

Subject: MSS "final"

## Patho

- \* **Ewing sarcoma**: the cell of origin is unknown, in the diaphysis of long bone  
↳ small blue cell tumor (PNET), ↑ N:C ratio, t(11;22)(q24;q12)  
"fusion of EWSR with FLI", Codman's triangle, the most sensitive test: FISH analysis
- \* **Giant cell tumor of bone (osteoclastoma)**: benign, the cell of origin is unknown, in the epiphyses of long bone, osteoclast-like giant cells, high levels of RANKL, bubble appearance without infiltration to the extra cortical space.
- \* **Aneurysmal bone cyst (ABC)**: benign, blood filled cyst, in the metaphysis of long bones, there's a debate whether it is a tumor or a reactive process.
- \* **Nonossifying fibroma (FCD, MFD)**: benign, maybe reactive not a true neoplasm, well circumscribed, bland fibroblastic proliferation, resolve spontaneously, in metaphysis.
- \* **Fibrous dysplasia (FD)**: not a real tumor → developmental abnormality of bone genesis (mutations in GNAS1 gene "cAMP mediated osteoblast differentiation"), leads to cherubism in children
  - ↳ Mazabraud syndrome (FD + soft tissue myxoma)
  - ↳ McCune-Albright syndrome (polyostotic FD + cafe au lait skin pigmentation + endocrine abnormalities) → abnormal trabeculae, haphazard arrangement, Chinese letter appearance, the biopsy helps to differentiate between it & PAGT disease
- \* **Metastatic tumors to bone**: lytic, blastic or mixed
  - ↳ the primary source: carcinoma (adenocarcinoma in lungs) ←
  - ↳ the primary source: prostate →
- \* **Joints** → Non synovial (solid): synarthrosis, minimal movement.
  - ↳ Synovial (cavitated): wide motion, covered by hyalin cartilage (70% water, type II collagen, no blood supply, no nerves, no lymphatics "shock absorber")
- \* **Synovial membrane**: lacks basement membrane
  - ↳ A synoviocytes: diff. macrophages
  - ↳ B // : fibroblast like



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Primary idiopathic → aging process

- \* **Osteoarthritis (OA, DJD)**: degeneration of cartilage, secondary → pre-existing disease
  - ↳ cartilage loss, osteophytes (bone spurs) → loose bodies in the middle of the space, joint space narrowing, crepitus, impingement on vertebrae
  - ↳ Trx: NSAIDs, intra-articular steroids
  - ↳ grade 5 is very severe: subchondral reactions, sclerosis & cyst.

- \* **Rheumatoid arthritis**: chronic inflammatory disease, autoimmune, systemic disease, nonsuppurative inflammatory synovitis, pannus formation → ankylosis (fusion of the joint space) & destruction of the cartilage
  - ↳ pathogenesis → TH1 → IFN- $\gamma$  → activate macrophages & synovial cells.
    - ↳ TH17 → IL-17 → recruits neutrophils & monocytes.
    - ↳ T cells → RANKL
  - ↳ macrophages → TNF & IL-1 → (synovial cells → proteases "destroy hyaline cartilage")
  - ↳ polyarthritides, severe blue cells, leads to chronic granulomatous inflammation, waxing & waning chronic (having normal days & bad days), ulnar deviation, boutonniere deformity of thumb, swan-neck deformity of fingers.
  - ↳ 2 tests → Anti-citrullinated protein antibody (ACPA)
    - ↳ Rheumatoid factor; negative rheumatoid factor doesn't rule out RA
  - ↳ Trx: steroids, MTX, anti-TNF

- \* **Juvenile idiopathic arthritis (JIA)**: < 16 years for at least 6 weeks, oligoarthritis, systemic disease, large joints are more affected, rheumatoid nodules & rheum factor are usually absent (-)
  - ↳ screening test: anti nuclear antibody seropositivity

- \* **Seronegative spondyloarthropathies**: associated with HLA-B27, rheumatoid factor is absent, ligamentitis, ankylosis of sacroiliac joint. Trx: anti IL-17

- \* **Suppurative arthritis**: hematogenous spread, acute, systemic manifestation
  - ↑ ESR, X-ray may show that everything is normal but the MRI may show some collections (more sensitive), Trx: aspiration of joint & antibiotics.

