Fig. 47.2).
- **8. Randomisation** — method (simple, block, adaptive/minimisation, response-adaptive) and **allocation concealment** from patients and investigators (CUM).
- **9. Blinding** — single or double; blinded end-point review when sham treatment is impractical (CUM, SM).
- **10. Interventions** — exact experimental and control treatments with **quality assurance** and centre credentialing (SM).
- **11. Follow-up schedule and data collection** — fixed visits and measures (HOPON: 3, 6 and 12 months; healing, QOL, pain, photographs, radiographs) (SM).
- **12. Measuring instruments** — validated scales (reliability, validity, responsiveness, low burden) for “soft” outcomes such as QOL; accurate, protocol-driven data collection is the solution to bias (CUM).
- **13. Safety** — how adverse events are collected and reported (CUM).
- **14. Statistical analysis plan** — tests chosen beforehand, intention-to-treat $\pm$ per-protocol, interim analysis, effect size with 95% CI (CUM, SM).
- **15. Ethics** — balanced trial information approved by an **ethics committee / institutional review board** (SM).
- **16. Funding and management** — costs (including excess treatment costs), trial group, public and patient involvement, reporting (SM).

PEARLS

- Protocol = **a priori** plan: question → end points → population → sample size → randomisation → blinding → interventions → follow-up → analysis → ethics.
- Primary end point and analysis must be fixed before the data are seen.
- Ethics approval, consent and quality assurance are part of the protocol, not afterthoughts.

495. Pilot study

ASKED 1* · 3-mark answer

Asked in: Paper I · Dec 2024 · Q6(b)

Q: Pilot study. [3]

SOURCE

- Cummings Otolaryngology (8e, Vol 1) — ch. 2 Interpreting Medical Data — \$Habit 4 (Bayesian approach); \$Understanding Sample Size — pp. 17, 25
- Scott-Brown's Otorhinolaryngology (9e, Vol 2) — ch. 225 Obstructive sleep apnoea and snoring — p. 2468
- Stell & Maran's Head and Neck Surgery and Oncology (6e) — ch. 9 Prehabilitation in head and neck cancer — p. 163; ch. 45 The surgical innovation continuum — p. 835; ch. 47 Becoming a clinical trialist: How and why? — \$Challenges in surgical trial delivery; \$Role of the surgeon; Boxes 47.5, 47.7 — pp. 859–860, 864–865
- W1 · CONSORT / PAFS consensus group — CONSORT 2010 statement: extension to randomised pilot and feasibility trials (Eldridge SM et al., BMJ 355:i5239) — 2016

NOT COVERED IN SOURCE

Not found as a defined topic in the four books. Searched full text of CUM Vols 1–3, SB, GS and SM for “pilot study/studies/trial/data”, “feasibility study/trial”, “preliminary data/study”, “run-in”, “interim analysis” and “early-phase”; the book indexes (SB pp. 2836–2874, GS pp. 1114–1147, SM pp. 956–977 — no “pilot” entry); and the research chapters (CUM ch. 1 Outcomes Research, ch. 2 Interpreting Medical Data; SM ch. 45, 47). The books use pilot studies but give no formal definition, aims list or design. Closely related book material follows.

What the books say about pilot studies (related material)

- A **small preliminary study** done before the main trial — e.g. a pilot of exercise prehabilitation with only **20 participants**, “therefore **not powered** to identify statistically significant findings” (SM).
- Supplies planning data** for the main study: an estimate of the **SD (variance)** for the sample-size calculation (CUM), and prior efficacy (e.g. animal or pilot data suggesting 50% efficacy) for Bayesian analysis of an RCT (CUM).
- Tests feasibility** — preclinical work on mannequins, cadavers and animals led to an IRB-approved prospective human **feasibility trial** of TORS, which established surgical equipoise for later trials (SM).
- Prevents failed main trials:** early-stage preparatory work is needed so that pragmatic, deliverable studies are designed; in HOPON the methodological difficulties were underestimated at the proposal stage and the assumed 30% ORN incidence proved wrong (SM).
- Limitations:**
 - small, often without a standardised comparison — e.g. most OSA tongue-base procedures are reported only as pilot studies (SB);
 - results do not transfer out of the “piloted setting” automatically (SM);
 - practice should not change on early-phase data — the ARTDECO phase III trial failed to confirm phase II benefit (SM).

