Fred Y. Lin · Zara M. Patel
Editors

ENT Board Prep

High Yield Review for the Otolaryngology In-service and Board Exams

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Dedication

To my wife, Gigi, for all her love and support, to my mother, Karen, for her devotion to family and the sacrifices she made, and in loving memory of my father, Fusen.

Fred Y. Lin

To my husband and the love of my life, André, to my sister and best friend, Cheherazade, and to my parents and loving guides, Marzban and Shireen.

Zara M. Patel

Preface

As the field of Otolaryngology grows, the depth and breadth of information that we are responsible for as otolaryngologists have also expanded. Along with the many recent advances in the subspecialties of Head and Neck, Plastics, Otology, Laryngology, Rhinology, and Pediatrics, we must also know Allergy, Sleep Medicine, Trauma, and the fundamentals of Fluid Balance, Nutrition, and those Systemic diseases that so frequently manifest in the head and neck region. The Board examination is designed to verify our grasp of this ever-increasing body of knowledge.

When we studied for our Board exam, we spent hours poring over textbooks, searching the Internet for answers we could not find in those books and then going back to those sources over and over as the review books we were using would remind us, but not inform us, of something more in depth that we had forgotten by those last few weeks leading up to the exam.

We found ourselves in need of a different kind of study guide. We wished for a directed review book to use as our source; brief enough to get through in the 1–2 weeks leading up to the exam, yet in depth enough so we would not need to go back to another source for more information.

As a result, we have compiled this review guide. It covers all the topics noted above. We have asked experts in all subspecialties to serve as section editors, and we thank them for their excellent contributions. We hope it serves future residents and fellows in those crucial weeks leading up to the exam, and that it consolidates the years of training they have gone through to join our specialty.

Fred Y. Lin — New York, NY
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PART I
Pediatrics
Section Editor: Jeffery Cheng, MD

Chapter 1
Embryology

Jeffrey Cheng and Eric Berg

PEARLS

- Understanding of embryologic derivatives will help to understand anatomy and pathophysiology when there are abnormalities in development.
- A child who presents with a midline nasal mass requires imaging prior to intervention.
- Imaging is usually not part of the work-up of a child presenting with atresia; the initial management step is to amplify; radiography is delayed until later when surgical intervention is potentially entertained

BRANCHIAL ARCH DERIVATIVES

- First arch structures
  - Nerve: trigeminal (V_3)
  - Muscle: muscles of mastication, tensor veli palatini, mylohyoid, anterior digastric, tensor tympani; sphenomandibular ligament, anterior malleolar ligament
  - Cartilage: head and neck of malleus, incus body, mandible
  - Artery: maxillary
- Second arch structures
  - Nerve: facial (VII)
  - Muscle: muscles of facial expression, posterior auricular, stapedius, posterior digastric, stylohyoid
  - Cartilage: manubrium of malleus, long process of incus, stapes suprastructure (footplate comes from otic capsule), lesser cornu, and upper body of hyoid
  - Artery: stapedial
- Third arch structures
  - Nerve: glossopharyngeal (IX)
  - Muscle: stylopharyngeus
  - Cartilage: greater cornu and lower body of hyoid
  - Artery: common and internal carotid
- Fourth arch structures
  - Nerve: superior laryngeal nerve (X)
  - Muscle: constrictors of pharynx, cricothyroid
  - Cartilage: laryngeal cartilages
  - Artery: subclavian on right, arch of aorta on left

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- Sixth arch structures
  - Nerve: recurrent laryngeal nerve (X)
  - Muscle: intrinsic laryngeal muscles
  - Cartilage: laryngeal cartilages
  - Artery: pulmonary artery on right, ductus arteriosus on left

BRANCHIAL ARCH ANOMALIES: CYSTS, SINUS, FISTULAE

- Run deep to artery and vein of named arch, superficial to artery and vein of next
- First branchial
  - Work classification
    - Type I
      - Epidermoid elements only (no cartilage or adnexal structures)
      - Duplication anomaly of the EAC
      - Medial to concha, extends to postauricular crease
      - Lateral to facial nerve, parallel to EAC
    - Type II
      - More common than type I
      - Ectodermal and mesodermal elements
      - May present in neck, typically at angle of mandible
      - Variable relationship to the facial nerve
      - End inferior to EAC or into bony/cartilaginous junction
- Second branchial
  - Most common type of branchial anomaly
  - Pathway
    - External opening along anterior border of SCM in lower third of neck
    - Internal opening found in tonsillar fossa, associated with posterior pillar
    - Penetrates through platysma muscle
    - Runs between ECA and ICA
    - Runs lateral to CN IX and XII on ascent into oropharynx
- Third/fourth branchial
  - Rare anomalies
  - Pathway
    - Also present lower in neck anterior to SCM
    - Deep to third arch structures—CN IX, internal carotid
    - Superficial to fourth arch structures—vagus nerve
    - Enters pharynx at thyrohyoid membrane or pyriform sinus
  - Treatment: controversial, but may include endoscopic approach with cauterization of opening into pyriform sinus/hypopharyx and excision of skin lesion OR if open approach, may need to include hemithyroidectomy with resection of tract

OTOLOGIC DEVELOPMENT

- Six Hillocks of His (1–3 = first arch, 4–6 = second arch)
  - 1: tragus, 2: helical crus, 3: helix, 4: antihelix, 5: antitragus, 6: lobule
- Adult configuration and location at birth, 85 % of adult size when 5 years old, adult size when 9 years old
- EAC and tympanic membrane: product of first branchial cleft
- Eustachian tube: 50 % adult length at birth; moves from horizontal to more vertical position by 5–7 years
- Ossicles: adult-sized at birth
  - Mastoid increases in size and pneumatization from birth to ~3 years (note that facial nerve is located more superficially at birth and is medialized with mastoid development)
- Microtia
  - Class I: mild, auricle decreased in size

- Class II: all major structures present but with tissue deficiency
- Class III: rudimentary soft tissue without recognizable structure
- Anotia: complete absence

- Aural atresia
  - Jahrsdoerfer grading system: 10-point grading system
    - Six favorable for surgical intervention
    - 2 points for stapes; 1 point mastoid pneumatization, oval window status, round window status, malleus, incus, facial nerve course, status of middle ear, and external ear appearance
- Syndromes associated with microtia/atresia: CHARGE, Crouzon's, Goldenhar's, hemifacial microsomia, Pierre Robin sequence, Treacher Collins, VATER
- Management principles for microtia/atresia
  - Early bone-conducting hearing aids for bilateral atresia
  - Defer surgical intervention until 5–8 years, no radiography indicated unless neural component of hearing loss or suspect cholesteatoma (middle ear or canal); usually obtain around 3–5 years old—if/when planning surgical intervention, not earlier
  - Microtia repair before atresiaplasty to preserve vascularity of tissue flaps
  - Canal cholesteatoma may be associated with atresia and requires prompt intervention

MIDLINE NASAL MASSES

- Nasal development
  - Nose formed from frontonasal process and bilateral nasal placodes
  - Origin of intranasal structures:
    - Maxilloturbinal → inferior turbinate
    - First ethmoturbinal → agger nasi cell, uncinate process
    - Second ethmoturbinal → middle turbinate
    - Third ethmoturbinal → superior turbinate
    - Fourth ethmoturbinal → supreme turbinate
  - Erroneous closure of embryologic spaces may lead to persistent communication and/or trapped neural or epithelial tissue elements and resultant congenital midline nasal pathology:
    - Anterior neuropore: most distal end of the ectoderm-derived neural tube, vulnerable to developmental errors
    - Foramen cecum: pathway between frontal and ethmoid bones that usually obliterates itself, continuous with the prenasal space
    - Fonticulus nasofrontalis: embryonic space between the frontal and nasal bones
    - Prenasal space: potential space during development between the nasal bones and the cartilaginous precursors of the septum
- Imaging: CT scan may show bifid crista galli with intracranial communication but can be indeterminate due to incomplete ossification of skull base; MRI more specific in evaluation
- Differential diagnosis
  - Dermoid cyst (most common): rare dural connection, rarely transilluminate, negative Furstenberg test (expansion of a nasal mass with compression of the IJVs)
    - Rarely associated with meningitis
    - Found in midline as a fluctuating cyst with a sinus tract leading to the skin; epithelium lined, contains skin appendages, may penetrate deep to the nasal bone
    - Treatment: surgery; manage any intracranial portion first; neurosurgical consultation
    - Surgical approaches for nasal component: vertical midline dorsal excision, external rhinoplasty, bicoronal
  - Neurogenic: glioma, encephalocele, neurofibroma
    - Glioma: trapped neural tissue without persistent dural connection, do not transilluminate, negative Furstenberg test, not associated with meningitis, a solid mass of glial tissue with a fibrous stalk
      - Usually found at the glabella, can also present as lateral nasal mass

- Encephalocele: always has a dural connection, transilluminates, positive Furstenberg test, associated with meningitis, histologically an ependymal lined sac that communicates with the CSF spaces
- Hemangioma

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Chapter 2
General Pediatric Otolaryngology

Jeffrey Cheng and Eric Berg

PEARLS

- Croup-like symptoms on presentation for the child <6 months of age should be of concern for possible subglottic hemangioma
- After maximization of medical therapy, adenoidectomy is the first-line surgical option for recurrent, acute sinusitis/adenoiditis in children
- Consider adenoidectomy to help treat underlying Eustachian tube dysfunction
- Nasal polyposis in a child should prompt a work-up for cystic fibrosis
- Torticollis or decreased neck range of motion post-tonsillectomy should be suspicious for Grisel's syndrome
- Neck masses in children are most commonly the result of an infectious process

PEDIATRIC SINUSITIS

- Major criteria for chronic pediatric sinusitis
  - Nasal obstruction
  - Purulent nasal discharge
- Other presenting symptoms
  - Headache
  - Chronic cough
  - Behavioral change, irritability
  - Halitosis
  - Postnasal drainage
  - Daytime cough with exacerbation at night
- Predisposing factors
  - Environmental
  - Allergy
  - Tobacco smoke
  - GERD
  - Immunodeficiency
  - Cystic fibrosis
    - Nasal polyps in a pediatric patient suggest CF until proven otherwise.
  - Ciliary dyskinesia
  - Infectious—viral, etc

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- Complications of pediatric rhinosinusitis
  - Meningitis
  - Epidural/subdural/intraparenchymal brain abscess
  - Orbital complications
    - Chandler classification
      - I: Periorbital cellulitis (pre-septal)
      - II: Orbital cellulitis
      - III: Sub-periosteal abscess
      - IV: Orbital abscess
      - V: Cavernous sinus thrombosis
    - Stage I and II can generally be managed with intravenous antibiotics. Stage IV and V require urgent surgical intervention. Small medial sub-periosteal abscesses may be treated with a trial of intravenous antibiotics with close observation and a low threshold for surgical intervention if clinical improvement is not seen
  - Indications for CT scanning for pediatric rhinosinusitis
    - Severe illness or toxic condition
    - Acute rhinosinusitis that does not improve with medical therapy in 48–72 h
    - Immunocompromised host
    - Presence of a suppurative complication other than orbital cellulitis
  - Bacteriology of acute pediatric sinusitis
    - Aerobes: *Pneumococcus*, *Moraxella catarrhalis*, *Haemophilus influenzae*, *Staphylococcus aureus*, *α-hemolytic Strep*, *Pseudomonas*
    - Anaerobes: *Peptococcus*, *Peptostreptococcus*, *Bacteroides*
  - Bacteriology of chronic pediatric sinusitis
    - Aerobes: *S. aureus*, *Streptococcus pneumoniae*, *H. influenzae*
    - Anaerobes: *Prevotella*, *Porphyromonas*, *Fusobacterium*

VELOPHARYNGEAL INSUFFICIENCY

- Four patterns of velopharyngeal closure
  - Coronal (55 %, most common)
  - Sagittal (10–15 %, least common)
  - Circular (10–20 %)
  - Circular with Passavant's ridge (15–20 %)
- Management of velopharyngeal insufficiency (VPI)
  - Medical
    - Speech therapy
    - Prosthetics: palatal lift or obturator
    - Biofeedback with nasometry
  - Surgical
    - Pharyngoplasty
    - Use when good anterior–posterior motion, poor lateral motion
    - Pharyngeal flaps
    - Use when good lateral motion, poor anterior–posterior motion
    - Posterior pharyngeal wall augmentation

UPPER AIRWAY INFECTIONS

- Laryngotracheitis (Croup)
  - Viral etiology (most commonly associated with parainfluenza)
  - Slow onset with URI prodrome leading to barky cough and inspiratory stridor
  - Presents in patients aged 6 months–3 years
  - AP neck X-ray with "steeple sign" (subglottic narrowing)
  - Supportive care with humidification, racemic epinephrine, ±steroids
  - Intubation rarely required and should be avoided if possible

- Supraglottitis (epiglottitis)
  - Bacterial etiology (classically *H. Influenza B*)
  - Rapid onset with high fevers, dysphagia, drooling, and toxic appearance
  - Presents most commonly in patients aged 1–8 years
  - Lateral neck X-ray with "thumbprint sign" (swollen epiglottis)
  - Secure airway, IV antibiotics
    - OR intubation/bronchoscopy with tracheotomy equipment available; extubate once edema decreased and air leak present
- Bacterial tracheitis
  - Bacterial etiology (*S. Aureus*, *S. Pyogenes*, *H. Influenza*, *M. Catarrhalis*)
  - May be bacterial superinfection after viral laryngotracheitis
  - URI prodrome with rapid escalation to toxic symptoms with high fevers, cough, hoarseness, and respiratory distress
  - IV antibiotics
  - OR intubation/bronchoscopy with therapeutic removal and culture of tracheal exudates
- Retropharyngeal abscess
  - Mixed aerobic/anaerobic bacterial etiology
  - URI prodrome with slowly progressive sore throat, dysphagia, drooling, and decreased neck range of movement
  - Lateral neck X-ray (widening of pre-vertebral soft tissues) vs. CT scan
  - IV antibiotics—may obviate the need for surgical drainage
  - Secure airway as needed; possible OR drainage (trans-oral vs. trans-cervical)

ADENOTONSILLAR DISEASE

- Adenoid anatomy
  - Blood supply
    - Pharyngeal branch of the internal maxillary (major supply)
    - Ascending palatine branch of the facial artery
    - Ascending cervical branch of thyrocervical trunk
    - Ascending pharyngeal artery
  - Innervation: CNs IX and X
    - Histology: ciliated pseudostratified columnar, stratified squamous and transitional epithelia present; presence of inflammation increases specialized squamous epithelium proportion and decreases respiratory proportion
  - Indications for adenoidectomy
    - Infection
    - Recurrent/chronic adenoiditis
    - Chronic otitis media with or without effusion (kids >4 years)
    - Obstruction
      - Adenoid hyperplasia with chronic nasal obstruction or obligate mouth breathing
      - OSA or sleep disturbances
      - Associated with cor pulmonale, failure to thrive (FTT)
    - Craniofacial growth abnormalities
    - Occlusion abnormalities
    - Speech abnormalities
    - Swallowing abnormalities
    - Others
      - Suspected neoplasm
      - Chronic sinusitis
- Tonsil anatomy
  - Blood supply to the tonsil
    - Facial artery (tonsillar branch, ascending palatine branch)
    - Dorsal lingual branch of lingual artery

        - Internal maxillary artery (descending palatine, greater palatine artery)
        - Ascending pharyngeal artery
    - Etiology of pseudomembranous tonsillitis
        - Epstein–Barr virus (mononucleosis)
        - Candidiasis
        - Vincent's angina
        - *Neisseria gonnorhoeae*
        - Syphilis
        - *Corynebacterium diphtheria*
        - Group A β-hemolytic *Streptococcus*
    - Indications for tonsillectomy
        - Infection
            - Recurrent acute infections >7 in 1 year, >5/year in 2 years, >3/year in 3 or more years
            - Recurrent acute infections with complications (cardiac valve disease, febrile seizures)
            - Chronic tonsillitis associated with halitosis, persistent sore throat, tender cervical adenitis, unresponsive to medical therapy
            - *Streptococcus* carrier
            - Peritonsillar abscess
            - Tonsillitis with cervical abscess
            - Mononucleosis with obstructing tonsils unresponsive to therapy
            - PFAPA (*see below*: syndrome of periodic fever, aphthous stomatitis, pharyngitis, and adenitis)
            - Obstruction
            - Suspicion of malignancy
- AAO-HNS guidelines for overnight admission post adenotonsillectomy
    - Severe OSA (AHI >10) or other craniofacial abnormalities
    - Emesis or hemorrhage
    - Age <3 years
    - Patient lives greater than 60 min away from hospital
    - Poor socioeconomic class which may predispose to neglect
    - Any other medical comorbidity which requires attention postoperatively (diabetes, seizures, Down syndrome, asthma, cardiac disease, etc.)
- Complications of adenotonsillectomy
    - Postoperative hemorrhage: 0.5–10 %
    - Postoperative pulmonary edema: due to loss of auto-PEEP from chronic obstruction and decreased intrathoracic pressure. Treat with diuretics, fluid restriction, CPAP. Intubation if necessary to control O_2 saturation
    - Hypoxemia: loss of hypercapneic respiratory drive
    - VPI
    - Nasopharyngeal stenosis
    - Atlantoaxial subluxation (Grisel's syndrome): deep calcification of anterior arch of atlas, laxity of anterior transverse ligament; Down syndrome children more prone to this
        - Diagnosis: MRI or CT C-spine
        - Treatment: muscle relaxants, benzodiazepines, spine consultation/traction, cervical collar, NSAIDs
    - Malodorous breath (most common complaint)
- PFAPA syndrome
    - Periodic high fevers, aphthous stomatitis, pharyngitis, cervical adenitis occurring every 3–5 weeks for at least 6 months
    - Repeated negative throat and viral cultures
    - Medical management with steroids, definitive surgical management with adenotonsillectomy
- Pediatric Autoimmune Neuropsychiatric Disorders Associated with Streptococcal infections (PANDAS)
    - Not validated as a disease entity
        - Dx: GABHS-Ig

- Rapid onset of obsessive compulsive disorder (OCD) in association with group A β-hemolytic streptococcal infections (GABHS)
- Treatment: psychiatric medications for OCD, PCN/abx

PEDIATRIC HEAD AND NECK MASSES

Most common neck mass in a child is inflammatory adenitis:

- Treatment with antibiotics
- Suppurative adenitis likely to require incision and drainage
- Deep-space neck infection may present with neck mass/fullness
- Cat scratch fever
  - *Bartonella henselae*
  - History of cat exposure
  - Dx: serum titer measurement
- Atypical mycobacterial infection
  - Childhood disease, non-tender slowly enlarging neck mass, no pulmonary involvement or systemic, drug therapy usually ineffective (biaxin may be effective)
  - Tx: incision and drainage/curretage, may cause fistulization

SALIVARY GLAND MASSES

- Most common pediatric salivary gland mass is hemangioma
- Most common pediatric salivary gland neoplasm is pleomorphic adenoma
- Most common pediatric salivary gland malignancy is mucoepidermoid carcinoma
- Overall ~50 % of parotid gland neoplasms in children are malignant (vs. ~20 % in adults)

SMALL BLUE-CELL MALIGNANCIES IN CHILDREN

- Lymphoma
- Sarcoma
- Rhabdomyosarcoma
  - Most common sites (descending order)
    - Orbit
    - Nasopharynx
    - Middle ear/mastoid
    - Sinonasal cavity
  - Metastatic sites
    - Lung
    - Bone
    - Bone marrow
  - Histopathology
    - Embryonal (75 %): most common in infants and children
      - Spindle-shaped cells with eosinophilic cytoplasm, best prognosis
      - Botryoid variant
    - Alveolar (20 %): most common in adolescents
      - Small round cells separated by fibrous septae into alveolar groups
    - Pleomorphic: most common in adults
- PNET (neuroendocrine tumor)

DIFFERENTIAL DIAGNOSIS FOR MIDLINE NECK MASS

- Thyroglossal duct cyst
  - Embryologic remnant of tract from descent of thyroid gland from foramen cecum to natural anatomic position

  - Evaluate for the presence of normal thyroid gland using ultrasound prior to surgical management
  - Tx: Sistrunk procedure—excision of cyst, surrounding tissue, and central portion of hyoid; variable tract path
- Teratoma
- Dermoid
- Lymphatic malformation
- Plunging ranula
- Thymic cyst
- Hemangioma

PEDIATRIC BASE OF TONGUE MASS

- Differential diagnosis
  - Lingual thyroid
  - Thyroglossal duct cyst
  - Vallecular cyst
- Evaluation
  - Thyroid function tests: TSH, T3/T4
  - CT or MRI
  - I-131 scan: identify other foci of functioning thyroid tissue
- Treatment of lingual thyroid: observation, thyroid suppression therapy, RAI, surgery

LYMPHATIC AND VASCULAR MALFORMATIONS

- PHACE syndrome
- Kasabach–Merritt syndrome
- Sturge–Weber syndrome
- Maffucci syndrome
- von Hippel Lindau syndrome
  - Autosomal dominant
  - Hemangioblastomas of CNS and retinas, renal cysts/carcinoma, pheochromocytoma, pancreatic cysts, papillary cystadenomas of epididymis
  - Associated with endolymphatic sac tumors

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Chapter 3
Congenital Syndromes

Jeffrey Cheng and Eric Berg

PEARLS

- A knowledge of embryology is essential to understanding the syndromes affecting the head and neck
- Many congenital syndromes are associated with hearing loss, making otologic evaluation and amplification important
- Coexistent syndromic conditions often make the prognosis for the patient more complicated, e.g., adenotonsillectomy may be less successful in treating syndromic children with sleep-disordered breathing/obstructive sleep apnea

PIERRE ROBIN SEQUENCE

- Classic triad
  - Retrognathia
  - Glossoptosis
  - Cleft palate
- Pathology: Retrognathia prevents descent of the tongue into the oral cavity which prevents secondary palate fusion
- Isolated or syndromic association in 50–80 % of cases
  - Most commonly Stickler, velocardiofacial syndromes
- Airway interventions (a progressive sequence)
  - Prone positioning
  - Nasopharyngeal airway
  - Endotracheal intubation
  - Surgical interventions
    - Tongue–lip adhesion
    - Mandibular distraction osteogenesis
    - Tracheostomy

ACHONDROPLASIA

- Most common cause of short-limb dwarfism, normal cognitive function
- Autosomal dominant, most cases spontaneous, due to mutation of FGFR-3 gene (4p16.3)
- Clinical features: short stature, shortened limbs, long narrow trunk, frontal bossing, midface hypoplasia, lumbar lordosis, limited elbow extension, genu varum, trident hand

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VATER SYNDROME: VERTEBRAL/VASCULAR ANOMALIES, ANAL ATRESIA, TRACHEAL ANOMALIES, ESOPHAGEAL ANOMALIES, RENAL/RADIAL BONE ANOMALIES

- VACTERL syndrome
  - VATER plus cardiac anomalies, limb anomalies

TRISOMY 21 (DOWN'S SYNDROME)

- Craniofacial features
  - Brachycephaly
  - Flat occiput
  - Abnormal small ears
  - Upslanting palpebral fissures
  - Epicanthic folds
  - Short small nose
  - Midface hypoplasia
  - Large fissured lips
  - Large fissured tongue
  - Dental abnormalities
  - Short neck
  - Atlantoaxial subluxation and instability—C-spine films and/or MRI may help to delineate if special precautions need to be taken, but all patients should be managed with as little manipulation of the cervical spine as possible

AUTOSOMAL DOMINANT SYNDROMES (WANTBCS)

- Waardenburg syndrome
  - Common findings
    - Pigmentary abnormalities (white forelock)
    - Craniofacial anomalies (dystopia canthorum, broad nasal root, synophrys)
    - Unilateral or bilateral SNHL
  - Type I: with dystopia canthorum; 20 % SNHL; mutation of PAX3 gene
  - Type II: without dystopia canthorum; 50 % SNHL; mutation of MiTF gene (microphthalmia transcription factor)
  - Type III: features of Type I plus skeletal dysplasias and muscular hypotonia
  - Type IV: features of Type II plus Hirschsprung megacolon (AR)
- Apert (acrocephalosyndactyly) and Crouzon (craniofacial dysostosis)
  - Both due to mutation of FGFR-2 gene (10q26)
  - Common findings
    - Craniosynostosis
    - Hypertelorism
    - Exophthalmos
    - Midface hypoplasia
    - Mandibular prognathism
    - Parrot-beaked nose
    - Syndactyly and cervical fusion
    - Cognitive function normal to severe mental retardation
  - Pfeiffer's syndrome—similar to Apert's syndrome, but digital broadening rather than syndactyly
    - Associated with tracheal sleeve (complete rings)
- Neurofibromatosis
  - Type I (Von Recklinghausen's disease)
    - Mutation on chromosome 17
    - Diagnostic criteria including café au lait spots, Lisch nodules, cutaneous neurofibromas

        - Acoustic neuromas in 5 %
        - CNS involvement may lead to SNHL, MR, blindness
    - Type II
        - Mutation of tumor-suppressor gene on chromosome 22
        - AD; 50 % due to spontaneous mutation
        - Greater CNS involvement
        - 95 % incidence of bilateral acoustic neuromas before 21 years
        - Only FDA-approved indication for auditory brainstem implant
- Treacher Collins (mandibulofacial dysostosis)
    - TCOF1 gene found on chromosome 5q (TREACLE gene)
    - Malformation of 1st (and 2nd) branchial arches
    - Clinical features
        - Otologic: Malformed ossicles, auricular deformity, aural atresia, CHL present 30 % of time, occasional SNHL
            - 50 % will have hearing impairment from EAC and/or middle ear malformations
        - Preauricular fistulas, mandibular and malar hypoplasia, anti-mongoloid palpebral fissures, coloboma of the lower eyelids, may have cleft lip and palate, normal IQ
- Stickler
    - Mutation of COL2A1 gene on chromosome 12, responsible for type II collagen gene
    - Can be found in association with Pierre Robin sequence
    - Clinical features
        - Myopia with retinal detachment and cataracts
        - Hypermobility and enlarged joints, early-onset arthritis, occ. spondyloepiphyseal dysplasia
        - SNHL or mixed HL in 80 %, educationally significant in 15 %
- Branchio-oto-renal (Melnick–Fraser syndrome)
    - Involves 8q between D8S87 and D8S165 (EYA1 gene)
    - Clinical features
        - Branchial cleft anomalies (63 %): cysts or fistulae
        - Otologic malformations: hearing loss (89 %), preauricular pits (77 %), auricle abnormalities (41 %), ossicular and cochlear malformations, lacrimal duct stenosis
        - 2 % of children with severe/profound SNHL
        - Renal dysplasia (66 %): agenesis, polycystic kidneys, duplicated ureters, renal abnormalities identifiable on IVP or renal U/S

AUTOSOMAL RECESSIVE SYNDROMES (PUGJ-AR)

- Pendred syndrome
    - SNHL associated with iodine metabolism defect leading to euthyroid goiter
    - Associated with Mondini's dysplasia and enlarged vestibular aqueduct
    - Historically diagnosed with perchlorate discharge test
    - Genetic testing for pendrin gene mutation
- Usher syndrome
    - Represents 10 % of hereditary deafness
    - Clinical features: hearing loss, vestibular deficits, ataxia, retinitis pigmentosa (RP) causing progressive visual loss (apparent with electroretinography prior to fundoscopic exam)
    - Type I: most common (90 %), profound deafness, RP by age 10, absent vestibular response
    - Type II: moderate/severe deafness, RP by teens/twenties, normal or slightly decreased vestibular response
    - Type III: progressive HL, RP begins with puberty
    - Type IV: X-linked; clinically similar to type II

- Goldenhar syndrome (oculoauriculovertebral spectrum)
  - Characterized by unilateral facial asymmetry, unilateral external and middle ear changes, vertebral malformations
  - Ocular findings: upper lid colobomata
  - Otologic findings: mildly deformed ears to anotia, EAC atresia, ossicular abnormalities
  - Underdevelopment of mandible, orbit, facial muscles, also may have hemivertebrae of vertebral column
  - Hemifacial microsomia often placed in this category, possible vascular insult not of genetic cause
  - Most cases sporadic, some autosomal dominant transmission reported
- Jervell–Lange-Nielsen syndrome
  - Profound bilateral SNHL
  - Cardiac defects: prolonged QT interval, large T waves, Stokes–Adams attacks
  - Recurrent syncopal episodes, may lead to sudden death
  - Screen with EKG
  - Treat with beta-blockade

X-LINKED RECESSIVE SYNDROMES

- Alport syndrome
  - X-linked and AR subtypes
  - Progressive SNHL and varying degrees of renal disease
  - Defect in renal basement membrane and stria vascularis
- Norrie syndrome
  - Caused by mutations in the *NDP* gene, located on Xp11.4
  - Primarily affects the eye, leads often to blindness
  - 30–50 % developmental delay or mental retardation
  - Early-onset SNHL common
- Otopalatodigital syndrome
  - Craniofacial anomalies
  - Widely spaced first and second toes
  - Conductive hearing loss due to ossicular malformation
- Wildervaank syndrome
  - Klippel–Feil malformation (congenitally fused segment of cervical spine)
  - Sensorineural or mixed hearing loss
  - CN VI paralysis

22Q DELETION SYNDROMES

- Velocardiofacial syndrome
  - Autosomal dominant disease, characterized by abnormal facies, VPI, and cardiac anomalies
  - Deletion of 22q11
  - Almond-shaped palpebral fissures, deficient nasal alae, tubular nose with bulbous tip, small mouth
  - Long face with vertical maxillary excess, malar flatness, mandibular retrusion
  - Palatal clefting ranges from submucous clefting to overt wide cleft palate with hypernasality
  - Cardiac anomalies in 80 %, most commonly VSD; other anomalies include right-sided aortic arch, tetralogy of Fallot, aortic valve disease
  - Medial displacement of ICA's present in up to 25 % of patients
- DiGeorge syndrome
  - CATCH-22
    - Cardiac anomalies (tetralogy of Fallot)
    - Abnormal facies

    - Thymic aplasia
    - Cleft palate
    - Hypocalcemia/hypoparathyroidism
  - Improper development of 3rd and 4th branchial arches
    - Thymic aplasia—T cell qualitative immunodeficiency
  - Laryngeal findings—anterior glottic web, patient may present with hoarseness alone or with other respiratory complaints

OTHER CRANIOFACIAL SYNDROMES

- Congenital pyriform aperture stenosis
  - Central megaincisor
  - Cerebral malformations—holoprosencephaly; obtain MRI
- Choanal atresia
  - Incidence 1:5,000–8,000 births, F:M 2:1
  - 50 % have other congenital abnormalities (75 % of bilateral cases associated with other anomalies)
  - 30 % bony, 70 % mixed bony-membranous
  - 65–75 % unilateral, rest are bilateral
  - Results from persistence of buccopharyngeal membrane
  - Severity of presentation depends on whether unilateral or bilateral; bilateral atresia presents with immediate cyclical cyanosis (cyanosis interrupted by crying spells); unilateral atresia can remain hidden for years and present with unilateral nasal obstruction and rhinorrhea
  - Four parts to the anatomic deformity
    - Narrow nasal cavity
    - Lateral bony obstruction from pterygoid plate
    - Medial bony obstruction from vomer
    - Membranous obstruction
  - General management approach
    - Unilateral atresia: non-urgent repair, can wait until ~1 year of age
    - Bilateral atresia: establish temporary airway and feeding pathway (McGovern nipple, oropharyngeal airway; intubation not necessary unless mechanical ventilation required) and prepare for surgical correction
  - Surgical repair approaches
    - Transnasal
    - Transpalatal (reserved for older children d/t orthodontic growth)
    - Transantral
    - Transseptal
  - Syndromes associated with choanal atresia (ACT TV)
    - Apert syndrome
    - Crouzon disease
    - Treacher Collins syndrome
    - Trisomy 18
    - Velocardiofacial syndrome
- CHARGE syndrome
  - Coloboma
  - Heart disease or hearing defect
  - Atresia (choanal)
  - Retardation of growth
  - Genital defects (in males)
  - Endocardial cushion defect or ear anomalies and deafness

CLEFT LIP AND PALATE

- Cleft palate results from failure of bilateral palatine shelves (from maxillary processes) to fuse at midline with developing nasal septum (from frontonasal process and bilateral medial nasal processes)
- Cleft lip results from failure of fusion of maxillary swelling with medial nasal process.
- Septum deviated to the cleft side
- Signs of submucous cleft palate:
  - Bifid uvula
  - Zona pellucida
  - Notched hard palate
- Dehiscence of palatal sling including levator veli palatini leads to significant Eustachian tube dysfunction and nearly universal incidence of chronic otitis media
  - Wide range of congenital insults and genetic errors have been linked:
    - Drugs: phenytoin, vitamin A derivatives, folic acid antagonists
    - Smoking and alcohol use in first trimester
    - X-linked cleft palate syndrome has been described
  - Incidence of CL ± CP is about 1/700 live births overall, increased in Native American and Asian populations and decreased in Caucasians and African Americans
  - More common in males (2/3)
  - 80 % of clefts are unilateral, more common on left (2/3)
  - Surgical repair of cleft lip and palate:
    - Lip adhesion: if done, performed at 2–4 weeks of age with definitive repair at 4–6 months of age
    - Cleft lip repair: if no contraindications and no previous lip adhesion, repair performed at 10–12 weeks; rule of 10's (10 weeks old, 10 kg weight, hemoglobin of 10)
      - Straight-line closure (rarely used)
      - Millard rotation advancement technique
      - Tennison-Randall (single) triangular flap interdigitation
      - Bardach (double) triangular flap interdigitation
      - Bilateral cleft repair (Millard)
    - Cleft palate repair: performed 9–12 months up to 18 months of age if child is growing and gaining weight; restoration of soft palate sling incorporating tensor veli palatini and levator veli palatini
      - Schweckendiek: closure of soft palate only
      - Von Langenbeck
      - Bardach two flap palatoplasty (for complete CP repair)
      - Furlow double Z-plasty (for secondary CP repair)
      - V-Y pushback technique (for secondary CP repair)

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Chapter 4
Pediatric Airway

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PEARLS

- Recommend using a ½ size smaller endotracheal tube, based on the formula (age + 16)/4.
- Endotracheal tube cuff pressures >20 mmHg will exceed the capillary filling pressure and cause ischemic damage over time
- More severe airway pathology is less likely to respond to endoscopic versus open interventions
- The history is essential to providing a complete and focused differential diagnosis to pediatric airway pathology
- Voice dysfunction in children may become more of an issue as they are introduced to more social environments; they may become withdrawn if they are not able to be easily understood or communicate with other children/adults and the emotional/social impact is not yet well elucidated but should not be ignored

DIFFERENCE BETWEEN PEDIATRIC AND ADULT LARYNX

- Pediatric larynx higher in neck (C2, descends to C6 with age)
- Epiglottis curved/omega shaped, in contact with soft palate
- Thyroid cartilage oblique, no defining angle
- Infant vocal cords shorter, 4–4.5 mm long at birth, adults 14–23 mm
  - True vocal cord in infants, 50 % composes vocal process compared to 25–33 % in adults
- Infant subglottis narrowest part (cricoid complete ring): 4.5–7 mm in full-term infant
  - Circumferential mucosal edema in infant narrows subglottis by >60 %

CLINICAL EVALUATION

- Location of stridor by its pattern
  - Inspiratory: supraglottic, glottic
  - Biphasic: subglottic
  - Expiratory: fixed intrathoracic trachea
- SPECSR mnemonic
  - Subjective—parents' impressions
  - Progression
  - Eating/feeding difficulties
  - Cyanosis
  - Sleep-disordered breathing
  - Radiography

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- Pediatric airway abnormalities improved in prone position
  - Laryngomalacia
  - Pierre Robin sequence
  - Vascular compression
  - Mediastinal mass
- Common GERD-related laryngeal disorders
  - Recurrent croup
  - Chronic cough
  - Laryngospasm
  - Hoarseness
  - Subglottic stenosis
  - Aspiration
  - Laryngomalacia

RADIOGRAPHIC EXAMINATION

- Signs of obstruction
  - Dilated hypopharynx
  - Indistinct vocal cords (infectious process)
  - Collapse of subglottis on inspiration, dilation on expiration
  - Steeple sign (infection): AP view
  - "Thumb" sign: lateral view (supraglottitis)

CLINICAL SCENARIOS

- Less than 6 months old
  - New-onset biphasic stridor, no foreign body history: subglottic hemangioma
  - Laryngomalacia: most common cause of inspiratory stridor, stridor worse with crying and lying supine
    - Uncertain pathophysiology, thought to be affected by
      - Anatomic factors: shortened aryepiglottic folds, anterior cuneiform cartilage collapse
      - Immature neuromuscular control
      - GERD
    - Indications for intervention
      - Severe stridor with failure to thrive
      - Obstructive sleep apnea
      - Weight loss
      - Severe chest deformity
      - Cyanotic attacks
      - Pulmonary hypertension, cor pulmonale
    - Medical
      - Reflux control
      - Speech–language pathology (SLP) evaluation, feeding strategies
    - Surgical approaches
      - Division of aryepiglottic folds
      - Epiglottic adhesion
      - Removal of redundant mucosa, cuneiform, and corniculate cartilages
      - Tracheostomy
      - Possible Nissen/g-tube adjunct for severe cases
  - If prior history of intubation, NICU, prematurity, etc.: subglottic stenosis, subglottic cyst
    - Also evaluate for vallecular cyst on bedside laryngoscopy

CLASSIFICATION OF LARYNGEAL CLEFT

- Type 1: supraglottic interarytenoid cleft above the level of vocal cords
  - Treatment: observation, modified diet, injection laryngoplasty, endoscopic repair
- Type 2: partial cricoid cleft, extends below the level of vocal cords
  - Treatment: observation, diet modification, injection laryngoplasty, endoscopic/open repair
- Type 3: total cricoid cleft, without extension into cervical tracheoesophageal wall
  - Treatment: diet modification, endoscopic/open repair
- Type 4: laryngotracheoesophageal cleft, almost universally fatal

VOCAL CORD PARESIS/IMMOBILITY

- Differential diagnosis of vocal cord palsy, unilateral or bilateral
  - Idiopathic
  - History of cardiac surgery (esp. PDA ligation with left cord paresis)
  - Birth trauma, other trauma
  - Neurologic disease
    - Arnold–Chiari malformation
    - Hydrocephalus
    - Cerebral palsy
    - Hypoxic encephalopathy
  - Malignant disease: familial, brainstem lesions
  - Drug related: vinca alkaloids (neurotoxic)
- Diagnostic work-up
  - MRI brain
  - Modified barium swallow
  - SLP evaluation
- Treatment
  - Unilateral—rarely any airway/respiratory issues, primarily voice and swallowing
    - Observation
    - Speech therapy
    - Injection laryngoplasty
    - Recurrent laryngeal nerve-ansa cervicalis anastomosis
  - Bilateral—almost all present with some component of respiratory problems
    - Observation—spontaneous recovery possible, 5–7 years of age
    - Lateral cordotomy, partial arytenoidectomy
    - Lateralization suture
    - Cricoid split—endoscopic, open, possible late failures secondary to synkinesis
    - Tracheostomy

RECURRENT RESPIRATORY PAPILLOMATOSIS

- Etiology: HPV 6, 11; develops at the junction of squamous and respiratory epithelium
  - Vertical maternal transmission, presents with hoarseness, stridor, respiratory distress, ball-valving glottic lesion
  - Pulmonary dissemination nearly uniformly fatal
- Types
  - Juvenile onset (<12 years old): more common, more aggressive
  - Adult onset
- Treatment
  - Surgical debulking: laser, microdebrider, cold knife
  - Tracheostomy, avoid unless absolutely necessary
  - Adjuvant therapies: interferon, cidofovir
    - Indications >4 surgeries/year, distal pulmonary spread, rapid regrowth of disease with airway compromise

SUBGLOTTIC STENOSIS

- Congenital
- Acquired: trauma/intubation, chronic infection, chronic inflammatory disease, neoplastic disease
- Cotton–Myer grading system
  - I: < 50 %
  - II: 51–70 %
  - III: 71–99 %
  - IV: no detectable lumen, complete obliteration
- Surgical treatment
  - Grade I/II: laser, dilation, cold knife
  - Grade III/IV: tracheostomy, laryngotracheal reconstruction (cricoid split with anterior ± posterior cricoid augmentation), cricotracheal resection
  - Single stage (no postoperative tracheotomy present) versus double stage (persistent postoperative tracheotomy with staged decannulation)

POSTERIOR GLOTTIC STENOSIS

- Classification
  - I: interarytenoid adhesion
    - Treatment: observation, endoscopic lysis
  - II: posterior commissure stenosis
    - Treatment: observation, endoscopic/open repair
  - III: posterior commissure stenosis with unilateral cricoarytenoid fixation
    - Treatment: endoscopic/open repair, tracheostomy
  - IV: posterior commissure stenosis with bilateral cricoarytenoid fixation
    - Treatment: tracheostomy, open repair

TRACHEAL OBSTRUCTION

- Tracheal stenosis
  - Acquired/inflammatory
  - Complete tracheal rings (congenital)
  - Surgical management: observation, endoscopic excision, tracheoplasty, segmental resection, slide tracheoplasty
- Tracheobronchomalacia
  - Immature tracheal cartilage with dynamic collapse
  - May require surgical decompression if due to extrinsic vascular compression
    - Innominate artery (anterior)
    - Double-aortic arch
    - Right aortic arch
    - Anomalous right subclavian artery (dysphagia lusoria)
    - Pulmonary artery sling
    - Pulmonary artery dilation

TRACHEOESOPHAGEAL FISTULA

- Types
  - Esophageal atresia with distal TEF (85 %)
  - Isolated esophageal atresia (10 %)
  - H-Type TEF (4 %)
  - Esophageal atresia with proximal TEF (0.5–1.0 %)
  - Esophageal atresia with proximal and distal TEF (0.5 %)

- Generally present with immediate feeding problems and aspiration with inability to pass feeding tube
  - H-type may present later with recurrent pneumonia
  - Diagnosed with fluoroscopy, endoscopy
  - Surgical correction required, risk of postoperative stricture

CAUSTIC INGESTION

- Acidic ingestion leads to coagulative necrosis (superficial)
- Alkaline ingestion leads to liquefactive necrosis (deep)
- Management:
  - NPO; IVF; do not induce vomiting
  - Reflux management
  - Empiric antibiotics debated
  - Lathyrogens may inhibit stricture formation
  - Esophagoscopy at 24–72 h
    - Consider nasogastric tube placement (stent)
    - Increased risk of iatrogenic perforation after 72 h
  - Grading:
    - Grade 1: mucosal erythema
    - Grade 2: mucosal erythema with non-circumferential exudates
    - Grade 3: circumferential exudates
    - Grade 4: circumferential exudates with perforation
  - Observation for grade 1–2 lesions; consider steroids
  - More aggressive management for grade 3–4 lesions; may require esophagectomy

ESOPHAGEAL FOREIGN BODIES

- Anatomical structures compressing esophagus, points of potential location for foreign bodies
  - Cricopharyngeus
  - Aortic arch
  - Left mainstem bronchus
  - Lower esophageal sphincter
- Some foreign bodies can be followed with serial X-rays to ensure passage, observation for 24 h
- Batteries ("double-halo sign") and sharp objects may lead to catastrophic complications and mortality and should be promptly removed
- Food impaction
  - Consider evaluation for esophageal stricture, peristaltic dysfunction, and/or biopsy for eosinophilic esophagitis (>15 eosinophils per high-power field)

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Chapter 5
Pediatric Otology and Cochlear Implants

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PEARLS

- The work-up for congenital sensorineural hearing loss should consist of at least an EKG, ophthalmologic evaluation, and an imaging study (MRI/CT)
  - MRI can be obtained early on when infant is very young, and may sleep through study without the need for sedation
  - Eye exam is important if patient has at least one special sensory impairment
  - Genetics evaluation may be useful for counseling and prognostic information
  - Other studies can be obtained as dictated by individual cases, but "shotgun" approach to testing may be expensive and unnecessary
- Aural polyps in the external auditory canal should trigger suspicion for an associated underlying cause for exuberant inflammatory/granulation tissue reaction
  - Prior to biopsy of external auditory canal lesion, should consider imaging—rule out vascular or intracranial connection
- Steroids may be protective for sensorineural hearing loss in cases of meningitis; however, if persistent hearing loss, then may recommend cochlear implantation
- The importance of binaural hearing is becoming more accepted—hearing in noise, summation, squelch, and directionality
  - Bilateral cochlear implants demonstrate some improved objective measures

EXTERNAL AUDITORY CANAL PATHOLOGY

- External otitis
  - Most commonly caused by *Pseudomonas*, second most common—*Staphyloccous aureus*
  - Treatment: aural hygiene, debridement, ototopical antibiotic drops
- Aural polyps—granulation tissue formation which may be associated with any of the following:
  - Chronic suppurative otitis media, with or without cholesteatoma
  - Necrotizing otitis externa (temporal bone osteomyelitis)
    - Susceptible populations
      - Diabetes, poorly controlled
      - Immunosuppressed—leukemia, bone marrow transplant, organ transplant, etc.
  - Rhabdomyosarcoma
  - Langerhan's cell histiocytosis
    - Eosinophilic granuloma
      - Solitary or few indolent and chronic lesions of bone or other organs

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- Hand–Schuller–Christian disease
  - Multifocal, chronic disease commonly presenting with diabetes insipidus, proptosis, and lytic bone lesions
- Letterer–Siwe disease
  - Acute, fulminant disseminated disease

OTITIS MEDIA

- Shorter, narrower, more horizontal eustachian tube makes children uniquely prone to chronic and acute otitis media
- Risk factors: Gender, bottle feeding, sibling history of OM, daycare attendance, lower socioeconomic status, maternal smoking, craniofacial abnormalities, immunodeficiency
- Etiologic agents: *Streptococcus pneumoniae*, *Haemophilus influenza*, *Moraxella catarrhalis*, Group A *Strep*
- Sequelae: adhesive otitis media, chronic suppurative otitis media, tympanic membrane perforation, tympanosclerosis, tympanic membrane retraction pocket, cholesteatoma, ossicular necrosis, hearing loss, mastoiditis
  - Adenoidectomy may help with eustachian tube dysfunction—retraction pockets, recurrent need for tympanostomy tubes, etc
- Acute indications for myringotomy ± tympanostomy tube placement:
  - AOM in a seriously ill or toxic child, AOM unresponsive to antibiotics, suppurative complications of AOM, AOM in newborn or immunocompromised patient, AOM with facial paralysis, AOM with meningitis or other intracranial process
- Indications for tympanostomy tube placement:
  - Recurrent AOM (>3 episodes in 6 months, >4 episodes in 12 months)
  - Bilateral COME >3 months, unilateral COME >6 months; earlier for significant (>25 dB) hearing loss, speech/language delay, severe retraction pocket, disequilibrium/vertigo, tinnitus
- Complications of tympanostomy tube placement:
  - Otorrhea, granulation tissue, myringosclerosis, tympanic membrane perforation, cholesteatoma, early extrusion, plugged tube, loss of tube in middle ear, persistence