- Sick cell disease → Salmonella
- < 2 years → H. influenza
- adults → S. aureus.



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\* Lyme arthritis: systemic disease, by spirochetes (most commonly: *Borrelia burgdorferi* → neuro borreliosis)  
↳ erythema migrans rash & neuritis with cranial nerve palsy  
↳ primary immune response (IgM), late immune response (IgG) "when spirochetes are disseminated"

\* Crystal-induced arthritis: crystals deposition → inflammatory reaction  
↳ destroys cartilage

① Gout: deposition of MSU → activation of multiple inflammatory cells → IL-1β  
- risk factors: hyperuricemia, thiazides / is occurred mainly in big toe.  
- morphologic changes → acute arthritis: (-ve) birefringent  
↳ chronic tophaceous arthritis: repetitive attacks & crystals deposition.  
↳ Tophi  
↳ gouty nephropathy: nephrolithiasis & pyelonephritis

- Trx: life-style modifications (decrease amount of meat)

NSAIDs & colchicine in acute gout

Xanthine oxidase inhibitors (Allopurinol) in chronic gout

② Pseudogout: deposition of CPPD, increase with age, (+ve) birefringent  
idiopathic secondary (are associated with DM, HPTH, hemochromatosis → iron deposition)

- Trx: Supportive, non-curative treatment, no preventive measures

CPP appear shorter than MSU

↳ rhomboid-shaped & blue      ↳ needle shaped & yellow



## Benign joint tumors

- ① Ganglion cyst: cystic bulge, mainly in the dorsum of wrist.  
↳ is not a true cyst → herniation of synovial membranes.  
↳ degeneration of joint space (pseudocyst)

- Trx: aspiration (surgical removal)

- Under microscope: dense fibrovascular connective tissue with myxoid degeneration.

- True synovial cyst (baker cyst): big cyst filled with fluid or a herniation process, around the knee joint, leads to deep vein thrombosis.

- ② Tenosynovial giant cell tumor: T(1;2)(p13q;37) → affects type IV collagen  $\alpha-3$

↳ Diffuse: brown pigment (hemosiderin macrophages)

↳ evidence of previous bleeding

↳ PVNS "finger like projection", most commonly in knee

↳ localized small hands tendons: in the distal aspect of joints of hand.

## Soft tissue tumors (Sarcoma)

- no precursor or preneoplastic lesions, most common site: extremities (high), most common site of metastasis: lung / risk factor: NF1, Gardner, Li-Fraumeni & Osler webber-rendu syndromes.

- 15-20% → simple karyotype, ex: ewing & synovial sarcoma

- 80-85% → complex / genomic instability & a lot of mutations → investigating these tumors for genetic abnormality is not useful, ex: LMS & pleomorphic sarcoma, Dx: grading & staging

## Adipose tissue tumors

### Lipoma

in subcutaneous tissue (subcutis), soft shiny yellow appearance, well-encapsulated & well-circumscribed, mature fat cells (adipocytes).

### Liposarcoma

in extremities & retroperitoneum  
well-differentiated: "atypical lipomatous tumor", MDM2 gene mutation, looks like lipoma → difficult to diagnose  
myxoid: t(12,16)  
pleomorphic: aggressive, bad prognosis

## Fibrous tumors

- ① Nodular fasciitis: reactive process, clonal, t(17,22) producing MYH9-USP6 fusion gene, may be self limiting, classical appearance: culture-like histology

The most important thing is not to mistakenly diagnose it as malignant.



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- ② Fibromas: benign, cutaneous & subcutaneous, has fibroblast appearance & chemical features. immunostim
- ③ Fibrosarcoma: malignant, storiform (woven), superficial cutaneous, elongated nuclei.
- ④ Superficial fibromatoses: cutaneous & subcutaneous, infiltrative but they're benign (don't metastasize), (A) Palmar (Dupuytren contraction) (B) Planter: in the sole of foot (C) Penile (Peyronie disease).
- ⑤ Deep fibromatoses (desmoid tumor): in abdominal wall, mesentery & limbs, mutations in CTNFB1 ( $\beta$ -catenin) or APC  $\rightarrow$   $\uparrow$  Wnt signaling, kill by local infiltration. No metastasis.