PEARLS

- Pilot = small, underpowered, preparatory — tests feasibility and gives the SD/effect estimates for sample size.
- Preparatory evidence only — never practice-changing on its own.
- Books give no formal definition — main trial planning uses its SD and feasibility data.

CURRENT GUIDELINE

- **W1 · CONSORT extension for pilot and feasibility trials (2016).**
- **Feasibility study** (umbrella term): asks whether a future definitive RCT can be done, should be done, and how. **Pilot study:** a subset — the future trial, or part of it, run on a smaller scale.
- **Aim:** feasibility, not efficacy; each objective has a matching assessment (recruitment, consent, retention, adherence, outcome measurement).
- **Formal hypothesis testing for effectiveness is not recommended;** give estimates with 95% CI. Sample size is justified by feasibility objectives.
- Report **pre-specified progression criteria** (often “traffic-light”) for deciding whether and how to proceed to the main trial.

496. Case-control study — what it is, with a suitable example

ASKED 3* · 4-mark answer

Asked in: Paper I · Jun 2021 · Q2(a) · Paper I · Dec 2023 · Q10(a) · Paper I · Jun 2025 · Q10(b)

Q: What is a case control study? [4]

Q: What is a case control study? [4]

Q: Describe case control study with a suitable example. [3]

SOURCE

- Cummings Otolaryngology (8e, Vol 1) — ch. 1 Outcomes Research — §Case-Control Study — pp. 3–4; Table 1.1, p. 3
- Cummings Otolaryngology (8e, Vol 1) — ch. 2 Interpreting Medical Data — §Habit 1; §Habit 2; §Habit 4; §Habit 7 — pp. 10–14, 16, 19; Tables 2.2, 2.5, 2.6, 2.8, 2.11
- Scott-Brown's Otorhinolaryngology (9e, Vol 1) — ch. 5 Age-related sensorineural hearing impairment — p. 65; ch. 45 Vestibular schwannoma presentation and natural history — p. 466
- Stell & Maran's Head and Neck Surgery and Oncology (6e) — ch. 2 Epidemiology and prevention of head and neck cancer — §Aetiology; §Prevention — p. 18

Definition

- An **observational, controlled (analytic), retrospective** study that starts from the **outcome**: subjects **with** the disease (**cases**) and subjects **without** it (**controls**) are compared for **past exposure** to a suspected risk factor (CUM).
- The disease is the “outcome”; the direction of inquiry is opposite to cohort studies and RCTs, which start before exposure and follow forward (CUM).
- Used by epidemiologists to identify **risk factors**; most valuable when prospective study is not feasible — **rare disease** or a **long interval** between exposure and outcome (CUM).
- Data usually come from clinical care records or questioning (CUM Table 2.5); real-world databases and registries can also be used to build case-control studies (CUM).