CONGENITAL SENSORINEURAL HEARING LOSS

- 50 % acquired, 50 % hereditary
- 1/3 of hereditary cases syndromic, 2/3 non-syndromic
- 80 % non-syndromic cases autosomal recessive, 15 % autosomal dominant, 5 % X-linked/mitochondrial inheritance
- Auditory brainstem response (ABR):
  - Newborn ABR waves I/II (eighth nerve), III (olivary complex), V (inferior colliculus)
  - Otoacoustic emissions (OAEs)
    - Spontaneous
      - Of little clinical use, not present in all patients
    - Evoked
      - TEOAE
      - DPOAE
- Continuing campaign for universal newborn hearing screening using ABR or OAEs
  - Referral for formal audiometric testing/sedated ABR if failure
- Auditory testing:
  - Behavioral observational audiometry: 0–6 months
  - Visual reinforcement audiometry: 6 months–2 years
  - Conditioned play audiometry: 2–5 years

- Work-up considerations:
  - EKG
  - Ophthalmology consult, SNHL may be associated with visual problems and maximize sensory input
  - Imaging—indicated for evaluation for cochlear implantation, in children with recurrent meningitis, with a history of sudden or progressive SNHL especially following head trauma, or where imaging results will impact patient counseling
    - CT
      - Advantages:
        - Lower cost
        - Increased availability
        - Speed/resolution of capturing images
        - Better visualization of bony labyrinth and osseous, inner ear structures
      - Disadvantages:
        - Radiation exposure
        - Difficult to assess the presence of cochlear nerve
    - MRI
      - Advantages:
        - Superior visualization of membranous labyrinth, internal auditory canal (can visualize cochlear nerve), high T2 intensity
        - Lack of ionizing radiation
      - Disadvantages:
        - More expensive
        - Increased length of time
        - Availability
  - Genetics consultation:
    - Counseling
    - Genetic testing:
      - Pendred gene mutations
      - Connexin 26: Product of gene GJB2; present in 30 % of non-syndromic congenital hearing loss; most common mutation in Caucasians is 35delG
      - Connexin 30
  - Other possible testing:
    - U/A
    - Basic metabolic profile (BMP)
    - CBC
    - TFTs
- Cochlear implant criteria:
  - Age 12 months or greater (evaluation can begin sooner)
  - Bilateral severe to profound hearing loss
  - Limited benefit from hearing aids (usually 3–6-month trial)
  - Strong family commitment
  - Educational plan and resources that emphasize the development of auditory skills
  - Note that implantation may occur earlier and without trial of hearing aids in the setting of progressive post-meningitic cochlear ossification
  - Contraindications: narrow IAC, cochlear nerve aplasia, Michel aplasia
- Central auditory processing disorder
  - Auditory neuropathy:
    - Normal OAEs
    - Absent ABR
    - Suggests CN VIII dysfunction
    - Worse outcomes with cochlear implantation

CONDUCTIVE HEARING LOSS

- Bone-conducting hearing aids
  - Atresia/microtia
  - Chronic otorrhea or abnormally small EAC where air-conducting hearing aids are insufficient
  - Ossicular chain reconstruction if conductive hearing loss following cholesteatoma resection
  - Atresiaplasty only in carefully selected patients according to Jahrsdoerfer criteria
    - Presence of stapes, probably most important single factor for prognosis of good hearing outcome (closure of air-bone gap to <20 dB)
  - Middle-ear implants may be more available in the future, indications/applications still under review

CONGENITAL INNER EAR MALFORMATIONS

- Membranous (~80 %)
  - Not visible using current imaging modalities
  - Schiebe (cochleosaccular aplasia: most common), Bing-Siebenmann (membranous aplasia of both cochlear and vestibular portions, bony labyrinth wnl), and Alexander (cochlear duct aplasia, especially affecting basal turn) dysplasia
  - Associated with Jervell–Lange-Nielsen, Refsum, Usher, and Waardenburg syndromes
- Bony and membranous (~20 %)
  - Michel aplasia: complete labyrinthine aplasia (third week)
- Cochlear anomalies
  - Common cavity: fourth week
  - Cochlear aplasia: fifth week
  - Cochlear hypoplasia: sixth week
  - Incomplete cochlear partitions ("Mondini malformation"): seventh week
    - Associated with Pendred, branchio-oto-renal, Waardenburg, Treacher Collins, Wildervanck (Klippel–Feil), and Mobius syndromes
  - Labyrinthine anomalies
    - Present in 40 % of patients with cochlear anomalies
    - Dysplasia more common than aplasia
    - Lateral SCC develops last and is most commonly affected
  - Aqueductal anomalies
    - Enlarged vestibular aqueduct: >1.5 mm in diameter; ~40 % of patients will progress to profound SNHL classically precipitated by head trauma
    - Enlarged cochlear aqueduct: Normal ~3–4 mm diameter
  - Internal auditory canal anomalies
    - Narrow (<3 mm) associated with absent or hypoplastic CN VIII
    - Widened (>10 mm) associated with stapes gusher

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PART II
Rhinology/Allergy
Section Editor: Zara M. Patel, MD

Chapter 6
Rhinology

Katherine Hayes and Zara M. Patel

PEARLS

- Osteomas are the most common benign sinonasal lesion with the frontal sinus the most common location
- On sinus MRI, dried secretions show as hyperintense on T1, hypointense on T2, and polyps show hypointense on T1, hyperintense on T2
- Rhinoscleroma is caused by *Klebsiella rhinoscleromatis* with histopathology showing Mikulicz cells (macrophages containing pathogen) and Russell bodies (plasma cells)

ANATOMY

- Nasal Framework
  - Cartilages: Upper lateral, lower lateral, accessory sesamoid, quadrilateral septal
  - Bones: Nasal bones, vomer, perpendicular plate of the ethmoid, maxillary crest, palatine bone, anterior nasal spine of maxilla
  - Lateral nasal wall: inferior, middle, superior (sometimes supreme) turbinates
    - Inferior meatus (inferior to inferior turbinate): nasolacrimal duct opening (valve of Hasner)
    - Middle meatus (inferior to middle turbinate): Semilunar hiatus opens to ethmoid infundibulum which receives drainage from maxillary, anterior ethmoid, and frontal sinuses
    - Superior meatus (anteroinferior to superior turbinate): opening to posterior ethmoid sinuses
    - Sphenoethmoidal recess (posterosuperior to superior turbinate): opening to sphenoid sinuses
- Blood supply
  - External carotid system
    - Facial artery
      - Angular artery (located in alar-facial groove): nasal sidewall, tip, and dorsum
      - Superior labial artery: columella, lateral wall
    - Internal maxillary artery (divides into terminal branches in pterygopalatine fossa)
      - Sphenopalatine artery (enters sphenopalatine foramen on lateral wall at junction of middle turbinate basal lamella and orbital wall)
      - Lateral nasal artery: anterior portion of lateral nasal wall
      - Posterior septal artery: courses over sphenoid face and supplies nasal septum
      - Descending palatine artery (found in greater palatine canal, then enters nasal cavity via incisive foramen): anterior nasal septum and nasal floor

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- Internal Carotid System
  - Ophthalmic artery terminates into anterior and posterior ethmoid arteries
    - Anterior ethmoid: Anterior and superior septum, lateral wall, and roof of nasal cavity
    - Posterior ethmoid: Superior turbinate, posterior septum
- Nasal Plexuses
  - Kiesselbach's plexus (Little's area): anteroinferior 1/3 of nasal septum; junction of sphenopalatine, greater palatine, anterior ethmoid, and superior labial arteries
  - Woodruff's plexus: posterior portion of inferior meatus and nasopharynx; junction of posterior nasal, sphenopalatine, and ascending pharyngeal veins
- Venous drainage
  - Corresponds to arterial supply
  - "Danger triangle" = area of skin from the corners of the mouth to the bridge of the nose. Veins draining this region are valveless, so skin infection can easily spread retrograde intracranially via angular vein → inferior ophthalmic vein → cavernous sinus

- Lymphatics
  - Anterior → facial nodes or upper cervical nodes
  - Posterior → retropharyngeal nodes
- Innervation
  - Muscles of facial expression: CN VII
  - Sensory: branches of V1 and V2 for pain, temperature, and touch; CN I at roof of nasal cavity for olfaction
  - Parasympathetic (acetylcholine and VIP): superior salivatory nucleus of CN VII →greater superficial petrosal nerve → vidian nerve → sphenopalatine ganglion (synapse) → terminates on blood vessels and glands of the nasal mucosa (induces vasodilation and secretion)
  - Sympathetic (NE): superior cervical ganglion (synapse) → deep petrosal nerve → vidian nerve → terminates on blood vessels and glands of the nasal mucosa (induces vasoconstriction)
- Paranasal sinuses
  - Maxillary sinus
    - Two periods of growth: age 3 and age 7–12, coincides with dental growth periods
    - Volume 15 cm^3, triangular space completely bound within bone of maxilla
    - Ostium drains into middle meatus; accessory ostia present up to 30 % of the time
    - Separated from first and second molars by thin layer of bone, can be dehiscent; dental infections can spread to sinus via this route and chronic infection or removal of these teeth can cause an oroantral fistula
  - Ethmoid sinuses
    - Reach adult size by age 12, separated into anterior (2–8 cells)/posterior (1–5 cells) by basal lamella of middle turbinate, volume 15 cm^3
    - Bound by sphenoid face posteriorly, lamina papyracea laterally, middle and superior turbinates medially, and skull base superiorly
    - Keros classification: can assist in determining risk of violating skull base during FESS
      - I: Cribriform plate 1–3 mm inferior to fovea ethmoidalis
      - II: 4–7 mm inferior
      - III: 8–16 mm inferior
    - Lamellae of ethmoid sinus:
      - Uncinate process (forms medial wall of ethmoid infundibulum)
      - Ethmoid bulla (largest anterior ethmoid air cell)
      - Basal lamella of middle turbinate (separates anterior from posterior ethmoid)
      - Lamella of superior turbinate
    - Retrobullar recess = space posterior to ethmoid bulla if bulla not fused to basal lamella
    - Suprabullar recess = space superior to ethmoid bulla if not fused to skull base
    - Agger nasi = most anterior ethmoid air cell, pneumatization of lacrimal bone, can block frontal recess

- Supraorbital ethmoid cell = always posterolateral to true frontal sinus ostium can be confused for frontal sinus septation
- Haller cell = infraorbital ethmoid cell pneumatizing into the maxillary sinus, can block maxillary sinus ostium
- Onodi cell = posterior ethmoid cell located superolateral to sphenoid sinus, may interface with or contain the internal carotid and optic nerve
- Ostiomeatal complex vs. ethmoid infundibulum vs. semilunar hiatus
  - Semilunar hiatus = 2D gap between uncinate and ethmoid bulla
  - Infundibulum = 3D space bounded by uncinate medially, lamina papyracea laterally, and frontal process of maxilla anterosuperiorly = route of drainage for maxillary, anterior ethmoid, and frontal sinuses
  - Ostiomeatal complex = includes middle turbinate, uncinate process, semilunar hiatus, ethmoid bulla, and infundibulum = functional drainage pathway for maxillary, anterior ethmoid, and frontal sinuses

- Frontal sinus
  - Pneumatized portion of frontal bone
  - Drains through ostium into frontal recess (bounded by agger nasi anteriorly, ethmoid bulla posteriorly, lamina papyracea laterally, middle turbinate medially, skull base superiorly)
  - Drainage pattern determined by attachment of uncinate process (UP)
    - Attached to lamina papyracea (most common 60–70 %) → drains medial to UP
    - Attached to skull base (5–15 %) or middle turbinate (10–20 %) → drains lateral to UP
  - Visible on X-rays by age 2–6, continues growth into adolescence
  - Types of frontal cells:
    - I: Single cell above the agger nasi
    - II: Two or more cells above the agger nasi
    - III: Single cell extending from the agger nasi superiorly into frontal sinus
    - IV: Cell isolated within frontal sinus
- Sphenoid sinus
  - Pneumatization from age 3–18
  - Landmarks: 30° angle relative to nasal floor, 1/3 distance superiorly from choana to skull base, 7 cm from nasal sill, at the same latitude as the roof of the maxillary sinus
  - Closely related to internal carotid, optic nerve, vidian canal, foramen rotundum, cavernous sinus; extremely variable intersinus septum (Fig. 6.1)

PHYSIOLOGY

- Histology
  - Pseudostratified ciliated columnar epithelium covers majority of nasal cavity except nasal vestibule (covered by stratified squamous epithelium)
    - Ciliated columnar cells (9 + 2 microtubules w/dynein arms, beat 10–20×/s), nonciliated columnar cells (microvilli covering surface increase surface area for humidification and warming), basal cells, and goblet cells (produce mucin which traps irritants)
- Mucin physiology
  - Sol layer = deep lubricating layer, produced by microvilli
  - Gel layer = superficial viscous layer, produced by goblet cells, traps particles
  - Mucus flows → nasopharynx → secretions swallowed
- Olfactory epithelium
  - Located along upper 1/3 of septum, medial superior/supreme turbinates, roof of nasal cavity
  - Gets roughly 15 % of nasal airflow
  - Neural sensory contributions from CN I and small contribution from CN V
  - Pseudostratified columnar epithelium with multiple different cell types:
    - Bipolar olfactory neurons (develop from neuroblasts; have cilia that do NOT beat)

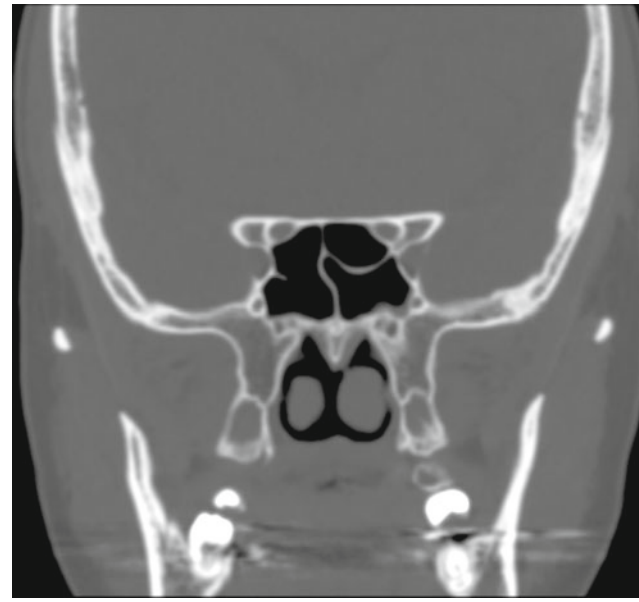

Fig. 6.1 Sphenoid sinus surrounded by critical structures (seen bilaterally, named from superior to inferior): optic nerve, carotid artery, V2, vidian nerve

- Sustentacular cells (support cells, have microvilli, protective function)
- Bowman's glands (produce secretions that bathe olfactory epithelium, required to dissolve odorants prior to nerve stimulation)
- Basal cells (differentiate into neurons or sustentacular cells)

- Hyposmia/Anosmia: Caused by damage to nerve itself, inflammation, or obstruction of airflow preventing odorants from reaching the nerve
  - Most common causes are obstructive sinonasal disease/polyps or URI with suspected viral attack on nerve causing inflammation and dysfunction
  - Also consider trauma, tumors, iatrogenic surgical damage, chemical irritant or medication-induced damage, endocrine or metabolic disorders (e.g., hypothyroidism), age-related loss of smell (presbyosmia), or early signs of neurologic disease (Alzheimer's or Parkinson's disease)
  - Foster Kennedy Syndrome = unilateral anosmia, optic atrophy, and papilledema due to frontal lobe masses
  - Kallman's syndrome = hypogonadotropic hypogonadism and anosmia (failure of hypothalamus to secrete GnRH, several types of inheritance including x-linked and autosomal dominant)
  - Evaluation and management of hyposmia/anosmia
    - Full history and physical examination including neurologic exam and rigid nasal endoscopy to identify any obvious possible underlying causes
    - Treat patients medically with course of oral steroids, nasal steroid spray, and nasal saline irrigations, then reevaluate in clinic to assess symptoms. Consider MRI for persistent symptoms to rule out masses/tumors.
    - UPSIT (University of Pennsylvania Smell Identification Test) can be used to identify malingering (score <10/40), for workman's compensation documentation, and for research purposes
- Evaluation of the nasal airway
  - Main functions: humidification, warming, filtration, olfaction, alteration of airway resistance
  - Nasal air flow = accounts for 50 % of total airway resistance
    - Internal nasal valve = most narrow part of nasal airway; bounded by nasal septum, upper lateral cartilage, head of inferior turbinate, and nasal floor

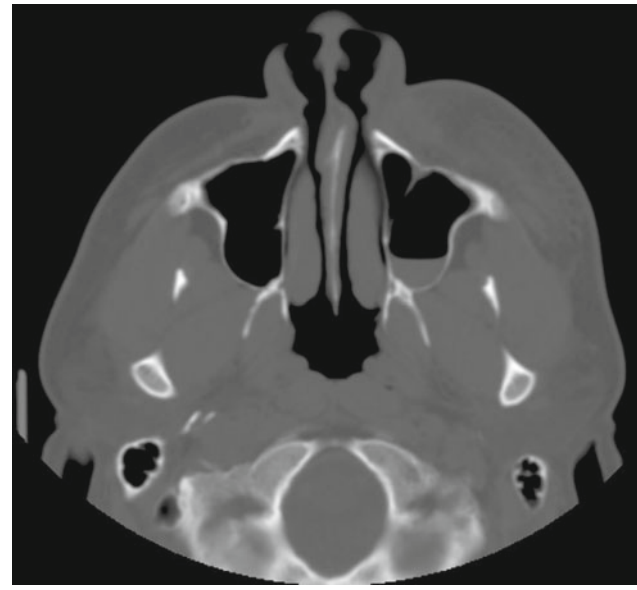

Fig. 6.2 Air-fluid level seen in left maxillary sinus, indicating purulent secretion (and not blood) in this case, as there is no history or sign of trauma

- Evaluated by Cottle maneuver (subjective improvement in nasal breathing with lateral distraction of the ipsilateral cheek indicates internal valve collapse)
- Nasal cycle = physiologic variation in vascular flow and sympathetic tone of nasal airway, engorgement of nasal tissue which alternates from one side to the other every 2–6 h

○ Objective measures of nasal airway resistance (commonly used only in research)

- Rhinomanometry = placement of sensors in the nose or nasopharynx which calculate pressure generated by nasal airflow through the nose before and after nasal decongestant administered. Cannot localize site of obstruction, used in research only.
  - > 35 % decrease in airway resistance = mucosal congestion
  - < 35 % decrease in airway resistance = structural abnormality
- Acoustic rhinometry = uses sound waves to measure the cross-sectional area at points along the nasal airway. Can identify narrow points in airway but unable to determine whether these narrow areas have any effect on nasal airflow.

IMAGING

- Air-fluid level = purulent secretions or blood after trauma (Fig. 6.2)
- Dried secretions = hyperintense on T1, hypointense on T2
- Polyps = hypointense on T1, hyperintense on T2
- Mycetoma (fungal ball) shows bony thickening of sinus walls on CT, hypointense on T1/T2
- Allergic fungal sinusitis CT findings include a rim of low density within sinus with central mucin, calcifications, and bony expansion/erosion (Fig. 6.3)
- Inverting papilloma shows bony thickening at attachment site on CT
- Juvenile nasal angiofibroma enhances on CT (Fig. 6.4), hyperintense on MRI with flow voids; Holman-Miller sign = anterior bowing of posterior maxillary sinus wall
- Fibrous dysplasia has ground-glass appearance on CT, hypointense on T2 MRI (Fig. 6.5)

RHINITIS

- Inflammation of nasal mucosa, affects 25 % of general population
  - ○ Allergic: IgE-mediated release of immune mediators (histamine, leukotrienes, etc.) from mast cells in response to allergen exposure, type I hypersensitivity reaction

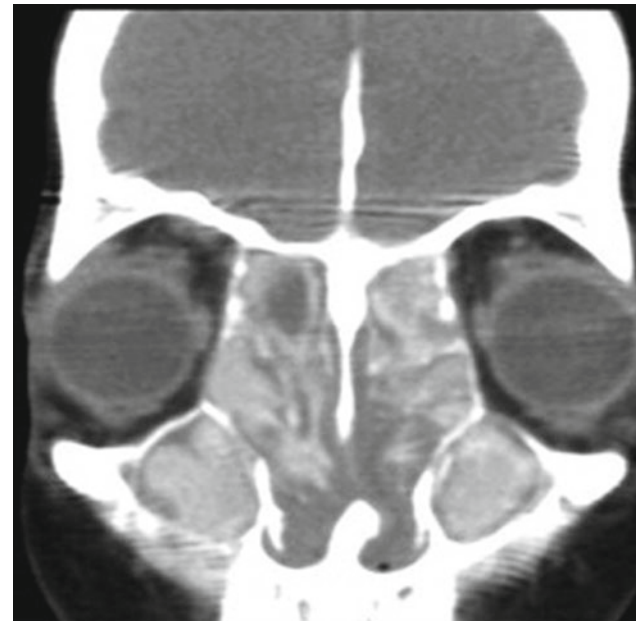

Fig. 6.3 Typical AFS imaging showing heterogeneous opacification of the sinuses and hypertelorism (fish eye effect) as the sinus cavity expands outwards, displacing the orbits laterally, to accommodate accumulating polyps and fungal mucin

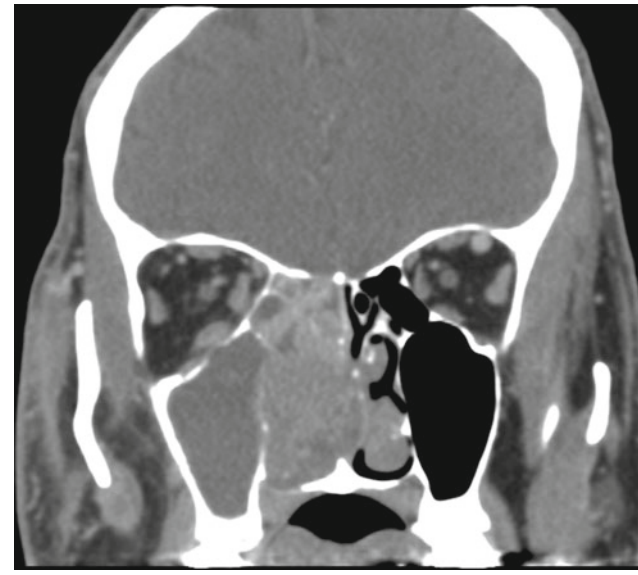

Fig. 6.4 Right maxillary sinus, obstructed by enhancing mass seen within the right nasal cavity and ethmoid region, showing accumulation of post-obstructive secretions

- Symptoms = nasal congestion, sneezing, eye irritation, thin clear rhinorrhea
- Immediate phase = within 5 min
  - Cross-linking of IgE and degranulation of mast cells releases histamine, leukotrienes, prostaglandin, and platelet activating factor (PAF)
  - Increases vascular permeability, produces main symptoms of rhinorrhea, sneezing, and congestion
- Late phase = peaks at 6 h, lasts up to 24 h
  - Recurrence of symptoms due to recruitment of inflammatory cells by previously released cytokines

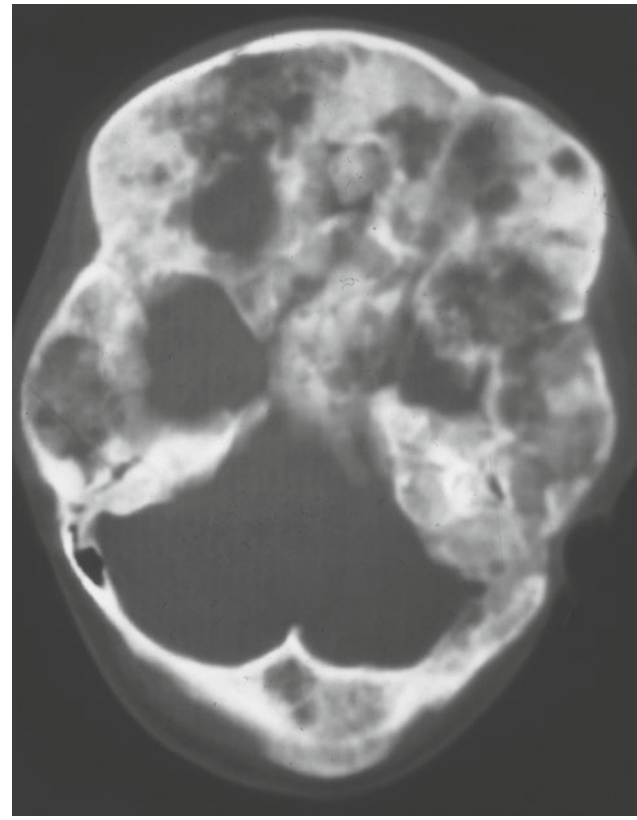

Fig. 6.5 Classic "ground-glass" appearance of the bone in fibrous dysplasia

- Perennial (i.e., dust mites, insects, dogs, or cats) versus seasonal (i.e., trees, grasses)
- Diagnosed via history, skin prick testing or serum RAST
- Treatment
  - Avoidance of specific allergens, topical antihistamine, anticholinergic, or steroid nasal sprays, oral antihistamines, antileukotrienes, antibody-directed immunomodulators, and subcutaneous or sublingual immunotherapy

○ Atrophic rhinitis
- Seen after radical nasal surgery with over-resection of inferior and middle turbinate tissue, termed by some "empty nose syndrome"
- Symptoms = mucosal atrophy, thick foul-smelling crust (ozena)
- Pathology = transformation of respiratory epithelium into keratinized squamous epithelium, +/– superinfection with *Klebsiella ozoena*
- Treatment = saline irrigations or gels, topical oil-based lubrication, alternative irrigations such as xylitol or alkalol. Surgical intervention limited to restructuring turbinate morphology

○ Nonallergic Rhinitis with Eosinophilia (NARES) = rhinorrhea, nasal pruritus, and sneezing related to asthma and aspirin sensitivity
- No association with IgE-mediated hypersensitivity, negative allergy tests
- Treatment = Symptomatic relief with nasal steroid spray, antihistamines

○ Vasomotor = excessive parasympathetic tone of nasal mucosa
- Symptoms similar to allergic rhinitis (with hypersecretion of clear, thin mucus as main symptom) but allergy does not play a role
- Triggers include exercise, anxiety, foods (gustatory rhinitis) or changes in temperature
- Can also be seen in autonomic dysregulation, commonly seen in elderly patients, or after stroke

- Treatment = Elimination of triggers and environmental irritants if possible, topical nasal steroid or anticholinergic sprays, or surgery (surface turbinate cautery, partial turbinectomy, or nasal branches of vidian neuronectomy)
- Medication-induced
  - Antihypertensives, antidepressants, anti-inflammatory drugs
  - Rhinitis medicamentosa = rebound congestion caused by prolonged use of topical alpha adrenergic medications
  - Treatment = stop use of topical vasoconstrictors, begin nasal saline +/– nasal steroid spray, may use oral steroid burst for severe nasal obstruction
- Hormone-induced (pregnancy, menstruation, oral contraceptives, hypothyroidism)
  - Estrogen inhibits ACh-esterase → elevated ACh levels → increased parasympathetic tone
  - Treatment = conservative measures including nasal saline, avoid decongestants while pregnant
- Infectious
  - Usually viral (most commonly rhinovirus, coronavirus) but can predispose to bacterial superinfection, managed symptomatically
  - Bacterial colonization:
    - MRSA colonization of anterior nasal cavity commonly found in health care workers, hospitalized patients, treated with Mupirocin ointment to nasal cavity
    - Rhinosporidiosis
      - *Rhinosporidium seeberi*, a eukaryotic parasitic pathogen
      - Symptoms = unilateral nasal obstruction, epistaxis, friable polyps
      - Pathology = pseudoepitheliomatous hyperplasia, chitinous shells
      - Treatment = surgical excision
    - Rhinoscleroma
      - *Klebsiella rhinoscleromatis*
      - Symptoms = three stages
        - Catarrhal (nonspecific crusting)
        - Granulomatous (epistaxis, friable mucosa, nodules throughout upper respiratory tract)
        - Sclerotic (sclerosis and fibrosis)
      - Pathology = Mikulicz cells (macrophages containing pathogen) and Russell bodies (plasma cells)
      - Common in Central America, Africa, India
      - Treatment = long-term antibiotics

RHINOSINUSITIS

- Fungal Sinusitis
  - Invasive
    - Acute
      - Occurs in immunocompromised patients (AIDS, malignancy, DM, immunosuppressive meds); fungal invasion into mucosa, soft tissues, and bone, seen as invasion of blood vessels on microscopy
      - Presents as pallor or eschar in nasal cavity or along palate +/– numbness or pain, CT findings of mucosal thickening, sinus opacification (usually maxillary sinus), and infiltration of retroantral fat
      - Rapidly progressive (over hours) and can be fatal due to intracranial extension
      - *Mucormycosis*: more common in uncontrolled DM (diabetic ketoacidosis), broad-based ribbon-like nonseptate hyphae with 90° branching
      - *Aspergillus fumigatus*: more common in immunocompromised patients, narrow septate hyphae with branching at acute 45° angles
      - Treatment = aggressive surgical debridement until healthy bleeding tissue is reached, IV antifungals, treatment of underlying disease process or adjustment of medications to alleviate immunosuppression

- Chronic Granulomatous
  - Fungal invasion of sinonasal tissue with indolent course, produces granulomatous inflammatory response
  - *Aspergillus flavus* most common
  - Treatment = surgical debridement + systemic antifungals
- Noninvasive
  - Mycetoma (fungus ball)
    - Isolated sinus opacification, usually maxillary or sphenoid
    - *Aspergillus* common, although fungal cultures can be negative
    - Treatment = surgical removal
  - Allergic fungal rhinosinusitis
    - Bent & Kuhn Criteria for diagnosis:
      - History of Type I Hypersensitivity
      - Nasal polyps
      - Allergic mucin (contains eosinophils or their breakdown products Charcot-Leyden crystals)
      - Presence of fungal elements on stain or culture (*Aspergillus* or dematiaceous fungi)
      - Characteristic CT findings (unilateral opacification, sinus wall erosion or expansion, heterogeneous density)
      - Lack of invasion
    - Treatment = FESS to open sinuses and remove accumulated thick mucus and polyps, allergy testing and immunotherapy if positive to prevent relapse, often these patients benefit from steroid, whether oral or topical

- Rhinosinusitis
  - Classification
    - Acute < 4 weeks
      - Recurrent ARS requires four or more episodes with complete resolution of symptoms between episodes
    - Subacute 4–12 weeks
    - Chronic > 12 weeks
      - CRSsNP (without nasal polyps) +/– eosinophilia or CRSwNP (with nasal polyps) +/– eosinophilia
      - Acute exacerbation of CRS = worsening of chronic symptoms with return to baseline after treatment but without complete resolution of symptoms
    - Criteria for diagnosis: inflammation of nose and paranasal sinuses characterized by specific symptoms
      - Older classification required two major factors (facial pain, nasal congestion, nasal discharge, hyposmia, purulence in nasal cavity) or one major factor and two minor factors (headache, fever, fatigue, cough, ear pain, or pressure)
      - 2012 European Position Paper on rhinology classification requires two symptoms—one must be nasal congestion or nasal discharge (other sx = endoscopic signs of edema, purulent discharge, polyps, and mucosal changes on CT)
        - Diagnosis should be supported by endoscopic or CT evidence of disease
- Acute rhinosinusitis
  - Etiology
    - Viral (most commonly rhinovirus, coronavirus) or bacterial (most commonly *Streptococcus pneumoniae, Haemophilus influenzae, Moraxella catarrhalis*)
    - Pathophysiology: Viral infection causes upregulation of inflammatory factors and leads to mucus hypersecretion and mucosal edema. In combination with a variety of predisposing factors (e.g., trauma, anatomic obstruction, ciliary dysmotility, immune factors), this can lead to mucus stasis or obstruction of sinus outflow tracts → provides ideal setting for bacterial growth

- Treatment
  - Supportive care and reassurance for mild symptoms
  - Antibiotics for severe symptoms (first line = amoxicillin or cephalosporins; if symptoms do not improve then second line = amoxicillin-clavulanate or respiratory quinolones), culture-directed, if possible
  - Nasal saline irrigations
  - Intranasal steroids, short course oral steroids (can improve facial pain, headache)
  - Oral analgesics and mucolytics
- Complications:
  - Orbital complications—described in increasing severity by Chandler's classification
    - Preseptal cellulitis
      - Periorbital soft tissue erythema/edema
      - No chemosis, vision changes, or dysmotility
      - Tx = oral antibiotics
    - Orbital cellulitis
      - Inflammation within orbit
      - Presence of chemosis, proptosis, limited mobility, and/or vision changes
      - Tx = IV antibiotics + functional endoscopic sinus surgery (FESS)
    - Subperiosteal abscess
      - Similar to orbital cellulitis WITH presence of pus between orbital periosteum and bone
      - Tx = IV antibiotics + FESS and surgical drainage of abscess. Can consider antibiotics alone for a small abscess in a clinically stable patient <2–4 years old without vision change, but should monitor closely with immediate surgical intervention available for signs of progression
    - Orbital abscess
      - Pus located within the orbit
      - Severe proptosis and ophthalmoplegia
      - Tx = IV antibiotics + FESS and surgical drainage
    - Cavernous sinus thrombosis
      - Structures which pass through cavernous sinus: CN III, IV, V1, V2, VI, internal carotid artery, and multiple venous channels
      - Symptoms = ophthalmoplagia, headache, periorbital sensory loss, papilledema/proptosis/periorbital edema/vision loss (from venous congestion); CN VI first to show effects
      - Tx = IV antibiotics + FESS (+/– anti-thrombotics, controversial)
      - Infections from sinuses spread directly or via hematogenous spread, most commonly from ethmoids
      - Always obtain ophthalmology consultation and document visual acuity, extent of proptosis, measurement of pressure, and eye movements (important to perform forced duction testing to examine if limit to EOM is due to pain or pathology)
      - General indications for OR = change in or loss of vision or EOM, or any other cranial nerve deficit
  - Intracranial complications
    - Epidural, subdural, or intracranial abscess (Tx = IV antibiotics +/– neurosurgical drainage)
    - Meningitis = headache, altered mental status, high fever, neck stiffness (Tx = first obtain head CT, LP if no intracranial mass seen on CT, IV antibiotics)
    - Infection spreads via direct extension, along olfactory nerve sheath, or hematogenously (foramina of Breschet = venous perforators connecting intracranial and extracranial vascular supply), most common from frontal sinus
  - Pott's Puffy Tumor
    - Osteomyelitis of anterior table of frontal sinus
    - Infection transmitted via diploic veins → swelling of adjacent forehead soft tissue
    - Tx = IV antibiotics, FESS and surgical debridement of sequestered bone

- Mucocele
  - Expansile collection of secretions trapped within an obstructed sinus
  - CT = sinus expansion and bony erosion; MRI T2 = hyperintense
  - Tx = FESS, with open procedures for inaccessible lesions
- Superior Orbital Fissure Syndrome
  - Due to infectious spread to or trauma involving superior orbital fissure
  - Structures included: III, IV, V1, VI, ophthalmic vein, and sympathetic fibers
  - Symptoms = ophthalmoplegia, ptosis, proptosis, ipsilateral forehead paresthesia, and fixed dilated pupil
- Orbital Apex Syndrome
  - Symptoms of superior orbital fissure syndrome + involvement of CN II (vision change or blindness)

- Chronic Rhinosinusitis (CRS)
  - Contributing factors
    - Microbial factors
      - Biofilms = aggregate of bacteria encased in self-produced polysaccharide matrix which confers antibiotic resistance
      - Superantigens = bacterial exotoxins which trigger a much larger downstream T-cell activation than traditional exotoxins without requiring antigen specificity
    - Environmental factors (smoking, pollution, allergens)
    - Anatomic factors (septal deviation, concha bullosa, infraorbital cells, scarring, etc.)
    - Mucociliary dysfunction
      - Primary ciliary dyskinesia (PCD) = AR defect in dynein arms of cilia of respiratory tract and reproductive system → URIs, otitis media, infertility
      - Kartagener's syndrome = PCD + situs inversus and bronchiectasis
      - Cystic fibrosis = AR mutation in CFTR gene which impairs chloride transport → thick mucus prevents clearing of bacteria (diagnosed with sweat chloride test)
    - Immunologic factors
      - Allergy
        - Nasal mucosal congestion which occurs in allergic rhinitis → obstruction of sinus ostia → impaired sinus ventilation → mucus retention and infection
      - Samter's Triad
        - Sinonasal polyposis, asthma, and aspirin sensitivity
        - ASA ingestion → inhibits cyclo-oxygenase metabolism of arachidonic acid → stimulates 5-lipo-oxygenase and production of leukotrienes → asthma and allergy effects
  - Pathophysiology is complex and multifactorial, involving any of the above listed factors which contribute to mucosal inflammation
  - Treatment
    - 3–6 weeks treatment with antibiotics (amoxicillin-clavulanate, respiratory quinolones, second-generation cephalosporins, etc.)
    - Topical nasal steroid spray, oral steroid taper, nasal saline irrigation, mucolytics
    - Treatment of any underlying allergy
    - Surgery for patients refractory to medical management, mucoceles, or signs of orbital/intracranial complications

EPISTAXIS

- Anterior source 90 % of the time
  - Etiologies
    - Local
      - Digital trauma, facial trauma
      - Inflammation or infection
      - Septal deviation or perforation (aberrant airflow causes drying of tissues which become friable)

- Dry nasal environment (CPAP, decongestants, dry climates)
- Foreign bodies (local irritation or secondary to attempts at removal)
- Tumors (secondary to erosion into vessels)
- Carotid aneurysm (rare, usually a late complication occurring several years after trauma accompanied by monocular blindness)

■ Systemic
- TB, Wegener's granulomatosis (respiratory tract granulomas, vasculitis, and glomerulonephritis), sarcoidosis (noncaseating granulomas), syphilis
- Symptoms = crusting, friable mucosa, septal perforation
- Osler Weber Rendu Disease (Hereditary hemorrhagic telangiectasia)
  - Autosomal dominant, numerous small vascular malformations of the skin and mucosal linings of the aerodigestive tract, AVMs of larger organs (lung, liver, brain)
  - Epistaxis and GI bleeding common, onset at puberty and worsens with age
  - Lack of normal vascular smooth muscle, impairs ability to contract
  - Treated with bipolar cautery or laser ablation, septodermoplasty, or nasal closure as a last resort
  - Use of bevacizumab (Avastin), a VEGF inhibitor, increasing, currently under study

■ Blood dyscrasias
- Alcoholism, malnutrition, malignancy, immunodeficiency, liver or kidney failure
- Characterized by reduced platelet aggregation, prolonged bleeding time; treat with platelet transfusion for severe bleeds
- Von Willebrand disease
  - Deficiency of von Willebrand protein leads to defective platelet adhesion and decreased activity of clotting factor VIII; treat with DDAVP, cryoprecipitate, or von Willebrand protein concentrate for severe bleeds
- Hemophilia
  - Deficiency in clotting factor VIII (type A) or IX (type B); treat with factor VIII or IX concentrate
- Drugs (i.e., NSAIDs, Plavix, Coumadin)
  - NSAIDs, ASA, and Plavix characterized by reduced platelet function; treat with platelet transfusion
  - Coumadin inhibits formation of multiple clotting factors; reverse with Vitamin K and FFP

○ Management: Determine acuity and remember ABCs; ensure patient is stable and address any systemic disease or obvious associated comorbidity

■ Topical vasoconstriction (e.g., oxymetazoline) and manual pressure for minor bleeds

■ Cauterization (silver nitrate, electric, or KTP/argon laser)

■ Nasal packing can be anterior or posterior, ranging from a variety of nasal tampon devices to vaseline gauze packing
- Anterior packing
  - Removed after 2–5 days depending on severity and etiology
  - Can be managed as an outpatient unless patient is elderly or has underlying coagulopathy which requires treatment
  - Complications: toxic shock syndrome (give anti-staphylococcal antibiotic while packing in place), sinusitis from blockage of sinus ostia, septal necrosis/perforation
- Posterior packing
  - Often requires sedation due to discomfort
  - Requires inpatient stay to monitor airway; elderly or frail patients and those with underlying cardiopulmonary disease should be monitored in intensive care unit with low threshold for intubation
  - Complications: airway compromise, nasal-vagal reflex (hypotension and bradycardia), alar necrosis

- Greater palatine foramen injection (local anesthetic 1 % lidocaine 1:100,000 epinephrine infiltrated into foramen—must aspirate prior to injection to ensure not in the vessel) helps control posterior bleeds
- Surgical evaluation with ligation of bleeding vessel(s)
  - Internal maxillary artery (IMA): open posterior maxillary sinus wall, identify branches of IMA in pterygopalatine foramen and ligate with clips
  - Sphenopalatine artery (SPA): endoscopically dissect in a subperiosteal plane along the medial inferior maxillary wall just anterior to lammellar attachment of middle turbinate, identify SPA as it exits at crista ethmoidalis and ligate with clip or cauterize
  - Anterior/posterior ethmoid arteries (AEA/PEA): can either identify endoscopically and cauterize with bipolar cautery within the nasal cavity or perform Lynch incision and dissect periorbita off medial orbital wall; AEA located 8–12 mm from lacrimal crest, PEA 10–12 mm from AEA, and optic nerve 4–6 mm from PEA
- Angiography and embolization
  - Angiography identifies site of active bleed, interventional radiologist performs embolization of specific branch or branches of external carotid
  - Complications: Blindness (more common with internal carotid branches, and embolization of these branches would only be undertaken in a life saving procedure), necrosis, stroke, facial pain, paresthesia

BENIGN MASSES/ABNORMALITIES

- Nasopharyngeal cysts
  - Rathke's pouch cyst or craniopharyngioma
    - Remnant of ectodermal tissue precursor of anterior pituitary gland
    - Tx = reassurance versus endoscopic marsupialization if symptomatic
  - Tornwaldt cyst
    - Remnant of caudal notochord
    - Tx = reassurance versus endoscopic marsupialization if symptomatic
- Midline nasal masses
  - Arise as a result of failure of closure of anterior nasopore
  - Persistence of fonticulus frontalis (opening between nasal and frontal bones in the embryo) allows for intracranial connection to prenasal space
  - MRI = allows for assessment of intracranial extension
  - Biopsy of midline nasal mass in children contraindicated due to risk of IC extension
  - Tx = open vs. endoscopic surgical excision, depending on whether or not external nasal structures involved.
  - Glioma
    - 60 % Extranasal, 30 % intranasal, 10 % combined
    - "Pinched off" glial tissue; can appear red and be confused with hemangioma
    - Symptoms = firm, nontender, noncompressible mass that does not transilluminate or change in size
  - Encephalocele, meningocele, meningoencephalocele
    - Herniation of meninges (meningocele), meninges + brain (meningoencephalocele), or meninges + brain + part of ventricular system (meningoencephalocytocele) through skull base defect
    - Sac of glial tissue lined with ependymal cells
    - 25 % Anterior (sincipital/external versus basal/internal) and 75 % posterior, or occipital in location
      - Sincipital/external: herniation occurs anterior to crista galli between frontal and ethmoid bones, presenting as external mass over nose or glabella
      - Basal/internal (less common): herniation occurs posterior to cribriform plate, presenting as an intranasal mass

        - Symptoms: soft, compressible mass that transilluminates and increases in size with crying (positive Furstenberg test)
    - Dermoid Cyst
        - Sequestration of ectodermal and mesodermal elements anywhere along a tract extending from foramen cecum to nasal tip
        - Symptoms = Fistulous tract, nasal pit with tuft of hair
    - Fibro-osseous lesions (*find also in Chap. 8*)
        - Osteoma = most common benign sinonasal lesion
            - Frontal sinus most common
            - Gardner's syndrome = skull osteomas, colonic polyps, and soft tissue tumors
        - Fibrous dysplasia
            - Two types: Monostotic (most common, 70–80 %) and polyostotic
            - McCune-Albright Syndrome = polyostotic lesions, precocious puberty, pigmented skin lesions
            - CT findings: Early = radiolucent; Late = "ground-glass" + calcifications
            - Tx = surgery only if symptomatic (debilitating pain or cosmetic deformity effecting quality of life), bisphosphonates
        - Ossifying fibroma
            - Solitary encapsulated slow growing monostotic tumor
            - CT findings = central lucency with eggshell rim
            - Tx = surgery

SINONASAL MALIGNANCY

See Head and Neck section

SURGICAL APPROACHES

- Endoscopic approach (Functional endoscopic sinus surgery or FESS)
    - Technique = Rigid nasal endoscopy +/– stereotactic image guidance, typical steps include medialization of middle turbinate, removal of uncinate process, maxillary antrostomy, ethmoidectomy, sphenoidotomy, and frontal recess exploration with sinosotomy as needed
    - Four lamellae encountered (anterior → posterior) = uncinate process → ethmoid bulla → vertical portion of middle turbinate basal lamella → vertical portion of superior turbinate basal lamella
    - Should be considered for any lesion or disease process (congenital, inflammatory, neoplastic, traumatic, etc.) which can be accessed endoscopically, but the rhinologic surgeon must be familiar with open approaches for lesions which are inaccessible or incompletely addressed via this approach
    - Complications = bleeding, synechiae, injury to the eye including blindness, CSF leak, nasolacrimal duct injury, brain injury
    - Specific endoscopic approaches to the frontal sinus:
        - Draf I: complete removal of the anterior ethmoid cells and uncinate process within the frontal recess leading to the frontal ostium. Obstructing frontal cells, if present, are removed. The frontal sinus ostium may then drain into a patent frontal recess, but the frontal sinus ostium itself is not instrumented.
        - Draf IIa: resecting all included in Draf I with the addition of widening the frontal sinus ostium itself, resecting all of the frontal sinus floor from lamina to the insertion of the middle turbinate medially
        - Draf IIb: resecting all included in Draf IIa with the addition of resecting the middle turbinate up to skull base and widening the frontal sinus medially to the septum
        - Draf III (aka Modified Lothrop): resecting all included in Draf II, with the addition of removing the intersinus septum and connecting bilateral frontal sinuses into one horseshoe-shaped sinus with a common drainage pathway