### Skeletal muscle tumors

- Rhabdomyoma: benign, occurs with TSC, in tongue & heart; aggressive
- Rhabdomyosarcoma (RMS): malignant, fleshy & hemorrhagic tumors
  - $\rightarrow$  embryonal, alveolar, pleomorphic

### Smooth muscle tumors

- Leiomyoma (LYM): benign, mostly in uterus, fumarate hydratase on chromosome 1q42.3, well circumscribed, not infiltrative, no necrosis, no hemorrhage
- Leiomyosarcoma: malignant, infiltrative, hemorrhage & necrosis.

### Tumors of uncertain origin

- ① Uncertain mesenchymal lineage.
- ② Synovial sarcoma: deep, t(X;18)(p11;q11) makes fusion genes SS18 monophasic (only spindle cells) or biphasic (spindle cells & glands), big mass close to joint.
- ③ Undifferentiated pleomorphic sarcoma (UPS): high grade, lack cell lineage, deep soft tissue & extremities, necrosis, poor prognosis.



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isn't enough to perform our everyday activities

(fully relaxation)

## Physio

- ① Simple muscle twitch: stimulus above threshold  $\rightarrow$  contraction followed by relaxation.  
 $\rightarrow$  latent period (needs time due to action potential) / contraction & relaxation periods.
- ② Recruitment / motor unit summation:  $\uparrow$  Voltage  $\rightarrow$   $\uparrow$  number of motor units contracting at the same time until we reach the maximum stimulation.
- ③ Frequency summation: stimulate the muscle before it fully relaxes  $\rightarrow$   $\uparrow$   $Ca^{++}$  can lead to tetanization.
- ④ Incomplete tetanization (unfused): is sustained but wavering contraction, it can only partially relax between stimuli.
- ⑤ Complete tetanization (fused): twitches can't be detected, it doesn't relax at all between stimuli, we reach maximum tension.
- ⑥ Fatigue: we are stimulating the muscle & the response is dropping.
- ⑦ Treppe effect (stair case effect): when a muscle begins to contract after a long period of rest its strength of contraction will gradually increase.



## Micro

- \* **Superficial Malassezia infections**: endogenous (normal commensals of skin),  
 (Lipophilic yeast → carboxylic acid → depigmentation)  
 → **pityriasis versicolor (tinea versicolor)**: asymptomatic, resolves spontaneously  
 Treatment is for cosmetic reasons, recurrence is common  
 Dx: Wood's ultra-violet light → greenish color / spaghetti & meatballs appearance.  
 → **seborrheic dermatitis** including dandruff

- \* **Cutaneous mycoses (ring worm, tinea)**: caused by dermatophytes  
 (Transmission → human to human → chronic response  
 ↳ zoophilic & geophilic → acute //  
 → red, itchy scaly rash, hair loss. - culture: SDA

- **Onychomycosis** (fungal infections of the nail) → painful (by candida)  
 ↳ painless (by dermatophytes)

- ②  
 \* **Candidiasis**: by *Candida albicans* → oval gram (+) budding yeast, opportunistic  
 endogenous, ferments glucose & maltose with acid & gas production,  
 chlamydo-spore & germ tube formation, creamy appearance

- \* **Subcutaneous mycoses**: ① **Madura foot**: caused by *Madurella mycetomatis*  
 ② **Sporotrichosis**: caused by *Sporothrix schenckii* → nodule

- \* **Endemic mycosis**: caused by dimorphic fungus, asymptomatic  
 (systemic // (soil inhabitant) ↳ pulmonary diseases  
 ↳ Transmission: through inhalation  
 ↳ Dx: antigen skin test → isn't significant (cross positivity)  
 - Serological tests are of limited value → not significant  
 - Detection of histoplasma antigen in blood & urine is significant.