Design

Flowchart 1. Design of a case-control study

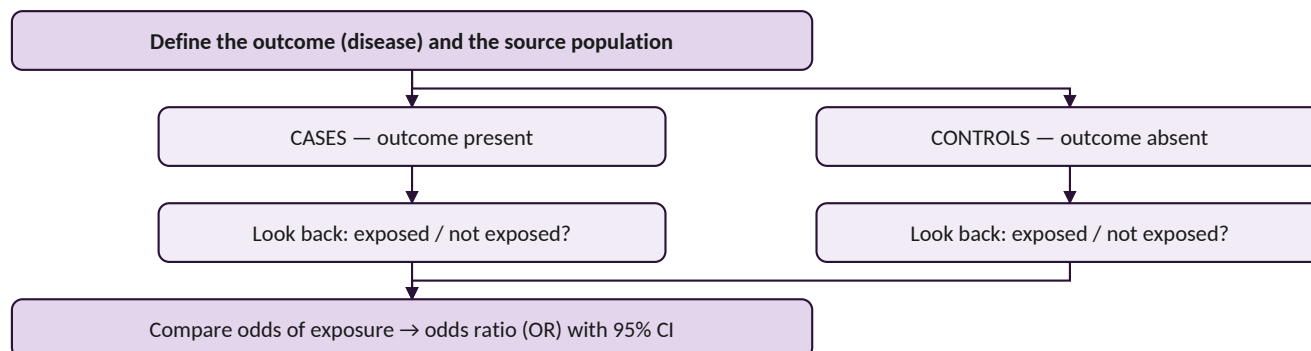


Table 1. The 2 × 2 table of a case-control study

	Cases (disease +)	Controls (disease -)
Exposed (risk factor present)	Exposed cases	Exposed controls
Not exposed	Unexposed cases	Unexposed controls
Comparison	Odds of exposure in cases	Odds of exposure in controls
Effect measure	Odds ratio = ratio of the two odds	OR = 1: no association

CUM ch. 2, Table 2.8, p. 13; p. 14.

- **Measures:** prevalence of the outcome and its **association** with the exposure; limited ability to assess causality, as the temporal relationship is not observed (CUM).
- **Effect measure: odds ratio** — e.g. OR 1.6 means bald subjects were 1.6 times more likely than non-bald controls to have had tonsillectomy (CUM).
- **Matched controls** (by age and sex) form related samples — analyse with McNemar test, not chi-squared (CUM Table 2.11).
- **Level of evidence:** 3 (CUM Table 1.1); 4 for treatment benefit in the OCEBM table (CUM Table 2.14).

Examples

- **Asbestos and laryngeal cancer:** a prospective study would need huge numbers and decades; identifying patients with and without laryngeal cancer and comparing their asbestos exposure answers the question faster (CUM).
- **Smoking and oral cancer:** pooled analysis of **12 case-control studies** — RR ≈ 3.43 (95% CI 2.37–4.94); involuntary smoking, 5 case-control studies — RR 1.51 (95% CI 1.20–1.91) (SM).
- **Smoking cessation:** case-control data from ex-, current and never smokers show oral cancer risk falls to never-smoker level after ≥20 years (SM).
- **Vestibular schwannoma:** 28 spontaneously regressing tumours (cases) vs growing tumours (controls) — regressing tumours were larger and further from the fundus (SB).
- **Family-based:** Framingham cohorts — hearing thresholds in spouse vs sibling or parent–child pairs to estimate the genetic share of age-related hearing loss (SB).

PEARLS

- Start from **outcome**, look back for **exposure**.
- Best for **rare diseases / long latency**; quick and cheap.
- Reports **odds ratio**; association, not proof of causation.

497. Strengths and weaknesses of a case-control study

ASKED 2* · 6-mark answer

Asked in: Paper I · Jun 2021 · Q2(b) · Paper I · Dec 2023 · Q10(b)

Q: Discuss the strength and weakness of a case control study. [6]

Q: Discuss the strength and weakness of a case control study. [6]

SOURCE

- Cummings Otolaryngology (8e, Vol 1) — ch. 1 Outcomes Research — §Bias and Confounding; §Fundamentals of Study Design; §Case-Control Study — pp. 2–4; Table 1.1, p. 3
- Cummings Otolaryngology (8e, Vol 1) — ch. 2 Interpreting Medical Data — §Habit 1; §Habit 2; §Habit 4; §Habit 6; §Habit 7; §Multivariate (Regression) Procedures — pp. 9–14, 16, 18–20, 22; Tables 2.2, 2.4, 2.5, 2.6, 2.8, 2.11, 2.12, 2.14
- Scott-Brown's Otorhinolaryngology (9e, Vol 1) — ch. 5 Age-related sensorineural hearing impairment — p. 65; ch. 45 Vestibular schwannoma presentation and natural history — p. 466
- Stell & Maran's Head and Neck Surgery and Oncology (6e) — ch. 2 Epidemiology and prevention of head and neck cancer — §Aetiology; §Prevention — p. 18

The design in one line

- An **observational, controlled, retrospective** study: subjects with the disease (**cases**) and without it (**controls**) are compared for **past exposure**; the disease is the outcome and the inquiry runs backwards in time (CUM).