OPEN APPROACHES

- Caldwell Luc
  - Used most often to gain access to the anterior wall of the maxillary sinus
  - Performed through canine fossa with incision at gingivobuccal sulcus
  - Can augment endoscopic surgery; good for anteriorly attached IP or other tumors, broader access to orbital floor and PPF
  - Complications = cheek edema/ecchymosis, numbness or pain with infraorbital nerve injury, oroantral fistula, epiphora if damage to nasolacrimal duct
- External ethmoidectomy
  - Provides access to ethmoid cavity, medial orbit, cribriform plate, and frontonasal area if endoscopy is not an option; can be employed to decompress subperiosteal abscess
  - Complications = eye injury including blindness and corneal abrasions, CSF leak, skull base injury, bleeding from AEA +/– retraction of vessel into eye
- External frontoethmoidectomy (Lynch procedure) or frontal trephine
  - Indications: uncommonly used now, when endoscopic approach is for any reason insufficient to address frontoethmoid mucocele, mucopyocele, rhinosinusitis with orbital complications, frontoethmoid or anterior skull base tumor, CSF leak repair, acute sinusitis with intracranial or orbital complications or not responsive to medical management and unable to access endoscopically, lateral frontal mucocele
  - Complications = bleeding, epiphora, frontal sinusitis, diplopia, blindness, CSF leak, intracranial hemorrhage
- Osteoplastic flap with frontal sinus obliteration or cranialization
  - Indications = when endoscopic approaches are insufficient or have failed to address osteomyelitis, frontal sinus tumor, recurrent persistent frontal sinusitis, trauma with comminuted anterior or posterior table fractures
- Open approaches to sphenoid sinus (historically used by neurosurgeons in pituitary surgery)
  - Transseptal: incision can be endonasal, sublabial, or transcolumellar
- Transfacial incisions
  - Lateral rhinotomy (incision made in naso-facial crease for small lesions of nasal cavity and medial maxilla), historically used for IP, no longer "gold standard"
  - Weber-Ferguson (incision for lateral rhinotomy extended laterally in subciliary crease and inferiorly along philtrum through vermilion border to split lip, provides wide access for most sinonasal tumors)
- Craniofacial resection
  - Bifrontal craniotomy with transfacial exposure of sinonasal cavity and orbits, allows for access to anterior cranial fossa
  - Used to approach skull base pathology including malignancy that cannot, for whatever reason, be accessed via the endoscopic approach

MAJOR COMPLICATIONS OF SINUS SURGERY

- Orbital
  - Includes blindness (direct injury or hematoma), penetration of orbit (may see fat herniation), diplopia (muscle injury), and epiphora (damage to lacrimal system)
  - Retrobulbar hematoma is an acute complication which must be recognized immediately and treated to avoid blindness
    - Cause = most commonly from venous injury near lamina papyracea or arterial injury to AEA during endoscopic surgery → retraction of vessel into orbit where pressure from hematoma compresses optic nerve
    - Sx = proptosis, chemosis, ecchymosis, vision change (if awake)
    - Treatment = immediate ophthalmology consult, ice packs, mannitol, remove any nasal packing if it has been placed, surgical intervention (lateral canthotomy, +/– medial orbital wall decompression)
    - Prevention = keep eyes visible during surgery and evaluate any imaging preoperatively to identify AEAs which run below skull base

- CSF leak
  - If identified at the time of surgery the defect should be repaired at that time (most common site of iatrogenic injury = lateral lamella of ethmoid roof)
  - If identified postoperatively (beta-2 transferrin positive thin watery rhinorrhea) can try conservative management first, although many surgeons would opt to go straight to surgery for repair
  - Conservative treatment = 7–10 days of bed rest, head elevation, stool softeners to avoid straining, lumbar drain for diversion (+/– antibiotics (prophylaxis for meningitis), no evidence to support use however most continue to use)
  - Surgical repair
    - Intracranial approach (50–70 % success rate) requires a coronal approach and carries risks of frontal lobe dysfunction, cerebral edema, seizures, and anosmia
    - Extracranial approach (80 % success rate) uses transfacial incisions, providing better visualization of the site of CSF leak but resulting in facial scarring
    - Endoscopic endonasal approach (95 % success rate) has the least morbidity
      - Overlay versus underlay repair (similar results) or both, using pedicled or free mucosal graft, pericranial flap, fat/fascia, synthetic dura are all options, with tissue glue/nasal packing per surgeon preference
      - Pedicled nasoseptal flaps when performing an endoscopic repair have dramatically reduced rate of recurrent CSF leak in the literature

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Chapter 7
Allergy and Immunology

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PEARLS

- Allergy skin prick testing—a wheal greater than 3 mm is considered positive
- Eosinophils contain peroxidase, neurotoxin, cationic protein, Charcot Leyden crystal protein, and major basic protein which induces release of histamine from mast cells and damages epithelial cells
- In vitro allergy testing is indicated if there is an inability to discontinue medications that would interfere with skin testing or prevent treatment of an anaphylactic response

EPIDEMIOLOGY

- Increasing incidence over the past 20 years
  - Increased allergen exposure
  - More hygienic living conditions for general population
- ~30 % of adults and ~40 % of children affected
- Seasonal allergies affect 20 % of population with perennial affecting 40 % of population
- Productivity lost approximately $639 million/year
- NHANES (National Health and Nutrition Examination Survey) study (2005): 53.9 % of study population tested positive to at least one antigen

RISK FACTORS

- Exposure to cigarette smoke
- Family history of atopy
- Higher socioeconomic status
- First born or only child
- Elevated total IgE

PATHOPHYSIOLOGY

Immunology

Classification

- Innate
  - *Nonspecific* response to foreign substances—not dependent on antigen recognition
  - For example, epithelial barrier, cellular and humoral defenses, complement activation

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- Adaptive
  - *Specific* response to foreign body—requires prior exposure/sensitization
  - Antigen recognition
    - Naturally acquired—contact with agent
    - Artificially acquired—vaccination
  - For example, antibodies, cytokines, T cells

Characteristics

- Recognition: self vs. non-self
- Surveillance
- Memory
- Specificity
- Diversity

Components

- Lymphocytes
  - Derived from bone marrow progenitor cells
  - T lymphocytes (cellular immunity)—all have CD2 and CD3 positivity
    - Bone marrow derived → maturation in thymus
    - Recognize fragments of foreign proteins via interaction with Major Histocompatibility Complex (MHC)
      - Cell bound proteins responsible for presenting antigens to T cells for recognition and proliferation of clonal lines
      - MHC 1: present on all nucleated cells
      - MHC 2: on antigen presenting cells and B cells
    - CD4 cells (T-helper cells) → primarily MHC2 interaction
      - 60 % of T lymphocytes—primarily located in periphery
      - TH0 cells: naïve cells → activated by intracellular pathogens or allergens
      - TH1 cells: mature subset which mediates defense against intracellular microbial infections
      - Major products IL-2 and IFN-gamma
      - TH2 cells: mature subset which down regulates TH1 and augments B-cell and Ig production
      - Major products IL- 4, 5, 6, and 10
    - CD8 cells (T-cytolytic cells) → primarily MHC1 interaction
      - 30 % of peripheral T lymphocytes
      - Defense against virus infected cells → mediates cell lysis
      - Response mediated by IL-2
    - T regulatory cells (T_{reg})
      - Modulate immune system, maintain tolerance to self-antigens, prevention of autoimmunity
      - Exploited in the therapeutic process of allergy immunotherapy
  - B lymphocytes (Humoral Immunity)
    - Mature in bone marrow → migrate to lymph nodes and spleen
    - T-dependent activation: B-cell processes antigen and express MHC 2 receptor allowing CD4 cell recognition → T-cell stimulates B cells via IL 2 and 4 secretion
    - T-independent activation: B-cell surface receptors activated by large antigens
      - Upon activation of B-cell via either pathway, cell produces plasma cells which secrete immunoglobulins
      - Made of two light and two heavy chains each with variable and constant chains—allows for diversity

- Allows antigen recognition, interaction with complement, phagocytosis
  - Ig*D*: distinct function unknown, receptor on naïve B cells, minor activation of basophils and mast cells
  - Ig*A*: dimer found in secretions/mucosa, often mediates first-line immune defense for pathogens entering the body via the oral cavity
  - Ig*M*: pentamer antibody
    - high avidity seen in early immune responses
  - Ig*E*: binds to allergens and triggers release of histamine and other mediators—*hypersensitivity reactions*
  - Ig*G*: major antibody in late immune responses
    - Crosses placenta to provide neonatal immunity
    - Complement fixation
- CD19 and CD21 positivity

- Natural Killer Cells
  - Maturation in bone marrow
  - Secrete cytokines
  - Role in innate immunity → kill virus infected cells
  - Activated by IL-2 → antibody-dependent cellular cytotoxicity
  - CD 16 and CD 56 positivity
- Antigen Presenting Cells
  - Located within skin, lymph nodes, and spleen
  - Process antigens for presentation via MHC 1 and 2 to T cells
  - For example, macrophages, Dendritic cells, B cells, Langerhans cells, monocytes
- Cytokines
  - Proteins secreted that allow for immunomodulation, pro-inflammation, and anti-inflammatory effects → intercellular "communication"
  - Modes of secretion:
    - Autocrine: cellular activation produces cytokine which affects secreting cell
    - Paracrine: cellular activation produces cytokine which affects nearby cells
    - Endocrine: cellular activation produces distant cellular effects
    - Role in inflammation
      - IL-1: stimulate IL-2 secretion, phagocyte activation, pyrogen
      - IL-2: stimulate T cells, B cells, and NK cells
      - IL-6: acute phase response
      - IL-12: proliferation of CD8, NK cells, IFN-gamma production, induce TH1 cells, suppress TH2
      - IL-18: induces IFN-gamma, enhances NK cell activity
      - Interferon (IFN): activates macrophages and NK cells, antiviral properties, increase MHC proteins, cytotoxic effects
        - Type I: IFN-alpha, beta → potent antiviral effects
        - Type II: IFN-gamma → potent immunomodulator, increases MHC expression
      - TNF: acute phase response, pyrogen
    - Role in allergy
      - IL-4: induces B cells and mast cells to increase IgE production
      - IL-5: activation and maturation of eosinophils
      - IL-13: induces B cells and mast cells to increase IgE production, induction of adhesion molecules at allergic sites
- Complement
  - Allows for the augmentation of immune function, mediates the interaction of antigen and antibody
  - Activation via two distinct pathways:
    - Classical pathway
      - Primary pathway
      - Activation via immune complexes, IgG and IgM of the C1 complex

        - Alternative pathway
            - Secondary pathway
            - Activated by viruses, bacteria, parasites, IgA, IgG via C3
        - Lectin pathway
            - Similar to classical pathway but utilize mannose-binding lectin instead of C1
    - Activation leads to opsonization "tagging," cellular migration and activation, cellular death via lysis
- Cells important in the allergic response
    - Neutrophils
        - Cell margination and migration to site of inflammation
        - Opsonized particles are recognized and undergo phagocytosis
    - Eosinophils
        - Receptors for cytokines, IgG and IgE which allow localization to inflamed endothelium
        - Contains peroxidase, neurotoxin, cationic protein, Charcot Leyden crystal protein, and major basic protein
            - Major basic protein → induces release of histamine from mast cells and damages epithelial cells
    - Monocytes
        - Immature-macrophages
        - Produces IL-1 allowing vascular permeability and production of acute phase proteins
    - Basophils
        - Circulating granulocytes rich in histamine and heparin
        - High-affinity IgE receptors → release histamine and cytokines IL-4, IL-13
        - Express IL-4
    - Mast cells
        - Granulocyte rich in histamine and heparin
        - Contained within connective tissue and mucosa—e.g., skin, mucosal lining of mouth and nose
        - When activated → histamine and cytokines TNF-alpha, IL-3, -4, -6, -8, -10, -11

CLASSIFICATION OF HYPERSENSITIVITY REACTIONS: GELL AND COOMBS

- Type I
    - *Mediator*: IgE hypersensitivity
    - *Time*: Immediate
    - *Agents*: environmental, food, medications
    - *Mechanism*: secondary to degranulating mast cells → histamine
    - *Manifestations*: systemic and localized anaphylaxis, sneezing, urticaria, congestion, wheals
- Type II
    - *Mediator*: IgG cytotoxicity hypersensitivity
    - *Mechanism*: antibody-directed against cell surface antigens → cell destruction via complement activation
    - *Manifestations*: Hemolytic anemia, transfusion reactions, Goodpasture syndrome, Myasthenia gravis
- Type III
    - *Mediator*: Immune complex mediated hypersensitivity (IgG)
    - *Agents*: Bacterial antigen, medications
    - *Mechanism*: Antigen–Antibody complex deposited on the surfaces of small vasculature, joints, and glomeruli with complement activation → massive infiltration of neutrophils
    - *Manifestations*: Serum sickness, post-streptococcal glomerulonephritis, angioedema, GI manifestations

- Type IV
  - *Mediator*: *Cell-mediated* hypersensitivity
  - *Time*: Delayed—up to several days
  - *Agents*: poison ivy, nickel reactions, chemicals
  - *Mechanism*: Sensitized TH1 cells release cytokines → activate macrophages or CD8 cells → direct cellular damage and inflammation
  - *Manifestations*: dermatitis, granulomatous disease, fungal disease

CELLULAR RESPONSE OF ALLERGIC REACTIONS

- First exposure
  - APC encounter allergen
    - Uptake and process → synthesize MHC2
    - Transform TH0 cells to TH2 via release of IL4
  - TH2 release IL4 → stimulate antigen-specific IgE production via B cells
  - Early response: within minutes of exposure to several hours
- Reexposure
  - Memory B cells maintains antibody response
  - Reexposure allows rapid proliferation to plasma cells → secrete high-affinity IgE
  - IgE binds and sensitizes mast cell → cross linking occurs with antigen → destabilization of mast cells → degranulate and release:
    - Histamine
      - Main mediator of allergic reactions
      - Vessel permeability, vasodilation, mucus secretion, tissue edema, bronchoconstriction
      - Receptors H1 and H2
    - Heparin
      - Anticoagulant
      - Enhances migration and phagocytosis
    - Leukotrienes
      - Derived from the lipoxygenase pathway
      - Vasodilation, mucus secretion, bronchial smooth muscle contraction, edema, increased vascular permeability
      - Act upon leukotriene receptors
    - Cytokines: allow cellular recruitment
    - PDG2: metabolite of arachidonic acid involved in innate and adaptive immune responses
    - PAF: mediator causing inflammation, platelet aggregation, and allergic response
- Late response: within several hours after exposure
  - Cytokine release (primarily IL4) causes accumulation of
    - TH2 cells
      - Orchestrate and maintain inflammatory response → IL-3, -4, -5, -13
    - Eosinophils
      - Production of oxygen-free radicals → damage epithelium and promotes inflammation
      - Release major basic protein
    - Basophils
    - B cells
    - Neutrophils

NEUROGENIC RESPONSE TO ALLERGEN

- Neurotransmitters play a pivotal role in pathogenesis
  - Altering secretions
  - Smooth muscle tone
  - Vasodilation
  - Cellular recruitment

- "Neurogenic inflammation"
  - Activation of peripheral terminals of sensory neurons → release neurotransmitters to act on mast cells and vascular smooth muscle
    - Redness and warmth due to vasodilation
    - Swelling due to plasma extravasation
    - Hypersensitivity due to alterations in excitability

ALLERGIC RHINITIS

Diagnosis

- History
  - Primary symptoms, duration, frequency, alleviating/exacerbating factors, associated symptoms or conditions, recent changes in job, environment, diet
  - Past medical history: History of asthma, anaphylaxis, eczema, allergen exposure, formula intolerance
  - Past Surgical History: e.g., T + A, BMT, FESS
  - Family history: allergic rhinitis, asthma, eczema, angioedema, food intolerance, anaphylaxis
    - Chance of having atopy with:
      - 0 Allergic parents: 10–15 %
      - 1 Allergic parent: 30 %
      - 2 Allergic parents: 50 %
  - Social history: Living accommodations, tobacco exposure, occupation
  - Medication use
- Physical
  - Eyes: lid edema and erythema, injection of conjunctiva and sclera, chemosis, itching, watery, photophobia, "allergic shiners," "Dennies lines"
  - Nose: supratip crease, facial grimacing, itching, nasal obstruction, inferior turbinate hypertrophy, rhinorrhea, increased mucus, sneezing
  - Ears: Tympanic membrane retraction, eustachian tube dysfunction, middle ear effusion
  - Oropharynx: "cobblestoning" of posterior pharyngeal wall, hypertrophy of lateral pharyngeal bands, mouth breathing, angioedema
  - Laryngeal: excess secretions, vocal fold edema, laryngeal drying, erythematous arytenoids, viscous mucus
  - Possible related systemic findings:
    - Skin: eczema, contact dermatitis, urticaria,
    - Lungs: wheezing, dyspnea, cough

Diagnostic Testing

- *In Vivo testing*
  - Although testing is generally safe, necessary medications and airway equipment to treat systemic anaphylaxis must be available
  - Skin Testing
    - Epicutaneously
      - Prick test
        - More specific testing than intradermal (fewer false-positive results)
        - False-negative rate is 5 %
        - Various antigens introduced in controlled manner—to determine reactivity and severity
        - Few drops of selected antigen are placed on skin surface after small prick with needle
        - Reaction >3 mm in diameter is considered positive

- Intradermal
  - Typically recommended to be performed after negative prick test, but specific sensitivity is suspected.
  - Not appropriate for food allergens due to high risk of false positives and risk of anaphylaxis
  - Small amount of allergen injected subcutaneously
  - More reproducible and sensitive testing than prick testing (fewer false negatives)
  - Skin end point titration
    - Intradermal injections of allergen at increasing concentrations starting with an anticipated non-reacting dose
    - Wheal which initiates positive reaction is safe starting point for immunotherapy
    - Technique
      - Start with diluent injection (inert) typically forms 5 mm wheal measured at 10 min
      - Injection of antigen at lowest reactive concentration (increasing concentration 1:5) until wheal enlarges by 2 mm → "endpoint"
        "Endpoint": concentration that produces positive wheal that continues to increase in size
        Considered safe point for starting skin testing
      - Injection of next stronger concentration that results in further 2 mm in growth → confirmatory concentration
      - 13 mm growth → major reaction, testing stopped
- Factors which affect wheal response:
  - Recent exposure
  - Prior immunotherapy
  - Area of body tested—i.e., upper back → lower arm
  - Age of patient—pediatric and geriatric tend to have less response
  - Medications: steroids, leukotriene inhibitors, bronchodilators, NSAIDs

- *In Vitro testing*
  - Serum test
  - Detects specific IgE to allergens
    - Suspected allergen bound to insoluble material → patient serum added
      - If IgE present in serum → binding to allergen occurs
      - Marker labeled anti-IgE added → washed
      - Detection of marker
        - Radiation: RAST (Radioallergosorbent test)
        - Fluorescent: ELISA
  - Indications:
    - Inability to discontinue medications that would interfere with skin testing or prevent treatment of an anaphylactic response—i.e., antihistamines, H2 blockers, tricyclic anti depressants, long-term topical steroids, β-blockers
    - Severe eczema or psoriasis precluding skin testing
    - Extraordinarily high sensitivity to suspected allergens that may lead to potentially serious side effects (i.e., anaphylaxis)
    - Poorly controlled reactive airway disease
  - Scoring:
    - 0–6 Based on level of IgE in specimen
  - More specific in determining allergen sensitivity, less sensitive than skin tests

MANAGEMENT OF ALLERGY SYMPTOMS

Nonpharmacologic

- Avoidance
  - Goals include:
    - Remove sources of allergens
    - Remove accumulated allergens
    - Prevent allergens from returning
  - Outdoor
    - Pollen
      - Types
        - Trees—February through May
        - Grass—June through August
        - Weeds—August until frost
      - Counts highest in morning, hot, dry windy days
      - Strategies of avoidance:
        - Shift outdoor activities to evening
        - Keep doors and windows closed, utilize AC
    - Mold (can be found both outdoor and indoor)
      - Present year round
  - Indoor
    - Dust mites
      - Keep surfaces clear
      - Remove carpeting
      - HEPA filters
      - Wash sheets and pillow case weekly in hot water >130°
    - Pet Dander
      - Avoidance of pet, especially keeping pet out of bed and bedroom
      - Eliminate carpeting

Pharmacologic Therapy

- Symptomatic Relief
- Decongestants
  - Reduce blood flow → agonistic action on alpha 1 and 2 adrenergic receptors
    - Endothelial cells within nasal vessels
    - Contraction of sphincters of the venous plexus within turbinate
  - Oral agents
    - Less chance for rebound congestion
    - Systemic effects: irritability, insomnia, headache, tachycardia, hypertension, increased intraocular pressure, urinary retention
    - Caution use in patients: hypertension, coronary disease, hyperthyroidism, glaucoma, urinary retention
    - For example, pseudoephedrine and phenylephrine
  - Topical nasal agents
    - Rapid onset <5 min with duration of 6 h
    - High local potency with fewer systemic effects
    - Over use >3–5 days leads to lost effectiveness and rebound congestion. Long-term use can lead to rhinitis medicamentosa
    - For example, oxymetazoline, neosynephrine, phenylephrine
- Maintenance
- Antihistamines
  - Competitively bind to H1 receptors → reduced vascular permeability, smooth muscle contraction, mucus secretion, vasodilation, pruritis

- Oral
  - First Generation—available over the counter, cheap
    - Limited due to potential for sedative effects → high lipophilicity → crosses blood brain barrier
    - Anticholinergic effects → dry mucus membranes, urinary retention, constipation, tachycardia, blurred vision: limit use in elderly
    - For example, diphenhydramine, chlorpheniramine, hydroxyzine
  - Second Generation
    - Lower CNS penetration and thus less sedating
    - Less anticholinergic effects
    - Lower interaction with cytochrome P 450
    - Better specificity for H1 receptor blockade
    - For example, loratidine, cetirizine, fexofenadine
- Topical nasal spray
  - Advantage of delivering high local concentration
  - Allows higher anti-inflammatory effects, reduction of systemic exposure, reducing potential for systemic side effects
  - Typically recommended for patients with seasonal allergic rhinitis
  - For example, azelastaline

- Anti-leukotriene
  - Limited role given the lack of efficacy noted
  - Combined use with antihistamines typically with additive effect
  - Synthesis blockade
    - Blockade of 5-lipoxygenase → prevention of LTA4 synthesis formation
    - For example, Zileuton
  - Receptor blockade
    - Reduces number of peripheral blood eosinophils
    - For example, Montelukast, zafirlukast
- Corticosteroids
  - Available as oral, injection or topical intranasal delivery
    - Multiple anti-inflammatory effects
      - Decreased capillary permeability
      - Promotes IL-10 production and IL-1 receptor antagonism
      - Decreased arachidonic metabolism → decreased prostaglandins, leukotrienes, thromboxane
      - Allows inhibition of cytokines and chemokines
      - Decreased recruitment and migration of eosinophils
      - Decreased activity of basophils and mast cells
      - Decreased migration of APC, T cells, B cells
  - Topical Intranasal delivery
    - Recommended for persistent nasal congestion
    - Systemic absorption and side effects are a theoretical concern but not well supported by the literature
      - (i.e., Inhibition of growth in children, metabolic disturbances, glaucoma, cataract formation, immunosuppression, skin thinning)
    - Effectiveness
      - Effective for all symptoms of SAR and PAR
      - Appropriate for mixed rhinitis
      - Clinical response equivocal for all available steroids
    - Topical side effects: Local burning, stinging, irritation, dryness
    - For example, beclomethasone, budesonide, flunisolide, triamcinolone, fluticasone, mometasone

- Mast cell stabilizers
  - Inhibit Ca^{2+}-dependent mast cell degranulation
  - Inhibit migration and survival of macrophages, eosinophils, monocytes
  - When used prophylactically can prevent and treat symptoms, although commonly need to be used as adjunct and not first-line therapy
  - Side effects: nasal burning, stinging, sneezing
  - For example, Cromolyns, olpatadine (dual antihistamine/mast cell stabilizer)
- Anticholinergic agents
  - Muscarinic receptor blockade → inhibits rhinorrhea, congestion, and sneezing
  - Side effects: dry mouth, dizziness, blurred vision, conjunctivitis, hoarseness
  - Typically suggested for treatment of rhinorrhea
  - Caution in use with elderly with glaucoma and urinary retention
  - For example, ipratropium

IMMUNOMODULATION

- Allergen-specific immunotherapy
  - Treats IgE-mediated allergy → regular and progressive doses of appropriate allergen → downregulation of immune response and control of symptoms
  - Benefits include:
    - Improvement in quality of life
    - Reduction of symptoms
    - Decrease reliance on medications
    - Long-term benefit after stopping treatment if they complete 3–5 years of therapy
    - Decrease risk of developing asthma
    - Prevent new sensitizations
  - Indications for therapy
    - Demonstration of IgE-mediated disease correlates with symptoms
    - Insufficient response to avoidance and pharmacotherapy
    - Significant side effects with medical therapy
    - Unable to comply with medical therapy and avoidance of allergens
    - Moderate to severe symptoms which last for majority of year or spanning across 2 or more seasons
  - Effective to following antigens:
    - Grass
    - Tree
    - Pollen
    - Animal dander
    - Insect venom
    - House dust mites
    - Mold
  - Relative contraindications
    - Concomitant therapy with beta-blocker
    - Contraindication to administration of epinephrine
    - Non-compliance of patient
    - Autoimmune disease
    - Pregnancy
    - Uncontrolled asthma
    - HIV or other immunodeficiency
  - Mechanism of action
    - With initial treatments → 2–3 months of increased antigen-specific IgE followed by gradual decline over 2 years
    - Decline does not correlate to clinical improvement
    - With decline in IgE → rise in IgG1 and IgG4

- Increase in IgG4 correlates with symptom relief
- Increase in antigen-specific suppressor T cells
- Shift TH2 cells to TH1 via increased IFN-gamma and IL12
- Decline in levels of pro-allergenic cytokines
- Reduced basophil, mast cell and lymphocyte reactivity
- Blunting of post-seasonal rise in specific IgE antibody
- Gradual decrease in symptoms with repeated exposure to same allergen level

- Schedule of treatment
  - Total treatment period is 3–5 years
  - Escalation phase → first year
    - Rapid escalation versus standard schedules
      - Allows for the attainment of maintenance doses in as low as 6 days through the use of increased frequency dosing (q 3–4 h) versus 3–6 months with standard schedules
      - The most rapid of escalation schedules typically necessitate hospitalization during the escalation period
  - Maintenance phase → up to 5 years
    - Every 1 week for first year, every 2 weeks for second year, every 3 weeks for third year
- Modes of Delivery
  - Subcutaneous Immunotherapy (SCIT)
  - Sublingual Immunotherapy (SLIT)
- Comparing SCIT and SLIT
  - Safety:
    - Fatal reactions from SCIT occur at rate of 1 in 2–2.5 million → 3.4 deaths/year
    - Between 2006 and 2009, six possible reported anaphylaxis in SLIT patients, none resulting in fatalities
  - Efficacy:
    - A 2007 Cochrane meta-analysis showed that immunotherapy reduced medication use, decreased clinical symptoms, and improved quality of life.
    - Efficacy has been shown to last as long as 3 years post immunotherapy cessation.
    - SLIT still has minor edge over SCIT in total efficacy, although many studies showing nearing equivalence
  - Dosing
    - Optimum SCIT maintenance dose is 5–20 μg of major allergen
    - Optimum SLIT maintenance dose not elucidated, but median monthly dosing is 49× that of SCIT
  - Cost
    - As of 2013, SLIT is not currently covered by insurance companies and considered an out of pocket expense.
    - Cost of SCIT varies dramatically according to insurance plans, while SLIT varies between practices
    - When loss of productivity and travel expense is added into the cost of SCIT, SLIT may be comparable in cost and more convenient for the patient.
- Complications
  - Typically secondary to
    - Presence, severity, control status of asthma
    - Dosing—inadvertent mistakes in antigen selection or concentration calculation
    - Accelerated dosing schedules
    - Treatment during peak pollen season
    - Extensive sensitivity to allergen
  - Local
    - SCIT: induration, wheal
    - SLIT: oral itching, irritation

        - Systemic
            - SCIT: coughing, wheezing, shortness of breath, urticarial, anaphylaxis
            - SLIT: Gastointestinal, i.e., abdominal pain, nausea, vomiting; can also have anaphylaxis
- Monoclonal Antibody
    - Recombinant humanized monoclonal anti-IgE antibody → forms complexes with free IgE → blocks interaction with receptors on mast cells and basophils
        - Profound reductions
            - Nasal eosinophils
            - IgE receptors on dendritic cells
            - T and B cells
    - Onset of action: typically 7–14 days
    - Clinical benefit shown in seasonal AR and perennial AR
    - Typically recommended for patient with refractory AR
    - Well tolerated with low rate of anaphylaxis
    - Disadvantage: Costly

SEVERE MANIFESTATIONS OF ALLERGIC RESPONSE

Anaphylaxis

- Definition
    - Immediate, severe, whole body, life-threatening, immunologic reaction characterized by the contraction of smooth muscle and dilatation of capillaries
- Epidemiology
    - Approximately 1,000 deaths/year in the United States
    - One of every 3,000 patients suffers an anaphylactic reaction in the US hospitals every year
    - Risk of death is twofold:
        - Airway edema—asphyxiation
        - Hypotension—shock/organ failure
    - Causes: Food (e.g., peanuts) → idiopathic → insect stings (e.g., bees) → medications (e.g., Beta-Lactam antibiotics)
- Treatment
    - Epinephrine: alpha- and beta-agonist
        - Adult dose: 0.3–0.5 cm^3 (1:1,000) IM or SC
        - Pediatric dose: 0.01 mg/kg (1:1,000) IM or SC
        - May repeat dose in 10–15 min
        - 10 % dose reduction with concomitant Monoamide oxidase inhibitors (MAOI) and Tricyclic Antidepressants (TCA)
    - Antihistamine: H1 and H2 antagonists
        - Effect on symptoms, i.e., hives, but no effect on hypotension, shock or airway obstruction
        - H1 blocker: Diphenhydramine 1 mg/kg IV or IM
        - H2 blocker: Ranitidine or Cimetidine via IV push
    - Steroids:
        - Typically used in asthmatic patients
        - Beneficial for late phase reactions
        - Prednisone 40 mg PO
        - Dexamethasone 20 mg IV
    - Bronchodilators:
        - Beta-agonist: Albuterol to break bronchospasm or overcome beta-blockade
        - Anticholinergic: Ipratropium
    - Dopamine: useful for maintenance of blood pressure
        - Initial dose 1 mcg/kg/min IV and titrate to 20 mcg/kg/min
        - Doses below 10 mcg typically act as beta-agonist

Angioedema

- Hereditary angioedema
  - Classification
    - Type I: 80 %—secondary to decreased production of C1-esterase inhibitor (C1-INH)
    - Type II: 20 %—normal or elevated functionally impaired C1-INH
  - Importance of C1-INH
    - Complement cascade: C1-INH prevents activation of C1
      - Preventing activation of C4, C3, C5
      - Decrease capillary permeability, fluid extravasation, edema
    - Kallikrein/kinin system:
      - C1-INH inactivates: Factor XII, plasmin, kallikrein
      - Prevents kininogen to be converted to bradykinin
      - Decrease vasodilation, nonvascular smooth muscle contraction, edema
  - Symptoms: edema of one of following organs
    - Skin
    - GI tract
    - Respiratory tract
  - Clinical Presentation
    - Symptoms associated with trauma, medical procedures, emotional stress, menstruation, infections, medication use (i.e., ACE-inhibitors)
    - Typically symptoms last 2–5 days with spontaneous resolution
    - Non-pitting skin edema
    - Facial area involvement (lips, eyelids, tongue)
    - Laryngeal involvement must be ruled out
  - Testing:
    - C1-INH levels
    - C1q levels
    - C2 and C4 levels—typically markedly decreased/undetectable
    - Genetic screening: autosomal dominant trait
  - Management
    - Genetic counseling
    - Intravenous C1 esterase inhibitor concentrate
    - Attenuated androgens, i.e., danazol, stanozolol
    - Trial of antihistamines, glucocorticoids, epinephrine
      - Although some reports suggest no response
    - Intubation if airway involved
    - Cessation of any offending agents, i.e., ACE-Inhibitors
- Acquired Angioedema
  - Secondary to increased destruction or metabolism of C1-INH
  - Typically noted in patients with rheumatologic disorders, B-cell lymphoproliferative disease, IgG autoantibodies against C1-INH
- ACE-Inhibitor therapy Induced
  - Associated with 0.1–0.5 % of patients
  - No sex predominance
  - Onset may occur during first week to as far as several years post initiation
  - Symptom resolution with 24–48 h
  - Typically with normal C1-INH levels and function
  - Treatment: discontinue ACE-I, start antihistamines, anticholinergics, corticosteroids

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Chapter 8
Systemic, Infectious, and Inflammatory Diseases

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PEARLS

- Wegener's Granulomatosis is the most common granulomatous disease to affect the upper airway with necrotizing granulomas, and small and medium vessel vasculitis
- Behcet's syndrome is a relapsing and remitting autoimmune disease with a triad of oral or genital ulcers, iritis/uveitis, and progressive sensorineural hearing loss
- Paget's disease, also known as, osteitis deformans, is an autosomal dominant idiopathic, chronic, and at times progressive disease of bone, osteolytic and osteoblastic changes that affect axial skeleton

GENETICS

Genetic Transmission

- Genotype: genetic constitution of an organism, set of alleles that determine expression of a trait/phenotype
- Phenotype: observable characteristics of an organism controlled by a specific genotype and environmental factors
- Allele: corresponding form of a gene found on each chromosome
- Homozygosity: two identical alleles at an autosomal gene locus
- Heterozygosity: two different alleles at an autosomal gene locus

Mendelian Inheritance

- Autosomal dominant inheritance: gene traits expressed in heterozygotes, 50 % chance of passing gene to next generation. *Penetrance*—percentage of individuals with a genotype that express a phenotype, can be complete or incomplete. *Expressivity*—variations in phenotype among individuals carrying a particular genotype
- Autosomal recessive inheritance: homozygous state is expression of disease; heterozygous state implies carrier status. Transmission of disease with two heterozygous parents is 25 %; 50 % chance of offspring being carriers, e.g., ataxia telangiectasia
- Sex-linked inheritance: can be either Y- or X-linked. Most commonly X-linked—mother transmits to offspring 50 % of time. Male offspring homozygous for disease; female offspring are carriers

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Non-mendelian Inheritance Patterns

- Mitochondrial inheritance: maternal mitochondria inherited through ovum; maternal inheritance
- Dynamic mutation: e.g., trinucleotide repeat—Fragile X, CAG repeat (Huntington's disease, spinocerebellar ataxia, Frederich's ataxia). CAG translates to glutamine = "polyQ." Autosomal dominant presentation, demonstrates *anticipation*—earlier onset, more severe onset as disease is transmitted to subsequent generations
- Genetic Imprinting: expression depends on parent of origin, one active copy, one inactive copy; inactive allele is highly methylated, e.g., Angelman Syndrome and Prader-Willi syndrome—both involve same region of chromosome 15 (Angelman misses maternal copy, Prader-Willi misses paternal copy)
- Mosaicism: presence of two or more genetically different cell lines within one individual, can be somatic or germline
- Uniparental disomy: inheritance of two copies of one chromosome (or part of chromosome) from one parent, none from other parent. Can be isodisomy (meiosis II error) or heterodisomy (meiosis I error). Also a cause of Angelman and Prader-Willi syndrome

Cancer Genetics

- Regulation of cell growth: proto-oncogenes—gene that normally act to regulate cell growth and differentiation, execution of mitogenic signals. Single mutation can lead to oncogene
- Tumor suppressor gene (TSG): encodes proteins that have a dampening/repressive effect on cell growth, may promote apoptosis
- Two-hit hypothesis: both copies of allele of TSG need to take it for mutation to occur

Oncogenes Classified Based on Function

- Growth factor: int-2
- Growth factor receptor: erbB2/neu (epidermal growth factor receptor)
- Protein kinases: c-raf
- Intracellular signal transduction protein: ras
- Transcription regulators: myc

Genes Involved in Head and Neck Squamous Cell Carcinoma (SCC)

- p53: tumor suppressor gene involved in cell cycle regulation and apoptosis. Mutation found in 50–66 % of head and neck SCC. Located on chromosome 17p13.1. Binds cyclin-dependent kinins and arrests cell replication in G1. If DNA repair mechanisms fail, induces apoptosis
- p16&p21: tumor suppressor proteins; suppress cyclin and cyclin-dependent kinase pathways
- Cyclin D1: protein that promotes progression through cell cycle
- bcl-2: oncogene that inhibits apoptosis, counteracts p53
- RET: proto-oncogene, cell surface tyrosine kinase receptor involved in signal transduction pathways for cell growth, associated with MEN II

CIRCULATORY

Osler Weber Rendu Syndrome (Hereditary Hemorrhagic Telangiectasia or HHT)

- Autosomal dominant
- Multiple telangiectasias of the skin and mucosa
- Present with recurrent epistaxis, pulmonary, gastrointestinal, and CNS bleeds due to ateriovenous malformations
- Treatment: manage anemia/acute bleeds; recurrent laser or bipolar cautery, possible septal dermoplasty for epistaxis

Kawasaki Disease (Mucocutaneous Lymph Node Syndrome)

Small vessel vasculitis, usually presents <5 years of age

Acute febrile illness of childhood, most common cause of acquired heart disease in children

- Symptoms and diagnosis: Clinical diagnosis—must have fever >5 days and have 4–5 of following symptoms. (1) Acute nonpurulent cervical lymphadenopathy >1.5 cm, typically unilateral, (2) erythematous desquamative rash of palms and soles, (3) truncal rash, (4) bilateral painless conjunctivitis, (5) erythema of tongue (strawberry tongue—protuberance of papillae), lips, oral cavity
- Workup: may also have elevated CRP, thrombocytopenia, chest radiograph with reticulogranular pattern, echocardiogram with pericardial effusion, coronary artery dilation, abdominal ultrasound demonstrating acalculus cholecystitis. 7–20 % develop coronary artery aneurysms, MI within 2–12 weeks of disease onset, facial palsy reported but rare, resolves in 1–12 weeks, due to ischemia injury to nerve
- Treatment: (1) Immunoglobulin, (2) high-dose aspirin

Giant Cell Arteritis (Temporal Arteritis)

Granulomatous large vessel vasculitis, commonly involves superficial temporal and ophthalmic arteries but can involve any large vessel, thrombi contain microabscesses. More common in females, presents >50 years of age

- Symptoms: jaw claudication, persistent throbbing pre-auricular pain, prominent and tender artery, low-grade fever, possible visual disturbances—ipsilateral blindness, elevated ESR, polymyalgia rheumatica with normal serum creatine kinase
- Diagnosis/workup: biopsy of vessel—multinucleated giant cell granulomas
- Treatment: high-dose oral corticosteroids. If presents with vision loss, high-dose IV steroids

Cogan's Syndrome

Assumed to be an autoimmune disease, non-syphilitic interstitial keratitis and vestibuloauditory symptoms (typical symptoms)

- Symptoms
  - Most patients have typical syndrome; atypical syndrome patients have hearing loss and ocular pathology other than keratitis such as scleritis, episcleritis, papilledema, retinal detachment that is not coincident; ocular manifestations can occur up to 2 years later
  - Meniere-like hearing loss but more pronounced and long-standing: initial unilateral, high-frequency loss, followed by bilateral and progressive, can become profound
  - Vestibular symptoms: sudden true vertigo, ataxia, vegetative symptoms
  - Systemic inflammatory involvement in 30 % of patients: systemic vasculitis, aortitis, musculoskeletal complaints, neurological symptoms
  - Viral prodrome, upper respiratory, within 7–10 days of initial onset of ocular and vestibular symptoms
  - If untreated, may lead to profound sensorineural hearing loss and loss of vestibular function
- Treatment: corticosteroids (systemic and topical—ocular), cyclophosphamide

Human Immunodeficiency Virus (HIV)

Retroviridae family of viruses, expression of disease correlates with CD4 count. Virus binds CD4 on T-cells and macrophages. Ultimately affects humoral and cell-mediated immunity

Presentation

- Acute retroviral syndrome, persistent generalized lymphadenopathy (PGL), acute HIV infection—occurs 1–4 weeks after exposure, lasts days to weeks then subsides. Symptoms include fever, malaise, myalgias, LAD, sore throat, headache (CD4 >500 cells/μL)
- Clinical latency/asymptomatic HIV/chronic HIV, if untreated lasts ~8 years. May develop PGL, weight loss, fever, myalgias, gastrointestinal problems (CD4 200–499 cells/μL)
- Acquired Immunodeficiency Syndrome (AIDS): CD4 count <200 cells/μL or presence of specific disease. CD4 count associated with disease
- Non-Hodgkin's lymphoma: <200 cells/μL
- Kaposi's sarcoma (HHV-8): <100 cells/μL
- Hodgkin's lymphoma: wide range of CD4
- Sinonasal lymphoma (NHL, typically B cell, not EBV related[5]): <200 cells/μL
- Invasive fungal sinusitis: <150 cells/μL
- Crytococcal menintigitis: <100 cells/μL
- Aspergillus: <50 cells/μL
- Cervical disease in HIV: progressive generalized LAD present in 12–45 %, differential diagnosis includes mycobacterium tuberculosis, pneumocystis jerovecii pneumonia, lymphoma, Kaposi sarcoma
  - Indications for open biopsy of lymphadenopathy in HIV: FNA suggesting malignancy, FNA negative for malignancy with any of the following—enlarging node; asymmetric, localized, unilateral; nodes >2 cm; low CD4 with new LAD; fever, weight loss, night sweats; significant mediastinal or abdominal lymphadenopathy
- Oral manifestations of HIV/AIDS: oral hairy leukoplakia, oral candidiasis, Kaposi's sarcoma, herpes simplex infections.
- Oral hairy leukoplakia: painless white patches on lateral tongue, not premalignant, caused by EBV infection, if HIV+ and develop OHL, 100 % chance of developing AIDS within 5 years

AUTOIMMUNE

Granulomatous Diseases—commonly involve tissues of airway, specifically nasal passages

Wegener's Granulomatosis

Most common granulomatous disease to affect upper airway

Necrotizing granulomas, small and medium vessel vasculitis, triad of upper/lower airway necrotizing granulomas, systemic vasculitis, focal necrotizing/proliferative glomerulonephritis

- Head and Neck symptoms
  - Nasal (90 %): rhinorrhea, anosmia, nasal congestion, may progress to sinusitis, septal perforation, crusting, epistaxis, nasal airway stenosis, saddlenose deformity. Diffuse nasal mucosal ulceration, less likely to be unilateral mucosal ulceration
  - Otologic (25 %): conductive hearing loss, suppurative otitis media, sensorineural hearing loss (can be bilateral and profound)
  - Orolaryngeal: gingival hyperplasia, gingivitis, laryngeal ulceration and edema (25 %), subglottic stenosis (8.5 %)
- Three clinical presentations
  - Type 1—upper airway involvement, few systemic manifestations
  - Type 2—similar to Type 1, prolonged upper airway symptoms with ulceration, pulmonary involvement
  - Type 3—disseminated disease with nasal involvement as in Type 1 and Type 2, and pulmonary involvement, cutaneous lesions, renal involvement
- Diagnosis: clinical presentation, anemia, elevated CRP, ESR, c-ANCA positive antibody against cytoplasmic antiproteinase-3 (specificity 90 % in systemic vasculitis stage, 65 % in granulomatous phase, 30 % in remission), and nasal biopsy after thorough removal of nasal crusting

- Histologic findings: (1) small and medium vasculitis, (2) fibrinous necrosis, (3) necrotizing granuloma, (4) mixed plasma cell, lymphocyte, histiocyte, and macrophage infiltrate
- Treatment: (1) Prednisone 1 mg/kg/day × 4 weeks then taper. (2) Cyclophosphamide 2 mg/kg/day for 6–12 months. Use methotrexate or azathioprine if develops hemorrhagic cystitis. (3) IVIg in immunosuppression nonresponders. (4) After symptoms stabilized, maintenance on trimethoprim-sulfamethoxazole (Bactrim/Septra)

Sarcoidosis

Unknown etiology, possibly exposure to beryllium, zirconium, pine pollen, peanut dust; can involve any organ but most commonly seen in the lungs. Nasal symptoms rare, though among first manifestation of disease. Female predominance, black predominance. Spontaneous resolution within 2 years, though 10 % progress to pulmonary fibrosis

- Nonspecific, noncaseating granulomas, epitheloid cells surrounded by lymphocytes and fibroblasts, multinucleated giant cells within granulomas
- Nasal symptoms: nasal obstruction, epistaxis, nasal pain, epiphora, anosmia. Affects septal mucosa and inferior turbinates, dry and friable nasal mucosa with crusting, yellow submucosal nodules (granulomas) with irregular polypoid mucosa, bony lesions of nasal bones
- Other sites of involvement: larynx (appears as "turban-like" thickening), epiglottis, supraglottis, subglottis (stenosis), typically spares vocal folds, unilateral/bilateral facial paralysis, recurrent bilateral parotid swelling, enlarging lacrimal gland
- Diagnosis: sinus CT demonstrating paranasal sinus mucosal thickening, osteoporosis or bony destruction, hilar LAD on chest X-ray, elevated serum/urinary calcium, elevated ACE (83 % of patients)
- Treatment: systemic corticosteroids—PO prednisone 10–40 mg/day, intranasal steroids, or methotrexate 30 mg weekly for nasal sarcoidosis
- Heerfordt's disease (uveoparotid disease): variant of sarcoidosis; seen in third to fourth decades; prodrome of fever, malaise, weakness, nausea, night sweats; 5 % of patients with parotitis, uveitis, CN paralysis (VII in 50 %); diagnose with elevated ACE level; treatment—corticosteroids, methotrexate, or azathioprine