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## Embryo

\* 1<sup>st</sup> pharyngeal arch → maxillary process (maxilla, zygomatic bone & lower part of temporal //)

mandibular process → meckel's cartilage → middle part (ventral part (ramus of mandible) anterior ligament of malleus & sphenomandibular ligament) → dorsal part (malleus & incus)

is supplied by mandibular n. → (tensor tympani, tensor veli palatini, muscles of mastication, mylohyoid & anterior belly of digastric)

\* 1<sup>st</sup> pharyngeal cleft → (external auditory meatus & outer layer of tympanic membrane)

\* 1<sup>st</sup> // pouch → (middle ear, eustachian tube & inner layer of tympanic //)

\* 2<sup>nd</sup> (hyoid) pharyngeal arch

→ ventral part (upper part of the body of hyoid bone & lesser horn of hyoid bone)

→ reichert's cartilage → middle // (stylohyoid ligament)

→ dorsal // (stapes & styloid process)

is supplied by facial n. → (muscle of facial expression, stapedius, stylohyoid & post. belly of digastric)

\* 2<sup>nd</sup> pharyngeal cleft: downward growth, cover the other clefts with a space in between (cervical sinus)

\* 2<sup>nd</sup> // pouch → (palatine tonsils)



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- Oblique facial cleft: failure of fusion between maxillary & fronto-nasal processes.
- Macrostomia (or micro): // // // // maxillary & mandibular //
- Cleft (hare) lip: // // // // maxillary process & intermaxillary segment.
- Median cleft lip: // // // // of medial nasal prominences.
- Cleft lower lip: // // // // mandibular processes.
- // of the primary palate: // // // // between maxillary process & intermaxillary segment (ant. to incisive foramen)
- // // // secondary //: // // // // processes. (post. to incisive foramen).



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# Anatomy

\* The eye :-

\* Sclera : white due to irregularity of the type I collagen fibers

\* Cornea : transparent due to uniform arrangement of collagen fibrils / avascular /

Nerve supply : long ciliary n. / the most important refractive medium of the eye

→ 5 layers → ① external stratified squamous epithelium non keratinized (corneal covering epithelium)

② anterior limiting membrane (Bowman's membrane) 5-6 cell layers

③ Substantia propria (stroma) : dense connective tissue

④ posterior limiting membrane (Descemet's membrane)

⑤ inner monolayer of epithelial cells (endothelium) : maintains a fluid balance

- Uvea : choroid, ciliary body & iris → pigmented, controls pupil diameter by sphincter & dilator pupillae

brown, vascularized, pigmented (absorbs light)

connected to lens by suspensory ligaments (zonular fibers)

secrete aqueous humor (by ciliary processes)

Nerve supply : oculomotor n. (parasympathetic) / Action : accommodation of the eye, for near vision (ciliary muscle contracts & suspensory ligaments are relaxed) the opposite for far vision

- Canal of Schlemm : reabsorbs aqueous humor

- Presbyopia : ↓ ability to accommodate (lens become denser & less elastic)

- Cataract : lens become opaque (due to denaturation of crystallins)

\* Retina → Macula lutea : avascular, contain fovea centralis (point of sharpest

vision : ↑ conc. of cones), inferolateral to optic disc (vascular, blind spot)

- Central artery of retina → Anatomical end artery (don't anastomose)

→ 10 layers → ① pigment epithelium : prevent the scattering of light & enhance clarity of vision

↳ Neural retina (9 layers) → ① photoreceptor layer (rod & cone) (for black/white vision "deficiency of V.A → night blindness") (for color vision)

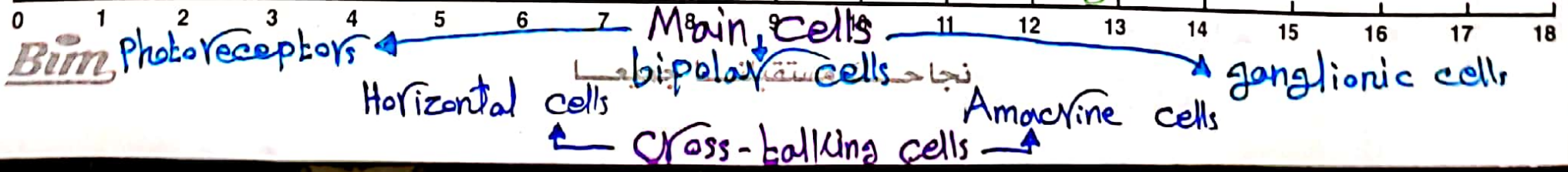
② outer limiting layer ③ outer nuclear layer ④ outer plexiform layer