Strengths

- **Efficient for rare diseases** — cases are gathered directly instead of waiting for them to arise in a huge cohort (CUM Table 1.1).
- **Efficient for delayed outcomes / long latency** — asbestos and laryngeal cancer would need a tremendous number of patients and decades of prospective observation; comparing exposure in patients with and without laryngeal cancer answers it far sooner (CUM).
- **Cheaper than a cohort study**, and much cheaper and simpler than an RCT (CUM Table 1.1).
- **Uses existing data** — records from routine clinical care (CUM Table 2.5); large real-world databases and registries can be used to create case-control studies of association (CUM).
- **Has a control group** — so it permits **analytic** statements about association, unlike a case series, which is purely descriptive (CUM Table 2.2).
- **Quantifies association** with an **odds ratio** and its 95% CI (CUM Table 2.8).
- **Answers questions that lack intervention studies** — e.g. no intervention studies of smoking cessation exist, but case-control data from ex-, current and never smokers show oral cancer risk returns to never-smoker level after ≥20 years (SM).
- **Can show dose-response** — case-control and cohort studies both show strong dose-response for alcohol and oral cancer (SM).
- **Results can be pooled** — pooled analysis of 12 case-control studies: smoking and oral cancer RR ≈ 3.43 (95% CI 2.37–4.94); meta-analysis of 5 case-control studies: involuntary smoking RR 1.51 (SM).
- **Flexible variants** — family-based case-control designs within cohorts (Framingham hearing study) and studies of natural history (regressing vs growing vestibular schwannomas) (SB).
- **Higher evidence than case series** — Level 3 vs Level 4 (CUM Table 1.1).

Weaknesses

- **Must rely on retrospective data** — quality limited by the consistency, accuracy, availability and completeness of source records (CUM Tables 1.1, 2.2).
- **Recall bias** — inaccuracies of retrospective assessment of exposure; reduced only by prospective data collection (CUM).
- **Observer / information bias** — exposure measured differently in cases and controls; reduced by blinded data collection (CUM).

- **Selection bias** — systematic differences between the groups compared, or between the sample and the target population (e.g. clinic or tertiary-care samples, volunteers) (CUM Table 2.12).
- **Confounding** — a variable linked to both exposure and outcome (e.g. smoking linking stained teeth with laryngeal cancer); multivariate analysis or propensity scores adjust only for factors that were measured (CUM).
- **Directionality unclear** — the temporal relationship between exposure and outcome is not observed, so **no causal judgement** is possible; the asbestos–laryngeal cancer link remains controversial (CUM).
- **Measures prevalence, not incidence** — association only, with limited ability to assess causality (CUM Table 2.6); **relative risk** needs a prospective study (CUM Table 2.8).
- **Odds ratio approximates relative risk only when the event is rare**; for common events they diverge widely (CUM).
- **Database problems** when built from real-world data — misclassification bias, dichotomous-variable bias, lead-time bias; “garbage in, garbage out” (CUM).
- **Matched designs need paired analysis** (McNemar), never independent-sample tests (CUM Table 2.11).
- **Missing data** may bias results if only complete cases are analysed (CUM).
- **Lower level of evidence** than cohort studies and RCTs (CUM).

Table 1. Strengths and weaknesses of a case-control study at a glance

Strengths	Weaknesses
Rare disease, long latency	Retrospective data — recall and information bias
Cheaper and quicker than cohort or RCT	Selection bias in choosing cases and controls
Existing records and databases usable	Confounding; unmeasured factors cannot be adjusted
Control group — association, odds ratio	Temporal sequence unclear — no proof of causation
Answers questions lacking intervention studies (smoking cessation)	No incidence or relative risk; OR $\approx$ RR only for rare events
Dose–response; pooled analyses	Level 3–4 evidence

CUM ch. 1, Table 1.1, pp. 2–4; ch. 2, Tables 2.2, 2.6, 2.8, 2.12, pp. 10–14, 18; SM ch. 2, p. 18.