Churg-Strauss Syndrome

"Allergic granulomatous angiitis," autoimmune vasculitis to small and medium sized vessels, leads to necrosis

- Triad of (1) asthma, (2) allergic rhinitis, and (3) eosinophilia
- 70 % with nasal involvement, symptoms include polyps, obstruction, rhinorrhea, crusting, polyps, and asthma (differs from Wegener's)
- Three phases of disease: (1) Prodromal—atopy and allergic rhinitis; (2) Eosinophilic infiltrative phase—chronic eosinophilia, eosinophilic tissue infiltration, pneumonia/gastroenteritis; (3) systemic phase—systemic necrotizing vasculitis
- Diagnosis: biopsy, p-ANCA positive in 70 %
- Treatment: high-dose corticosteroids, cyclophosphamide in life-threatening cases or poor prognosis

Amyloidosis

Idiopathic, extracellular deposition of insoluble fibrillar proteins, derived from soluble variants. Classified based on three parameters:

- *Fibrillar protein comprising deposit:* AA, AL, etc.
- Clinical description of associated disease process
  - Primary systemic (56 %): mesenchymal organs (heart, tongue, gastrointestinal tract)
  - Secondary systemic (8 %): in context of chronic destructive disease (tuberculosis, rheumatoid arthritis, osteomyelitis), deposits in kidneys, adrenals, spleen, liver
  - Myeloma-associated (26 %)

  - Localized (9 %): larynx most common head and neck site, most commonly in true and false vocal folds and ventricles, presents with hoarseness, light chain Ig type
  - Familial
  - Hemodialysis-associated
- Pathology
  - Light microscopy: acellular, amorphous, homogeneous, eosinophilic appearance after H&E stain. Primary/myeloma—light-chain Ig (kappa/lambda); secondary—amyloid-associated protein
  - Biopsy: apple green birefringence with Congo red staining under polarizing light; reversal with potassium permanganate infers secondary amyloid
- Clinical Presentation: primary—tongue most commonly involved; localized: orbit most commonly involved, larynx most common site of deposition in respiratory tract followed by trachea—can present as subglottic stenosis
- Treatment: conservative removal of deposits; steroids and antimetabolites not helpful

Relapsing Polychondritis

Rare idiopathic inflammatory disease that causes episodic inflammation of cartilaginous structures including ears, nose, eyes, larynx, bronchi, costal cartilages, articular joints

- Pathology: chondritis with mixed inflammatory cell infiltrate comprised of PMNs, lymphocytes, plasma cells, eosinophils. Primary stage—loss of matrix mucopolysaccharides, secondary—perichondrial inflammatory reaction
- Clinical: 50–55 % develop airway involvement (tracheomalacia), most common site—bilateral chondritis of auricles; 10–50 % mortality rate when laryngobronchial tree involved
- Treatment: airway protection, may require tracheostomy, initially high-dose corticosteroids, maintenance with low-dose corticosteroids and methotrexate

Systemic Lupus Erythematosis

Autoimmune connective tissue disease, type III hypersensitivity—circulating antibody/antigen/complement immune complex and deposition in basement membrane of dermal–epidermal junction. Involves heart, joints, kidneys, skin, blood vessels, nervous system

- Head and neck manifestations
  - Malar rash (50 %)
  - Painful oral mucosal ulcers (25 %)
  - Telangectasias
  - Septal ulceration/perforation (3–5 %)
  - Laryngeal/tracheal: true vocal cord thickening/paralysis, cricoarytenoid arthritis, subglottic stenosis
  - Acute parotid enlargement (10 %)
  - Chronic xerostomia
  - Cranial neuropathy (15 %)
- Treatment: NSAIDs, antimalarials, glucocorticoids; azathioprine and cyclophosphamide for resistant cases

Rheumatoid Arthritis

Autoimmune disease of synovial tissue. Can have false-positive VDRL, heterophile antibody test for infectious mononucleosis; HLA DR1 and HLA DR4—most common serotypes associated with RA. HLA-linked RA susceptibility locus accounts for <20 % RA in general population, higher in familial RA

- Head and neck manifestations include:
  - Larynx involved in 25–30 % of cases.
  - Acute laryngeal involvement—tender, edematous and erythematous arytenoids

- Chronic: cricoarytenoid (CA) joint involvement with ankylosis (86 %), can lead to bilateral vocal fold impairment and fixation in adducted position; subluxed CA joint can be seen on CT scan; submucosal nodules similar in histology to other RA nodules—presents with hoarseness that improves with removal of nodules. Methotrexate associated with development of laryngeal nodules in case reports
- Temporomandibular joint dysfunction: pain, tenderness of joint/overlying muscles; mandible ankylosis
- Otologic: tympanometric alterations, autoimmune inner ear disease (bilateral sensorineural hearing loss that progresses over weeks to months and responds to steroids)
- Cervical pain, decreased range of motion; basilar impression/invagination (10 %), mandible ankylosis

- Treatment: analgesics and NSAIDs; disease modifying anti-rheumatic drugs (DMARDs)—methotrexate, hydrochloroquine, sulfasalazine

Behcet's Syndrome

Relapsing and remitting autoimmune disease

- Triad of symptoms
  - Oral aphthous ulceration, genital ulcers, painful punched out lesions—typically first symptom
  - Iritis/uveitis in (43–72 %), loss of site (25 %)
  - Progressive sensorineural hearing loss
- Treatment: corticosteroid cream for ulcers, mydriatics, and ocular corticosteroid drops

Sjogren's Syndrome

Chronic autoimmune disease of exocrine glands, lymphocyte mediated

- Triad of symptoms
- Keratoconjunctivitis
- Xerostomia
- Associated with other autoimmune diseases (if just 1. and 2. present, is called sicca complex)

Other symptoms include altered taste and bilateral/unilateral salivary gland enlargement

- Diagnosis
  - Biopsy of minor salivary gland (lip, septum, hard palate); Focus score (positive if ≥1 in 4 mm^2 field)—50+ lymphocytes, histiocytes, plasma cells
- Blood tests
  - Primary: SS-A/Ro (60 %), SS-B/La (30 %), HLA-DW3, HLA-B8
  - Secondary: HLA-DW4
  - Other positive findings: RF, ANA
- Radiology (sialography): punctate to globular contrast collections, progress to complete gland destruction
- Treatment: symptomatic treatment (eye lubrication, sialogogues)

Myasthenia Gravis

Autoimmune neurologic disease, antibodies against postsynaptic acetylcholine nicotinic receptors at the neuromuscular junction, impaired receptors prevents sufficient sodium ions from entering myocyte, so no muscle contraction. A second form of MG caused by antibody against muscle-specific kinase (anti-MuSK), a tyrosine kinase receptor at the neuromuscular junction

- Symptoms: fatigability and weakness of striated muscles resulting in ptosis, diplopia, dysarthria, dysphagia, olfactory dysfunction
- Diagnosis: physical examination—have patient gaze upward for 30 s, repeat "ee-ee-ee" while evaluating palate and larynx. Tensilon (edrophonium) or neostigmine test rarely used—IV edrophonium/neostigmine administered, prevents breakdown of ACh, weakness

improves in patient with MG; serology—85 % have positive anti-AChR antibodies; anti-MuSK antibodies present in 40 % patients who do not have anti-AChR antibodies
- Treatment: acetylcholinesterase inhibitors: edrophonium, neostygmine, pyridostigmine, thymectomy

Pemphigus Vulgaris

Autoimmune disease that affects skin and mucous membranes, formation of blebs secondary to loosening of epidermal-dermal junction. Antibody against desmoglein 3, which is found in oral and oropharyngeal mucosa, in contrast to Pemphigus foliaceus—antibody against desmoglein 1, found in skin

- Symptoms: painful bleeding oral ulcers after vesicles rupture; epistaxis; laryngeal involvement presenting as hoarseness, stridor, dsypnea
- Exam: oral ulcerations of palate, gingival buccal mucosa and tongue—oral manifestation most common in head and neck region; involvement of laryngeal surface of epiglottis, aryepiglottic folds, and arytenoids mucosa, blebs not typically seen; tan fibrous base with halo of erythema. Scarring can lead to supraglottic narrowing. Positive Nikolsky sign
- Histology: separation of parabasal and superficial epithelium from the basal layer which remains adherent to basement membrane, tombstone effect, formation of Tzanck cells, acantholysis. IgG and/or C3 localized to intracellular spaces of epithelium
- Treatment: oral corticosteroids, azathioprine, cyclophosphamide, cyclosporine

Pemphigoid

Group of autoimmune diseases, subepithelial vesiculobullous disease, deposition of IgG and C3 at mucosal basement membrane antibodies against various antigens—including bullous pemphigoid antigen 2, bullous pemphigoid hemidesmosomal antigen 180, laminin 5

- Two main types: bullous—confined to skin; cicatricial—confined to mucosa
- Symptoms: oral mucosa involvement most common in head and neck region, followed by ocular, nasal (25–50 %, affects anterior nasal cavity), and nasopharyngeal. Slower healing and more scarring than pemphigus vulgaris, ocular scarring is most common
- Exam: oral ulcerations—erythema with patchy distribution of vesicles and bullae
- Histology: separation of mucosal epithelium from underlying lamina propria, linear immune deposits of epithelial basement membrane with immunoflourescent staining. Absence of acantholysis
- Treatment: if multiple sites involved—dapsone for 12 weeks; can use topical corticosteroids for isolated oral mucosal involvement

Scleroderma

Autoimmune disease, primarily of skin, unknown etiology, characterized by fibrosis and collagen deposition, can be associated with Sjogren's or CREST (see below)

- Head and neck manifestations: difficulty opening mouth secondary to fibrosis of masticator muscles, wide periodontal ligament spaces, gingivitis; nasal cavity telangiectasias leading to epistaxis
- Esophageal manifestations: aperistalsis of lower 2/3 of esophagus and esophageal dilation; absent lower esophageal sphincter contraction allowing reflux
  - Can be limited or diffuse. Limited = CREST
  - Calcinosis (soft tissue calcium deposits)
  - Raynaud's phenomenon (90 %)
  - Esophageal stenosis
  - Sclerodactyly
  - Telangiectasias
- Treatment: symptomatic—Raynaud's treated with nifedipine, amlodipine, diltiazam. Immuno-suppressants—methtrexate, cyclophosphamide, mycophenolate, azathioprine

INFECTIOUS

Actinomyces

Endogenous saprophytic organism of oral cavity and tonsils

- Clinical presentation: palpable firm neck mass after dental surgery, neck mass is most common H&N manifestation, 51 % with visible sinus tracts, 40 % with lymphadenopathy, concurrent dental, sinus, or perimandibular disease
- Histologic: multifilamented, anaerobic gram-positive rod; sulfur granules (collections of Actinomyces organisms), granuloma formation
- Treatment: surgical debridement, penicillin G IV for 2–6 weeks, tetracycline, or erythromycin if penicillin allergic

Rhinoscleroma

Chronic granulomatous disease of the nose, caused by *Klebsiella rhinoscleromatis*—gram-negative coccobacillus

- Histologic signs
  - Mikulicz cells—vacuolated, large macrophage with clear cytoplasm that contains bacilli
  - Large foamy histiocytes
  - Russell bodies—eosinophilic, large, immunoglobulin-containing inclusions found in plasma cells
- Stages
  - Catarrhal: foul-smelling purulent rhinorrhea lasting weeks to months
  - Atrophic: large foul crusts simulating atrophic rhinitis
  - Granulomatous: large granulomas of upper respiratory tract
  - Fibrosis: progressive stenosis of nares, with possible involvement of nasopharynx and trachea
- Treatment: debridement, long-term streptomycin and tetracycline, supportive airway management

Cat Scratch Disease

Caused by Bartonella (aka Rochalimaea) henselae, intracellular pleomorphic gram negative bacillus, visible on Warthin Starry silver staining. Reservoir for Bartonella is kittens; vector is cat flea

- Diagnosis: history of exposure to cats, papule/pustule 1–2 weeks after exposure, local lymphadenopathy; 10–30 % spontaneously suppurates. Cultures require 6-week incubation period). Test for antibodies to *B. henselae*
- Atypical presentation: Parinaud's oculoglandular syndrome—unilateral granulomatous conjunctivitis, associated with ipsilateral pre-auricular or submandibular lymphadenopathy. Bacillary angiomatosis—cutaneous proliferative vascular lesions
- Treatment: reassurance, self-limiting spontaneously resolving disease in 1–2 months; rifampin, azithromycin, not beta-lactams

Tuberculosis

Acid-fast bacilli, mycobacterium tuberculosis, leading cause of death in HIV-positive patients

- Head and neck manifestations
  - Cervical lymphadenopathy (scrofula), most commonly anterior superior cervical region followed by posterior cervical. With overlying skin changes. Commonly seen in HIV-positive patients
  - Otitis media (0.05–0.9 %) with lymphadenopathy in high jugular chain
  - Larynx—involvement of vocal folds, ventricular folds, aryepiglottic folds, posterior glottis
  - Salivary glands—may become encapsulated in intraglandular lymph nodes of parotid gland. Rarely involves facial nerve

  - May present as acute inflammatory lesion with diffuse glandular edema (could be confused with sialadenitis)
  - May present as chronic, slow-growing mass that mimics neoplasm
- Diagnosis: cultures positive for AFB. Test for HIV. FNA demonstrates granulomatous inflammation and epitheloid histiocytes. Calcification on CT
- Treatment: antituberculous medication, incision and drainage versus excision of LAD with abscess, depending on location

Leprosy (Hanson's Disease)

- Mycobacterium leprae, aerobic, intracellular, pleomorphic acid-fast bacilli, transmitted by aerosolized droplets, can be highly contagious, though only 5–10 % develop disease. Difficult to culture ex vivo, cultured in armadillos
- Diagnosis: skin and peripheral nerve involvement. Painless, insensate skin patches. Tissue staining shows acid-fast bacilli and granuloma formation. Hypercalcemia
- Head and neck manifestations: in disseminated disease, >1/3 have laryngeal involvement; laryngeal and upper tracheal stenosis. Rhinitis
- Treatment: dapsone, rifampin, clofazimine for 1–2 years

Histoplasmosis

Dimorphic fungus *Histoplasma capsulatum*, in Ohio and Mississippi River Valley. Exists in soil in mycelial form, converts to yeast when exposed to higher temperature (human body). Can present as acute or chronic pulmonary infection, or an acute or chronic disseminated infection with systemic symptoms. Is an AIDS-defining illness. Oral histoplasmosis lesions strongly associated with HIV/AIDS, CD4 <50 cells/μL

- Presentation: acute pulmonary, chronic pulmonary, or disseminated infection. If disseminated, flat, plaque-like, nontender elevation, become tender after ulceration, can resemble squamous cell carcinoma or TB
- Oral lesions: painful erythematous patches that progress to raised, granulomatous lesions covered with pseudomembrane, may have cervical adenopathy
- Larynx: hoarseness, aspiration, dysphagia
- Otologic: via ascending infection along Eustachian tube, superinfection of existing chronic otitis media, or hematogenous embolic dissemination. Granulomas of temporal bone
- Diagnosis: tissue biopsy shows poorly defined granulomas with macrophages and multinucleated giant cells on H&E stains. Wright Giemsa or methenamine silver stain shows macrophages with intracellular oval and round bodies (fungi in yeast form)
- Treatment: amphotericin B × 1–2 weeks, itraconazole prophylaxis if CD4 <150 cells/μL or other immunosuppression and with recurrent disease

Blastomycosis

Caused by dimorphic fungus *Blastomyces dermatitidis*. Endemic in Mississippi and Ohio River basins. Primary point of entry is lungs. Hematogenous spread (including laryngeal involvement)

- Presentation: Skin most common system involved. Larynx involved 2 %—manifest with hoarseness. True vocal folds most common subsite with extension into ventricular folds—exophytic lesions or ulcerative lesions. Must biopsy
- Histologic findings: acute and chronic inflammation, microabscesses, giant cell formation, pseudoepitheliomatous hyperplasia is hallmark finding
- Diagnosis: fungal stain on Gomori methenamine silver shows double-walled sphere, 8–15 mm diameter, broad-based buds
- Treatment: prolonged oral ketoconazole or itraconazole. Amphotericin B with CNS involvement

Cryptococcosis

Caused by Cryptococcus neoformans, yeast-like fungus with thick polysaccharide capsule, found in pigeon dropping-contaminated areas. Contracted via spore inhalation

- Presentation: Subclinical presentation in immunocompetent patients. Immunocompromised—systemic infection, usually CNS meningitis, fever, fatigue, chest pain, dry cough, headache, blurry vision. Rare laryngeal involvement—hoarseness, true vocal fold involvement
- Diagnosis: cryptococcal antigen in culture of CSF, sputum, and/or urine. India ink stain. Biopsy of glottic lesion—budding yeasts, may see pseudoepitheliomatous hyperplasia
- Treatment: amphotericin B + flucytosine/fluconazole

Coccidioidomycosis

AKA: San Joaquin Valley fever, caused by *Coccidioides immitis*, endemic to Southwest USA and Mexico. Contracted via spore inhalation

- Presentation: 40 % develop flu-like symptoms 1–3 weeks after infection. 60 % of infections unrecognized. Larynx site of inoculation in some patients—hoarseness, odynophagia, stridor
- Diagnosis: culture from sputum, involved tissue biopsy, DNA detection of *C. immitis*, fungal antigen, or host antibody
- Treatment: amphotericin B

Candidiasis

Caused by *Candida albicans*, a diploid fungus that grows as yeast and filamentous cell. Infection usually in immunocompromised patients, systemic or localized (steroid inhalers). Most common opportunistic infection of oral cavity, oropharynx, corners of mouth, isolated laryngeal involvement with inhaled steroid use, associated with failure of tracheoesophageal puncture voice prosthesis

- Presentation—six clinical forms
- Pseudomembranous candidiasis (thrush, classic presentation)—white sessile (curd-like) plaques on erythematous base, plaques can be scraped off
- Acute atrophic candidiasis—antibiotic sore mouth, associated with broad-spectrum antibiotic use, burning sensation in mouth, atrophy of dorsal lingual papillae
- Chronic atrophic candidiasis (most common)—erythematous, associated with dentures/oral appliance, in distribution of appliance
- Hyperplastic candidiasis (increased epithelial atypia and malignant transformation), "candida leukoplakia," rarest type, involves buccal mucosa along occlusal line, raised white plaques that cannot be scraped off
- Median rhomboid glossitis—"central papillary atrophy," rhomboid area of atrophy with associated corresponding palatal area of atrophy, satellite/kissing lesions
- Mucocutaneous candidiasis—angular cheilitis, tender and erythematous fissures and ulcers at oral commisure, superimposed bacterial infection with *S. aureus*
- Risk factors: xerostomia, inhaled steroids, heavy smoking, poorly controlled diabetes, oral foreign bodies (e.g., dentures)
- Diagnosis: clinical presentation sufficient to initiate treatment; mucosal surface scraping and KOH placement, or tissue prep with periodic acid-Schiff (PAS) or methenamine silver. Can culture on Sabouraud medium
- Treatment: topical nystatin, PO fluconazole, "magic mouthwash" may help alleviate symptoms as well as treat infection

Diptheria

Caused by *Cornybacterium diphtheriae*, gram + facultative anaerobe, produces diptheria toxin

- Presentation: sore throat, low-grade fever, dysphagia, odynophagia, dysphonia, cervical lymphadenopathy, pseudomembrane on tonsil, pharynx, and/or nasal cavity, associated myocarditis in 20 %, peripheral neuropathy 10 %. Contagious, aerosolized particles
- Diagnosis: isolate organism on gram stain or throat culture; Albert's Stain
- Treatment: airway management, diptheria antitoxin (does not neutralize toxin already bound to tissue), metronidazole, erythromycin PO/IV × 14 days, penicillin G IM × 14 days

Lemierre Syndrome

Typically caused by *Fusobacterium necrophorum*, internal jugular vein thrombophlebitis. Spread via tonsillar veins to internal jugular system, bacteria endotoxin causes platelet aggregation

- Presentation: initial presentation of pharyngitis, lateral neck tenderness, otalgia; blood-stained, foul-smelling otorrhea; spiking fever ("picket fence"); engorged optic disks; increased CSF pressure; SCM tenderness; neck stiffness; metastatic lung abscesses; septic arthritis
- Diagnosis: CT neck with contrast, Griesinger's sign—erythema and edema over mastoid process, Queckenstadt (Toby-Ayer) test—measuring CSF pressure with LP while compressing one or both IJVs. If no change/slow change in ICP, likely thrombosis. Normal IJV—rapid rise in ICP
- Treatment: first line—beta-lactamase resistant antibiotics +/– heparin, drainage of infection, ligation of IJV, anticoagulation controversial

Ludwig's Angina

Rapid, gangrenous cellulitis involving all three primary spaces of the oral cavity (spaces where infection spreads from teeth to bone): sublingual, submandibular, and submental spaces bilaterally; typically extends posteriorly to involve secondary spaces causing trismus: masseteric, pterygomandibular, and temporal spaces; usually mixed flora

- Symptoms: trismus, drooling, tachypnea, floor of mouth, submental, and submandibular swelling, tachycardia, difficulty swallowing, eventual airway distress secondary to posteriorly displaced tongue, kinks the supraglottis
- Treatment: airway control, incision and drainage of abscess/phlegmon. IV penicillin, or IV clindamycin in penicillin-allergic patients

Necrotizing Fasciitis

Deep neck space infection, occurs more often in older patients (>60 years old), immunocompromised, poorly controlled diabetes. Origin commonly odontogenic, mixed flora—aerobes and anaerobes

- Presentation: progressive cellulitis, pitting neck edema, orange peel appearance secondary to obstructed dermal lymphatics, +/– crepitus; CT neck with contrast—subcutaneous gas, diffuse loculated hypodense areas without rim-enhancement consistent with liquefactive necrosis
- Treatment: broad-spectrum IV antibiotics: clindamycin + ceftriaxone + flagyl; intensive care and airway securement; surgical exploration and debridement of necrotic tissue until tissue bleeds, irrigate, pack with moist dressing, second look procedure in 2–3 days; adjuvant hyperbaric oxygen. Mortality of 20–30 % in treated patients

Epstein-Barr Virus

Double-stranded capsid DNA in herpes viridae family, remains latent in B lymphocytes, 80–90 % people worldwide are seropositive; causative agent in infectious mononucleosis,

implicated in nasopharyngeal carcinoma, Burkitt's lymphoma, oral hairy leukoplakia, sensorineural hearing loss

- Infectious mononucleosis (IM): virus replicates in oropharyngeal epithelial cells and is transmitted via saliva, incubation period of 3–7 weeks; prodrome of fever, malaise, chills; followed by sore 1–2 weeks sore throat, fever, cervical adenopathy
- Symptoms: erythematous and enlarged tonsils with exudates, diffuse hyperplasia of Waldeyer's ring, petechiae at hard-soft palate junction, splenomegaly, hepatomegaly, periorbital edema. Presence of atypical lymphocytes on blood smear, symptoms caused by robust cytotoxic T-cell response. Diagnose with monospot test (detects presence of heterophile antibodies)
- Complications include secondary bacterial infection—group A beta-hemolytic streptococcus in 30 %, Guillain-Barré in 1–5 %, cranial nerve VII neuropathy, spontaneous splenic rupture, hemolytic anemia
- Treatment: supportive care, avoid contact sports, antibiotics for secondary bacterial infection though avoid ampicillin/amoxicillin—causes maculopapular rash in patients with IM
- Nasopharyngeal carcinoma (NPC): not all patients with EBV develop NPC. IgA antibodies to viral capsid antigen (VCA) and nuclear core early antigen most specific tests for diagnosis, titers ~85 % positive in cases of WHO II & III NPC. Antibody-dependent cellular cytotoxicity (ADCC) titers: can be used to predict prognosis of WHO II & III NPC, significant relationship between lower titers and progression—lower titers correlate with poorer prognosis
- Burkitt's lymphoma: non-Hodgkin's lymphoma, high incidence in children in equatorial Africa and Brazil, Burkitt's accounts for 50 % of these, associated with EBV. Translocation of myc gene on chromosome 8 to chromosome 14
- Histology: "starry sky," characterized by homogenous small non-cleaved cells with minimal variability in nuclei size and shape
- Symptoms: primarily in abdomen in patients in Africa, in head and neck in patients in USA
- Treatment: chemotherapy and CNS prophylaxis (intrathecal methotrexate and ara-C). Tumor lysis syndrome common; do not give steroids

Herpes Simplex Virus (HSV)

- Double-stranded DNA virus in herpes viridae, HSV 1 and HSV 2. HSV 1 more often associated with head and neck pathology
- Causative agent in primary herpetic gingivostomatitis, pharyngitis, laryngitis, sensorineural hearing loss, herpes labialis (cold sore—indication of reactivation, not primary infection), and oral ulcerations. In oral ulcerations, high concentration of virus present in ulcers in first few days, small round ulcers without erythematous halo, multinucleated giant cells seen in a Tzanck smear
- Treatment: initiate as soon as symptomatic, topical or oral acyclovir

Varicella-Zoster Virus (VZV)

Human herpes virus 3, member of herpesviridae family. Initial infection results in "chicken pox," virus lies dormant in sensory ganglia, reactivation presents with dermatomal distribution ("shingles")

- Symptoms: in head and neck region, reactivation causes unilateral painful vesicles on skin or in oral cavity, distributed in ophthalmic, maxillary, or mandibular divisions of trigeminal sensory nerves. If ear involved (herpes oticus), vesicles in canal and conchal bowl, virus thought to be harbored in geniculate ganglion and spreads along sensory fibers of CN VII. Can result in blindness (V1 distribution), facial paralysis/paresis (Ramsay Hunt syndrome), vertigo, hearing loss
- Treatment: antivirals (i.e., acyclovir, valcyclovir), analgesia, high-dose steroids for sensorineural hearing loss and facial paralysis

Human Papilloma Virus (HPV)

Member of papilloma viridae family, over 200 types, HPV 6 and 11 causative agents in recurrent respiratory papilloma and genital condyloma. HPV 16 and 18 causative agents in squamous cell carcinoma of head and neck and cervix

- Treatment modalities for RRP
  - Tracheostomy associated with increased risk of distal spread, avoid unless absolutely necessary
  - Surgical debulking the standard of care: remove as much disease as possible while preserving normal structures. Modalities include CO_2 laser, KTP laser; microlaryngoscopy with cold knife or microdebrider; cryosurgery
  - Adjuvant therapy: 20 % of patients will require some form; criteria include >4 surgeries/year, distal multisite spread of disease, rapid regrowth with airway compromise. Modalities include: cidofovir (use discouraged in children), Avastin (bevacizumab)—newer agent, monoclonal antibody inhibits VEGF-A; interferon therapy, autogenous vaccine, Indole-3-carbamol diet supplementation (found in cruciferous vegetables), ribavirin (used in RSV pneumonia, some promise), mitomycin C, mumps vaccine (some promise), antireflux therapy

OSTEODYSTROPHIES

Fibrous Dysplasia

Genetically based developmental anomaly, defect in osteoblastic differentiation, replacement of normal medullary bone by fibrous tissue and immature woven bone. Presents <age 30, lesions present as painless enlarging bony swelling. 25 % occurs in head and neck, mainly maxilla

- Three clinical presentations
  - Monostotic (80 %), most commonly in ribs and femur
  - Polyostotic (17 %)
  - Disseminated (McCune-Albright syndrome) *(3 %)*: polyostotic disease associated with triad of hyperpigmentation, precocious puberty, and endocrinopathy
- Histology: not encapsulated (versus ossifying fibroma, which has a capsule), immature bone without osteoblastic activity
- Symptoms: sinonasal obstruction and associated pain; if compressing optic nerve, diplopia, aesthetic deformity
- Workup: computed tomography—findings depend on density of mineralization—in early disease higher density of fibrous tissue, appears radiolucent or lytic, similar to bone cyst. As disease progresses, ground-glass appearance. MR—hypointense on T1, variable findings T2, nonhomogeneous after gadolinium
- Treatment (only for cosmetic deformity, or impingement of critical structures causing pain or functional deficit) surgical debulking, curettage, and excision. Medical management with bisphosphonates (pamidronate) to inhibit osteoclastic activity. Radiotherapy contraindicated due to possible malignant conversion

Ossifying Fibroma

Benign neoplasm. Occurs in third to fourth decade, more common in black females, psammomatoid variant occurs in men at younger age, more aggressive

- Histology: encapsulated, variant with small ossicles in stroma that appear like psammoma bodies
- Symptoms: space occupying lesion in nasal cavity, temporal bone
- Workup: endoscopic exam—lesion covered by intact mucosa. Computed tomography—well-defined, multiloculated lesion, bordered by egg-shell-like rim. MR—hyperintense on T2; on T1 central portion intermediately to hyperintense central portion with hypointense outer portion
- Treatment: surgical radical resection due to high rate of aggressive recurrence with local destructive potential. Radiotherapy contraindicated due to possible malignant conversion

Paget's Disease

Osteitis deformans, idiopathic chronic and at times progressive disease of bone, osteolytic and osteoblastic changes that affect axial skeleton. Autosomal dominant pattern with high penetrance, associated with mutations in gene-encoding sequestosome 1, possibly related to viral infection. Age of onset >40, polyostotic most common, occurs in lumbar spine, in head and neck, skull and maxilla often involved

- Three phases of disease
  - Osteolytic phase
  - Mixed or combined phase
  - Osteoblastic "burn out" phase
- If temporal bone involvement—remodeling of inactive irregular bone into normal appearing lamellar bone
- Symptoms: enlarging head, kyphosis. If inner ear and/or internal auditory canal involved, tinnitus, mixed hearing loss (50 %) vestibular dysfunction. Facial nerve spared. Spacing and mobility of teeth if maxilla involved
- Histology: osteoclastic resorption, increased vascularity and formation of fibrous tissue, mosaic pattern of new bone formation
- Workup/diagnosis: elevated serum alkaline phosphatase, thickened skull table, lytic lesions in calvarium
- Treatment: calcitonin, bisphosponates

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PART III
General
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Chapter 9

Sleep-Disordered Breathing and Obstructive Sleep Apnea

Lucia Olarte and Fred Y. Lin

PEARLS

- Apnea–Hypopnea Index
  - AHI <5—Normal, Snoring, or Upper Airway Resistance Syndrome (UARS)
  - AHI 5–15—Mild Sleep Apnea
  - AHI 15–30—Moderate Sleep Apnea
  - AHI >30—Severe Sleep Apnea
- Sleep Syndromes:
  - Snoring
  - Upper airway resistance syndrome: daytime hypersomnolence, normal PSG
  - Obstructive sleep apnea syndrome: daytime hypersomnolence
    - Apnea and hypopnea (AHI >5)
- Definitions:
  - Apneic event: cessation of ventilation for 10 s or longer leading to an arousal
  - Hypopneic event: a decrease in airflow of 30 % with a 4 % decrease in oxygen saturation or a 50 % decrease in airflow with a 3 % decrease in oxygen saturation
  - Respiratory effort-related arousal (RERA): absence of apnea–hypopnea with a 10 s or more duration of progressive negative esophageal pressure leading to an arousal or microarousal
  - Apnea Index (AI): number of apneas in an hour period
  - Respiratory distress index (RDI): number of apneas, hypopneas, and RERA's in an hour. No longer used in defining sleep apnea

Sleep Physiology

Normal Sleep:

- Non-rapid eye movement (NREM), "quiet" sleep stage:
  - Steady, slow heart rate
  - Slow respiratory rate
  - Low blood pressure
- Rapid eye movement (REM)
  - Bursts of rapid conjugate eye movement
  - Increased autonomic activity
  - Large fluctuations in heart rate, respiratory rate, blood pressure
  - Dreaming

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TABLE 9.1 Sleep architecture of young healthy adult

Stage		Arousal threshold	EEG pattern	Sleep distribution (%)
NREM sleep	N1	Low	Theta waves	2–5
	N2	High	K complex/sleep spindles	45–55
	N3	Higher	Delta waves ("slow-wave sleep")	5–20
REM sleep		Variable	Sawtooth waves	20–25

- Age Distribution
  - Infants and children under age 10
    - Higher percentage of REM sleep and stage 3 NREM sleep
  - >10 Years old adults
    - See Table 9.1
  - > 60 Years old
    - Stage 3 diminished, may no longer be present
- Sex distribution
  - With aging, women maintain slow-wave sleep longer than men

Obstructive Sleep Disorders

Definitions:

- Apneic event: cessation of ventilation for 10 s or longer leading to an arousal
- Hypopneic event: a decrease in airflow of 30 % with a 4 % decrease in oxygen saturation or a 50 % decrease in airflow with a 3 % decrease in oxygen saturation
- Respiratory effort-related arousal (RERA): absence of apnea–hypopnea with a 10 s or more duration of progressive negative esophageal pressure leading to an arousal or microarousal
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- Respiratory effort-related arousal (RERA): absence of apnea–hypopnea with a 10 s or more duration of progressive negative esophageal pressure leading to an arousal or microarousal
- Patterns of arousal
  - Obstructive: lack of airflow despite ventilatory effort
  - Central: lack of airflow resulting from an absence of ventilatory effort
  - Mixed: usually begins as a central apneic event, ends as an obstructive event

Snoring:

- An undesirable sound that occurs predominantly during sleep
- Nonapneic snoring can be associated with arousal or sleep fragmentation
- Does imply upper airway resistance

Upper Airway Resistance Syndrome:

- Mild sleep-related upper airway system closure
- No true apnea or hypopnea events
- Does lead to arousals, sleep fragmentation, and excessive daytime sleepiness
- Repetitive alpha EEG arousals with sleep fragmentation
- 15 or more RERAs per hour
- More often seen in women, nonobese patients, and young adults

Obstructive Sleep Hypopnea Syndrome:

- Daytime hypersomnolence
- Greater than 15 hypopneas per hour
- No apneas

Obstructive Sleep Apnea Syndrome:

- Apnea–hypopnea index (AHI) of 5 or more
- Mild: AHI 5–15
- Moderate: AHI 15–30
- Severe: AHI ≥30

Physiology of Upper Airway Obstruction

Multifactorial interaction

- Collapsible airway
  - Obesity, soft tissue hypertrophy, craniofacial abnormalities, neuromuscular tone
- Pharyngeal dilator muscle relaxation
  - Reflex pathway from the central nervous system fails to maintain pharyngeal patency
- Nasal obstruction can worsen OSA
  - Open-mouth breathing when asleep that can increase upper airway collapsibility and decrease dilator muscle efficacy
  - Mouth breathing leads to a backward rotation of the jaw displacing tongue base posteriorly, lowers hyoid, leads to pharyngeal collapse
  - Increased resistance upstream leading to an increased collapse downstream via loss of nasal reflex

Symptoms of OSAS

- Snoring
- Witnessed episodes of gasping or choking
- Frequent movements that disrupt sleep
- Restless sleep
- Fatigue
- Waking feeling tired and unrefreshed regardless of time slept
- Excessive daytime sleepiness
- Forgetfulness
- Irritability
- Sexual dysfunction
- Motor vehicle accidents (MVAs)
- Job-related accidents
- The degree of daytime sleepiness and its impact on quality of life correlate poorly with the frequency and severity of respiratory events

Consequence of Untreated OSA

Increased mortality

Cardiovascular disease

- Hypertension
  - Likely related to increased sympathetic tone from hypoxemia and frequent arousals
  - Treatment of OSA improves hypertension
  - Apneic event: decreased cardiac output, increased sympathetic nervous system activation, increased systemic vascular resistance
  - Resolution of apneic episode: increased venous return to the right side of the heart leading to an increased cardiac output against the increased vascular resistance, abrupt increase in blood pressure
  - Multiple cycles, eventual increased sympathetic nervous system activation persists
- Coronary artery disease
  - Recurrent apneas can cause acute thrombotic events, secondary to an increase in platelet activation, and chronic atherosclerosis

- Congestive heart failure
  - Increased afterload on an already failing heart leading to reduced cardiac output
  - Release of catecholamines from the apneic event can worsen cardiac function
- Arrhythmia
  - Bradytachyarrythmia are the most common seen
  - Bradycardia starts at cessation of respiration followed by tachycardia at the resumption of respiration as a result of the increased sympathetic activity from the hypoxia and arousal
  - Supraventricular tachycardia, premature ventricular contractions, changes in QT interval
- Myocardial infarcts
  - Acute ischemia can occur as a result of a depletion of myocardial oxygen supply during apneic events
- Stroke
  - Cerebral vascular similar stress as cardiac vasculature
  - Apnea leads to decreased systemic pressure and increase in intracranial pressure leading to a decrease in cerebral perfusion, increasing the chance for an ischemic event
  - Fluctuations in cerebral blood flow, increase in atherosclerotic changes to endothelium, increased risk of thrombotic events
- Risk for insulin resistance
- Sudden death
- Pulmonary hypertension

Neurocognitive difficulties

- Problems with attention, working memory and executive function

Increased risk of fatal and nonfatal motor vehicle accidents (MVA)

Diagnosis

Common symptoms

- Loud snoring, restless sleep, daytime hypersomnolence
- In women: insomnia, heart palpitations, ankle edema

Screening

- Epworth Sleepiness Scale Score >10
  - 0 = would never doze
  - 1 = slight change of dozing
  - 2 = moderate chance of dozing
  - 3 = high chance of dozing

Situation	Chance of dozing (0–3)
Sitting and reading	
Watching TV	
Sitting inactive in a public place	
As a passenger in a car for an hour without a break	
Lying down to rest in the afternoon when circumstances permit	
Sitting and talking to someone	
Sitting quietly after lunch without alcohol	
In a car, while stopping for a few minutes in traffic	

Rule out other disorders causing fatigue

Examination

- BMI, blood pressure, neck circumference
- Body habitus, size of mandible/maxilla, retrognathia/prognathia, facial character
- Nasal: size, deformity, valve, septum, turbinates, polyps/masses, adenoids
- Oral Cavity/Oropharynx: size/position of tongue, elongated palate/uvula, tonsils, Mallampati score/Friedman classification, dentition, crowding of oral pharynx

- Hypopharynx: size/position of tongue base, lingual tonsillar hypertrophy
- Larynx: mobility of vocal cords, masses/polyps
- Neck: size, placement of hyoid, jaw/retrognathia
- Flexible nasolaryngoscopy: awake, asleep, lying down
  - Müller maneuver: nose pinched close with mouth closed, inhale against closed airway examining retropalatal and retrolingual areas for collapse
- Drug-induced sleep videoendoscopy
  - Propofol-induced sleep
  - Evaluate degree of obstruction from lateral pharyngeal folds, retropalatal, retrolingual areas

Imaging

- Cephalometric radiograph
  - Inferiorly displaced hyoid, small posterior airway space, long palate
  - Mandibular plane to hyoid distance <21 mm associated with higher success in patients with mild to moderate OSA undergoing uvulopalatopharyngoplasty (UPPP)
- CT Scan
  - Poor sensitivity for OSA
- MRI
  - Also poor sensitivity for OSA but excellent evaluation of soft tissue
- Fluoroscopy
  - Can improve UPPP selection/outcomes
  - Time intensive, radiation exposure
- Nocturnal Polysomnography (PSG): Gold Standard
- Level 1:
  - Electroencephalogram (EEG)
  - Electro-oculogram (EOG)
  - Submental electromyogram (EMG)
  - Electrocardiogram (ECG)
  - Nasal and oral airflow
  - Thoracoabdominal effort
  - Blood oxygen concentration/Oximetry (SaO_2)
  - Body position
  - Snoring
- Level 2:
  - Unattended study performed in the patient's home, limited by lack of technician to perform hookup
  - Same measures as Level 1
- Level 3:
  - Unattended, same limitations as Level 2
  - Heart rate
  - Airflow
  - Oximetry
  - May underestimate AHI because does not determine sleep versus wake
- Level 4:
  - Unattended
  - 1–2 parameters, including oxygen saturation

Treatment

Medical

- Conservative/Behavioral Modifications
  - Avoid alcohol, sedatives at bedtime
    - Sedatives can promote deep sleep, make apnea more pronounced, blunt drive to arouse and resume breathing

- Weight loss
- Positional therapy: supine position, tongue falls posteriorly enhancing obstruction
- Bariatric surgery consult for morbidly obese patients

- CPAP (Continuous positive airway pressure): Gold Standard
  - Pneumatic splint, prevents upper airway collapse, constant intraluminal pressure during inspiration and expiration
  - Moderate to severe OSA
    - Reduces AHI, improved subjective and objective sleep measures, quality of life measures, decreased cardiovascular events, decreased MVAs
  - Complicated by patient adherence
    - Compliance considered at least 4 h per night, 5 days/week
- BiPAP
  - Separately adjustable lower expiratory and higher inspiratory PAP: tolerated better by some
- APAP (Autoadjusting PAP)
  - Autotitrate PAP to select an effective level of CPAP to prevent upper airway collapse
  - Pressure changes in response to variations, snoring, impedence
- Oral Appliances
  - Mild to moderate OSA
  - Mobilizes mandible and base of tongue anteriorly, maintains patency of posterior oropharyngeal airway
  - Complicated by tooth/jaw pain, increase in salivation overnight, dry mouth
  - Cost effective but more effective for milder cases
- Medications
  - Insufficient evidence. Theory: increase upper airway dilator muscle tone, increase ventilatory drive, increase cholinergic tone during sleep versus a decrease in percent of REM sleep, decreased airway resistance, decreased surface tension in the upper airway
  - Progesterone: respiratory stimulant
  - Acetazolamide: increases hydrogen concentration in blood
  - Theophylline: increases hypoxic ventilatory drive
  - Protryptiline: reduce REM sleep
  - Oxygen therapy
  - Fluticasone: if allergic rhinitis component
  - Montelukast (Leukotriene receptor antagonist): decreased adenoid size in children with mild OSA
  - Modafinil (Central post alpha-adrenergic receptor): promotes alertness, used to treat narcolepsy and idiopathic hypersomnia, adjuvant for patients on CPAP who continue to experience excessive daytime sleepiness
  - Nasal Strips
    - Can decrease snoring, mouth breathing, sleepiness
    - Can improve UPPP selection/outcomes

Surgical: Determined by the site of obstruction

- Counseling possibility of multiple or staged procedures, possibility of tracheostomy
- Nasal: can reduce CPAP requirements, rarely cures OSA
  - Septoplasty
  - Turbinate surgery
  - Nasal valve repair
  - Sinus surgery
  - Adenoidectomy
- Palatal
  - UPPP with or without tonsillectomy
    - Remove uvula, redundant tissue from the soft palate and anterior tonsillar pillars
    - Posterior tonsillar pillars advanced lateral-cephalad direction
    - Enlarge nasopharyngeal airway in anterior to posterior dimension
    - Risk of nasal reflux temporarily, infection, change in speech

- Transpalatal advancement pharyngoplasty after UPPP if persistent OSA
  - Remove 1 cm of the hard palate, advance the soft palate, secure to tensor aponeurosis
- Expansion sphincteroplasty
  - Variation of UPPP
- Uvulopalatal flap
  - Variation of UPPP
  - Advancement flap, suture uvula and distal soft palatal tissue upward onto soft palate
  - If VPI, procedure is reversible
  - Contraindicated in patients with excessively thick palates or uvulas
- Z-palatoplasty
- Laser-assisted uvulopalatoplasty (LAUP)
  - Primarily for snoring
  - CO_2 laser, 2 vertical cuts in soft palate on either side of uvula, amputate lower two-thirds to three-fourths of the uvula
  - Scar retraction and stiffening of the palate is achieved
- Cautery-assisted palatal stiffening (CAPSO)
  - Remove mucosa off midline of soft palate, induces scar tissue resulting in stiffer palate
- Radiofrequency ablation of soft palate
  - Soft palate coagulation necrosis causes scarring and contraction of tissue, shorter stiffer soft palate
  - Office-based procedure, local anesthesia
- Palate implant
  - Used for snoring
  - 3 to 5 implantable rods inserted into the palate for scar formation
  - Risk of implant extrusion
- Injection snoreplasty
  - Office-based procedure for snoring
  - Inject sclerosing agent (alcohol, sodium tetradecyl sulfate) into midline of soft palate

- Tongue Base
  - Partial midline glossectomy
    - CO_2 laser, electrocautery, plasma knife, coblation
    - Risk of bleeding from lingual artery, hypoglossal nerve injury, hematoma, abscess, dysphagia, taste disturbance
  - Lingualplasty
  - Lingual tonsillectomy
  - Radiofrequency tongue base ablation
    - Four lesions at circumvallate papilla to reduce tissue volume at the tongue base
- Hypopharyngeal
  - Genioglossus advancement
    - More anteriorly positioned tongue with increased tension on the genioglossus
    - Rectangular geniotubercle osteotomy with advancement
    - Risk of dental root injury, mandible fracture, hematoma
  - Hyoid myotomy/suspension
    - Hyoid mobilized anteriorly and superiorly via attachment to the mandible or to thyroid cartilage
    - Risk of numbness, infection, seroma, fracture, death
  - Tongue suspension
    - Base of tongue to anterior floor of mouth
  - Maxillomandibular advancement
    - Most effective surgical procedure for OSA
    - Enlarges pharyngeal and hypopharyngeal airway
    - Risk of malocclusion, relapse, nerve paresthesia, nonunion, malunion, temporomandibular joint tenderness, infection

- Tracheotomy
  - Bypass the site of upper airway obstruction
  - Indications: morbid obesity, arrhythmia with apnea, severe apnea with desaturation, cor pulmonale, no response to dietary modifications or CPAP, chronic alveolar hypoventilation

Postoperative care

- There is an increased risk of airway compromise from edema, respiratory rate alteration secondary to narcotics, possibility of bleeding and difficulty with intubation
- Repeat polysomnography at 3–4 months postoperatively

Sleep Disorders

Insomnia

- Recurrent difficulty with sleep initiation, maintenance, consolidation, or quality causing daytime dysfunction. May include non-restorative sleep or sleep of poor quality
- Daytime symptoms must include at least one:
  - Fatigue or malaise, cognitive impairment (attention, concentration, or memory), social/vocational difficulty or poor school performance, mood impairment or irritability, daytime sleepiness, reduced motivation or energy, tendency to be accident-prone, headache, muscle tension, gastrointestinal upset, concerns about sleep itself