⑤ inner nuclear layer : nuclei of bipolar cells, amacrine cells, horizontal cells & Muller cells (form the outer & inner limiting layer) ⑥ inner plexiform layer

⑦ ganglionic layer ⑧ nerve fiber layer ⑨ inner limiting layer

\* The first (5) layers receive O<sub>2</sub> & nutrients from choroidal capillaries

\* The last (5) layers are supplied by branches of central artery of retina



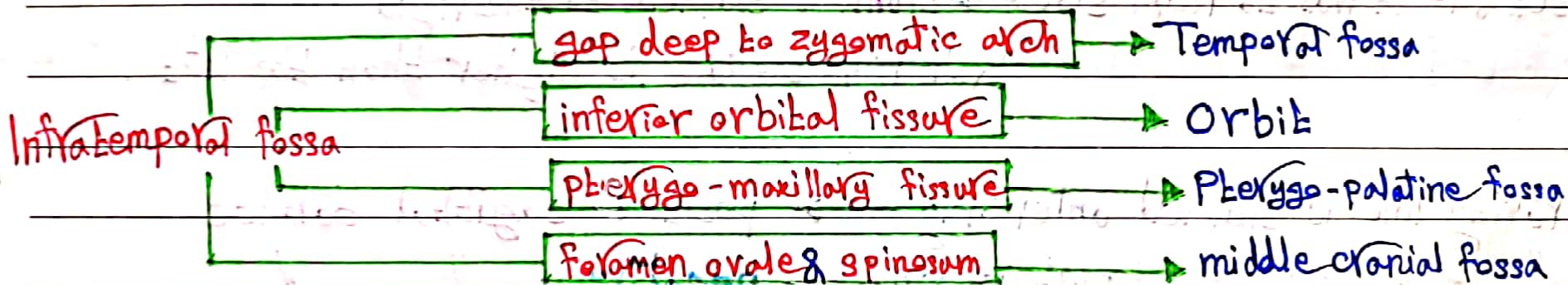


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Muscles of Mastication (Nerve supply: mandibular n.)

Muscle	Origin	Insertion	Action
Temporalis	Temporal fossa	Coronoid process	Closing jaws, elevation & retraction of the mandible
Masseter	Zygomatic arch, maxillary process of zygomatic bone	Lateral surface of the mandible	Closing jaws, elevation of mandible
Medial pterygoid	Medial surface of the lateral pterygoid plate	Medial surface of the mandible near the angle	Closing jaw, elevation of mandible
Lateral pterygoid	Upper head: roof of the infratemporal fossa (greater wing of sphenoid) Lower head: lateral surface of lateral pterygoid plate	Neck of mandible (Pterygoid fovea)	Protraction of the mandible

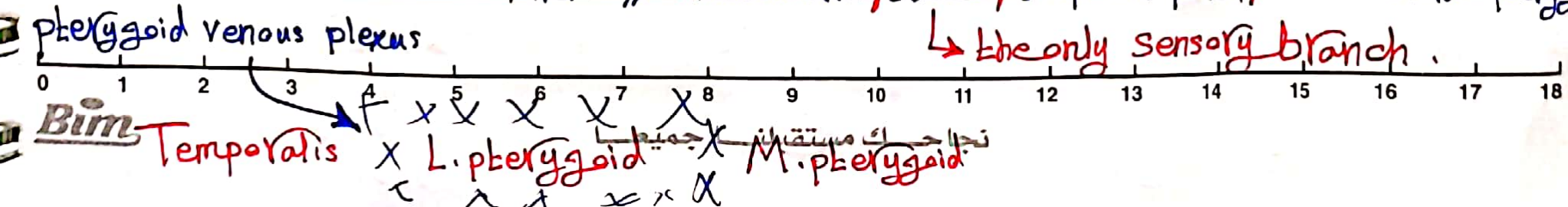
\* Contents of Temporal fossa: superficial, middle & deep Temporal artery / deep Temporal nerve, auriculotemporal & zygomaticotemporal nerves, Temporal branch of facial nerve