Table 2. Bias in case-control studies and how the books reduce it

Bias	Mechanism	Remedy
Recall	Inaccurate retrospective assessment of past exposure	Prospective data collection
Observer (information)	Exposure recorded differently in cases and controls	Blinded data collection
Selection	Groups or sample differ systematically from the target population	Representative (random, consecutive) sampling; clear selection criteria
Confounding	Third variable linked to exposure and outcome	Multivariate analysis, propensity-score matching

CUM ch. 1, p. 2; ch. 2, Tables 2.4, 2.12, 2.13, pp. 11, 18.

Worked example — strengths and weaknesses together

- **Question:** does tonsillectomy cause baldness? **Case-control design:** bald subjects (cases) and non-bald subjects (controls) are questioned about prior tonsillectomy (CUM Table 2.6).
- **Strength shown:** quick, cheap, uses existing subjects; gives an odds ratio — OR 1.6 means bald subjects were 1.6 times more likely to have had tonsillectomy (CUM).
- **Weakness shown:** measures prevalence of baldness and association only; exposure history depends on recall; confounders linked to both tonsillectomy and baldness must be adjusted; causality can be judged only by a cohort study or RCT, which measure incidence (CUM Table 2.6).
- **Reporting:** OR, RR and rate difference compare two groups of dichotomous data; no association exists when OR equals 1 (CUM).

Examinable book difference — level of evidence

Table 3. Level assigned to a case-control study

Cummings ch. 1 (Outcomes Research)	Cummings ch. 2 (OCEBM 2011 levels)
Level 3 — below RCT (1–2) and controlled cohort (2), above case series (4)	Level 4 for treatment benefit, prognosis and diagnosis — grouped with case series and historically controlled studies

CUM ch. 1, Table 1.1, p. 3; ch. 2, Table 2.14, p. 20.

PEARLS

- Case-control = **outcome** — **exposure**; best for **rare diseases and long latency**.
- Main weakness: **recall bias** and unclear temporality — association, not causation.
- Gives **odds ratio**, not relative risk or incidence.
- OR ≈ RR only when the outcome is rare.
- Level 3 (CUM ch. 1) or Level 4 (OCEBM, CUM ch. 2).

498. Differences between case-control and cohort studies

ASKED 1* · 4-mark answer

Asked in: Paper I · Dec 2025 · Q6(a)

Q: Differentiate between case control and cohort study. [4]

SOURCE

- Cummings Otolaryngology (8e, Vol 1) — ch. 1 Outcomes Research — §Bias and Confounding; §Cohort Study; §Case-Control Study — pp. 2–4; Table 1.1, p. 3
- Cummings Otolaryngology (8e, Vol 1) — ch. 2 Interpreting Medical Data — §Habit 1; §Habit 2; §Habit 7 — pp. 10–14, 20; Tables 2.2, 2.5, 2.6, 2.8, 2.14
- Stell & Maran's Head and Neck Surgery and Oncology (6e) — ch. 2 Epidemiology and prevention of head and neck cancer — §Aetiology — p. 18; ch. 47 Becoming a clinical trialist — Box 47.6 — pp. 864–865

Definitions

- **Cohort study**: subjects identified at baseline **before exposure** (or treatment) and followed **forward** to see who develops the outcome; may be prospective (longitudinal) or historical (retrospective, non-concurrent) (CUM).
- **Case-control study**: subjects identified by the **outcome** — with disease (cases) and without (controls) — and compared for **past exposure**; the opposite temporal direction (CUM).