Sleep-Related Breathing Disorders

- Central Sleep Apnea Syndromes
  - Primary central sleep apnea
  - Central sleep apnea due to Cheyne-Stokes breathing pattern (increased risk of CHF)
  - Central sleep apnea due to high-altitude periodic breathing
  - Central sleep apnea due to medical condition not Cheyne Stokes
  - Central sleep apnea due to drug or substance
  - Primary sleep apnea of infancy
- Obstructive Sleep Apnea Syndromes
  - Obstructive sleep apnea, adult
  - Obstructive sleep apnea, pediatric
- Other Sleep-Related Breathing Disorders
  - Sleep apnea/sleep-related breathing disorder, unspecified
  - Obesity-related hypoventilation

Hypersomnias of Central Origin

- Subclasses:
  - Narcolepsy
  - Recurrent hypersomnia
  - Klein-Levin syndrome
  - Menstrual-related hypersomnia
  - Idiopathic hypersomnia
  - Behaviorally induced insufficient sleep syndrome
  - Hypersomnia due to medical condition
  - Hypersomnia due to drug or substance

Circadian Rhythm Sleep Disorders

Parasomnias

- Disorders of Arousal
  - Confusional arousals
  - Sleepwalking
  - Sleep terrors
- Parasomnias usually associated with REM Sleep
  - REM sleep behavior disorder (including parasomnia overlap disorder and status dissociatus)
  - Recurrent isolated sleep paralysis
  - Nightmare disorder
    - Treatment: reassurance, cognitive-behavioral therapy, pharmacologic intervention

- Other Parasomnias
  - Sleep-related dissociative disorders
  - Sleep enuresis
  - Sleep-related groaning (catathrenia)
  - Exploding head syndrome
- Parasomnias Associated with Obstructive Sleep Apnea
  - OSA-induced arousals from REM sleep
  - OSA-induced arousals in NREM sleep
  - OSA-induced cerebral anoxic attacks or nocturnal seizures
  - REM rebound from CPAP use leading to:
    - Confusional arousals
    - Sleepwalking
    - Sleep terrors

Sleep-Related Movement Disorders

- Subclasses
  - Restless leg syndrome
    - Rule out iron deficiency
  - Periodic limb movement disorder
    - Treatment: clonazepam and dopamine agonist therapy
  - Sleep-related leg cramps
  - Sleep-related bruxism
  - Sleep-related movement disorder, unspecified
  - Sleep-related movement disorder due to drug or substance
  - Sleep-related movement disorder due to medical condition

Isolated Symptoms, Apparently Normal Variants, and Unresolved Issues

- Subclasses
  - Long sleeper
  - Short sleeper
  - Snoring
  - Sleep talking
  - Sleep starts (hypnic jerks)
  - Benign sleep myoclonus of infancy
  - Hypnagogic foot tremor and alternating leg muscle activation during sleep
  - Propriospinal myoclonus at sleep onset
  - Excessive fragmentary myoclonus

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Chapter 10
Fluids, Hemostasis, Nutrition, and Pulmonary Physiology

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PEARLS

- Fluid and electrolyte optimization serves an integral role in the management of the surgical patient
- Electrolyte disturbances should be addressed promptly and may require medical consultation particularly if there are symptoms
- Routine preoperative use of coagulation studies, platelet count may be unnecessary and should be guided by patient history and the surgical bleeding risk that accompanies the proposed procedure
- Alcohol abuse may be a co-contributor to nutritional deficiencies in this patient population

FLUIDS

- Fluid and Electrolyte Requirements
  - Total Body Fluid Volume (liters) is at least half of body weight
    - 60 % of lean body weight (kg) for males
    - 50 % of lean body weight (kg) for females
  - Maintenance fluid therapy replaces water and electrolytes lost in normal physiologic processes, i.e., respiratory tract, skin, stool, and urine
    - It can be given enterally or intravenously
    - Adults—4/2/1 rule
      - 4 ml/kg for first 10 kg
      - 2 ml/kg for next 10 kg
      - 1 ml/kg for anything over 20 kg
    - Typical maintenance fluid regimen to provide adequate water and electrolyte requirements:
      - D5 0.45 % NaCl + 20 mEq/L KCl
  - Repletion fluid therapy replaces water and electrolytes lost in pathologic processes, i.e., diarrhea, vomiting, trauma
    - If patient is in unstable clinical condition, administer a bolus of isotonic replacement fluid such as 0.9 % NS, Lactated Ringer's or Plasmalyte

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- Electrolyte Hemostasis
  - Sodium and Water
    - Normal serum sodium 135–145 mEq/L
    - Normal sodium intake 1 mEq/kg/24 h
    - Serum sodium disorders are due to changes in total body water balance or distribution
    - Hyponatremia (Sodium <135 mEq/L)
      - Pathophysiology: Excess of water relative to sodium
      - Treatment:
        - Correction with 0.9 % NS or 3 % NS should be guided by calculating the sodium deficit. Increase serum sodium at rate of 0.5 mEq/L/h to avoid central pontine myelinolysis
        - If CNS symptoms (seizures, cerebral edema, increased intracranial pressure), correct sodium rapidly with hypertonic saline (3 % NS). Increase serum sodium by 2 mEq/L/h until symptoms resolve
        - If asymptomatic, therapy will depend on the volume status of the patient
          - Hypovolemic: replete with 0.9 % NS
          - Euvolemic: free water restriction to 1–1.5 L/day and reverse underlying cause. Also consider loop diuretic
          - Hypervolemic: free water restriction to 1–1.5 L/day, dietary sodium restriction, loop diuretic
    - Hypernatremia (Sodium >145 mEq/L)
      - Pathophysiology: deficit of water relative to sodium or sodium gain in the setting of lack of access to free water or inability to concentrate urine
      - Treatment:
        - Correction of free water deficits with hypotonic solution (D5W, ½ NS, ¼ NS) should be guided by calculating the free water deficit. Decrease serum sodium at rate of 0.5 mEq/L/h to avoid cerebral edema
          - Water deficit = (Total body water) × (1 – (140/Na))
          - Total body water = Correction factor × Weight
          - The correction factor is 0.6 for men, 0.5 for women and elderly men, and 0.45 for elderly women
        - Hypovolemic: First give 0.9 % NS if hemodynamic instability. Replace free water deficit with hypotonic solution
        - Euvolemic: Central DI—dDAVP, Neurogenic DI—treat cause, thiazide diuretic + sodium restriction
        - Hypervolemic: loop diuretic and D5W or PO ingestion of free water
  - Potassium
    - Normal serum Potassium 3.5–5.0 mEq/L
    - Hypokalemia (Potassium <3.5 mEq/L)
      - Pathophysiology: due to transcellular shift or potassium depletion
      - Clinical: nausea, vomiting, anorexia, ileus, weakness, muscle cramps, polyuria, EKG changes—u waves, ventricular ectopy (PVCs), increased QT interval
      - Treatment:
        - Patients can tolerate mild hypokalemia (serum potassium 3–3.5 mEq/L)
        - Correct hypomagnesemia
        - Goal serum potassium = 4 for patients with underlying cardiac disease (i.e., CAD, arrhythmias) or on digoxin
        - Oral—preferable, safer route
        - IV—consider if patient is NPO or life-threatening hypokalemia
    - Hyperkalemia (Potassium >5.0 mEq/L)
      - Pathophysiology: due to transcellular shift or renal dysfunction
      - Clinical: weakness, nausea, paresthesias, palpitations, EKG: peaked t waves, long PR interval, increased QRS width, asystole/PEA

- Treatment: guided by the serum potassium level and if there are EKG changes
  - EKG changes or serum $K \geq 6.5$ mEq/L: Calcium gluconate or chloride (give 1st), regular insulin/D50, $NaHCO_3$
  - No EKG changes: Kayexalate PO/rectal
  - Renal insufficiency: consider hemodialysis, loop diuretic

○ Calcium
- ■ Normal serum total calcium 9–10 mg/dL, ionized calcium 1.1–1.3 mmol/L
- ■ 99 % of calcium is in the bone, remaining 1 % in the serum is ionized (active form) or complexed with anions or albumin (inactive form)
  - Total serum calcium value affected by change in anions or albumin levels
  - Calcium balance is regulated by PTH and calcitriol (1,25 vitamin D)
- ■ Hypocalcemia (serum total calcium <8.4 mg/dL, ionized calcium <1 mmol/L)
  - Pathophysiology: decreased PTH activity, vitamin D deficiency
  - Clinical: numbness, tingling, headaches, cramps, Chvostek sign (facial nerve irritability), Trousseau sign (carpal spasm), laryngospasm, growth failure, bone pain, osteomalacia, osteitis fibrosa cystica, cardiovascular instability, ventricular ectopy
  - Treatment: guided by cause and if there are symptoms
    - Replete hypomagnesemia first
    - Symptomatic: calcium gluconate or chloride 1–2 g IV, consider continuous infusion
    - Asymptomatic or chronic: calcium (1–3 g/day) + calcitriol PO
    - Parathyroidectomy: patients are at risk for hypocalcemia postoperatively, consult endocrinology to optimize vitamin D preoperatively, ionized calcium should be measured at least once every 6 hours postoperatively and repleted accordingly
- ■ Hypercalcemia (serum total calcium >10.6 mg/dL, ionized calcium >1.3 mmol/L)
  - Pathophysiology: Increased PTH, neoplasm
  - Clinical: symptoms usually with total serum calcium >12 mg/dL or ionized calcium >3 mmol/L
  - "bones, stones, abdominal groans, and psychiatric moans"—Nausea, vomiting, ileus, constipation, pancreatitis, cardiovascular instability, short QT interval, altered mental status, polyuria, nephrolithiasis, osteopenia, fractures
  - Treatment: manage acutely if symptoms or serum calcium >12 mg/dL, reverse underlying cause
    - Correct hypovolemia with 0.9 % NS
    - Furosemide IV q2–6 h (replace urinary loss with 0.9 % NS)
    - Bisphosphonate IV
    - Calcitonin
    - Malignancy—glucocorticoids
    - Parathyroidectomy

○ Magnesium
- ■ Normal serum levels 1.6–2.5 mEq/dL
- ■ Normal intake 20 mEq/day
- ■ No hormones affect magnesium balance
- ■ Magnesium concentration affects renal excretion
- ■ Hypomagnesemia (serum magnesium <1.4 mEq/dL)
  - Etiology: impaired intestinal absorption (alcohol abuse, malnutrition, NGT drainage, diarrhea), increased renal excretion (drugs, uncontrolled diabetes), chelation from the serum (pancreatitis, hungry bone syndrome)
  - Clinical: altered mental status, fasiculations, tremor, seizure, electrolyte abnormalities—hypocalcemia, hypokalemia, hypophosphatemia, EKG changes—prolonged PR and QT interval, torsade de pointes
  - Treatment:
    - Caution with renal insufficiency
    - Symptomatic: Magnesium sulfate 2 g bolus then infusion
    - Asymptomatic: Magnesium oral (associated with diarrhea)

- Hypermagnesemia (serum magnesium >2.2 mEq/dL)
  - Etiology: iatrogenic, renal insufficiency, DKA, tumor lysis syndrome
  - Clinical: hyporeflexia, lethargy, weakness, paralysis, hypotension, bradycardia, arrhythmias
  - Treatment:
    - Symptomatic: supportive care, calcium gluconate 1 g IV bolus, consider dialysis with renal insufficiency
    - Asymptomatic: with normal renal function, magnesium levels will return to normal, consider dialysis with renal insufficiency

- Phosphorus
  - Normal serum levels 3.0–4.5 mg/dL
  - Phosphorus balance affected by PTH, phosphorus concentration, insulin and calcitriol (1,25 vitamin D)
  - Hypophosphatemia (serum phosphorus <2.8 mg/dL)
    - Etiology: impaired intestinal absorption (malabsorption, oral phosphate binder use, alcoholism, vitamin D deficiency), increased renal excretion (hyperparathyroidism, DKA, sepsis), transcellular shift (refeeding syndrome, respiratory alkalosis)
    - Clinical: symptoms occur due to decreased ATP and tissue oxygen delivery—weakness, heart failure, impaired diaphragm function, paresthesia, altered mental status, hemolysis, platelet dysfunction
    - Treatment: serum phosphorus <1 mg/dl and/or symptoms: Replete with IV phosphorus otherwise replete with oral phosphorus
  - Hyperphosphatemia (serum magnesium >4.5 mg/dL)
    - Etiology: transcellular shift (rhabdomyolysis, tumor lysis syndrome, increased intake (Fleet enema, excess vitamin D), decreased renal excretion (renal insufficiency, hypoparathyroidism)
    - Clinical: calcium–phosphate complex deposition, acute hypocalcemia
    - Treatment:
      - Acute hyperphosphatemia: dialysis, 0.9 % NS, acetazolamide
      - Chronic hyperphosphatemia: minimize phosphorus intake, phosphate binders

- Acid Base Disorders
  - Acidemia: pH <7.37, due to processes that increase [H+] or decrease [HCO_3−]
  - Alkalemia pH >7.43, due to processes that decrease [H+] or increase [HCO_3−]
  - Approach to blood gas
    - Look at change in [HCO_3−] and/or pCO_2 to see if it can account for change in pH
    - If pH is normal or if compensation is less or more than predicted, then a mixed disorder is likely present
    - If metabolic acidosis, calculate anion gap (AG):
      - AG = [Na] − ([Cl] + [HCO_3])
      - AG >10, positive AG gap
  - Metabolic Acidosis
    - Anion Gap Metabolic Acidosis
    - Etiologies: "MUDPILES"
      - M—methanol
      - U—uremia
      - D—DKA
      - P—paraldehyde
      - I—Isoniazid, inborn errors of metabolism
      - L—Lactic acidosis
      - E—Ethylene glycol
      - S—Salicylates, acetaminophen
    - Non-anion Gap Metabolic Acidosis
    - Etiologies:
      - GI loss of [HCO_3−]—diarrhea, pancreatic fistula, or drainage
      - Renal causes—RTA, renal failure

- Ingestions—acetazolamide, sevelamer
- Dilutional—bicarbonate fluid infusion
- Post-hypocapnia
- Ureteral diversion
- Treatment: directed at cause, no benefit of sodium bicarbonate therapy with ketoacidosis and lactic acidosis

○ Metabolic Alkalosis
■ Etiologies:
- Loss of acid from GI tract or kidney—vomiting, NGT drainage, diuretics, Bartter/Gitelman syndrome, hyperaldosteronism
- Excess alkali
- Post-hypercapnia
- Treatment: directed at cause, replete hypokalemia

○ Respiratory Acidosis
■ Etiologies:
- CNS depression—drugs, brainstem lesions
- Upper airway abnormalities—OSA, laryngospasm
- Lower airway abnormalities—obstructive lung disease, pneumonia, pulmonary edema
- Thoracic cage abnormalities—pneumothorax, flail chest
- Neuromuscular failure—Guillain-Barre, ALS
- Treatment: directed at cause, improve ventilation, no role of sodium bicarbonate

○ Respiratory Alkalosis
■ Etiologies:
- Primary hyperventilation—CNS disorders, pain, anxiety, drugs, pregnancy, sepsis, hepatic encephalopathy, asthma exacerbation, mechanical ventilation
- Treatment: directed at cause, change ventilator settings

● Pediatric Concerns
○ Fluid and Electrolyte Needs
■ Bolus Fluid: 20 cc/kg over 30 min to 1 h
■ Maintenance Fluid: Many different methods, Holliday-Segar Method mostly used, 4:2:1 rule
- First 10 kg, 4 mL/kg/h
- Second 10 kg, 2 mL/kg/h
- Each additional kg, 1 mL/kg/h
- i.e., 25 kg child = 65 mL/h

■ Maintenance Electrolyte: 1:2:3 rule
- 1 mEq potassium/kg/day
- 2 mEq sodium/kg/day
- 3 mEq chloride/kg/day

■ Urine output should be at least 1 mL/kg/h

HEMOSTASIS

Components of Primary Hemostasis

● Blood Vessels
○ Vascular injury triggers vasoconstriction
○ Disorders of the vasculature clinically are exceedingly rare, but can be separated into acquired and heredity disorders:
■ Hereditary: Ehlers-Danlos syndrome, William-Beuren syndrome, Hereditary-Hemorrhagic Telengectasias (HHT aka Osler-Weber-Rendu syndrome), Osteogenesis imperfecta
■ Acquired: Scurvy, amyloidosis

- Platelets
  - Adhesion
    - High sheer-state of flowing blood require effective contact between platelets and the vascular endothelium
    - Generally, vascular injury leads to exposed collagen fibrils and an accessory molecule known as von Willebrand Factor (vWF)
    - Enabled by binding of GP1b surface receptor on platelets to vWF
    - In the presence of thrombin, factor VIII is activated and is released from vWF
    - vWF is capable of binding the exposed subendothelial connective tissue factors and also binds to the GP1b receptor expressed on platelet surfaces
  - Aggregation
    - Platelets undergo metamorphosis in which they assume a more spherical shape with cytoplasmic projections called pseudopods
    - Formation of a platelet plug is also enhanced by the production of specific cell-surface receptor proteins called GPIIb/IIIa which allows platelet aggregation to occur
    - GPIIb and GPIIIa are a part of class of proteins called integrins and together are assembled into a receptor complex on the surface of platelets
    - Platelets require an intermediary protein, fibrinogen, to bridge the "gap" between the GPIIb/IIIa receptors on individual platelets
  - Release
    - Occurs simultaneously with platelet aggregation following adhesion of platelets to vWF and platelet activation
    - Activated platelets release cytoplasmic-stored granules containing ADP and thromboxane A2 (TxA2)
    - TxA2 is produced from arachidonate in platelets by the aspirin-sensitive cycloxygenase pathway
    - Thrombin is a potent activator of platelets and will result in TxA2 production in addition to effect other intracellular processes that lead to platelet shape change, and aggregation

Components of Secondary Hemostasis

- Coagulation System
  - Primary hemostasis results in the formation of a platelet plug
  - Extrinsic Pathway
    - Primary physiologic driver of clot formation. Tissue Factor (TF), also known as thromboplastin, is integral to blood clotting
    - Once generated, TF binds to circulating VIIa. TF/VIIa complex then activates factor X directly, but also factor XI. The activation of IXa by TF/VII complex leads to a prolific production of Factor Xa, much more than that produced directly by TF/VIIa. Factor Xa then activates prothrombin to thrombin
    - Thrombin positively reinforces the cascade by activating:
      - Factor VIII which is cofactor of IX
      - Factor V
      - Factor XI
    - The end product is the generation of large amount of thrombin, and ultimately fibrin to form a mature hemostatic clot
  - Intrinsic Pathway
    - Less important clinically in terms of propensity for bleeding, but important in terms of in vitro testing of clot formation
    - Contact factors—prekallikrein, high-molecular-weight kininogen, and factor XII—initiate this pathway in vivo

Clinical Assessment

- History
  - A positive history suggestive of bleeding disorder is informative and can lead to appropriate additional testing
- Physical Examination
  - Several specific findings on physical examination can suggest an underlying hematologic condition
    - Petechiae or ecchymosis → thrombocytopenia or functionally deficient platelets
    - Telangiectasias → underlying liver disease, but if around the mouth and lips could suggest HHT
    - Presence of joint deformity suggestive of prior hemarthroses → severe factor deficiencies
    - Hematomas → factor deficiencies or inhibitors against a clotting factor
    - Hyperelasticity of skin, hyperextendible joints → Ehler-Danlos syndrome or other collagen vascular disorder
- Laboratory Testing
  - PT/PTT/INR
  - Bleeding time
- Differential Diagnosis for Abnormal Coagulation Studies
  - Increased PTT
    - Inherited deficiency of clotting factors (VIII, IX, XI, XII, PK, HK, and vWF which binds and prevents degradation of factor VIII)
    - XII, PK, HK deficiencies are not associated with increased risk for clinical bleeding
    - Acquired deficiencies of multiple clotting factors
      - Inhibitors—Lupus anticoagulant (associated with thrombosis rather than bleeding)
      - Inhibitors—directed against specific factors such as factor VIII
      - Heparin
      - Liver disease
      - Disseminated Intravascular Coagulation (DIC)
  - Increased PT
    - Inherited deficiencies of one or more clotting factors
    - Acquired deficiencies of multiple clotting factors
      - Coumadin (inhibition of Vitamin K-dependent factors II, VII, IX, X)
      - Vitamin K deficiency
      - Liver disease
      - DIC
      - Inhibitors (rare)

Anticoagulants

- Unfractionated Heparin (UFH)
  - Binds to anti-thrombin III (ATIII) in plasma to form AT–heparin complex which then selectively inhibits FIIa, Xa, IXa, XIa, XIIa
  - Monitored with aPTT
  - Reversal with protamine sulfate
  - Heparin-induced thrombocytopenia (HIT) has an incidence of 3–5 %. Results from widespread platelet activation and aggregation following development of an antibody to heparin-platelet factor 4. Defined by platelet count less than 150,000 or a 50 % reduction in baseline value 5–14 days after initiation. Treatment involves immediate cessation of heparin and use of direct thrombin inhibitors

- Low Molecular Weight Heparin (LMWH)
  - Comprised of much smaller molecules of heparin
  - Binds ATIII and as a complex selectively inhibits FXa and IIa in 4:1 ratio
  - Routine measurement of aPTT is not necessary
  - HIT is a known complication of LMWH; the incidence is roughly 1 %, lower than that for UFH
  - Has no proven complete reversal treatment
- Warfarin
  - Inhibits vitamin K epoxide reductase and thereby depletes vitamin K-dependent factors 2, 7, 9, 10 and protein C and S
  - In the case of overdose and no bleeding, administer vitamin K based on INR value
  - In the case of severe bleeding give Vit K 10 mg IV and FFP at 2–4 units IV q6–8 h
- Selective Xa Inhibitors
  - Includes Rivaroxaban administered orally and Fondaparinux administered parenterally
  - Effect exerted through direct inhibition of Factor Xa
  - These are mainly used in orthopedic patients as randomized controlled trials (RCTs) have shown both to be superior to enoxaparin in the prevention of venous thromboembolism
  - Rivaroxaban increases aPTT, PT, and heparin clotting time, while Fondaparinux exerts no effect on the coagulation profiles
  - No known reversal
- Direct Thrombin Inhibitors
  - Includes dabigatran, argatroban, lepirudin, and bivalirudin
  - Dabigatran has recently been shown in phase III trials to be superior to warfarin for the prevention of embolic stroke in patients with atrial fibrillation without increased adverse bleeding events

NUTRITION

Nutritional Evaluation

- History
  - Current nutritional intake
  - Aspiration risk
  - Recent weight loss
    - Unintentional loss >10 % is significant
  - Concomitant chronic conditions predisposing to protein-calorie malnutrition
  - Prior chemoradiation therapy → fibrosis of constrictor muscles, stricture formation
  - Previous operations/procedures, including gastrointestinal tract
    - Gastrectomy → vitamin B12 deficiency
    - Ileal resection → vitamin B12 and fat-soluble vitamin (ADEK) deficiencies
- Anthropometrics
  - Scientific study of body size, weight, and proportions
  - Body Mass Index (BMI)
    - Used to measure protein-calorie malnutrition, but also over-nutrition
    - Does not incorporate percentage body fat
    - Mass (kg)/(height (m))^2
    - Underweight <18.5
    - Normal weight = 18.5–24.9
    - Overweight = 25–29.9
    - Obesity >30
- Laboratory Evaluation:
  - Serum Proteins: used to assess nutritional status but can be influenced by many other factors including rate of synthesis, loss (gastrointestinal, renal, cutaneous), and hydration status (dehydration may result in false elevation of serum proteins)

        - Albumin
            - Half-life = 20 days
            - Large volume of distribution in tandem with long half-life causes serum values to fall and recover slowly with changes in nutrition
            - Serum levels plummet in critical illness due to transcapillary escape secondary to endothelial membrane dysfunction. Considered an acute phase reactant
            - Albumin less than 3.5 mg/dL predictive of increased perioperative morbidity and mortality and associated with increased length of hospital stay
        - Transferrin
            - Shorter half-life of 8–10 days and smaller volume of distribution
            - More sensitive indicator of adequate nutrition repletion than albumin
            - Dependent on variations in iron status; iron-deficiency anemia leads to increased levels
        - Prealbumin
            - Half-life = 2 days
            - More sensitive than transferrin
            - Decrease early with malnutrition; increases quickly with repletion
        - Retinol Binding Protein
            - Half-life = 12 h
            - Highly sensitive measure of protein synthesis
- Nutritional Indices
    - Allows risk-stratification among patients in an objective manner and can be used as a prognostic indicator
    - Subjective Global Assessment (SGA) is considered the gold standard as it is clinically validated as reproducible. SGA takes into consideration many components including:
        - Medical history
        - Changes in weight
        - Dietary intake
        - Functional capacity
        - Metabolic demands
        - Gastroinstestinal symptoms
        - Physical examination
- Determination of Energy Requirements
    - Harris-Benedict Equation
        - Derived from healthy human subjects and calculates basal energy requirements (BEE) based on height, weight, gender, and age
        - Total Energy Expenditure (TEE) accounts for the caloric demands of the body under physiologic stress conditions
        - Specific stress factors for various diseases are multiplied by BEE to calculate the TEE

Nutritional Therapy

- Enteral
    - Safer and less expensive than parenteral nutrition with added benefit of preserving gut functionality
    - "Feeding the gut" prevents opportunistic bacterial overgrowth by stimulation of immunoglobulin A, maintenance of normal gut pH and flora
    - Contraindications
        - Patients who require period of bowel rest—protracted emesis, gastrointestinal bleeding, active gastrointestinal ischemia
        - Patients under physiologic stress—hemodynamically unstable patients, those with vasopressor requirements

- Access
  - Gastrostomy
    - Percutaneous endoscopic versus open
    - Consider if long-term enteral feeding is expected
    - Prophylactic insertion of gastrostomy tubes in HNSCC patients prior to definitive chemoradiation is a controversial topic within the literature. While pretreatment gastrostomy tube insertion may off-set the weight loss attendant to chemoradiation and reduce hospitalization rates for dehydration, there is also evidence that insertion is associated with a higher incidence of esophageal stricture formation
    - Risk of tumor seeding the gastric wall and subcutaneous tissues has been reported when using the standard "pull-technique"
  - Jejunostomy
    - Consider for long-term enteral feeding in patients with contraindications to delivery of feeds in the stomach
- Types of Enteral Formulas
  - Polymeric
    - Composed of complex sources of protein, carbohydrates, and fat. Requires digestion and absorption by functional GI tract
  - Elemental
    - Nutrients are provided in predigested, readily absorbable form
  - Modular
    - Special formulas that address nutritional needs of specific clinical condition, i.e., renal insufficiency, pulmonary failure, hepatic dysfunction
- Complications
  - Nasogastric tube insertion may be associated with tracheobronchial intubation, visceral perforation, esophagitis, alar necrosis, sinusitis
  - Enteral feeds, in general, carry a risk of aspiration pneumonia, particularly in those patients with poor gag reflex and depressed mental status
  - Metabolic complications—such as electrolyte imbalances (Na, K, Mg, Phos, Ca) and hyperglycemia—can also occur and require viligant monitoring and appropriate correction

- Parenteral
  - Indications
    - Only utilized when the gastrointestinal tract cannot be utilized
  - Peripheral Parenteral Nutrition (PPN)
    - Avoids complications associated with central venous access; therefore, safer to administer than TPN
    - Considered in patients who require supplemental nutrition for less than 14 days
    - Requires large volumes of solution to fulfill the typical patients total nutritional requirements as the low-osmolar solutions (<1,000 mOsm) are required to avoid phlebitis of the infused vein
    - Prolonged therapy is rarely possible as the catheter must be moved frequently to prevent the development of phlebitis
  - Total Parenteral Nutrition (TPN)
    - High osmolarity of TPN requires administration via a central vein
    - Can be concentrated in patients who require fluid restriction (heart failure, renal failure)
    - Complications occur in 5 % of patients and mortality rate attributable to TPN is 0.2 %. Complications can be:
      - Technical: arterial puncture, pneumothorax, air embolism
      - Infectious: central line-associated sepsis
      - Metabolic: refeeding syndrome in severely malnourished patients, hepatic cholestasis/acalculous cholecystitis, steatosis, hypoglycemia if TPN abruptly withdrawn

PULMONARY PHYSIOLOGY

Components of the Thoracic Cavity

- Mediastinum
  - Boundaries: parietal pleura, stermum/manubrium, vertebrae, diaphragm, superior aperture of the thorax
  - Superior compartment
    - Between superior aperture of the throat superiorly, manubrium, sternothryoid and sternohyoid muscles anteriorly, upper thoracic vertebrae posteriorly, manubrium to 4th vertebra inferiorly
      - Contains thymus, brachiocephalic veins, SVC, aortic arch with three branches, trachea, esophagus, phrenic/vagus nerves, thoracic duct, and lymphatics
  - Inferior (anterior, middle, and posterior) compartments
    - Anterior: posterior to sternum, anterior to pericardium
      - Contains fat
    - Middle: posterior to anterior compartment, anterior to posterior compartment
      - Contains pericardium and heart
    - Posterior: posterior to heart, anterior to thoracic vertebrae
      - Contains esophagus with nerve plexus, thoracic aorta, lymphatics, thoracic duct, azygos/hemiazygous veins, sympathetic trunks
  - Brachiocephalic vein
    - In adults, crosses anterior to the trachea and posterior to the upper half of the manubrium
    - In children, it crosses over the superior border of the sternum
  - Trachea
    - Bifurcates at T4-T5 or about 6 cm from the suprasternal notch. In the elderly, trachea can bifurcate at T6
    - In adults, is 10–12 cm in length, has 16–20 rings, and with diameter 20 mm × 15 mm
    - Mediastinal fascial layers are a direct continuation of the cervical fascia
  - Esophagus
    - Four constricting points: cricopharyngeus muscle, aorta crossing, left main stem bronchus crossing, diaphragm
- Lungs
  - Lung development begins at 3–4 weeks, with true alveoli by 26–28 weeks. Alveoli development continues after birth
  - Bronchopulmonary segments: Lungs are divided according to bronchial distribution and not by fissures
    - Right lung: 10 segments
      - Right upper lobe (also known as eparterial bronchus)—apical, posterior, anterior
      - Middle lobe—superior, medial
      - Lower—superior, lateral basal, medial basal, posterior basal, anterior basal
    - Left lung: 8 segments
      - Upper—apical–posterior, anterior
      - Lingula—lateral, inferior
      - Lower—superior, anteromedial basal, lateral basal, posterior basal
  - Lymph nodes: divided into two groups per TNM staging
    - N1—pulmonary nodes
    - N2—mediastinal nodes
  - Arterial supply: Deoxygenated blood—pulmonary arteries, Oxygenated—bronchial arteries
  - Venous return: Deoxygenated blood—azygous-hemiazygous, Oxygenated—pulmonary veins
  - Lung: Right lung—3 lobes that give 55 % of lung volume; Left lung—45 % of lung volume

CHEST DISEASES

Mediastinal Masses

- Anterior: 50 % of mediastinal masses, presents with retrosternal pain, cough, dyspnea, SVC syndrome, chocking sensation
  - Thymic tumors (thymomas, carcinoma, carcinoid, lipomas) lymphangioma (children), goiters, teratoma, lymphoma
- Middle:
  - Adenopathy, aortic aneurysm, bronchogenic cyst, pericardial cyst
- Posterior:
  - Neurogenic tumor (schwannoma), esophageal lesion (tumor, diverticula)

Pulmonary

- Obstructive:
  - COPD, Asthma
- Restrictive
  - Sarcoidosis, idiopathic interstitial pneumonias, pneumoconioses, hypersensitivity pneumonitidies, collagen vascular disease, eosinophilic pneumonia
  - Neuromuscular Disorders
  - Pleural disease, chest wall cavity disorder (i.e., kyphoscoliosis)
- Other:
  - Obstructive Sleep Apnea–Hypopnea Syndrome—repetitive collapse of upper airway causing obstructive respiratory events (apnea or hypopnea), associated with hypoxemia, hypercapnia, daytime somnolence

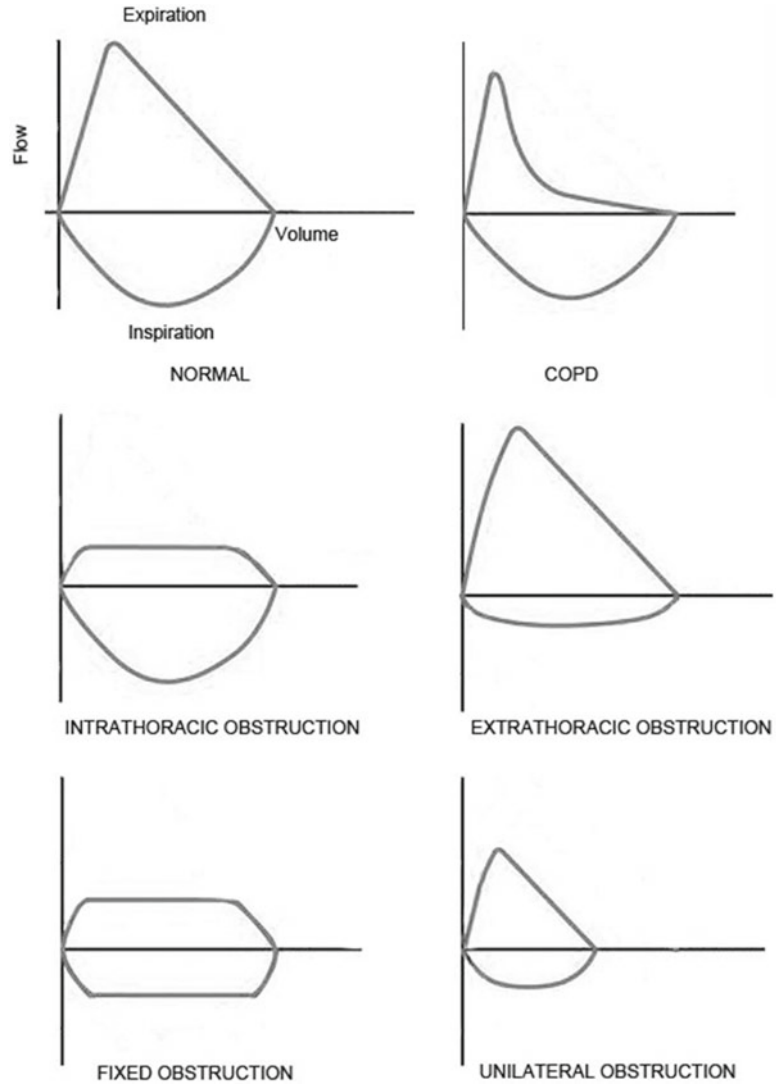
PULMONARY FUNCTION TEST

Provides objective measures of lung function. Can be used to diagnose and manage pulmonary diseases.

- Definitions
  - Tidal volume (TV) = amount of gas inspired and expired at rest
  - Residual Volume (RV) = volume of gas remaining after maximal expiration, prevents alveoli collapse
  - Functional Residual Capacity (FRC) = amount of gas in lungs after normal expiration
  - Total Lung Capacity (TLC) = total amount of gas in lungs after maximal inspiration
  - Forced Vital Capacity (FVC) = measurement of maximum expiration after maximum inspiration
  - Forced expiratory volume in 1 s (FEV1) = volume of the FVC that is expired within 1 s
  - Forced Expiratory Flow (FEF) = flow of exhaled air at different points in the FVC
    - Done at 25, 50, and 75 % of FVC
    - More sensitive in detecting early airway obstruction

Tests

- Spirometry: most readily available test, measures the rate at which lung changes volume with forced breathing maneuvers
  - Measures forced expiratory volume in one second (FEV1), forced vital capacity (FVC)
  - FEV1/FVC ratio is normal 75–85 %. Decreased ratio signifies obstructive process, low FEV1 with normal ratio signifies restrictive process
  - Flow volume loop is a plot of the inspiratory and expiratory flow against volume during the forced breathing maneuvers (See Figure below)
- Lung volumes—lung volumes of TLC, FRC, RV are measured
- Diffusing Capacity—diffusing capacity of carbon monoxide (DLCO) used to evaluate obstructive and restrictive lung diseases. Obstructive disease with decreased DLCO is emphysema. Restrictive lung disease with decreased DLCO is interstitial lung disease



Procedures

- Mediastinoscopy—for diagnostic assessment of medistinal nodes
  - Complications of mediastinoscopy—hemorrhage, vocal cord dysfunction, tracheal injury, pneumothorax
- Bronchoscopy—diagnostic bronchoscopy used for upper airway obstruction, tracheotomy decannulation, persistent cough, hemoptysis, hoarseness, persistent atelectasis, foreign body, lung cancer, neck mass, head and neck neoplasm workup
  - Flexible—visualize segmental bronchi and upper lobe bronchi for lung cancer staging
  - Rigid—obtain biopsy, culture, remove foreign body, surgical intervention
  - Complications of bronchoscopy—hypoxia, respiratory failure, fever, infection, sore throat, pneumothorax
- Tracheotomy—indicated for patients unable to be removed from mechanical ventilation, airway stenosis
  - Complications of tracheotomy
    - Intraoperative
      - Great vessel injury, laryngeal damage, tracheoesophageal partition damage (perforation), pneumothorax, pneumomediastinum

- Early postoperative
  - Obstruction, displacement, infection, pulmonary edema
- Late postoperative
  - Tracheal stenosis, Granulation tissue, Tracheal-inominate fistula, Tracheoesophageal fistula, right laryngeal nerve injury, sinusitis

- Esophagoscopy—indicated for dysphagia, odynophagia, hoarseness, respiratory distress (i.e., foreign body), diagnosis of lesions, GERD evaluation
  - Complications of esophagoscopy—esophageal perforation, trauma to oral cavity, aspiration, respiratory depression, cardiac instability, pneumothorax, bleeding

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Chapter 11

Therapeutics: Pharmacology, Chemotherapy, Radiation Oncology

Anthony G. Del Signore and Fred Y. Lin

PEARLS

- Lidocaine
  - Low to intermediate potency, 45–60 min duration
  - Dosage calculation 1 %, 2 %, 4 % = 10 mg/ml, 20 mg/ml, 40 mg/ml
  - Dosage max: w/o epinephrine: 5 mg/kg and w/epinephrine: 7 mg/kg
- Types of chemotherapeutic agents
  - *Alkylating agents*: substitution reactions, cross-linking, and strand-breaking reactions with DNA → inaccurate DNA replication → cell death
  - *Antimetabolite agents*: inhibit critical enzymes involved in nucleic acid synthesis or become incorporated into nucleic acid and produce incorrect codes → inhibition of DNA synthesis during S phase → cell death

ANESTHESIA

- Local Anesthetics
  - Irreversibly blocks sodium channels of lipid membranes in unmyelinated nerves (pain, autonomic, and temperature)
  - High margin of safety—therapeutic effect: toxic effect
  - Factors in efficacy:
    - Lipid solubility: potency and duration
    - Degree of ionization: penetrance across lipid membranes
    - Protein binding: duration
  - Two classes: mnemonic "2 I's" in amides versus "1 I" in esters
    - Amide
      - Metabolized in liver: N-dealkylation
      - i.e., Lidocaine, Mepivacaine, Bupivacaine
    - Esters
      - Metabolized by liver and plasma cholinesterases
      - i.e., Tetracaine, Benzocaine, Procaine, Cocaine
  - Cocaine
    - Blocks reuptake of norepinephrine and dobutamine at adrenergic nerve endings
    - Very high potency with slow onset, duration of 30–60 min
    - Maximum recommended dose: 2–3 mg/kg

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- Lidocaine
  - Low to intermediate potency, 45–60 min duration
  - Dosage calculation 1 %, 2 %, 4 % = 10 mg/ml, 20 mg/ml, 40 mg/ml
  - Dosage max: w/o epinephrine: 5 mg/kg and w/epinephrine: 7 mg/kg
  - Methemoglobinemia: oxidation of hemoglobin to ferric state → desaturations
    - Chocolate cyanosis: brown discoloration of lips, ears, mucous membranes
    - Minor cases: remove agent and provide oxygen
    - Severe cases: administer 1 % methylene blue slowly at dose of 1–2 mg/kg IV
- Toxicity
  - Local
    - Skin reactivity, cellulitis, ulceration
    - Watch injection technique and site of injection
  - Systemic
    - Central nervous system:
      - Excitatory to depressive effects
      - Agitation, tingling, light headedness, muscle twitching → tonic clonic seizures, unconsciousness, apnea
    - Cardiovascular system:
      - Profound hypotension secondary to systemic vasodilatation and reduced cardiac output, decreased myocardial contractility
  - Management
    - ABCs approach
    - Stop procedure → maintain airway and oxygenate
    - IV in place with fluid boluses if needed

- Common Local Blocks
  - Scalp Block
    - Innervated by supratrochlear and supraorbital nerves, zygomaticotemporal and zygomaticofacial nerves and the auriculotemporal nerves
    - Entire scalp block requires circumferential infiltration from ears to occiput to glabella
  - Supraorbital and Supratrochlear Nerve Block
    - Typically used for forehead anesthesia
    - Palpate supraorbital notch then insert needle until paresthesias are felt in distribution → injection of 3 ml of 2 % lidocaine with epinephrine
  - Infraorbital Nerve Block
    - Used commonly in rhinoplasty and sinus procedures
    - Targets the V2 distribution innervating the skin and soft tissue of midface
    - Infraorbital nerve exits foramen just below infraorbital rim at pupillary line
  - Sphenopalatine Nerve Block
    - Ganglion located within the pterygopalatine fossa
    - Palpate for depression in hard palate just medial to gum line at 2nd molar, this indicates greater palatine foramen. Bend needle at 2.5 cm at 45° to avoid damage to orbital structures superiorly
  - Otologic Nerve Blocks
    - Sensory innervation derived from greater auricular and auriculotemporal nerve (external) and branches of 7th, 9th, and 10th cranial nerves (EAC)
    - Injection performed around the ear circumferentially for external block
  - Laryngeal Nerve Blocks
    - Largely supplied by the superior laryngeal nerve with small contribution of the recurrent laryngeal nerve
    - Typically a combined transtracheal and superior laryngeal nerve block is used
      - Cricothyroid membrane is palpated and 2–4 cc of 4 % lidocaine is injected—a "popping" sound can be appreciated upon entrance of the needle into the trachea
      - Midway between the hyoid and thyroid cartilage an additional 2 cc of local is injected

- General Anesthesia
  - Four main stages of anesthesia
    - Stage 1: conscious and rational, perception of pain diminished
    - Stage 2: unconscious but responds to stimuli, breath holding (+), pharyngeal muscular tone (+), able to protect airway, pupils dilated and gaze discongugate
    - Stage 3: surgical anesthesia—increasing degrees of muscular relaxation, protective pharyngeal reflexes (–), unable to protect airway
    - Stage 4: medullary depression—cardiovascular and respiratory collapse
  - Inhalational agents
    - Potency: described by MAC (minimal alveolar concentration)—concentration of anesthetic that will prevent movement in response to surgical stimuli in 50 % of individuals
    - Agents are additive—2 drugs with 1/2 MAC of each will deliver 1 MAC
    - Nitrous Oxide
      - Low potency and low solubility in blood allowing rapid onset and recovery
      - Systemic effects: mild myocardial depression, minimal effect on respiration
    - Isoflurane
      - Low potency and low solubility
      - Systemic effects: depresses respiratory drive and ventilator response to hypoxemia, direct cardiac depressant, reduces systemic vascular resistance, potent vasodilator
      - Low level of metabolism in the body, eliminating nephrogenic or hepatic toxicity.
    - Sevoflurane
      - Low solubility
      - Systemic effects: mild respiratory and cardiac depression
      - Commonly used for pediatric inductions as not bronchoirrative
    - Desflurane
      - Low solubility
      - Bronchoirrative with high incidence of breath holding, coughing, and laryngeal spasm
  - Intravenous Anesthetic Agents
    - Non-opioids—provides hypnosis and blunting of reflexes
      - Typically used in conjunction for induction
      - Thiopenthal
        - Enhances inhibitory neurotransmission by enhancing GABA receptor function
        - Ultra short acting except with prolonged infusion
        - Cardiovascular and respiratory effects noted
        - Metabolism via liver
      - Etomidate
        - Enhances inhibitory neurotransmission by enhancing GABA receptor function
        - Ultra short acting
        - Less depressant effect on cardiovascular function
        - Can produce myoclonic movements and pain with injection
      - Ketamine
        - Noncompetitive antagonist of NMDA receptors in CNS
        - State of "dissociative anesthesia"—appear awake but no response to stimuli
        - Associated with unpleasant dreams/hallucinations
      - Propofol
        - Facilitates inhibitory neurotransmission by enhancing GABA receptors in CNS
        - Rapid onset and short duration with rapid metabolism
        - Decreases systemic blood pressure via vasodilation
    - Opioids—provide analgesia, produce unconsciousness and suppress response
      - Examples: Morphine, meperidine, fentanyl, remifentanil
      - Used as a supplement during induction or maintenance
      - Binds to mu-receptors in brain, spinal cord, and periphery
      - Onset within minutes and metabolism via liver and eliminated by kidneys
      - Minimal affect to cardiovascular but dose-dependent depression of respiration

- Neuromuscular blockers—allows interruption of transmission of synaptic signaling at neuromuscular junction
  - Depolarizing
    - Succinylcholine
      - Mimics the action of acetylcholine
      - Rapid onset within 40–60 s with effect of 4–6 min
      - Hydrolyzed by plasma cholinesterase
      - Side effects: myalgia (fasciculations), cardiac dysrhythmias, hyperkalemia
      - Caution in patient with history of malignant hyperthermia
      - Unable to use reversal by acetylcholinesterase inhibitors
  - Non-Depolarizing
    - Reversible competitive antagonism of acetylcholine
    - May be reversed with the use of anticholinesterase drugs
      - Edrophonium, neostigmine, pyridostigmine
    - Vecuronium
      - Intermediate acting agent
      - Metabolized by liver and excreted in bile and renally
      - Prolonged effect in elderly and those with liver/kidney disease
      - No cardiovascular effects noted
    - Rocuronium
      - Lower potency intermediate acting agent
      - Quick acting within 60 s, ideal for rapid sequence induction when succinylcholine contraindicated
      - No cardiovascular effects noted
  - Monitor peripherally by electronically stimulating the ulnar nerve and measuring adductor pollicis response
    - Monitor the decreased twitch height or fade of "train-of-four" twitches
    - Twitch response correlates with percentage of neuromuscular blockade