\* Contents of infratemporal fossa: medial & lateral pterygoid muscles, maxillary vein, middle meningeal vein, pterygoid venous plexus, sphenomandibular ligament (between sphenoid & lingula), maxillary artery (buccal, inferior alveolar, deep Temporal, middle meningeal arteries & pterygoid branches), mandibular n. (inferior alveolar, buccal, lingual & auriculotemporal nerves), chorda tympani & otic ganglion

→ 1<sup>st</sup> part (mandibular): middle meningeal & inferior alveolar arteries.  
 \* Maxillary artery → 2<sup>nd</sup> part (pterygoid): pterygoid branches, deep Temporal, buccal & masseteric arteries.  
 → 3<sup>rd</sup> part (pterygopalatine): infraorbital artery

\* Mandibular n. branches:  
 • meningeal branch  
 • nerve to medial pterygoid (Tensor Tympani, Tensor Veli Palatina)  
 • post. division → ALI (Auriculotemporal, Lingual & Inferior alveolar n.)  
 • Ant. // → masseteric, buccal, deep Temporal, nerve to lateral pterygoid.









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## Muscles of the back

### Extrinsic group

Muscle	Nerve supply	Action
First layer: Trapezius latissimus dorsi	Ventral rami of spinal nerves	No functional relation to the vertebral column.
Second layer: Levator scapulae Rhomboidus (minor & major)	Spinal nerves	
Third layer: Serratus posterior superior	2 <sup>nd</sup> to 5 <sup>th</sup> intercostal n.	elevation of ribs (2-5)
// // inferior	9 <sup>th</sup> to 11 <sup>th</sup> // n. & the subcostal n. (12 <sup>th</sup> )	depression of ribs

### Attachment of the thoracolumbar fascia

In the thoracic region	medially	to the spines of thoracic vertebrae
	laterally	to the ribs, near their angles
In the lumbar region	post. layer	to the spinous processes & supraspinous ligament
	middle //	to the tips of transverse processes & intertransversus ligaments
	ant. //	to the bases of // // // (covering quadratus lumborum)

### Splenius muscle

Nerve supply	dorsal rami of the cervical nerves (same as intrinsic group)
Action	extend the neck (antagonist of sternocleidomastoid muscle)

### Intrinsic group

Muscle	Nerve supply	Action
Superficial layer: Erector spinae (from medial to lateral)	spinalis longissimus iliocostalis	extends the spine, lateral flexion (ipsilateral)
Intermediate layer: Transverso spinalis (from superficial to deep)	Semispinalis capitis	greater occipital n. medial branches of posterior rami of spinal nerves
	Rotatores	medial branches of posterior rami of spinal nerves
Deep layer: Interspinales	posterior rami of spinal nerves	extension, ipsilateral, rotation (contralateral)
	Intertransversarii	posterior rami of spinal nerves
doesn't reach the skull	in cervical region: Ant. // // // //	Extension & contralateral rotation of thoracic spine
Levatores costarum	post. rami of spinal nerves (T1-T12)	extends cervical & lumbar spine lateral flexion & stabilize the spine elevate the ribs & rotate the thoracic vertebrae



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**Epidural hematoma**

**Subdural hematoma**

**The cause**

tumour over pterion → injury to anterior branch of middle meningeal artery

Violent shaking → injury to bridging veins (superior cerebral veins), Venous sinus

**Shape**

biconvex shaped

lunar (crescent) shaped

**Time**

Always acute

acute → hyperdense bleeding

(white like bone)

chronic → hypodense bleeding

(like CSF)

**Treatment**

Craniotomy

- \* The most common traumatic intracranial bleeding is subarachnoid hemorrhage.
- \* Base of skull fracture → raccoon eye, battle sign (hematoma behind ear), (pneumocephalus (subdural air in CT scan)) → meningitis, CSF rhinorea or otorrhea.

- \* Brain contusion "intra-parenchymal localized bleeding"  
↳ if > 3 cm → intra-cerebral hematoma.