Comparison

Table 1. Cohort study versus case-control study

Feature	Cohort study	Case-control study
Starting point	Exposure (present / absent); outcome-free	Outcome (cases / controls)
Direction of inquiry	Prospective: exposure → outcome	Retrospective: outcome → exposure
Data source	Clinical care or research	Clinical care records, recall
Temporal sequence	Clear — exposure precedes outcome	Unclear
Measures	Incidence (new events) and association	Prevalence (existing events) and association
Effect measure	Relative risk; rate difference	Odds ratio
Causality	Can be assessed after adjusting for confounders	Limited; no firm causal judgement
Best for	Treatment effectiveness in routine care; prognosis (inception cohort)	Rare disease; long latency between exposure and outcome
Sample size, duration	Large numbers, long follow-up (decades for cancer)	Smaller, quick
Cost	Cheaper than RCT	Cheaper than cohort study
Main problems	Finding a suitable control group; confounding	Recall, selection, confounding
Level of evidence	2 with control group, 4 without (CUM ch. 1); 3 (OCEBM)	3 (CUM ch. 1); 4 (OCEBM)

CUM ch. 1, Table 1.1, pp. 3–4; ch. 2, Tables 2.2, 2.5, 2.6, 2.8, 2.14, pp. 10–14, 20.

Key points

- **Direction is the key difference:** cohort = exposure → outcome; case-control = outcome → exposure (CUM).
- **Incidence and relative risk** come only from a cohort (prospective) design; a case-control study gives an **odds ratio**, which approximates relative risk only for rare events (CUM).
- **Choice:** a prospective cohort for asbestos and laryngeal cancer would need a tremendous number of patients and decades of observation — the case-control design answers it sooner, at the cost of causal certainty (CUM).
- **Examples:** cohort — COVIDSurg-HN international prospective cohort of 1137 patients (SM); a US cohort giving a 67% attributable fraction of oral cancer for tobacco and/or alcohol (SM). Case-control — pooled analysis of 12 case-control studies, smoking and oral cancer RR ≈ 3.43 (SM).
- **Historical cohort is not a case-control study:** both use past records, but the historical cohort starts from exposure (prior tonsillectomy vs intact tonsils) and measures incidence of the outcome, whereas the case-control study starts from the outcome (bald vs non-bald) (CUM Table 2.6).
- **Cohort advantages:** cheaper than an RCT, less stringent inclusion, treatment assigned in routine care, easy maintenance as no blinding is needed; **disadvantages:** suitable controls are hard to find and unmeasured confounding persists (CUM).
- **Case-control advantages:** cheaper than a cohort, efficient for rare diseases or delayed outcomes; **disadvantages:** must rely on retrospective data, and the direction between exposure and outcome is unclear (CUM Table 1.1).
- **Common ground:** both are observational and controlled, both need adjustment for confounding, and both support dose–response evidence (alcohol and oral cancer) (CUM, SM).

PEARLS

- Cohort: **exposure → outcome**, incidence, RR, clear temporality.
- Case-control: **outcome → exposure**, OR, rare diseases, recall bias.
- Historical cohort ≠ case-control: it starts from exposure and measures incidence.

499. Cross-sectional study and its difference from a case-control study

ASKED 1* · 4-mark answer

Asked in: Paper I · Jun 2024 · Q1(c)

Q: What is a cross sectional study and how it is different from case control study? [4]

SOURCE

- Cummings Otolaryngology (8e, Vol 1) — ch. 1 Outcomes Research — §Case-Control Study — p. 4
- Cummings Otolaryngology (8e, Vol 1) — ch. 2 Interpreting Medical Data — §Habit 1; §Habit 2; §Habit 6; §Habit 7 — pp. 10–14, 18–20; Tables 2.2, 2.5, 2.6, 2.8, 2.13, 2.14
- Cummings Otolaryngology (8e, Vol 1) — ch. 10 Head and Neck Manifestations in the Immunocompromised Host — p. 178; ch. 12 Otolaryngology in Older Adults — §Presbystasis — p. 199
- Scott-Brown's Otorhinolaryngology (9e, Vol 2) — ch. 130 Acute otitis media — §Epidemiology — p. 1392