- Complications
  - Malignant hyperthermia
    - Hypermetabolic syndrome secondary to increases in Ca^{2+} in sarcoplasmic reticulum
    - Autosomal dominant, variable expressivity
    - Offending agents include: halogenated inhaled agents and succinylcholine
    - Features include: tachycardia, hypercarbia, metabolic acidosis, muscle rigidity, hypoxemia, hyperkalemia, ventricular dysrhythmias
    - Treatment includes: dantrolene, sodium bicarbonate administration, insulin, and glucose
    - Muscular dystrophy patients increased risk
  - Laryngospasm
    - Typically due to irritative stimulus to airway during light anesthesia
      - Triggers: secretions, vomitus, blood, pungent volatile anesthetics, laryngoscopy
    - Treatment
      - Remove stimulus
      - Administer 100 % oxygen
      - Continuous positive pressure on airway and jaw thrust
      - Small dose succinylcholine

PHARMACOLOGY

- Antimicrobials
  - Bacteriostatic
    - Mechanism of action (MOA): prevents replication of bacteria
    - Function best during growth phase
  - Bacteriocidal
    - MOA: actively kills pathogen
    - Treats both multiplying and non-multiplying bacteria

- Penicillins
  - MOA: beta-lactam inhibits D-alanyl-D-alanine carboxypeptidase which cross links peptidoglycan
  - Examples: penicillin, oxacillin, methicillin, dicloxicillin, ampicillin, amoxicillin
  - Efficacy: Time-dependent killing, CNS penetration, gram (+), gram (–), spirochetes
  - Resistance with microbial beta-lactamase enzyme production
  - Side Effects (S.E.): hypersensitivity (~5 %), ampicillin associated rash with concurrent mononucleosis infection
- Penicillin + Beta-Lactamase inhibitor
  - MOA: irreversibly bind to beta-lactamase enzymes inhibiting activity
  - E.g.: amoxicillin+ clavulanate, ampicillin + sulbactam
  - Efficacy: gram (+) and gram (–) aerobes/anaerobes, +/– *pseudomonas*
  - S.E.: GI (nausea, vomiting, diarrhea)—minimized with concurrent meal
- Cephalosporins
  - MOA: Beta-lactam cell wall synthesis inhibitor
  - 1st Gen: Gram (+)/skin flora
    - Cefazolin, cephalaxin
    - S.E.: nausea
  - 2nd Gen: Less gram (+) and more gram (–)
    - Cefoxitin, cefuroxime
    - S.E.: diarrhea
  - 3rd Gen: Gram (–), no *pseudomonas* coverage
    - Cefdinir, ceftazidime, ceftriaxone (+ CSF penetration)
    - S.E.: risk of pseudomembranous colitis
  - 4th Gen: Pseudomonal coverage
    - Cefepime
    - Non-ototoxic alternatives to gentamicin for *pseudomonas* coverage
- Carbapenems
  - MOA: beta-lactam cell wall inhibitor
  - Ex: ertapenem, imipenem, meropenem
  - Efficacy: broad spectrum, typically for severe infections, not first line
  - S.E.: seizures (high doses)
- Monobactams
  - MOA: inhibition of mucopeptide synthesis of cell wall
  - E.g.: Aztreonam
  - Efficacy: Aerobic gram (–) including *pseudomonas*
  - S.E.: possible super-infection as highly selective against gram (–)
- Macrolides
  - MOA: binds to 50S ribosomal subunit → decrease protein synthesis
  - E.g.: erythromycin, clarithromycin, azithromycin
  - Efficacy: Gram (+) and (–), atypical bugs, no efficacy to MRSA
  - S.E.: + GI motility, inhibits cytochrome p 450, prolonged QT
- Lincosamides
  - MOA: binds to 50S ribosomal subunit, reduces toxin production
  - E.g.: Clindamycin
  - Efficacy: Anaerobes, +/– MRSA, some gram (+), no *pseudomonas*
  - S.E.: Pseudomembranous colitis (*C. difficile*)
- Tetracyclines
  - MOA: impairs 30S ribosomal subunit and tRNA binding
  - E.g.: doxycycline, tetracycline
  - Efficacy: broad spectrum
  - S.E.: grey-brown discoloration of teeth, interfere absorption Ca, Mg, Fe, Al, predisposition to sunburn

- Aminoglycosides
  - MOA: binds 30S ribosomal subunit, bacteriocidal due to misreading of mRNA
  - E.g.: amikacin, gentamycin, neomycin, tobramycin
  - Efficacy: *Pseudomonas*, gram (–), no anaerobes or MRSA coverage
  - S.E.: ototoxicity and nephrotoxicity
- Quinolones
  - MOA: inhibition of DNA gyrase
  - E.g.: ciprofloxin, levofloxacin, moxifloxacin, ofloxacin
  - Efficacy: gram (–) aerobes, gram (+), broad anaerobic coverage, pseudomonas
  - S.E.: peripheral neuropathy, tendon rupture in children, QT prolongation, epidermal necrolysis, rash
- Vancomycin
  - MOA: inhibition of N-acetylmuramic acid and N-acetylglucosamine into peptidoglycan
  - Efficacy: MRSA, *C. difficile*
  - S.E.: Nephrotoxic, ototoxic, "red man" syndrome
- Metronidazole
  - MOA: destabilization of anaerobic DNA
  - Efficacy: anaerobes
  - S.E.: metallic taste, bone marrow suppression, peripheral neuropathy
- Mupirocin
  - MOA: inhibition of RNA synthesis
  - Efficacy: MRSA
  - S.E.: contact dermatitis
- Sulfonamides
  - MOA: competitive antagonist para-aminobenzoic acid for bacterial folic acid synthesis
  - Efficacy: Broad spectrum, MRSA
  - S.E.: rash, bone marrow suppression

- Antifungals
  - Amphotericin B
    - MOA: binds ergosterol
    - Efficacy: works well against *Mucor;* increasing *Candida albicans* resistance
    - S.E.: infusion reactions, nephrotoxic, cardiotoxic, neurotoxic
  - Nystatin
    - MOA: binds ergosterol
    - Efficacy: broad fungal coverage
    - S.E.: rash, itching
  - Azoles
    - MOA: inhibits lanosterol conversion to ergosterol
    - E.g.: ketoconazole, fluconazole, clotrimazole, itraconazole
    - Efficacy: varied coverage
    - S.E.: similar to those listed for amphotericin but less severe
  - Caspofungin
    - MOA: inhibition of fungal cell wall synthesis
    - Efficacy: *Candida, Aspergillus*
    - S.E.: hepatotoxicity
- Antivirals
  - Acyclovir/Valcyclovir/Famciclovir
    - MOA: inhibitions of viral polymerase
    - Efficacy: *Herpes simplex* and *Herpes zoster*
    - S.E.: bone marrow suppression, Stevens-Johnson syndrome
  - Rimantidine
    - Efficacy: influenza type A—both active treatment and prophylaxis
  - Oseltamivir

- Efficacy: influenza type A + B—treatment must be initiated within 36 h of symptom onset

- Anti-reflux
  - Histamine blockers
    - MOA: block histamine-2 receptors
    - E.g.: ranitidine and famotidine
    - S.E.: cytochrome p 450 inhibition
  - Proton pump inhibitors
    - MOA: block H+/K+ ATPase pump on parietal cells on luminal surface of stomach, must be taken 30–60 min prior to meal
    - E.g.: omeprazole, lansoprazole, esomeprazole, pantoprazole
    - S.E.: cytochrome p 450 inhibitors
  - Promotility agents
    - MOA: dopamine receptor antagonist which increases tone of LES, increases contraction of gastric antrum and relaxes pylorus and duodenum
    - E.g.: metoclopramide
    - S.E.: extrapyramidal symptoms (i.e., movement disorders)
- Common rhinologic medications
  - Antihistamines
    - MOA: dose-dependent antagonism of histamine-1 receptor
    - E.g.: 1st gen: diphenhydramine 2nd gen: fexofenadine, loratadine
    - S.E.: 1st gen: sedation, anticholinergic
  - Anticholinergics
    - MOA: competitive antagonist of cholinergic receptors to decrease mucosal secretions
    - E.g.: ipratropium
    - S.E.: nasal irritation, drying
  - Decongestants
    - MOA: alpha agonist to cause vasoconstriction
    - E.g.: oxymetazoline, phenylephrine, pseudoephedrine
    - S.E.: hypertension, tachyphylaxis, rebound congestion with prolonged use (>3 days topical agents), long-term use results in *rhinitis medicamentosa* (atrophy of glands and chronic inflammation of mucosal lining)
  - Corticosteroids
    - MOA: inhibition of genetic transcription and protein synthesis to decrease inflammation
      - Topical corticosteroids
        - E.g.: Beclomethasone, flunisolide, fluticasone, mometasone
        - S.E.: mucosal dryness, epistaxis, tearing
      - Oral corticosteroids
        - E.g.: Prednisone, dexamethasone, methylprednisolone
        - S.E.: fluid imbalance, electrolyte disturbances, glycosuria, increase susceptibility to infections, hypertension, hyperglycemia, osteoporosis, cataracts, central obesity, hypothalamic-pituitary axis suppression
        - Interconversion of steroid compounds

Hydrocortisone	1
Prednisone	4
Methylprednisolone	5
Dexamethasone	25

    - Cromolyn Sodium
      - MOA: mast cell membrane stabilizer to inhibit release of histamine
      - Note: used for prophylaxis rather than active treatment
    - Leukotriene receptor antagonist
      - MOA: block leukotrienes from cellular activation
      - E.g.: Montelukast

- Botox
  - MOA: active component binds to presynaptic neuromuscular junction of motor neurons inhibiting acetylcholine release → flaccid paralysis
  - E.g.: *Botulinum* type A, *botulinum* type B
  - S.E.: nausea, pain at injection site, acne, unwanted paralysis and ptosis, bruising

CHEMOTHERAPY

- Types of chemotherapeutic agents
  - *Alkylating agents*: substitution reactions, cross-linking and strand-breaking reactions with DNA → inaccurate DNA replication → cell death
    - E.g.: Cisplatin, carboplatin
    - Renal toxicity is common, ototoxicity (obtain pretreatment audiogram), cumulative myelosuppression, peripheral neuropathy
  - *Antimetabolite agents*: inhibit critical enzymes involved in nucleic acid synthesis or become incorporated into nucleic acid and produce incorrect codes → inhibition of DNA synthesis during S phase → cell death
    - Methotrexate binds to dihydrofolate reductase preventing synthesis of DNA
    - 5-Fluorouracil (5FU) binds to thymidilate synthetase which blocks conversion of uridine to thymidine
    - S.E.: myelosuppression, mucositis, cardiac toxicity
  - *Antitumor antibiotics*: *Streptomycin* derived and cytotoxic
    - Affect structure and function of nucleic acids via intercalation of DNA base pairs, DNA strand fragmentation, or cross-linking of DNA
    - Doxorubicin, bleomycin, and mitomycin
  - *Alkaloids*: bind to free tubulin dimers and disrupt the balance between microtubule polymerization
    - Result in destruction of mitotic spindles and arrest of cells in metaphase
    - E.g.: vincristine and vinblastine
  - *Taxanes*: stabilize tubulin polymers and prevent cell division
    - E.g.: paclitaxel and docetaxel
    - S.E.: neutropenia, alopecia, mucositis
- Chemotherapy treatment schemes
  - Addition of chemotherapy:
    - Improved clinical outcomes in those with advanced disease
    - Demonstrates significant benefits in organ preservation
    - Promotes longer time to disease progression
    - Better locoregional control
    - Fewer distant metastasis
    - Longer survival times
  - Neoadjuvant chemotherapy: use of therapy prior to definitive radiation or surgical therapy (i.e., induction)
  - Concomitant chemotherapy: simultaneous use of chemotherapeutic and radiation treatments
  - Adjuvant chemotherapy: administered after definitive treatment with radiation, surgery, or chemotherapy

RADIATION ONCOLOGY

- Radiation Absorbed Dose: (rad)
  - Energy deposited by ionizing radiation per gram of tissue
  - 1 rad = 1 erg/cm^3
    - (1 Gray (Gy) = 1 J/kg, 1 J=10^7 ergs)
  - 1 Gy = 100 rads

- Fractionation
  - Standard fractionation
    - 70 Gy in 35 fractions over 7 weeks
  - Hyperfractionation
    - 81 Gy in 68 fractions over 6–8 weeks
    - Exploits differential sensitivity of tumor cells and normal tissue
      - Smaller dose fractions allows higher total dose administered
      - Delivered within the tolerance of late responding normal tissue
      - Higher biological dose against the tumor
    - Increased number of doses delivered
    - Decreased intensity per dose delivered (1.15–1.2 Gy per fraction)
    - Decreased risk of late complications
    - Increased acute side effects
  - Accelerated fractionation
    - 67 Gy in 42 fractions over 6 weeks
    - Allows shortening of total duration of XRT → reducing opportunity for tumor proliferation
    - Multiple fractions (higher dose) delivered (1.5–2 Gy)
    - Decreased total dose
    - Increased acute side effects
    - Decreased late side effects
- Adverse events (sequelae from chemotherapy) of the head and neck
  - Mucositis
    - Atrophy of squamous epithelial tissue, absence of vascular damage and inflammatory infiltrate
    - Transient effect, but usually exacerbated in patients with history of ETOH and tobacco use
    - Typically presents with hyperkeratinization → erythema
    - Severity in decreasing order: soft palate, mucosa of hypopharynx, cheek, base of tongue, lips, and dorsal tongue
    - Treatment centered around aggressive oral hygiene, topical anesthetic (magic mouthwash), ETOH, and tobacco cessation
  - Salivary gland damage
    - Secondary to progressive degeneration of acinar epithelium and onset of interstitial fibrosis
    - Substantial irreversible decrease in the production and output of saliva
    - Salivary thickening and mucoid, reduced pH → allowing flora to flourish
    - Increase in dental caries, sensitivity and periodontal disease
    - Treatment utilizes copious fluids with meals, salivary substitutes, pilocarpine, fluoride treatments
  - Osteoradionecrosis
    - Changes include hyperemia, endarteritis, thrombosis of vasculature
    - Fibrosis and fatty degeneration of marrow
    - Poor response to trauma and infection
    - Staging
      - I: Superficial involvement only involving cortical bone with exposure
      - II: Localized involvement of exposed cortical bone with underlying medullary bone necrosis
      - III: Diffuse involvement of bone with full thickness involvement
    - Treatment ranges from oral rinses, local debridement, hyperbaric oxygen therapy to radical resection, dental consultation, and pre-radiation dental extractions are essential
  - Alterations in taste
    - Typically due to damage to taste buds and decreased salivary flow

  - Trismus
    - Secondary to muscle and ligament fibrosis and scarring
    - Treatment: jaw exercises and stretching
  - Cutaneous reactions
    - Erythema, dryness, swelling, fibrosis
    - Treatment: moisturizers, mild cleansers, corticosteroids
  - Alopecia
  - Post radiation-induced cancer
    - Postoperative radiation therapy
- Indications
  - Close or positive surgical margins
  - Perineural spread
  - Lymphovascular invasion
  - Contiguous tumor extension into bone or skin
  - Multiple nodal involvement
  - Extra capsular extension of nodal disease
- Timing for delivery typically within 3–4 weeks
  - Radiotherapy completed within 11 weeks gave better outcome than >11 weeks
- Preoperative radiotherapy
  - Indications
    - Cancer with marginal resectability
    - Small radiocurable disease
    - Large adenopathy

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Chapter 12
Head and Neck Pathology

Lucia Olarte, Kelly R. Magliocca, and Fred Y. Lin

PEARLS

- Papillary carcinoma features the formation of papillae and unique nuclear features like "Orphan Annie Eye" nuclei and psammoma bodies
- Melanoma is characterized by melanin pigment and is S100+, HMB 45+, Melan A+ (melanocytic antigen), Tyrosinase+

LARYNX

Nodule (Fig. 12.1):

- Bilateral, usually on the true vocal cord, middle third
- Smooth, rounded, sessile or pedunculated excrescences
- Covered by squamous epithelium can be keratotic, hyperplastic
- Dysplastic core and loose myxoid connective tissue, myxoid stroma
- Variably fibrotic or punctuated by numerous vascular channels

Polyp (Fig. 12.2):

- Unilateral, usually anterior ½ true cord
- Submucosa is edematous and myxoid

Contact ulcer (Fig. 12.3):

- Polypoid, ulcerated lesion with associated granulation tissue and inflammation
- Ulcerative lesion (active) and hyperplastic squamous epithelium (healing/reactive)
- Associated necrosis, scattered multinucleated giant cells, granulation tissue
- Connective tissue
  - Granulation tissue
  - Radiating dilated vascular pattern
  - Prominent enlarged fibroblasts

Histoplasmosis (Fig. 12.4):

- Histiocytic and lymphoplasmacytic infiltrate
- May not have clear granuloma formation
- Intracellular organisms
  - Very small yeast forms with pale capsular halo
  - Difficult to see on H&E stain (arrow)
- Fungal stain: Gomori's methenamine silver (GMS)

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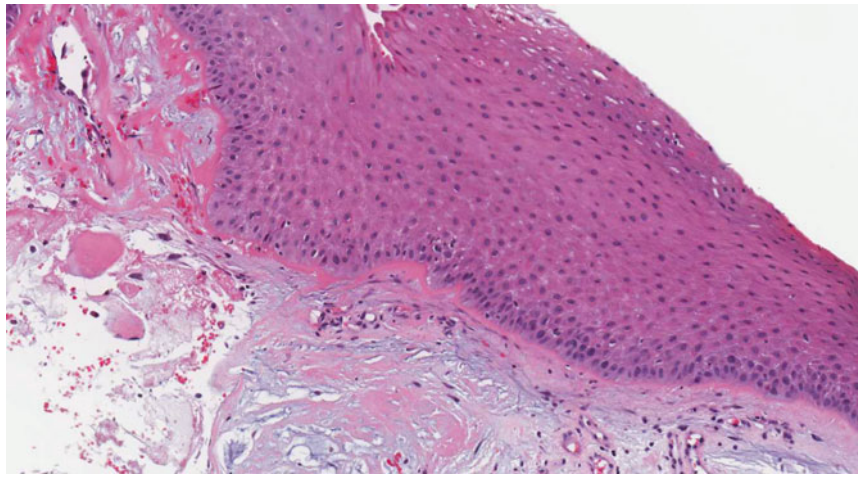

Fig. 12.1 Laryngeal nodule: Hyperplastic surface epithelium with normal maturation. Basophilic and hyalined stroma

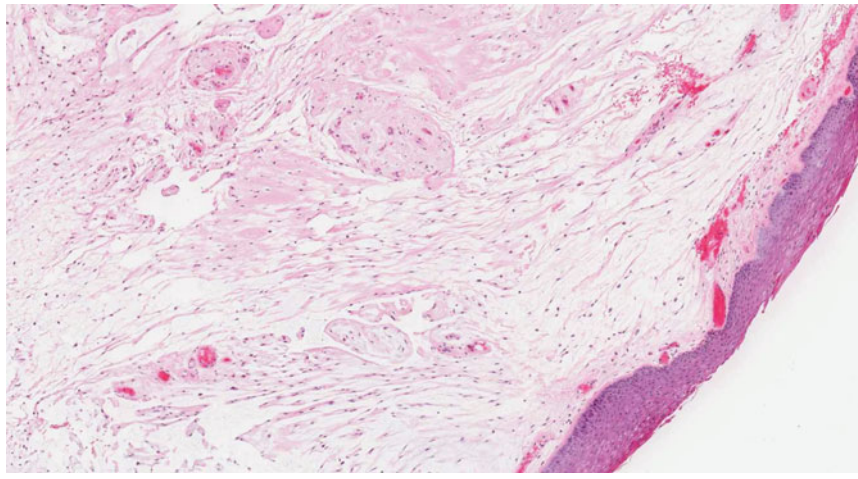

Fig. 12.2 Laryngeal polyp: Surface epithelium with normal maturation. Edematous stroma with increased vascularity

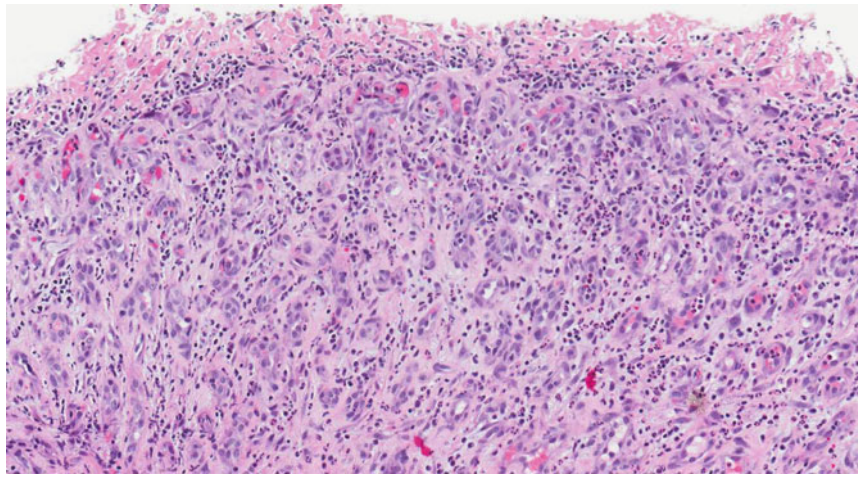

Fig. 12.3 Contact ulcer: Surface ulceration with exuberant formation of granulation tissue

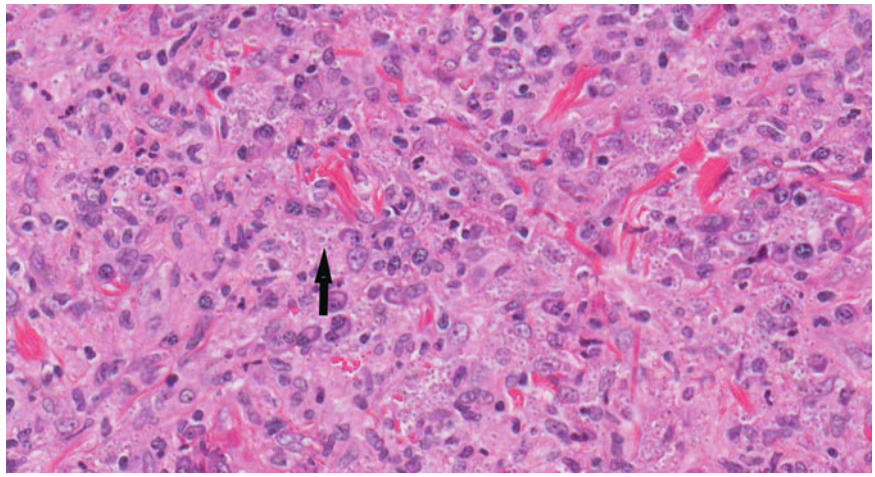

Fig. 12.4 Histoplasmosis: Intracellular fungal organisms (*arrow*)

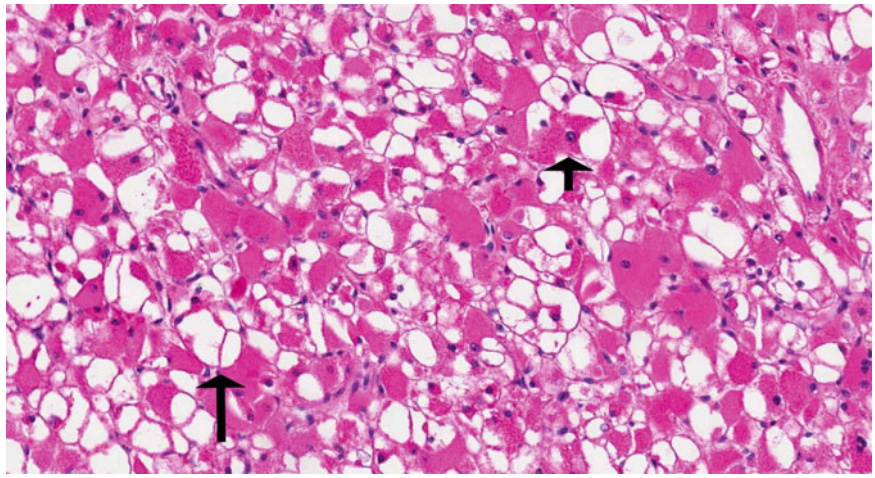

Fig. 12.5 Adult Rhabdomyoma: Glycogen results in clear cell change and development of "spider-webs" (*long arrow*). Granular appearance of eosinophilic muscle cells (*short arrow*)

Adult Rhabdomyoma (Fig. 12.5):

- Benign skeletal muscle lesion
- Large polygonal eosinophilic and clear cells, pink fibrillar cytoplasm
- Granular-appearing cross-striations common (short arrow), myoid differentiation
- Nuclei multiple and peripherally placed in cell
- Vacuolated cytoplasm due to glycogen content
  - Results in "spider-web" formations, i.e., pink intracellular strands (long arrow)
- PTAH (phosphotungstic-acid hematoxylin) stain: shows striations of myoid differentiation

Juvenile Laryngeal Papillomatosis (Fig. 12.6)

- HPV 6 and 11
- More aggressive 16 and 18 as seen in cervical type
- Low magnification silhouette reveals multiple slender, papillary or finger-like projections supported by central fibrovascular cores (arrows) and covered by stratified squamous epithelium

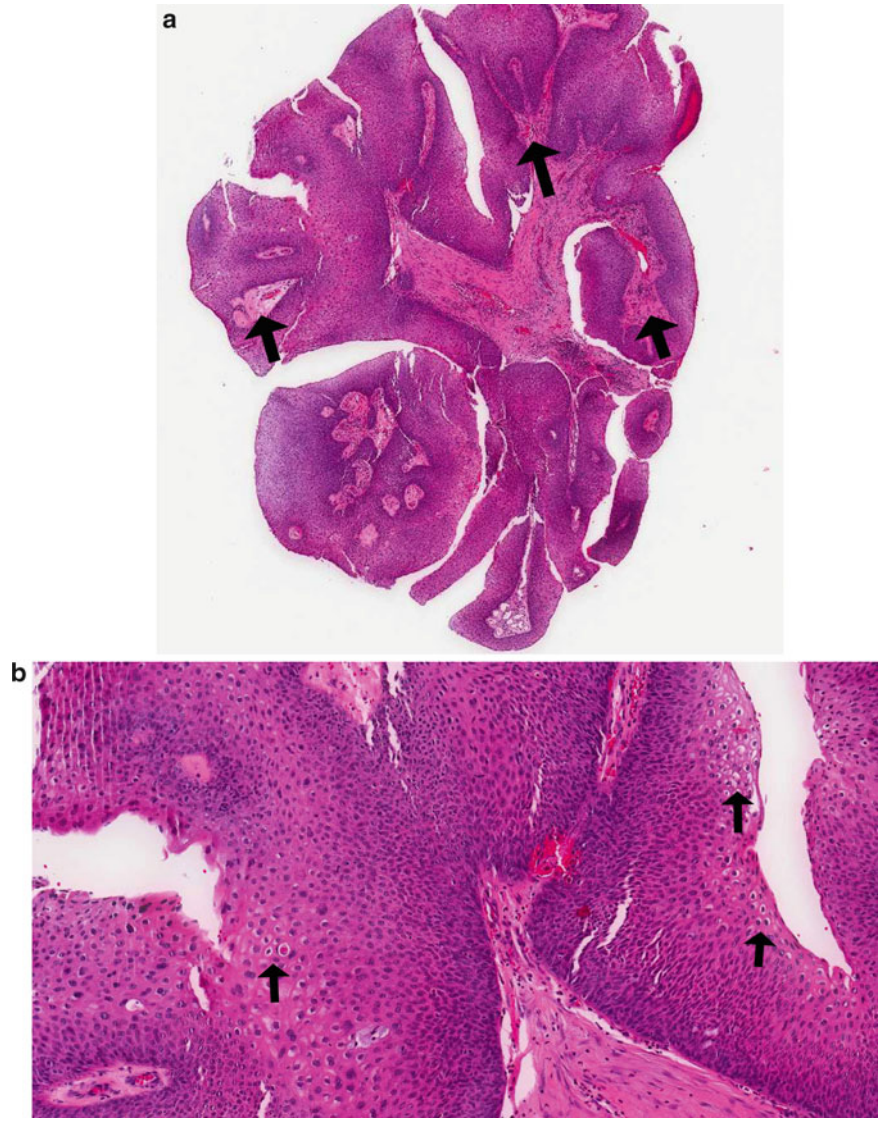

Fig. 12.6 Laryngeal Papillomatosis: (**a**) Low magnification of papillary silhouette. Fibrovascular cores support epithelium (*arrows*). (**b**) Koilocytosis, mild cellular and nuclear variability (*arrows*)

- Minor areas of keratinization in some
  - Extensive keratinization or dysplasia, more likely papillary squamous cell carcinoma
- Koilocytotic changes can be seen (arrows)
- Minor cytologic atypia common
- Malignant transformation: nuclear atypia, dysplasia, perineural invasion (Fig. 12.6)

Granular cell tumor (Fig. 12.7)

- Schwann cell origin, benign
- Pseudoepitheliomatous hyperplasia of overlying squamous epithelium
- Nuclei small round, centrally placed
- Large, polygonal cells with granular eosinophilic cytoplasm (lysosomes), resemble histiocytes
- Special stains and immunohistochemistry (IHC):
  - PAS (Periodic acid-Schiff) positive
  - Diastase resistant (lysosomes appear red)
  - S100+ (neural differentiation)

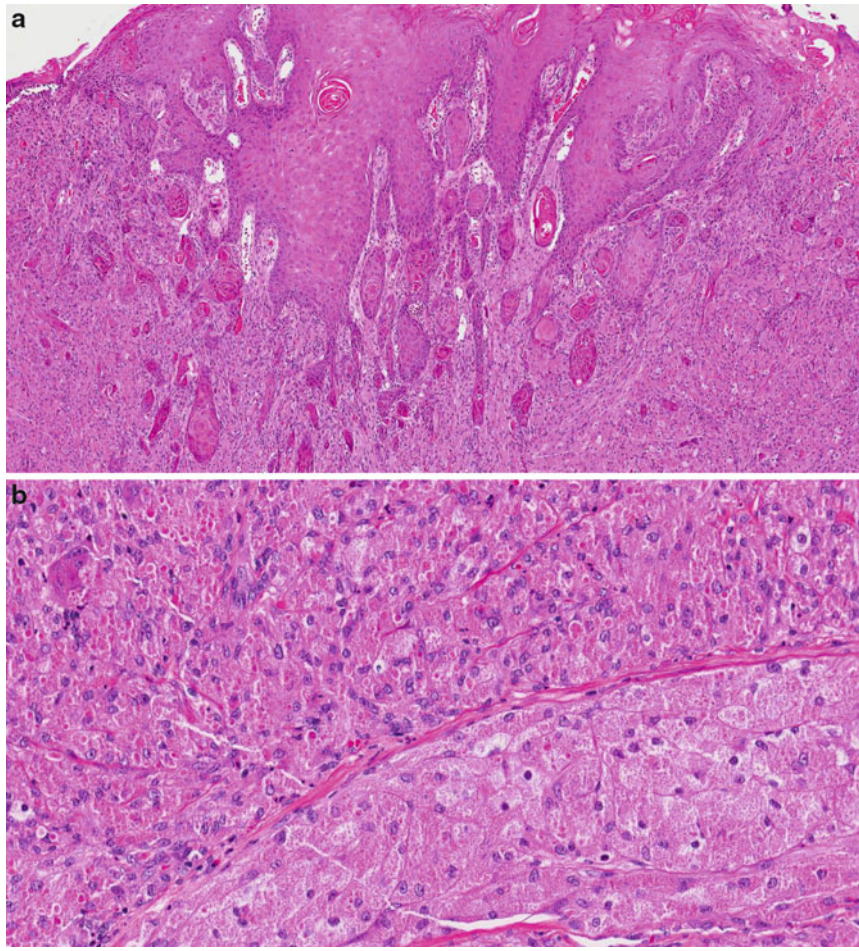

Fig. 12.7 Granular cell tumor: (**a**) Pseudoepitheliomatous ("pseudocarcinomatous") hyperplasia present in area overlying granular cell tumor. (**b**) Syncytium of large eosinophilic cells with granular cytoplasm

Squamous Cell Carcinoma (SCC) (Fig. 12.8)

- Dysplasia of upper respiratory tract begins in basal zone, advances through layers
  - Disorderly, hyperchromatic, enlarged nuclei, loss of polarity
- Most agree that biologic behavior of severe dysplasia equivalent to carcinoma in situ (CIS)
- Classical keratinizing SCC:
  - Keratin pearls
  - Desmoplasia: background stroma of dense fibrotic cells surround tumor
- Non-keratinizing SCC (Fig. 12.9):
  - Variant commonly affects oropharynx, high-risk HPV most likely
  - Immunohistochemical stain p16 commonly positive
- Basaloid SCC (Fig. 12.9):
  - Variant may have minimal keratinization
  - Often with basal palisading, comedonecrosis, high nuclear to cytoplasmic ratio
- Papillary SCC (Fig. 12.10):
  - Variant with low magnification silhouette giving appearance of cut "celery-stalks"
  - Filiform fronds covered by atypical epithelium (may range from mild to CIS)

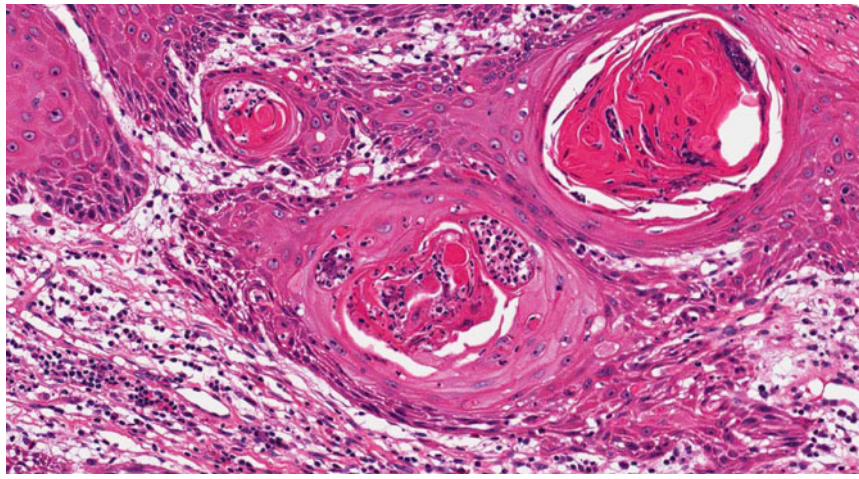

Fig. 12.8 Squamous cell carcinoma: Malignant epithelial proliferation forming keratin pearls within connective tissue

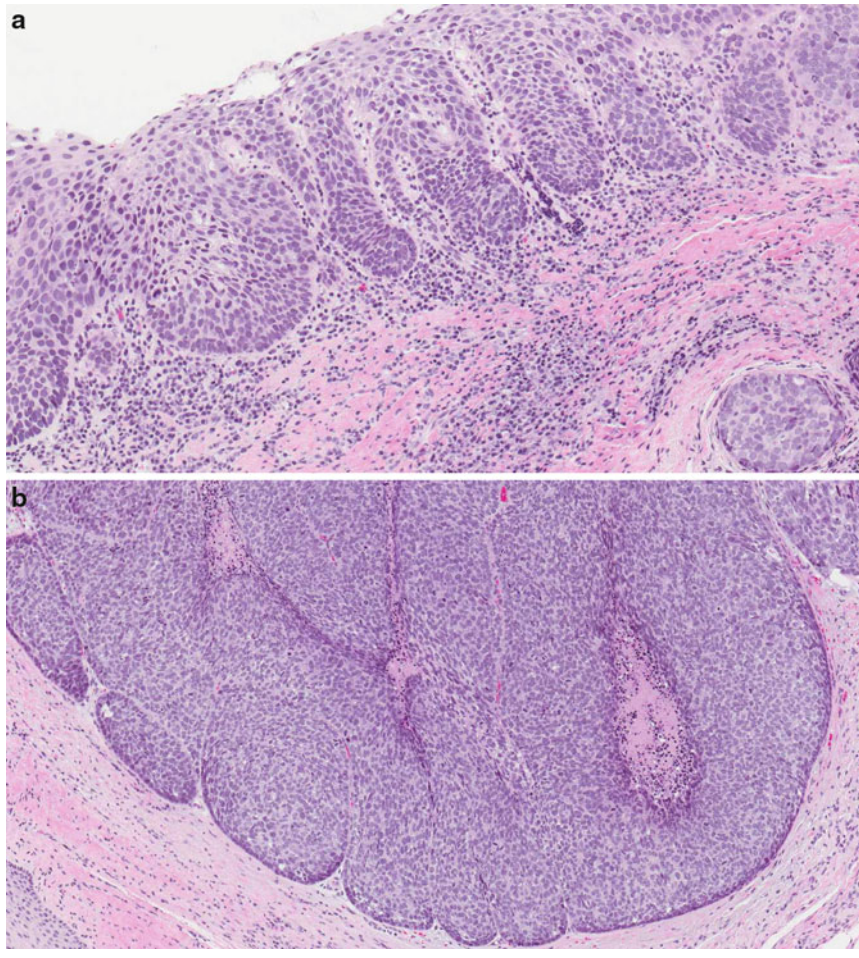

Fig. 12.9 Non-Keratinizing squamous cell carcinoma: (**a**) Basaloid squamous cell carcinoma: high grade dysplasia in epithelium overlying invasive basaloid squamous carcinoma. (**b**) Smooth contours, peripheral palisading and comedonecrosis

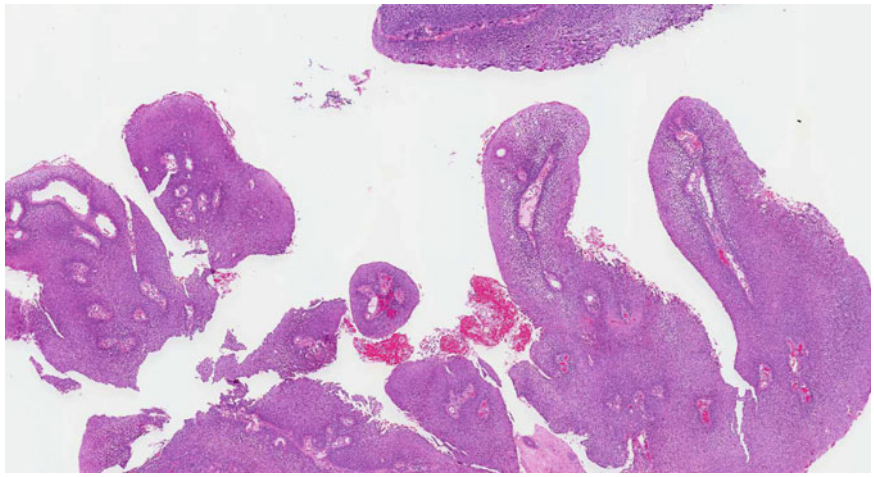

Fig. 12.10 Papillary squamous cell carcinoma: Low magnification of papillary silhouette. "Celery or cauliflower bunches" cut in cross section

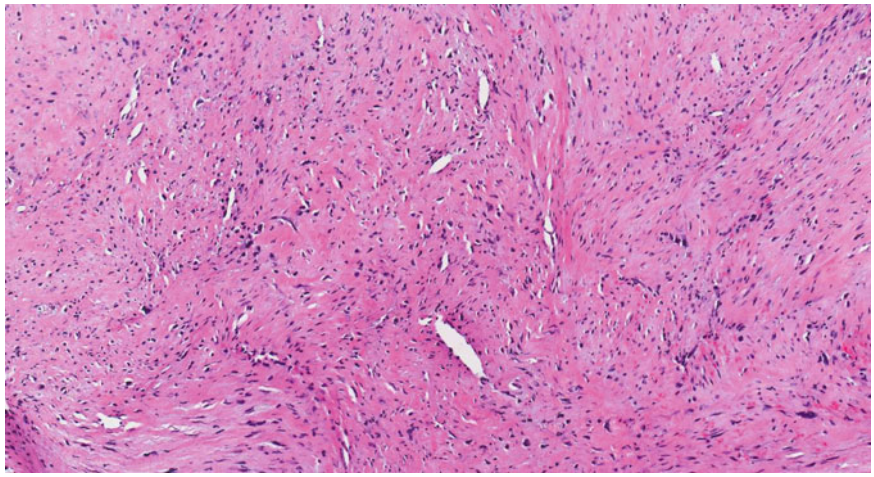

Fig. 12.11 Spindle cell carcinoma: Scattered atypical cells in a fibrotic stroma

Spindle Cell Carcinoma (Fig. 12.11)

- Variant of SCC, with microscopic sarcomatoid pattern
- Exophytic, polypoid lesions, often ulcerated
- Classically shows biphasic histology:
  - Areas of squamous differentiation or overlying epithelial dysplasia
  - Malignant spindle cell stroma underneath
- Spindled or pleomorphic cells with variable nuclear atypia and mitotic rate
- Dense cellularity, more cellular than reactive lesions
- Chondroid or osseous differentiation of stroma possible, regarded as metaplastic process
- IHC: Spindle cells in stroma generally cytokeratin/vimentin

Verrucous Carcinoma (Fig. 12.12)

- Well-differentiated variant of SCC
- Uniform squamous cells with little atypia and minimal mitotic activity above basal/parabasal layer

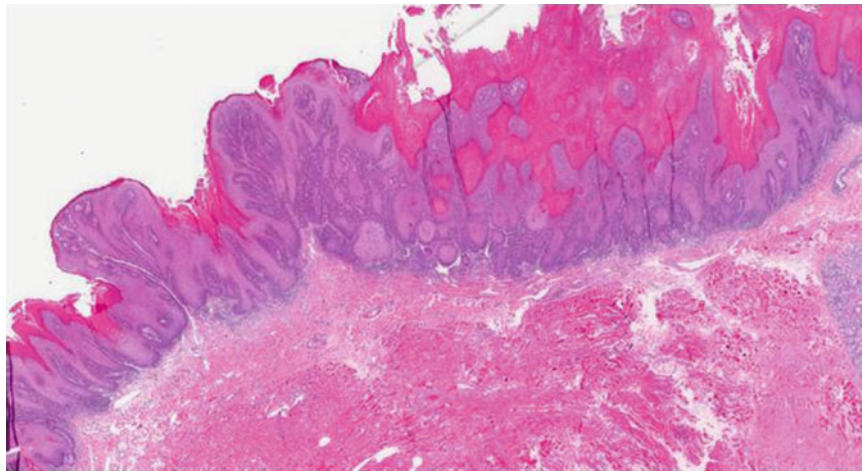

Fig. 12.12 Verrucous carcinoma: Warty surface silhouette of the well-differentiated neoplasm with broad pushing invasion into the lamina propria

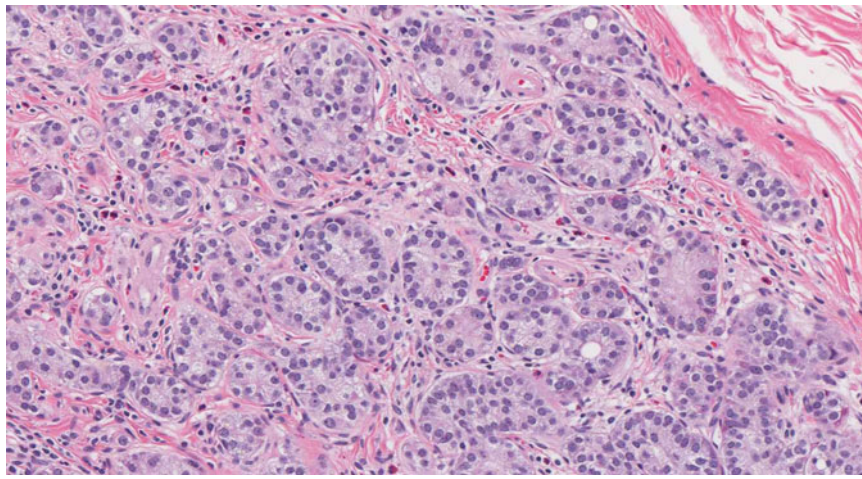

Fig. 12.13 Carcinoid: Organoid and trabeculae growth of uniform cells with abundant eosinophilic cytoplasm

- Marked surface parakeratinization (church spire-like) steeple-like projections and invaginations
- Broad bulbous pushing border with chronic inflammation but no irregular infiltration
- Dysplastic nuclei, irregular (conventional) invasion, and desmoplasia indicates conventional SCC

Neuroendocrine (NE) Carcinoma

- Epithelial and neuroendocrine differentiation
- IHC: cytokeratin + (epithelial differentiation), chromogranin/synaptophysin (NE cells)
- Carcinoid (low grade) (Fig. 12.13):
  - Nests, ribbons, and/or rosettes of uniform cells
  - Centrally located, small round salt-pepper nuclei
  - No pleomorphism, necrosis, or mitotic activity

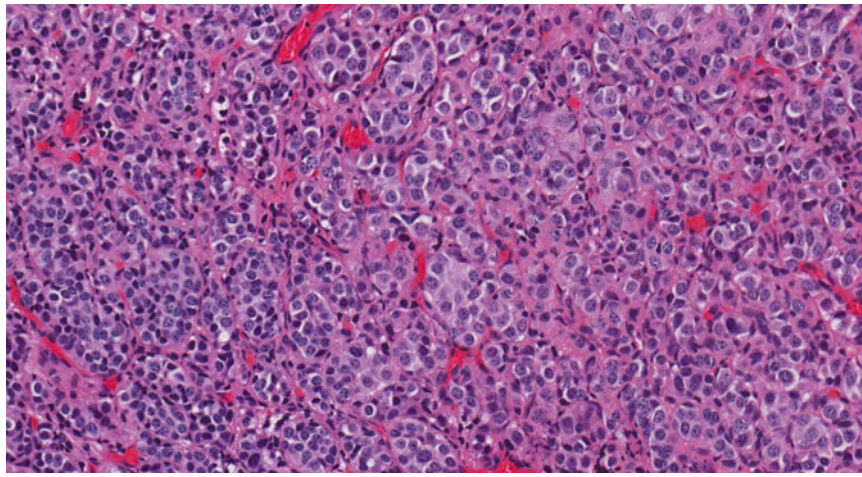

Fig. 12.14 Atypical Carcinoid: Trabeculae of cells with cellular pleomorphism, increased cellularity and a mitotic figure