Muscles of the neck	Nerve supply	Action
Sternocleidomastoid	spinal part of accessory & C2 & C3	extend head & flex neck
Scalene	Anterior (brachial plexus between them)	elevates 1 <sup>st</sup> rib & laterally flexes the cervical spine
	posterior	elevates 2 <sup>nd</sup> rib & laterally flexes the cervical spine
Infrahyoid	Sternohyoid	depresses hyoid bone
	omohyoid	
	Sternothyroid	depresses larynx
Suprahyoid	Thyrohyoid	elevates larynx & depresses hyoid bone
	stylohyoid	elevates hyoid bone
	digastric	ant. belly: nerve to mylohyoid post. //: facial nerve & depresses mandible
	mylohyoid	nerve to mylohyoid (inf. alveolar "mandibular n.") & elevates floor of mouth & hyoid bone
	Geniohyoid	C1 elevates hyoid bone & depresses mandible



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\* descending hypoglossi + descending cervicalis (C2+C3) → ansa cervicalis.  
(superior root) (inferior root)

\* Cutaneous branches of cervical plexus: lesser occipital (C2), great auricular (C2 & C3), transverse cervical (C2 & C3) & supraclavicular (C3 & C4) nerves

### Posterior triangle of the neck

\* **Boundaries**: anterior border of trapezius, posterior border of sternocleidomastoid, middle third of clavicle

\* **Roof**: investing layer

\* **Floor**: scalene, levator scapulae, splenius capitis

\* **Contents**: inferior belly of omohyoid, accessory n., brachial & cervical plexus, subclavian A. (3rd part), suprascapular A., transverse cervical A., occipital A.

// V. // V. // V.

external & anterior jugular veins

① Occipital triangle ② supraclavicular (subclavian) triangle

### Anterior triangle of the neck

\* **Boundaries**: - superiorly: mandible, anteriorly: midline, posteriorly: sternocleidomastoid

Triangle	Boundaries	Content
① Carotid	superior: posterior belly of digastric lateral: sternocleidomastoid inferior: superior belly of omohyoid	internal jugular vein, //, external & common carotid arteries, 10 <sup>th</sup> , 11 <sup>th</sup> & 12 <sup>th</sup> cranial nerves, ansa cervicalis
② Submandibular (digastric)	superiorly: mandible anteriorly: ant. belly of digastric posteriorly: post. // // //	submandibular gland & lymph nodes. Facial vein & artery
③ Submental	Inferiorly: hyoid bone Floor: mylohyoid muscle medially: midline laterally: ant. belly of digastric	submental lymph nodes
④ Muscular	superiorly: hyoid bone medially: midline supero-laterally: superior belly of omohyoid infero-laterally: sternocleidomastoid	pharynx, larynx, thyroid & parathyroid glands, trachea, esophagus

0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18



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- \* Middle ear (Tympanic cavity):
  - Roof: Tegmen tympani
  - Floor: internal jugular vein (N: mandibular division of Trigeminal)
  - Anterior wall: internal carotid artery, tensor tympani muscle, auditory (Eustachian) tube: "posterior inner third is bony"
  - Posterior wall: aditus → mastoid antrum "is related to sigmoid venous sinus"  
pyramid → stapedius muscle (N: facial nerve)  
vertical path of facial nerve
  - Medial wall: horizontal path of facial nerve  
Oval window (closed by base of stapes "fenestra vestibuli")  
Round // ( // // secondary tympanic membrane "fenestra cochleae")
  - Lateral wall: membranous wall

### \* Joints of the sternum :-

- 1) Manubriosternal joint: secondary cartilaginous joint
- 2) Xiphisternal // : // // // //

### \* Costovertebral joints :-

- 1) Costotransverse // : plane synovial joint, between tubercle of ribs & transverse process
  - 2) Costocorporeal // : // // // // head of rib & vertebral body
- 1<sup>st</sup> & last 3 ribs articulate with corresponding vertebral body only.

### \* Joints of the costal cartilage :-

- 1) Sternocostal joint: plane synovial joint
- 2) Chondrachondral // : cartilaginous // between ribs & costal cartilage (No movement)

### \* Intercostal muscles :-

- 1- External : its fibers are directed downward & forward
- 2- Internal : // // // // // & backward
- 3- Innermost : incomplete muscle layer
- 4- Subcostal : from internal surface of rib to internal surface of rib 2-3 levels below the origin.