Cross-sectional study

- An **observational** study in which subjects are identified at a **single time point**, regardless of outcome or disease, and exposure and outcome are measured **at the same time** (CUM Tables 2.2, 2.6).
- **Measures prevalence** (existing events) and, if a comparison group is included, **association** — but **not causality**, as there is no time-span component (CUM).
- **Place in the hierarchy**: above case series (which measure only prevalence or incidence) but below case-control, cohort and RCT designs for establishing a causal relationship (CUM Table 2.6).
- **Forms**: surveys, screening programmes and evaluation of diagnostic tests (CUM); data from clinical care or research, with or without a comparison group (CUM Table 2.5).
- **Analysis**: two groups of ordinal or numeric data, often from a cross-sectional study, are compared with a correlation coefficient (CUM).
- **Validity** needs a random, representative sample — a convenience sample cannot be generalised (CUM Table 2.13); diagnostic-test results depend on the prevalence in the sample tested (CUM).
- **Evidence**: a local, current random-sample survey (or census) is Level 1 for prevalence; a systematic review of cross-sectional studies with a consistent reference standard and blinding is Level 1 for diagnosis (CUM Table 2.14).
- **Examples**:
 - tonsils and baldness examined in the same subjects at one visit — prevalence of both and their association (CUM Table 2.6);
 - facial lipoatrophy in 54% of adults on ART for >12 months (CUM);
 - 50 adults aged ≥70 — increasing age associated mainly with decline in semicircular canal function (CUM);
 - cross-sectional population surveys of otitis media — prevalence 0–11% in children (SB).

Difference from a case-control study

PEARLS

- OS = death from **any cause**; Kaplan–Meier with censoring.
- Relative survival = observed ÷ expected; DSS counts only disease deaths.
- Median survival = time when cumulative survival is 0.5; compare curves by log-rank.

503. What do you understand by evidence-based medicine?

ASKED 1* · 3-mark answer

Asked in: Paper I · Dec 2022 · Q7(a)

Q: What do you understand by evidence-based medicine? [3]

SOURCE

- Cummings Otolaryngology (8e, Vol 1) — ch. 1 Outcomes Research — §Fundamentals of Study Design; §Grading of Evidence-Based Medicine Recommendations — pp. 3–4; Tables 1.1–1.2, pp. 3–4
- Cummings Otolaryngology (8e, Vol 1) — ch. 2 Interpreting Medical Data — §Habit 7: View Science as a Cumulative Process; §Importance of Principles — pp. 19–20, 26
- Cummings Otolaryngology (8e, Vol 1) — ch. 41 Chronic Rhinosinusitis: Evidence-Based Medical Treatment — §Introduction — pp. 667–668; Fig. 41.1, p. 668

Definition

- EBM is the “**conscientious, explicit, and judicious use of current best evidence** in making decisions about the care of individual patients” (CUM).
- It is a careful **integration of three elements**: best research evidence + individual **clinical expertise** + **patient values and preferences**.
- Formalised and popularised in the **1990s** as the medical literature grew exponentially; decision making based on EBM improves quality of care, clinical outcomes and value of care.

Key features

- **Level of evidence**: each study is ranked by design — Oxford Centre for Evidence-Based Medicine (OCEBM) levels 1 (systematic review of RCTs / high-quality RCT) to 5 (expert opinion).
- **Grades of recommendation** follow the level: A = level 1, B = level 2 or 3, C = level 4, D = level 5.
- **Aggregate grade** (body of evidence) + **benefit–harm balance** → strong recommendation, recommendation, option, no recommendation or recommend against.
- **Evidence synthesis**: systematic reviews/meta-analyses → clinical practice guidelines → consensus statements when evidence is weak.
- **Core competencies (5 steps)**: **ask** → **acquire** → **appraise and interpret** → **apply** → **evaluate**.
- **Caveat**: a higher level of evidence does not necessarily mean a lower risk of bias; validity and generalisability must still be appraised.

PEARLS

- EBM = best evidence + clinical expertise + patient values.
- Level of evidence (study) ≠ grade of recommendation (body of evidence).
- Steps: ask, acquire, appraise, apply, evaluate.



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