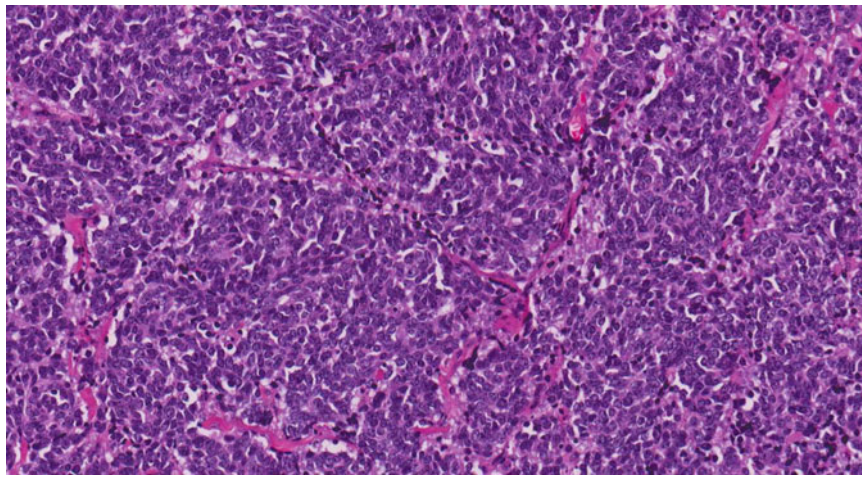

Fig. 12.15 Small cell neuroendocrine carcinoma: large, cellular nests of hyperchromatic oval and spindled tumor cells

- Atypical Carcinoid (intermediate grade) (Fig. 12.14):
  - Mitoses and/or necrosis seen, more atypia, pleomorphism in cells
- Small Cell Carcinoma (high grade) (Fig. 12.15):
  - Undifferentiated, small cells with scant cytoplasm, nuclear molding
  - High mitotic rate and necrosis
  - Resembles basaloid SCC or other "small round blue cell" tumors

SALIVARY GLAND

Necrotizing Sialometaplasia (Fig. 12.16):

- Intact or ulcerated surface epithelium
- Submucosal, lobular coagulative necrosis
- Acinus-sized pools of mucin with lobular architecture as a result of coagulative necrosis

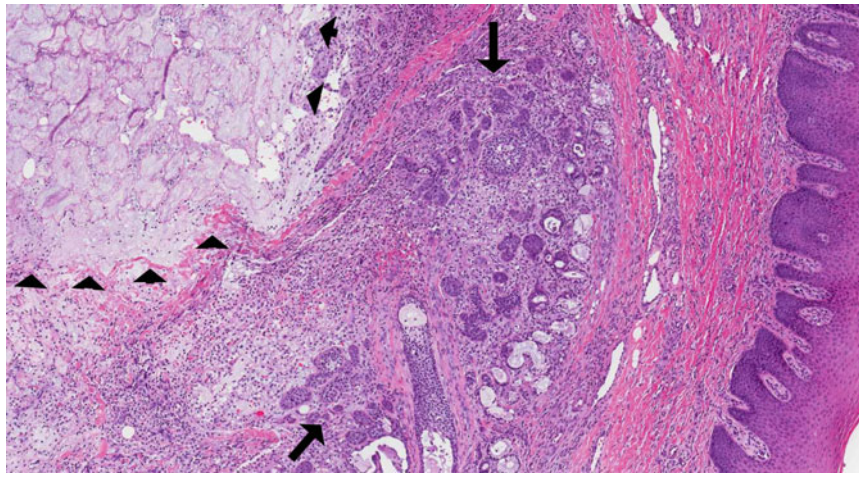

Fig. 12.16 Necrotizing sialometaplasia: coagulative necrosis of salivary gland acini (*arrowheads*), metaplastic salivary ducts (*arrows*), and inflammation

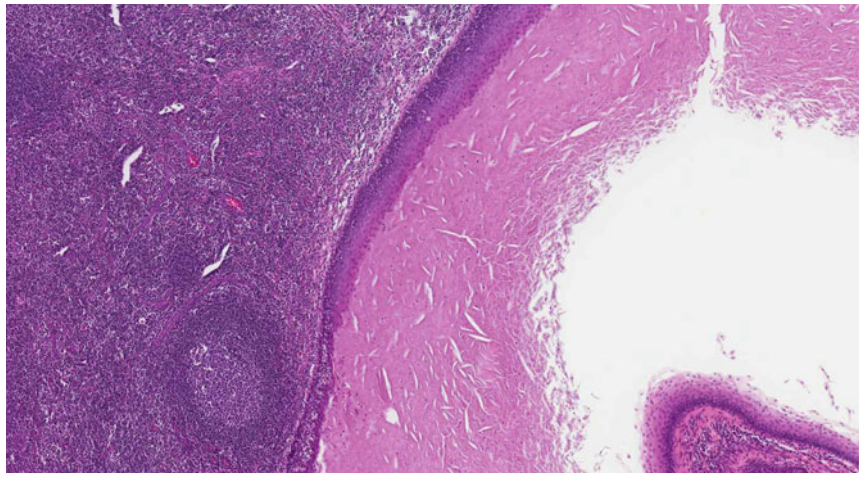

Fig. 12.17 Lymphoepithelial cyst: Squamous epithelial cyst lining present. Germinal center formation within cyst wall

- Squamous metaplasia of residual salivary ductal elements
- Bland squamous epithelium of ductal elements with uniform nuclei, unlike SCC
- Preservation of lobular pattern at low magnification unlike mucoepidermoid carcinoma

Lymphoepithelial Cyst (Fig. 12.17):

- Arise from lymphoid aggregates in salivary gland
- Lymphoid proliferation with central dilated cysts lined by bland squamous epithelium
- When associated with HIV:
  - Marked lymphoid hyperplasia, multiple "chambers," bilateral, usually parotid

Pleomorphic Adenoma (Fig. 12.18):

- Most common benign salivary gland neoplasm
- Major glands typically have capsule, minor glands often unencapsulated (pushing borders)

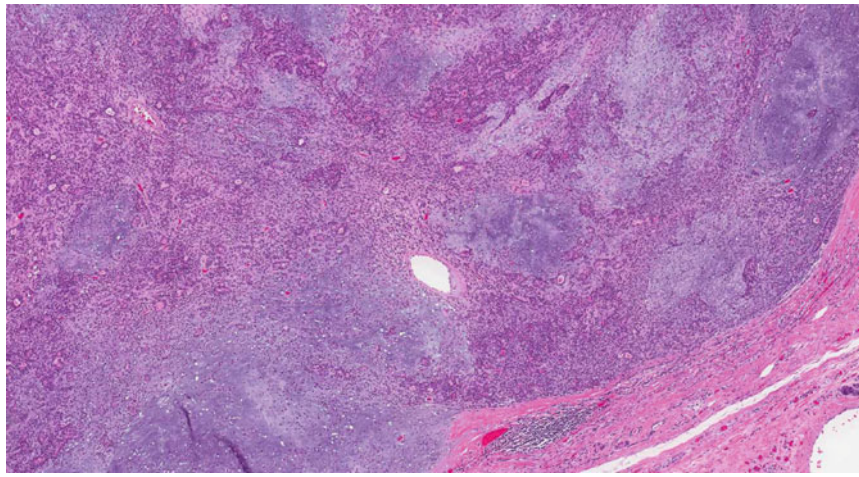

Fig. 12.18 Pleomorphic adenoma: Well-circumscribed neoplasm in parotid gland at low magnification with carilage, epithelial cells, and myoepithelial cells

- Biphasic pattern:
  - Epithelial differentiation:
    - Forms ductal elements and/or may see keratin formation
    - Probable origin of myoepithelial cells
  - Mesenchymal differentiation:
    - Chondrocytes, chondroid myxoid stroma, fat, bone
- Epithelial and myoepithelial elements dispersed throughout a non-homogenous matrix with varying degrees of myxoid, fatty, hyaline, chondroid (cartilaginous), and osseous tissue

Warthin's Tumor (Fig. 12.19):

- Benign tumor with lymphoid and double-layered papillary oncocytic epithelial component
  - Lymphoid: blue staining
  - Epithelial: basal layer of cells closer to lymphoid tissue, with presence of second epithelial cell type oxophilic/oncocytic/eosinophilic (pink granular cytoplasm) columnar cells closer to lumen (often a clear space) side.
    - Granularity due to increased number of mitochondria
- Papillary type architecture, cystic, lymphocytes, and often plasma cells
  - "Double lines" of papillary epithelium project into cystic lumen
  - Dense lymphoid stroma with germinal center formation present
- Malignant transformation rare but possible:
  - Epithelial component may transform to SCC, adenocarcinoma
  - Lymphoid component to lymphoma

Oncocytoma (Fig. 12.20):

- Benign, encapsulated tumor with large, granular-appearing epithelial cells
- Oncocytic cells
  - Abundant granular pink cytoplasm (due to mitochondria)
- Nuclei small and pyknotic
- Occasional clear cells
- Special Stains:
  - PTAH: binds to mitochondria

Mucoepidermoid Carcinoma (MEC) (Fig. 12.21):

- Malignant tumor with admixed mucus-secreting cells, intermediate cells, and epidermoid cells
  - Epidermoid: squamous differentiation

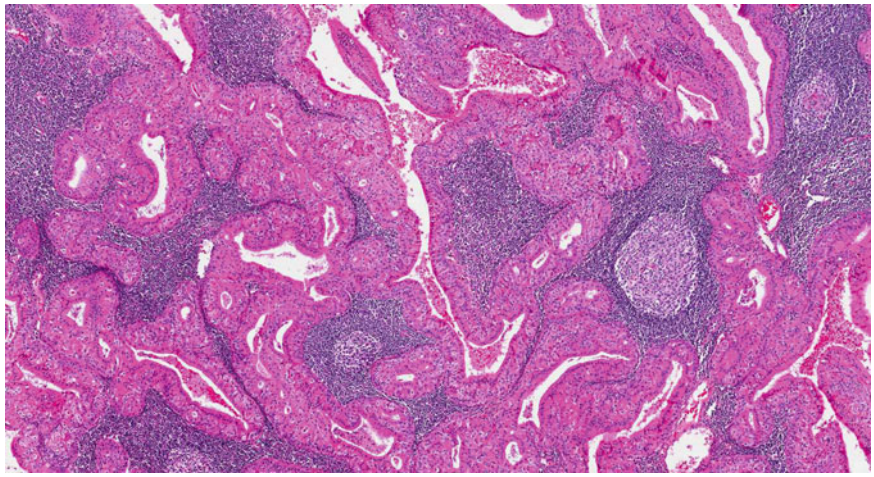

Fig. 12.19 Warthin's tumor. Eosinophilic epithelial cells forming papillary and cystic structures and surrounded by lymphoid cells

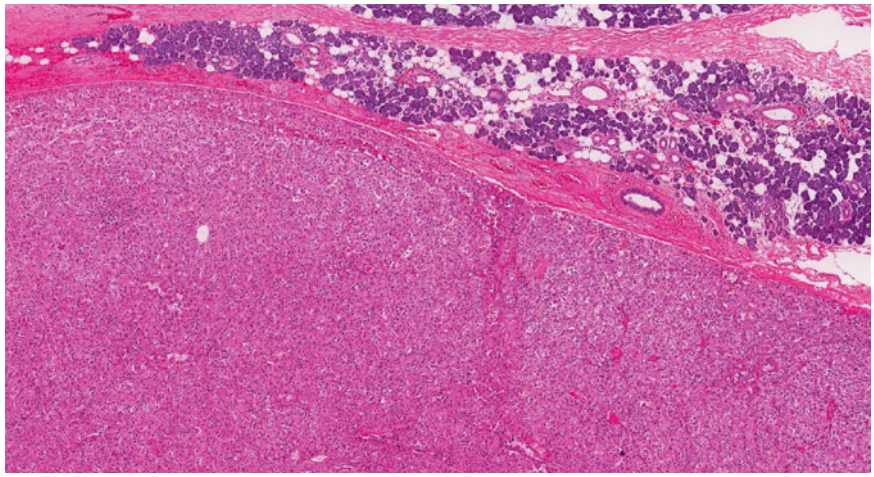

Fig. 12.20 Oncocytoma: Encapsulated eosinophilic salivary gland neoplasm in parotid gland

- Requires grading assignment into low, intermediate, or high grade category by pathologist
- Various grading scales exist
- Factors impacting grade
  - Small biopsy versus complete removal (i.e., sampling)
  - Ratio of mucous cells to epidermoid or intermediate cells
  - Percentage of cystic structure formation
  - Some consider perineural invasion or necrosis, mitoses

High grade MEC may be misdiagnosed as conventional SCC

- Special stains:
  - PAS positive
  - Mucicarmine positive: reddish-pink intracellular mucin

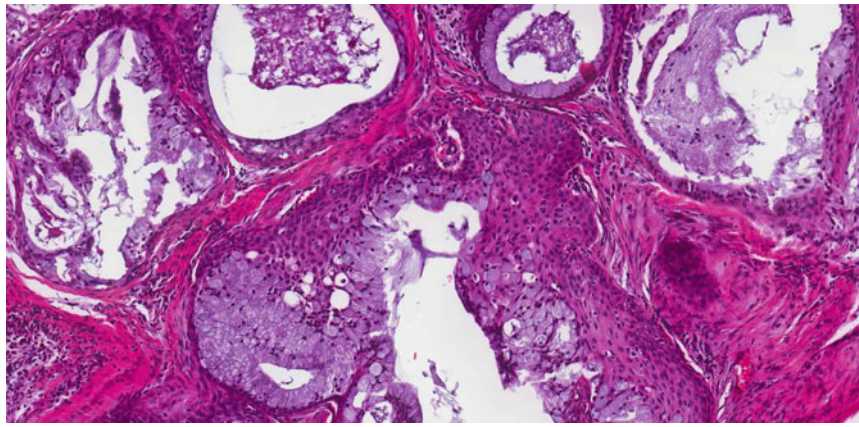

Fig. 12.21 Mucoepidermoid carcinoma: Tumor islands composed of epidermoid cells, intermediate cells, and mucous cells. Mucous cells line cystic spaces

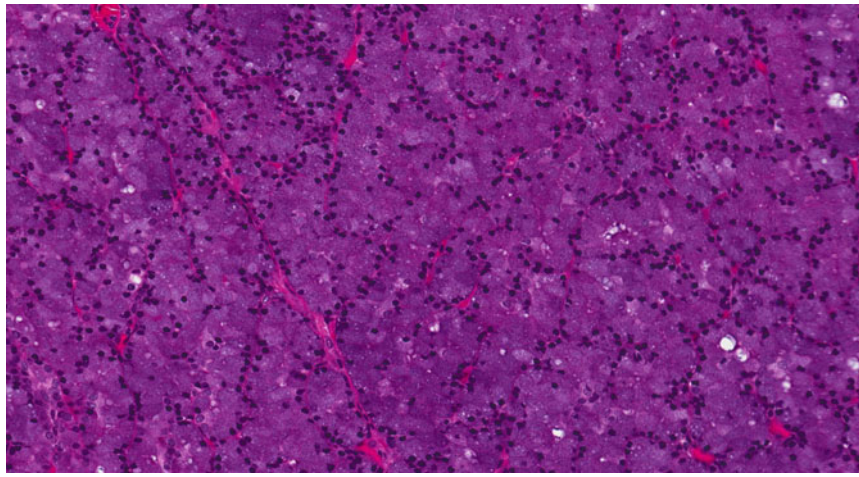

Fig. 12.22 Acinic cell carcinoma: Trabeculae of large, basophilic, slightly granular-appearing tumor cells. Eccentric position of the nucleus within cells

Acinic Cell Carcinoma (Fig. 12.22):

- Malignant salivary gland neoplasm with serous acinar differentiation
- Microscopic patterns: Solid/classic or "blue dot," microcystic, papillary or follicular
  - Solid type readily distinguishable by the purple granular basophilic cytoplasm
    - On FNA may be misdiagnosed as "normal" if very well-differentiated cells
  - Microcystic: small "holes" or circular clearing among syncytium of basophilic cells
  - Papillary pattern much more eosinophilic
    - Some (in addition to some eosinophilic microcystic cases) may actually represent recently characterized Mammary Analogue Secretory Carcinoma
- Special stain:
  - PAS positive and diastase resistant

Adenoid Cystic Carcinoma (AdCC) (Fig. 12.23):

- Slow growing malignant salivary gland neoplasm, with perineural invasion (PNI)
- Small cells with dark, compact nuclei, scant cytoplasm
- Space between cells filled with hyaline material (excess basement membrane), pseudoducts

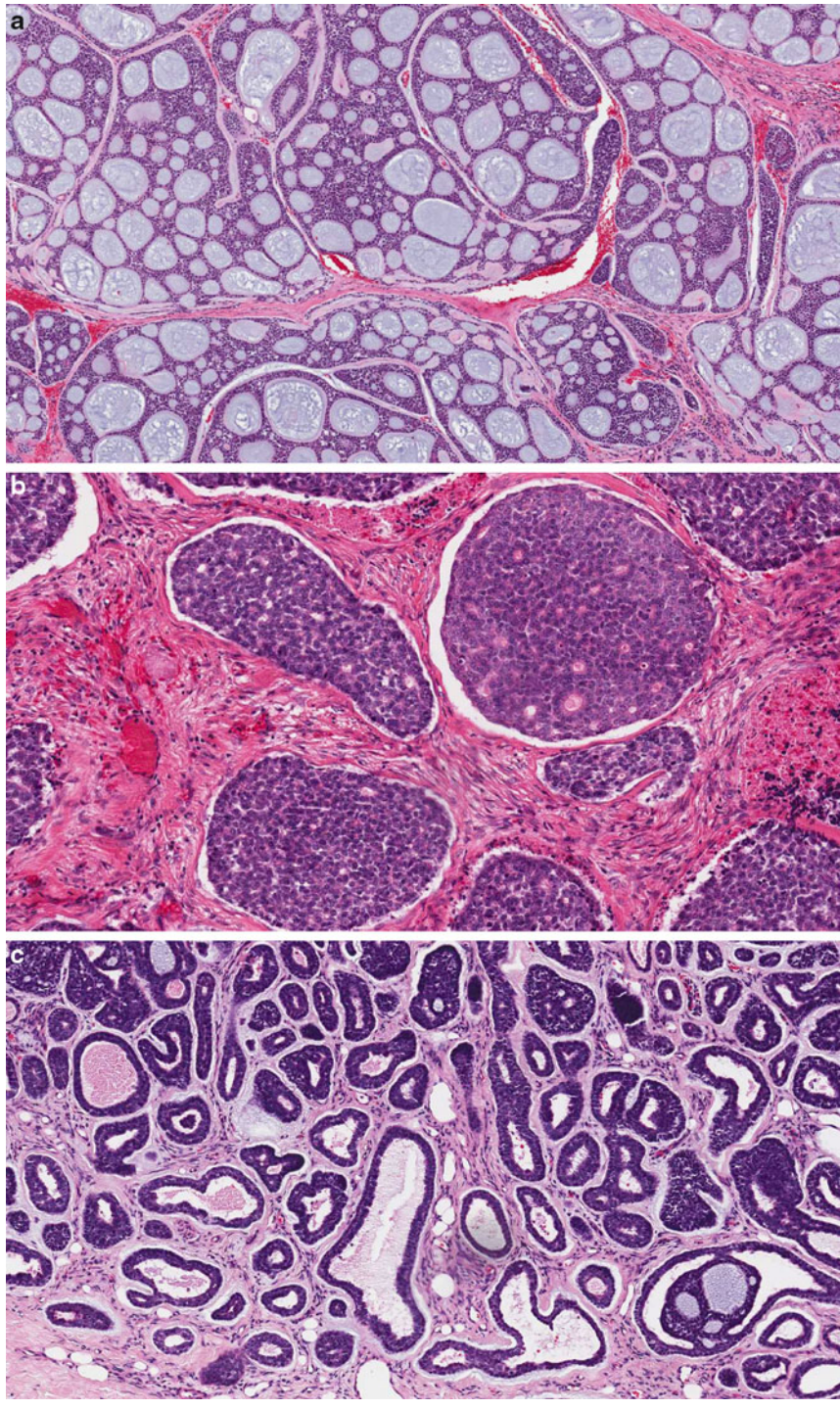

Fig. 12.23 Adenoid cystic carcinoma: (**a**) Cribriform pattern of growth. (**b**) Solid pattern. (**c**) Tubular pattern

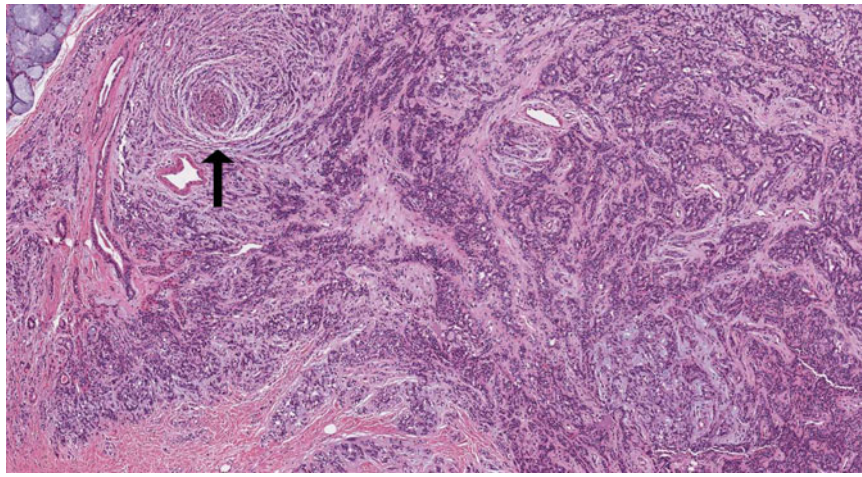

Fig. 12.24 Polymorphous low-grade adenocarcinoma: Tumor forms characteristic "onion-skinning" or "targetoid" pattern (*arrow*)

- True ductal structures also present
- Tubular, solid, cribriform microscopic patterns
- Cribriform (Swiss cheese pattern):
  - Islands of basaloid epithelial myoepithelial cells
  - Demarcated nests
  - Light pink or bluish tint in areas of a cellular clearing (i.e., the cheese holes)
- Solid:
  - Looks like basaloid tumor
  - Solid basaloid cells in hyalinized stroma
  - Worst prognosis
- Tubular:
  - Smaller tubular, sometimes trabecular duct-like arrays
  - Basaloid epithelial cells surrounding central lumen like space
  - Fibrous/hyalinized stroma

Polymorphous low-grade adenocarcinoma (PLGA) (Fig. 12.24):

- Syn: Lobular carcinoma, terminal duct carcinoma
- Shows PNI, similar to AdCC, however differentiated from AdCC by better prognosis in PLGA
- Low-grade behavior
- Relatively monomorphous in cell types present, but cells arranged in variable patterns (polymorphous architecture)
- Characteristic "targetoid" or "onion-skinning" pattern of tumor growth, often around a nerve
- May have cribriform growth similar to AdCC
- Cuboidal or low columnar with oval/elongated basophilic nuclei
- IHC:
  - CD117: tumor percent positivity characteristically higher in AdCC
  - S100: tumor percent positivity characteristically higher in PLGA

Carcinoma Ex-Pleomorphic Adenoma (Fig. 12.25):

- Malignant transformation of a preexisting benign mixed tumor
- Can have cartilage, hyaline, ductal, benign looking neoplasm adjacent to areas of high mitotic, activity, large nuclei, atypia or frank malignancy
  - Evaluate the capsule of the neoplasm for extracapsular extension
  - Malignant component invasion of less than 1.5 mm has better prognosis

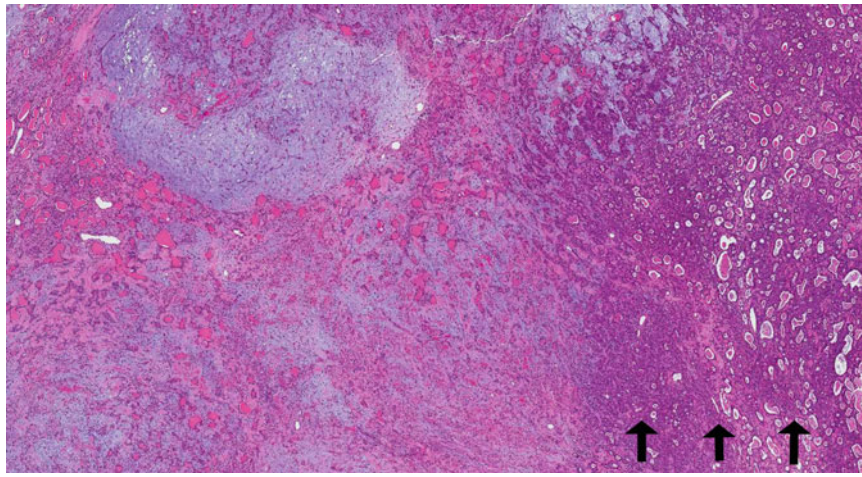

Fig. 12.25 Carcinoma ex-pleomorphic adenoma: Bland basophilic material between benign epithelial and myoepithelial cells. Adjacent hyperchromatic, hypercellular malignant ductal proliferation (*above arrows*)

- Malignant epithelial component: various types adenocarcinoma or SCC possible
- Malignant mesenchymal component: chondrosarcoma, osteosarcoma, and others possible
  - Malignant transformation of epithelial and mensenchymal = carcinosarcoma

SINONASAL

Nasal Glial Heterotopia (Nasal Glioma) (Fig. 12.26):

- Extranasal/Intranasal (presents as a polyp)/Mixed type (10 %, communicate via bony defect)
- Homogeneous, polypoid appearance
- Extracranial, ectopic glial tissue without neurons
- Astrocytes + glial fibers, neurons rare
- Gemistocytes (swollen, reactive astrocytes)
- IHC:
  - S100 + (neurons, glia, nerve sheath cells)
  - GFAP + (glial fibrillary acidic protein)

Polyps (Fig. 12.27):

- Localized outgrowth of lamina propria secondary to the accumulation of fluid with proliferation of fibroblasts and acute and/or chronic inflammation
- Epithelial lining: respiratory or squamous (chronic irritation causes squamous metaplasia)
- Connective tissue/stroma:
  - Myxoid: pale, edematous changes
- Many inflammatory cells:
  - Lymphocytes, plasma cells, eosinophils, neutrophils
- Atypical stromal cells possible:
  - Large stromal cells, usually after trauma

Allergic Fungal Sinusitis (AFS) (Fig. 12.28):

- Hypersensitivity reaction, not infection
- Inspissated mucin:
  - Thick, tenacious, brown-green mucus
  - "Peanut butter," "thick rubbery material," "rubber cement"
- H&E: Pinkish mucin with dark blue areas of "stacked coins" or "tide lines" or "ripple" formation
  - These formations are degenerating inflammatory cells, debris, intermixed with mucin
  - Contains eosinophils (degenerating and intact) in sheets

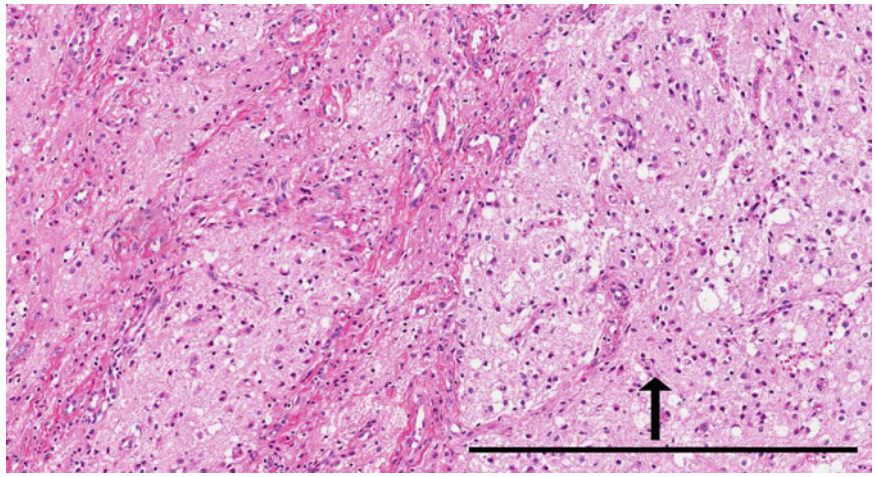

Fig. 12.26 Nasal glioma (nasal glial heterotopia): Sheets and islands of delicate pink fibrillary material (*above arrow*) positioned between fibrovascular connective tissue

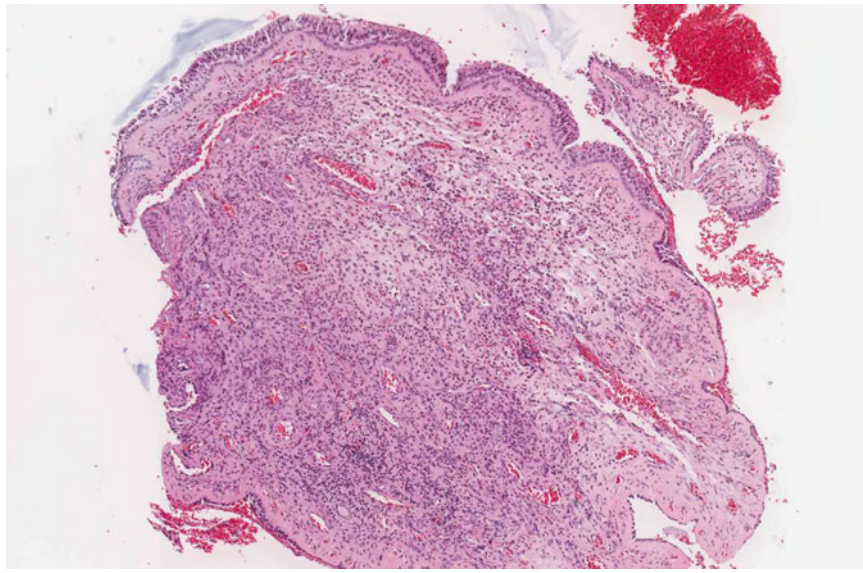

Fig. 12.27 Nasal polyps: Nasal polyp, chronically inflamed

- Charcot-Leyden crystals:
  - Pale rod-like crystalline structure
  - Represent degenerated eosinophils
- GMS fungal stain can be done, fungal hyphae may be seen, not required
- Cultures: Aspergillus, Curvularia, Dreshella, Bipolaris, Exserohilium

Rhinoscleroma (Fig. 12.29):

- Gram negative bacilli: Klebsiella rhinoscleromatis
- Stages: rhinitic, florid, fibrotic
- Variable types chronic inflammatory cells (lymphocytes and plasma cells) comingled with pale, clear or slightly granular-appearing macrophages
  - Mikulicz cells: Macrophages with clear to foamy/granular cytoplasm containing bacilli
  - Russell bodies: immunoglobulin in plasma cells (but completely nonspecific)

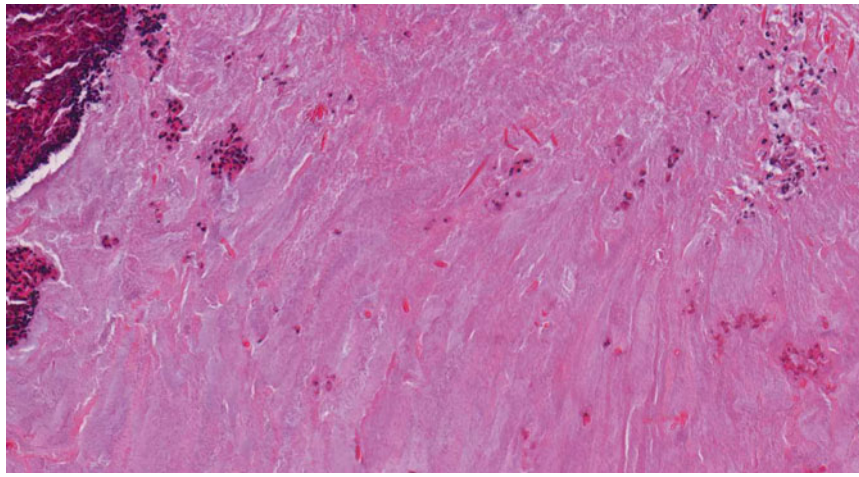

Fig. 12.28 Allergic fungal sinusitis: Charcot-Leyden crystals

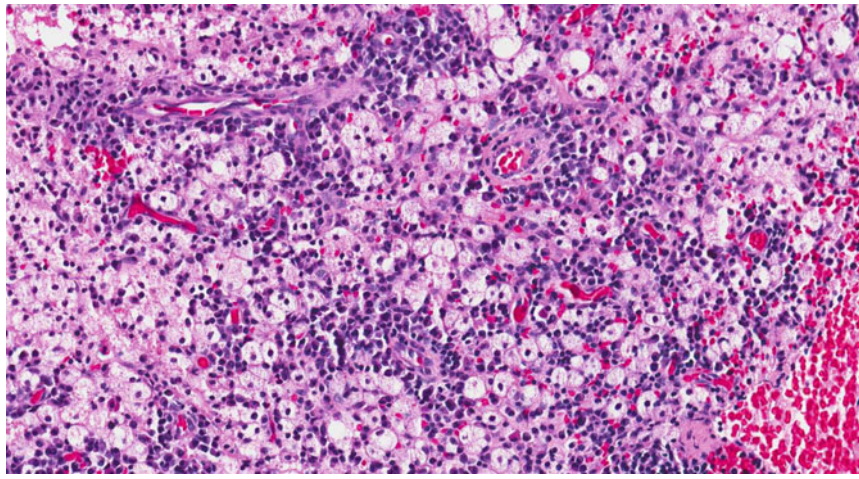

Fig. 12.29 Rhinoscleroma: numerous foamy macrophages (Mikulicz cells) intermixed with chronic inflammatory cells

- Warthin-Starry stain: positive good for small bacteria, stain silver
  - Also used for syphilis: detection of spirochetes

Rhinosporidiosis (Fig. 12.30):

- Zoonotic: Rhinosporidium seeberi
- Pseudoepitheliomatous hyperplasia may be present
- Respiratory epithelium and/or submucosa exhibits round structures, often containing spores
  - Submucosal cyst/sporangia (10–300 μm) with endospores
  - Chronic inflammatory response: lymphocytes, plasma cells, eosinophils

Lobular Capillary Hemangioma (Fig. 12.31):

- Larger branches centrally, smaller vessels peripherally
- Lobular capillaries with surrounding connective tissue
  - Bundles of small vessels surrounded by pink stroma
- Proliferation of small vessels and capillaries

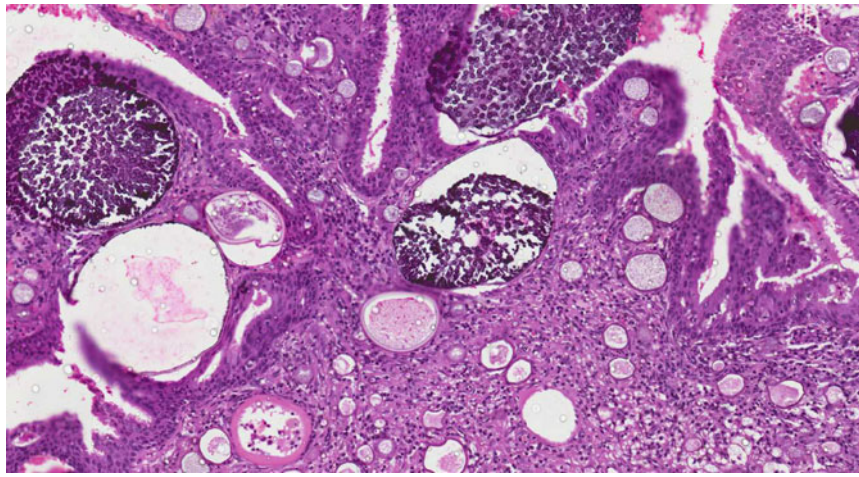

Fig. 12.30 Rhinosporidiosis: Dilated thick- or thin-walled structures which may appear empty or contain numerous endospores (latter has a bag of marbles appearance)

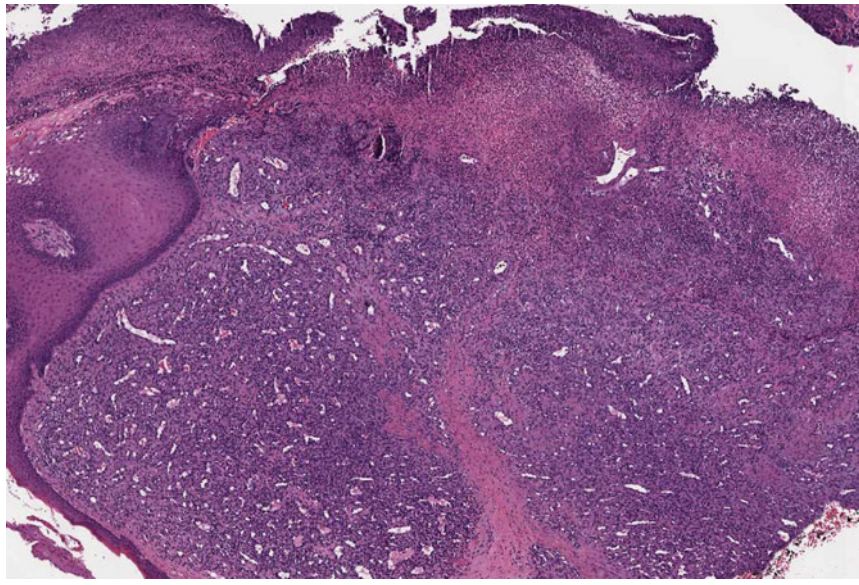

Fig. 12.31 Lobular capillary hemangioma: Numerous endothelial-lined vascular channels

Juvenile Nasopharyngeal Angiofibroma (JNA) (Fig. 12.32):

- Syn: nasopharyngeal angiofibroma
- Syndromic association possible: Gardner syndrome, autosomal dominant
- Large and small vessels embedded within dense collagenous stroma.
  - No branching small vessels
  - Vessels ectatic, gaping… "held open" by the dense stroma
  - Some, not all vessels with muscular coat
  - Histology may reveal thromboembolic material introduced preoperatively

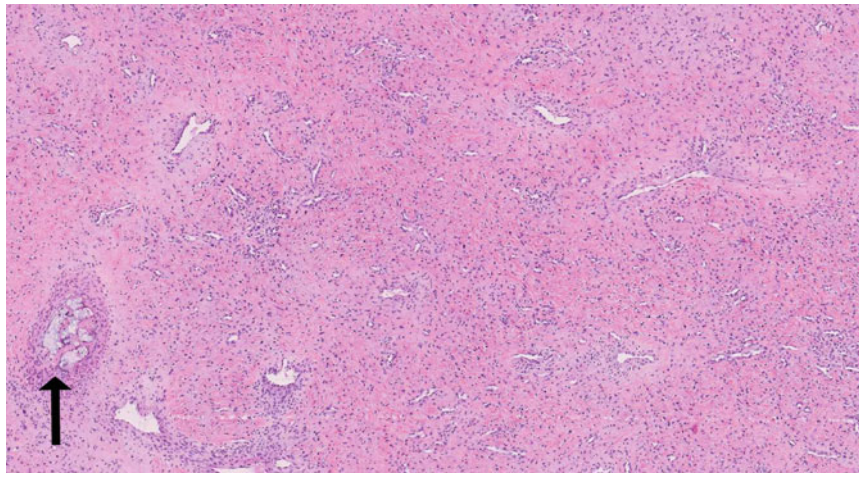

Fig. 12.32 Nasopharyngeal fibroma: Ectatic vascular channels embedded in a bland fibrous stroma. Thromboembolic material presents as a result of preoperative embolization of the neoplasm (*arrow*)

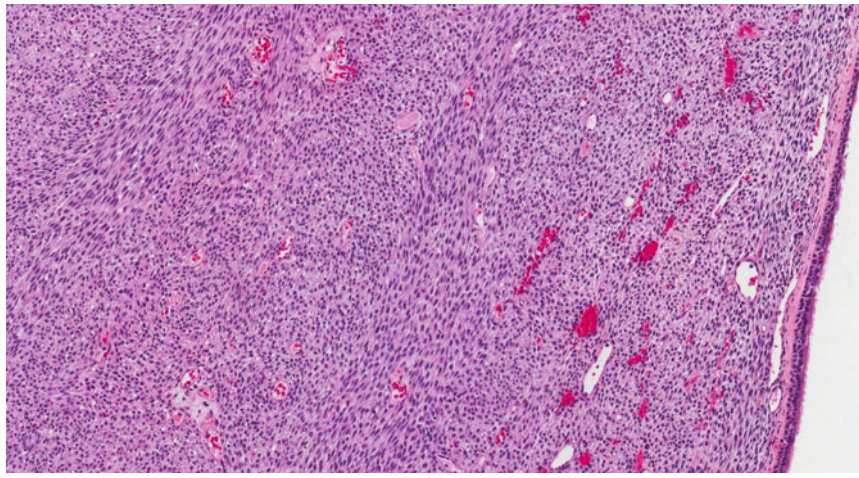

Fig. 12.33 Sinonasal-type hemangiopericytoma (glomangiopericytoma): Short fascicles of spindled and ovoid cells with intervening vascular channels, all surfaced by intact respiratory epithelium

Sinonasal-type Hemangiopericytoma (Fig. 12.33):

- Syn: glomangiopericytoma
- Diffuse, cellular neoplasm composed of spindled or ovoid neoplastic cells
- More cellular tumor, arranged in short fascicles or whorls, tumor appears more blue
- Usually large, dilated vessels often with perivascular hyalinization (pink rind)
  - Staghorn vessels possible
- IHC: Actin positive (myoid differentiation) and negative for CD34 (vascular marker)

Sinonasal Papilloma (Schneiderian papilloma) (Fig. 12.34):

- Inverted (47 %): lateral nasal wall, burrowing pattern
  - Mixed respiratory and non-keratinizing squamous epithelium
  - Mucus cysts, goblet cells (mucocytes, pale blue areas) with many polymorphonuclear leukocytes (PMNs)
  - Surface keratinization may suggest underlying dysplasia
  - Epithelium burrows below submucosa to form elongated tubular structures

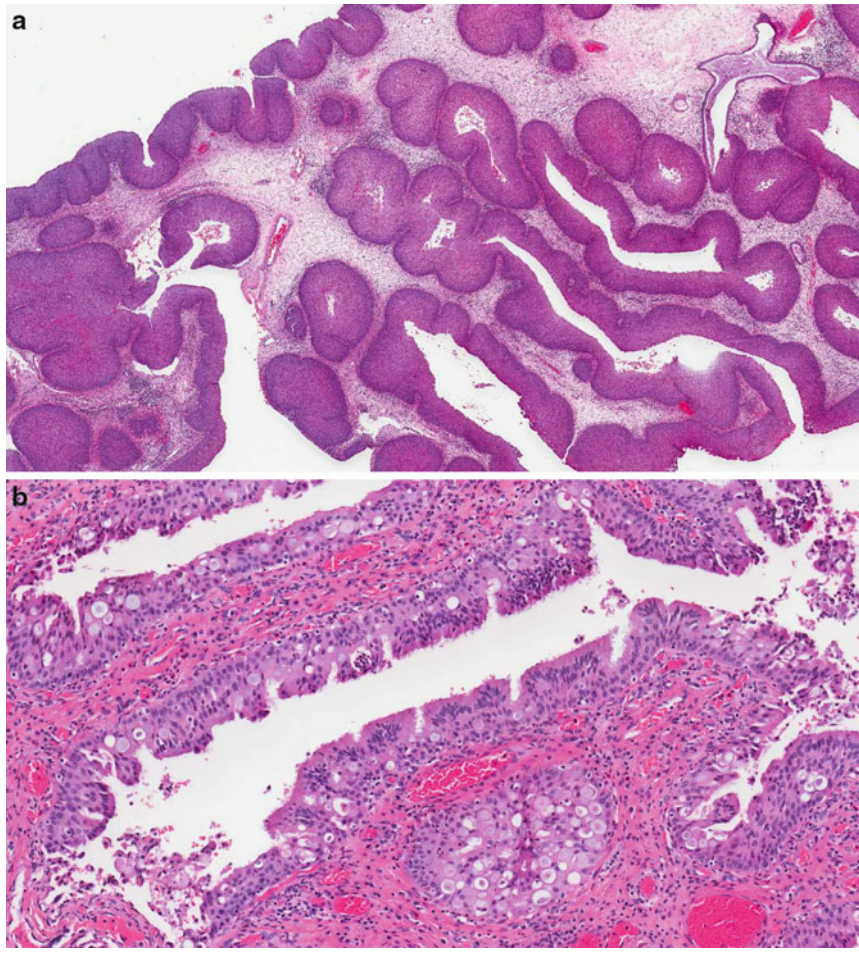

Fig. 12.34 Sinonasal papillomatosis: (**a**) Inverted papilloma: Marked hyperplasia of epithelial component. Epithelium "burrows" or "inverts" into the stromal tissue. (**b**) Oncocytic variant

- Fungiform (50 %)
  - Non-keratinizing squamous epithelium
  - Exophytic, septal lesions
  - Fewer mucous cells
  - Malignant transformation less common
- Cylindrical (3 %)
  - Oncocytic schneiderian papilloma
  - Mucus cysts, goblet cells, cilia, PMNs
  - Papillary pattern (papilla, branching) with multilayered columnar cells with cilia, pink cytoplasm
  - Elongated cells with mucus cysts, cylindrical appearing

MALIGNANT SINONASAL NEOPLASMS

Nasopharyngeal Carcinoma (NPC) (Fig. 12.35):

- Keratinizing type: most differentiated, worst prognosis
  - Looks like SCC
  - Jagged irregular islands of tumor

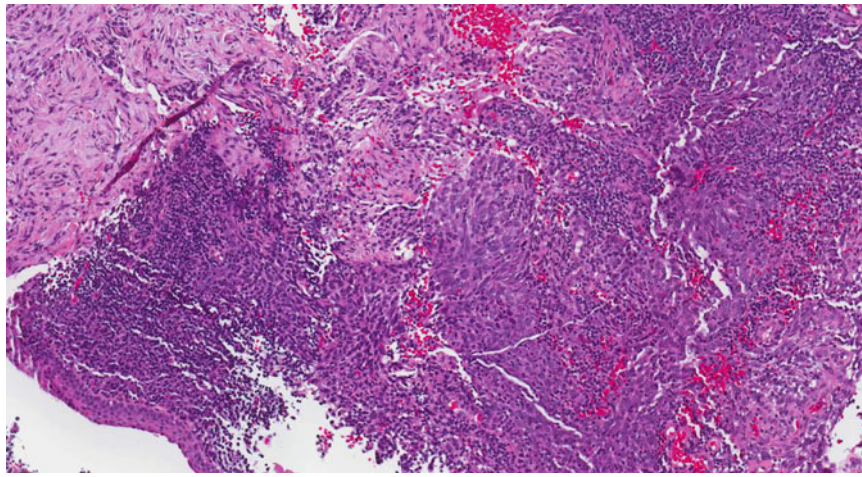

Fig. 12.35 Nasopharyngeal carcinoma: Non-keratinizing malignant proliferation in connective tissue

- Polygonal, boat shape, pink cytoplasm
- Occasional intercellular bridges, keratin pearls
- Does not respond well to radiation therapy (XRT)

- Non-Keratinizing
  - Epstein-Barr Virus association
  - Broad-based bands
  - Pushing border, non-infiltrative pattern
  - Nuclear crowding
- Undifferentiated: best prognosis (responds best to XRT)
  - Epstein-Barr Virus association
  - Dense tumoral lymphoplasmacytic infiltrate
  - Pale vesicular nucleus with prominent nucleolus
  - IHC: Cytokeratin (CK) + (epithelial differentiation)

Sinonasal undifferentiated carcinoma (SNUC) (Fig. 12.36):

- Aggressive malignancy, histogenesis not very well defined
- Undifferentiated "medium-sized" pleomorphic cells
- Nucleoli usually large
- Eosinophilic cytoplasm with distinct cell borders
- Vascular invasion, necrosis
- Lacks keratinization, rosettes, or glandular differentiation
- IHC:
  - CK+
  - EMA+/–
  - Neuron-specific enolase (NSE)+/–
  - Synaptophysin (SYN)-, Chromogranin (Chr)-

Olfactory Neuroblastoma/Esthesioneuroblastoma (Fig. 12.37):

- Neuroepithelial tumor, originates from olfactory membrane
- 4-Tier grading system: Hymes
- Low grade:
  - Lobular pattern, surrounded by vascular tissue
  - Background dark nuclei appear like lymphocytes
    - Lymphocyte-like nuclei
  - Neurofibrillary matrix: pink, cob-web or cotton-candy appearance
  - Homer-Wright rosettes: nuclei ring around fibrillary matrix

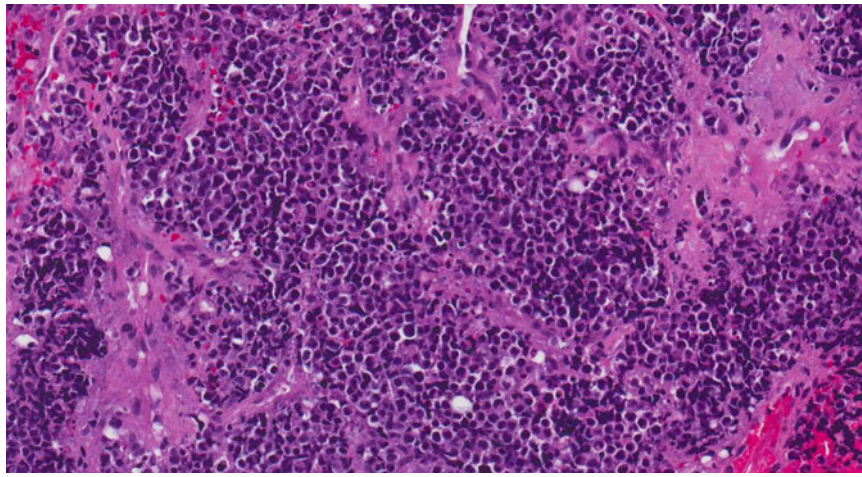

Fig. 12.36 Sinonasal undifferentiated carcinoma: high grade malignancy with necrosis

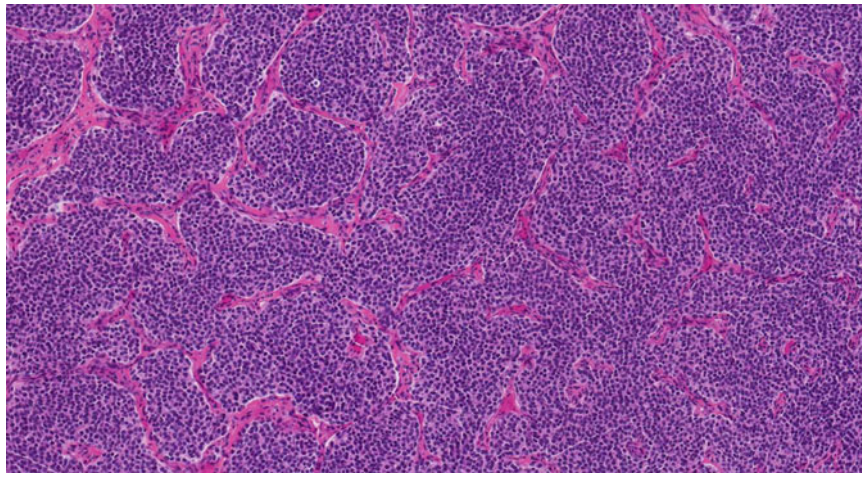

Fig. 12.37 Esthesioneuroblastoma: Lobular aggregates separated by fibrovascular tissue

- High grade:
  - Trends towards SNUC appearance
  - Less differentiated, less cob-web matrix
  - Flexner-Wintersteiner rosettes
  - Nuclei ring without matrix in between
  - Increased mitotic rate with increasing grade
- IHC:
  - NSE+
  - SYN/Chr+
  - S100+
  - CK–, EMA–

Sinonasal Adenocarcinoma (Fig. 12.38):

- Salivary Gland Type:
  - Tumors resemble their salivary gland counterparts
  - Example: MEC, AdCC

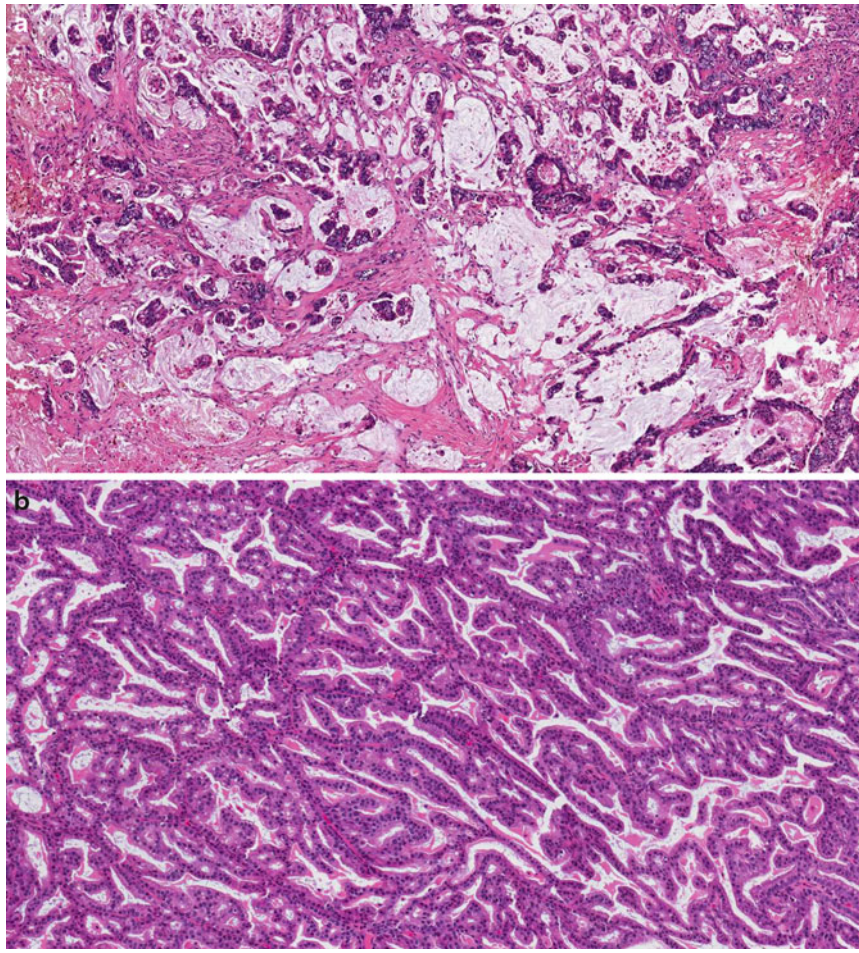

Fig. 12.38 Sinonasal adenocarcinoma: (**a**) Intestinal type adenocarcinoma (ITAC): abundant mucin intermixed with malignant epithelium with resemblance to colonic epithelium. (**b**) Low-grade non-salivary gland, non-itac adenocarcinoma: low-grade morphology, back-to-back glandular proliferation

- Non-Salivary Gland Type:
  - Intestinal Type Adenocarcinoma (ITAC)
    - Associated occupational exposures: woodworking
    - IHC: Positive CDX-2, CK20, CK7+/–
  - Non-ITAC
    - Low grade: back- to-back glandular formation
    - High grade: poorly defined

Sinonasal Mucosal Melanoma (Fig. 12.39):

- Melanin pigment: brown/black pigment
- Spindle, round, epitheliod cells with large nucleoli ("cherry red" or "stop sign")
- Remember the pathology adage: "melanoma can look like anything"
- SNUC-like appearance, small round blue cell, vaguely neuroendocrine appearance
- IHC:
  - S100+
  - HMB 45+
  - Melan A (melanocytic antigen)
  - Tyrosinase + (produced by melanoma)

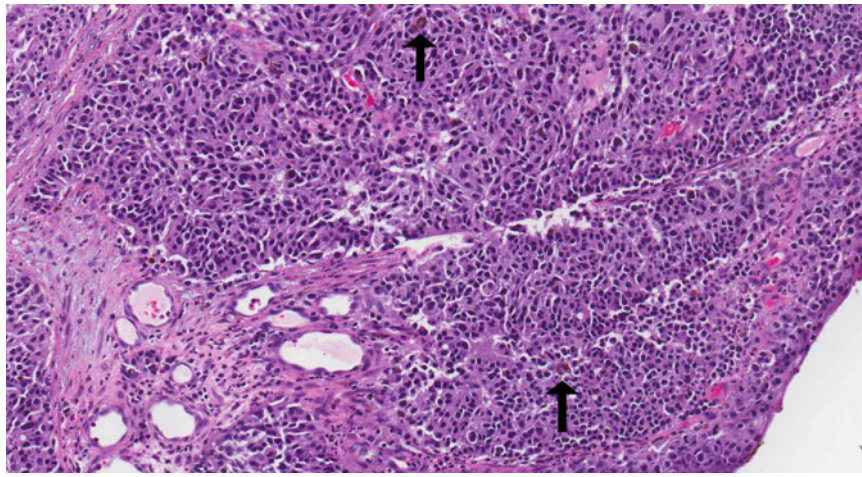

Fig. 12.39 Mucosal melanoma: Occasional cells with melanin (*arrows*) within tumor proliferation

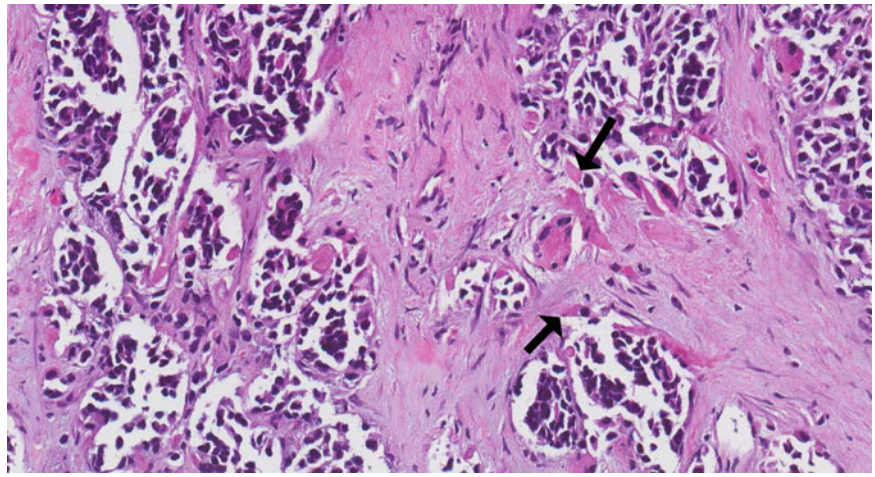

Fig. 12.40 Rhabdomyosarcoma: Dyscohesive cells in groups. Strap cells (*arrow*) and scattered large pink cells with myoid differentiation

Rhabdomyosarcoma (RMS) (Fig. 12.40):

- Embryonal RMS, most common in H&N:
  - "Sarcoma botryoides" in cavitary spaces (sinuses, "aural polyp") is ERMS variant
  - Clinical appearance of pale, polypoid cluster of gelatinous grapes
  - Alternating Hypo/Hypercellular areas:
    - Hypercellular: cambium layer
      - Condensed cellularity adjacent to mucosa/epithelium
    - Hypocellular:
      - Myxoid background- pale loose background with developing rhabdomyoblasts
  - Embryonal RMS often with primitive "small round blue cell" appearance
    - Clues to diagnosis include eccentric eosinophilic cytoplasm and strap cells
    - Strap cells: long tail, nucleus off to side, fibrillar/stringy cytoplasm
- Alveolar RMS:
  - Groups of dyscohesive dark cells separated by bands of fibrous stroma
  - Low power silhouette may appear similar to lung alveoli

- Malignant cells with 'small blue cell' appearance, focal muscle differentiation
- Muscle differentiation: eosinophilic cytoplasm, "strap cells," rarely cross-striations

- IHC:
  - Desmin
  - Myoglobin
  - MyoD1
  - MSA

DDx of small round blue cell tumors of the sinonasal tract:

- Melanoma (+HMB, +S 100, Melan A, tyrosinase+)
- SNUC (epithelial markers)
- Esthesioneuroblasoma
- Lymphoma (lymphocyte markers, especially leukocyte common antigen)
- Poorly differentiated SCC/Adenocarcinoma
- Rhabdomyosarcoma (myocyte markers)

INFECTIOUS/INFLAMMATORY

Tuberculosis (Fig. 12.41):

- Granulomatous:
  - Elongated-epithelial histiocytes, palisading appearance
  - Central acellular necrotic debris
- AFB: bright red on acid-fast/Ziehl-Neelsen stain

Mucormycosis/Fycomycosis/Zygomycosis (Fig. 12.42):

- Caused by *Mucor, Rhizopus, Absidia*
- Angioinvasive lesions: Thrombosis of blood vessels with necrosis of soft tissue
- Immunocompromised
- Fungal organism:
  - Branching organisms
  - Non-septate fungal hyphae

Wegener's granulomatosis (Fig. 12.43):

- Idiopathic granulomatous necrotizing inflammation with multinucleated giant cells
- c-ANCA +
- Geographic appearance of the necrotic areas:
  - Neutrophilic debris with basophilia (bluish as opposed to usual pink debris)
- Vasculitis:
  - Destruction of blood vessel walls with inflammatory cell migration

Natural Killer (NK)-T cell Lymphoma/Lethal Midline Granuloma/Midline Malignant Reticulosis (Fig. 12.44):

- Malignant proliferation of NK-T cells
- Angiocentric pattern with massive necrosis yields tissue loss
  - Therefore tissue biopsied often nonviable and non-diagnostic
- Site: most often found at midline of sinonasal cavity
- Epstein-Barr virus associated (detect virus with in situ hybridization, called EBER)
- Polymorphous:
  - Cell variability indicating malignancy (usually indicates reactive process)
- IHC:
  - CD3+ (T-cells)
  - CD56+ (NK cells)
  - TIA-1 + (NK cell marker)

EAR

Keloid (Fig. 12.45):

- Abnormal degradation of fibroblasts after local injury
- Epidermis often attenuated, absent hair follicles in area
- Haphazardly arranged dermal collagen bundles
- Eosinophilic hyalinized appearance "strips of bubble gum" collagen

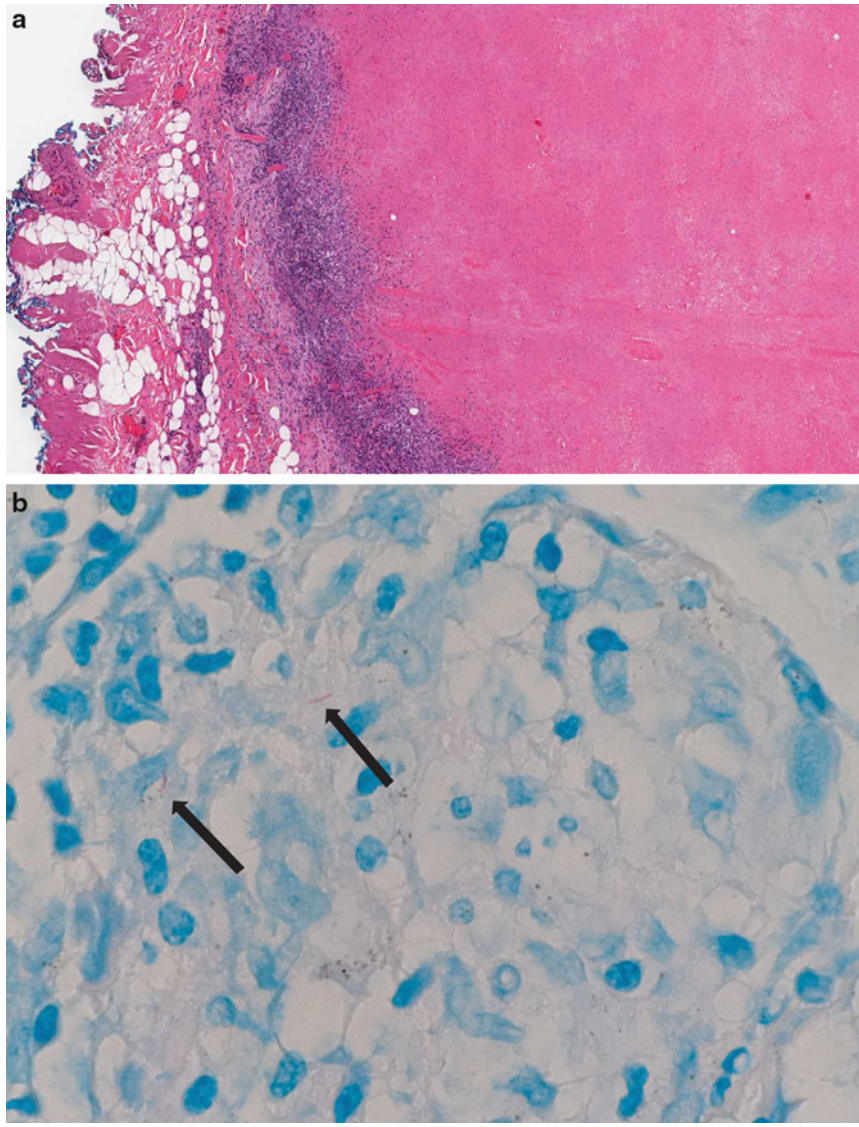

Fig. 12.41 Tuberculosis: (**a**) Uniformly pink necrotic area surrounded by histiocytes in this necrotizing granuloma. (**b**) Rod shaped, *red color* of mycobacterium stained with AFB

Gout (Fig. 12.46):
- Microscopic appearance depends on processing:
- Formalin: monosodium urate crystals (MSU) dissolve but leave pale fluffy, amorphous deposits
- Without processing: MSU crystals are refractile and needle-shaped under polarized light
- Regardless of processing: Crystals cause foreign body giant cell reaction in tissue (tophi)

Exostoses (Fig. 12.47):
- Broad based bony outgrowth, bilateral, multiple in external auditory canal (EAC)
- Dense lamellar bone deposition with onion-skin appearance
- No marrow spaces or trabecula

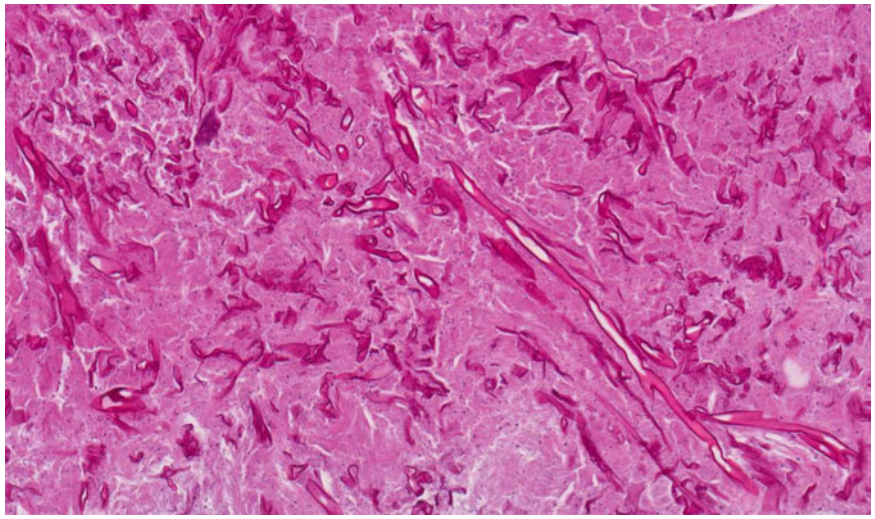

Fig. 12.42 Mucormycosis: Branching, ribbon-like fungal organisms

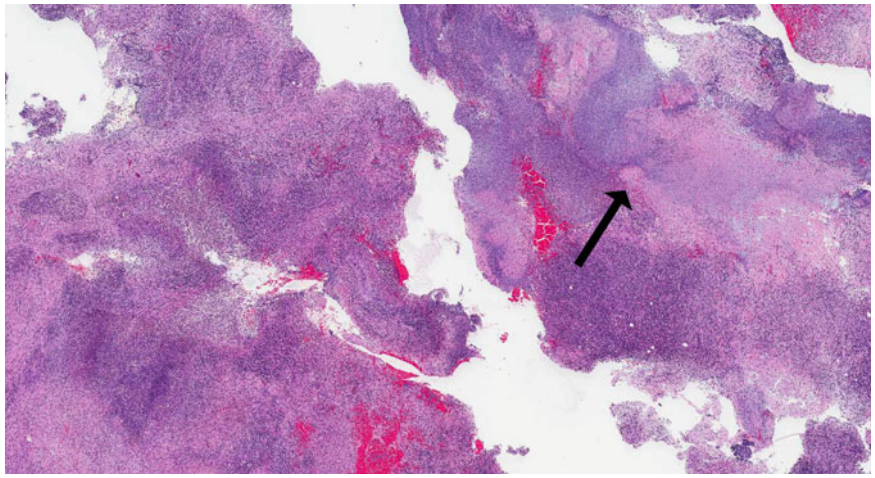

Fig. 12.43 Wegener's granulomatosis: Neutrophilic debris with basophilia (*arrow*)

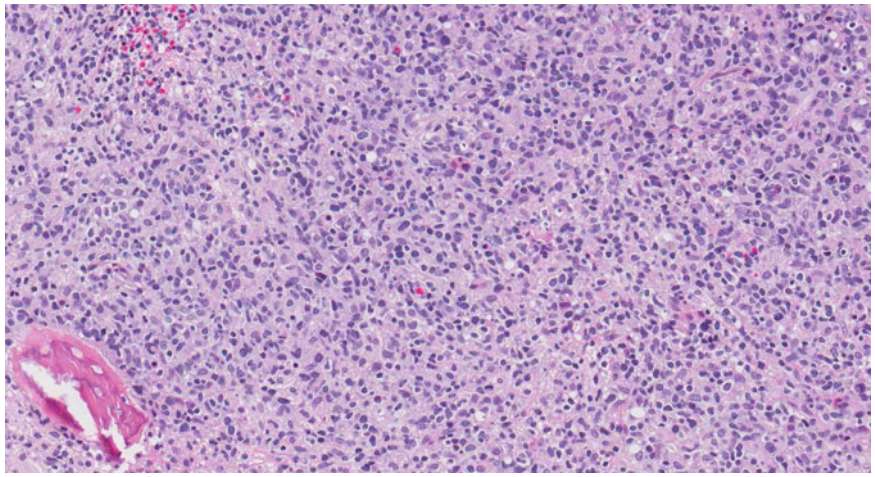

Fig. 12.44 NK-T cell lymphoma: Cellular, dense proliferation of neoplastic lymphocytes

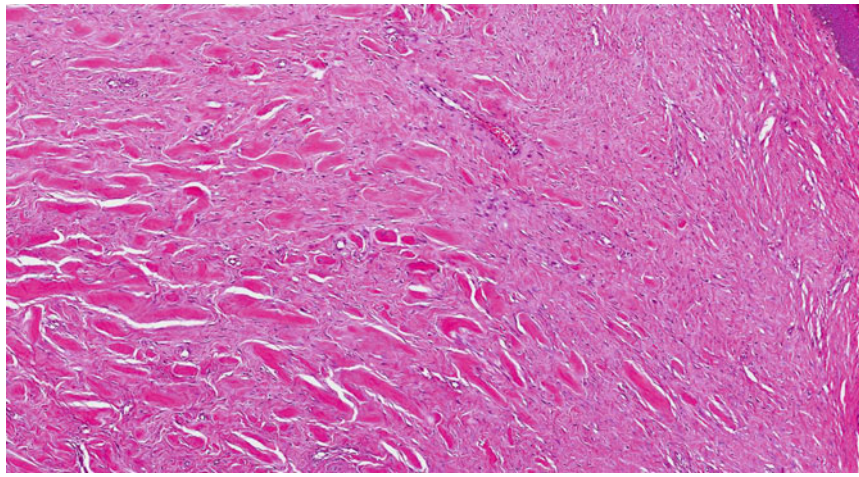

Fig. 12.45 Keloid: Broad bands of densely eosinophilic keloidal collagen ("bubble gum")

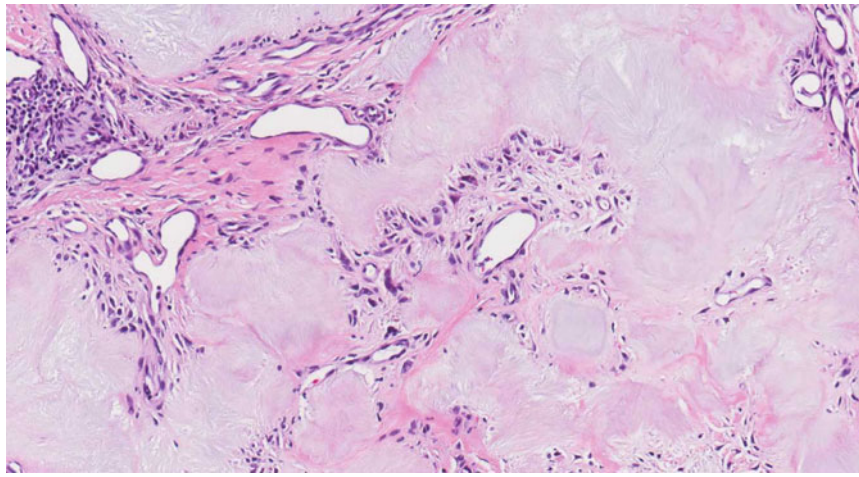

Fig. 12.46 Gout: Amorphous fluffy deposits surrounded by inflammation

Osteoma (Fig. 12.48):
- Benign neoplasm
- Solitary, pedunculated bony mass
- Viable bone with marrow spaces and trabeculae with osteoblasts

Ceruminous Adenoma (Fig. 12.49):
- Unencapsulated proliferation of closely packed glandular structures
- Irregular distribution of glands, but banal cytologically
- Two-cell lining:
  - Luminal (inner) layer lined with cuboidal to columnar cells
    - Brightly eosinophilic cytoplasm with apocrine "snouts"
  - Flattened myoepithelial layer encircles the inner layer of epithelium

Cutaneous Squamous Cell Carcinoma (Fig. 12.50):
- Conventional SCC:
  - Keratinaceous debris, possible keratin pearl formation, intercellular bridges/desmosomes, eosinophilic glassy cytoplasm

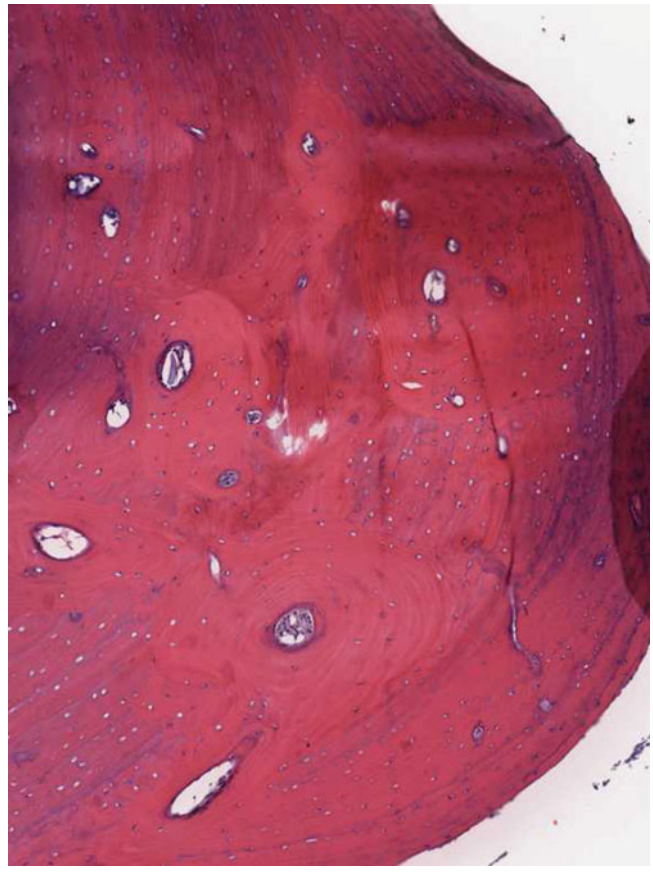

Fig. 12.47 Exostoses: Dense lamellar bone

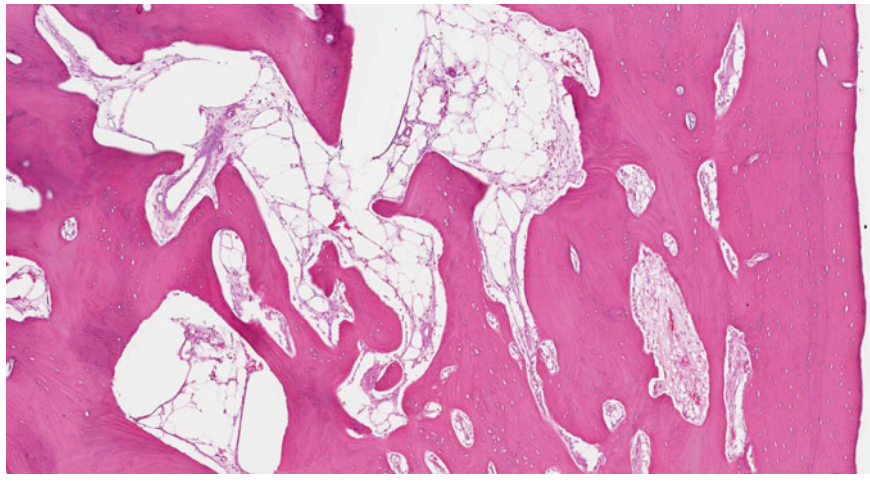

Fig. 12.48 Osteoma: Trabeculae of bone with fibrovascular spaces

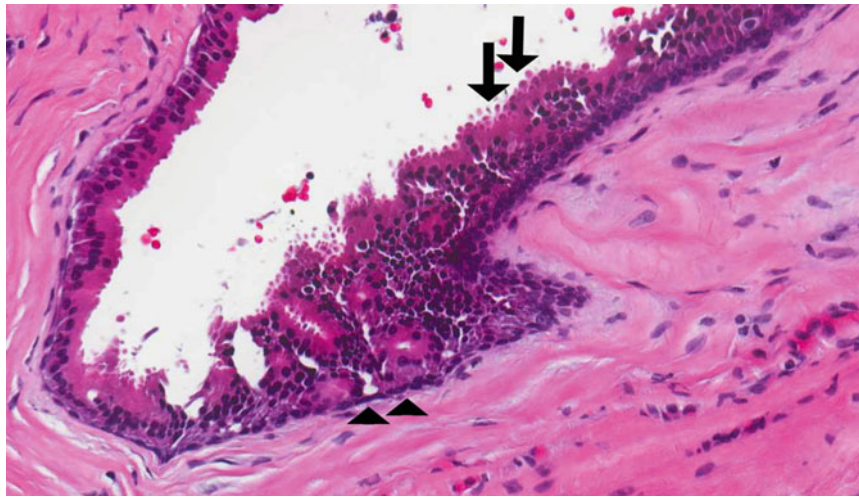

Fig. 12.49 Ceruminous adenoma: Myoepithelial layer surrounding cells with apocrine "snouting"

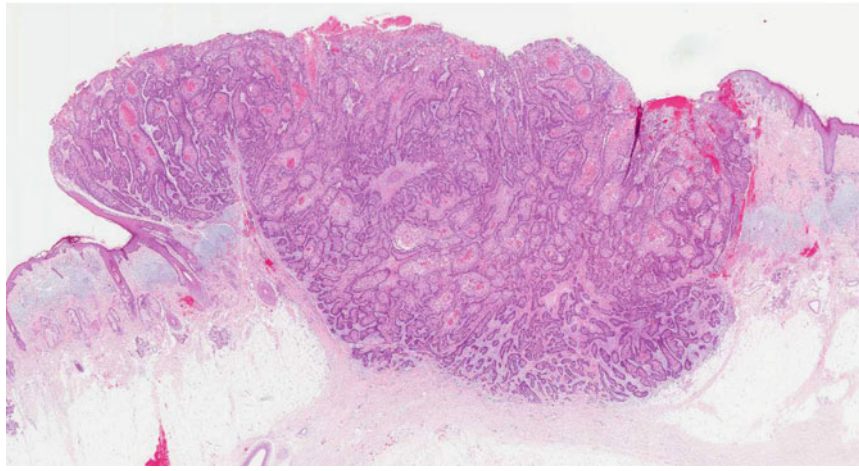

Fig. 12.50 Cutaneous squamous cell carcinoma: Exophytic and endophytic proliferation

- Spindle SCC:
  - Spindle cells with focal differentiation into squamous differentiation or overlying squamous dysplasia
- Adenoid SCC:
  - Acantholysis (lack of cell cohesion) causes pseudoglandular pattern

Basal Cell Carcinoma (Fig. 12.51):

- Clinical: pearly papules or shiny plaque, traversed by microvasculature
- Epithelial cells: very little cytoplasm, large nuclei imparts basaloid appearance, mitoses+, peripheral palisading
- Stroma: Often mucinous. Cleft or separation often develops between stroma and neoplastic epithelial island interface

Cutaneous Melanoma (Fig. 12.52):

- Malignant melanocytes within epithelial layer (pagetoid spread), but importantly, invasion of connective tissue is seen

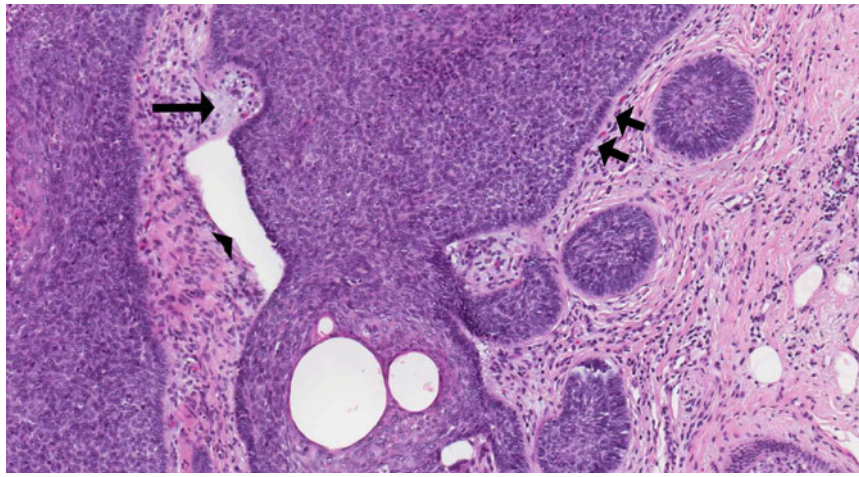

Fig. 12.51 Basal cell carcinoma: Peripheral palisading (*double arrows*), tumor-stromal clefting (*arrowhead*), stromal mucin (*single arrow*)

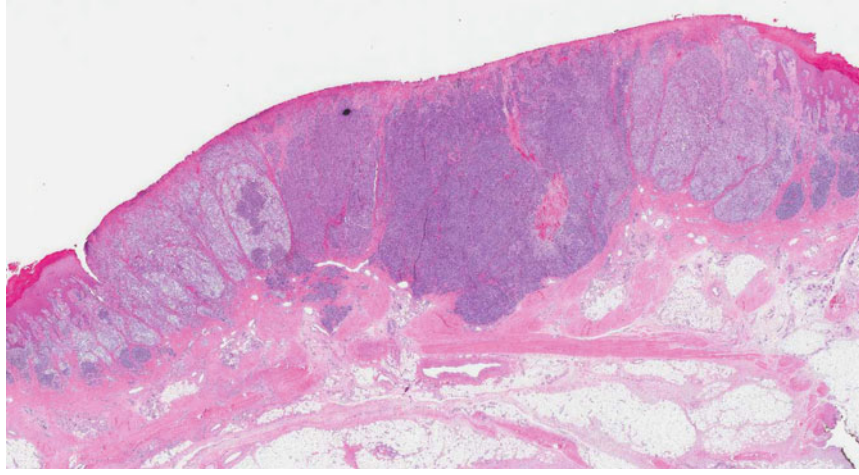

Fig. 12.52 Cutaneous melanoma: Invasive melanocytic proliferation

- Melanin may be seen, pigmented cells
- Spindle, round, polygonal epithelioid cells with large "cherry red" or "stop sign" nucleolus
- IHC: S100 +, HMB45

Cholesterol Granuloma (Fig. 12.53):

- Cholesterol cleft: from degrading RBCs → forms crystals, which dissolve upon processing
- Appear as clear, "needle-like" spaces microscopically
- Foreign body giant cells often present alongside granulation tissue
- Hemosiderin present, as focal hemorrhage resolves

Cholesteatoma (Fig. 12.54):

- Clinical: keratinous debris, cheesy/white
- Cystic lesions, 1–4 cm diameter, lined by keratinizing squamous epithelium or metaplastic mucus-secreting epithelium

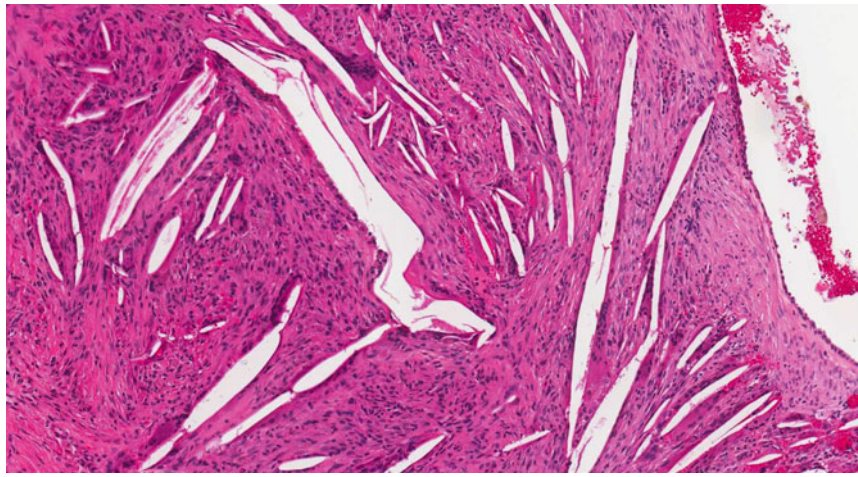

Fig. 12.53 Cholesterol granuloma: needle-like spaces of cholesterol clefts

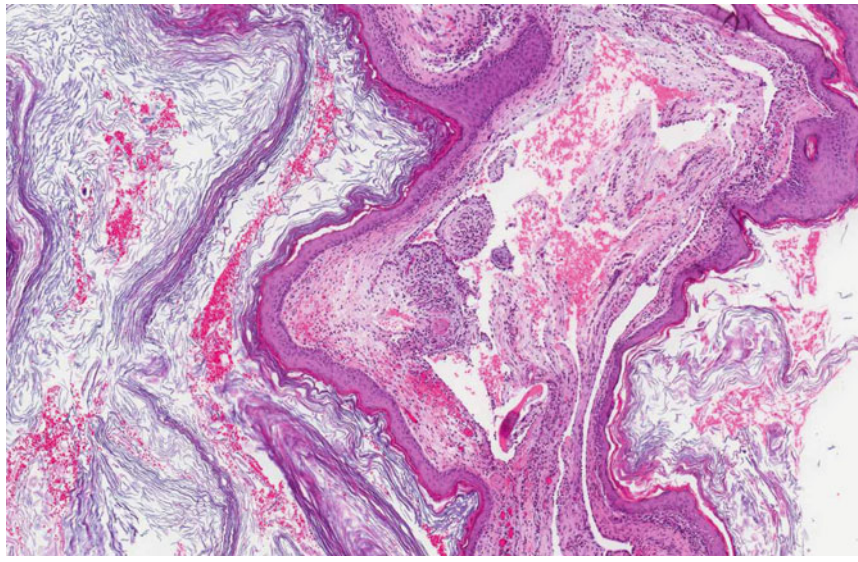

Fig. 12.54 Cholesteatoma: benign squamous epithelium, keratin debris and inflamed stromal tissue

- Three components for diagnosis
  - Epithelium: nearly always keratinizing squamous epithelium
  - Keratinaceous debris: flakes, scales, desquamated keratin
  - Stromal tissue: Granulation tissue often chronically inflamed
- Can occur with foci of cholesterol cleft formation or with cholesterol granuloma

Langerhans Cell Histiocytosis (Fig. 12.55):

- Focal lesion: Eosinophilic granuloma
- Collection of neoplastic histiocytes exhibiting pale eosinophilic cytoplasm and irregular, often grooved nuclei (reniform)
- Admixed eosinophils, multinucleated giant cells, neutrophils, lymphocytes, plasma cells

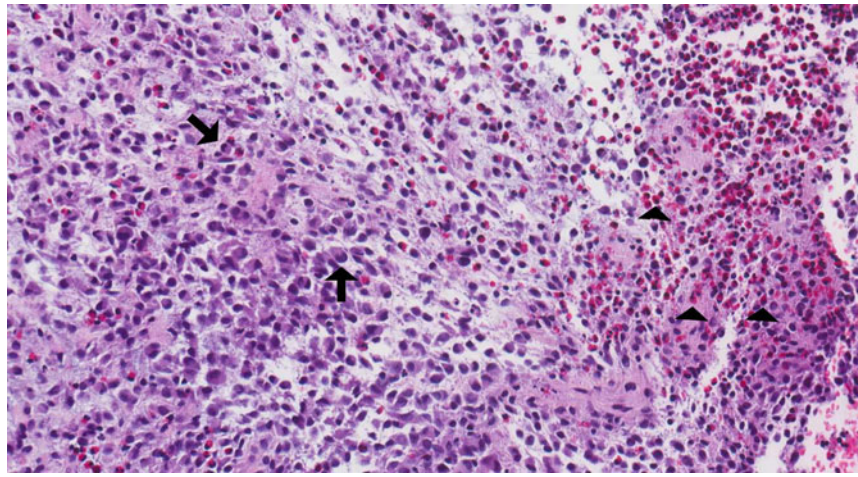

Fig. 12.55 Langerhan's cell histiocytosis: Langerhan's cells (*arrows*) and associated eosinophils (*arrowheads*)

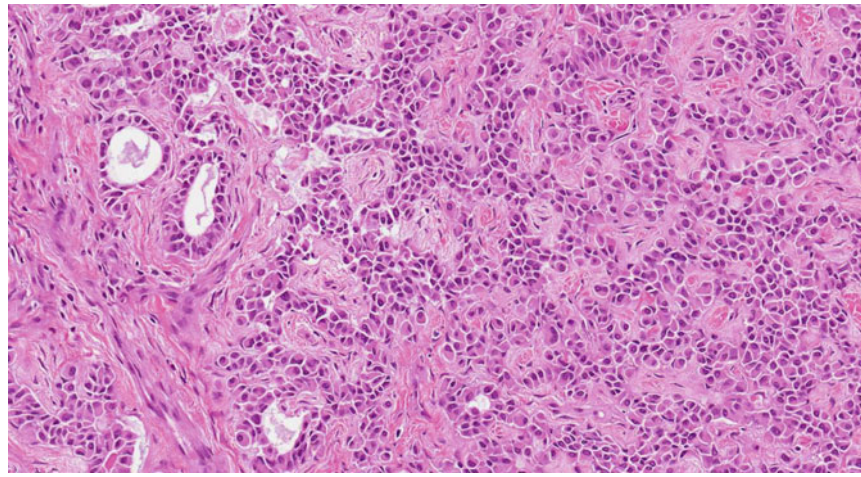

Fig. 12.56 Middle ear adenoma: cords of neoplastic cells with plasmacytoid appearance. Ductal formation

- IHC:
  - S100+
  - CD1a+
- Electron microscopy: Birbeck granules (appear like zippers or tennis rackets)

Middle Ear Adenoma (Fig. 12.56):

- Unencapsulated, benign glandular proliferation
- Columnar to cuboidal occasionally plasmacytoid cells organized into various patterns
  - Solid, trabecular, tubular, papillary
- Often reminiscent of carcinoid with ribbon-like pattern and salt-pepper nuclei
- May demonstrate neuroendocrine differentiation
- IHC:
  - S100+
  - SYN+

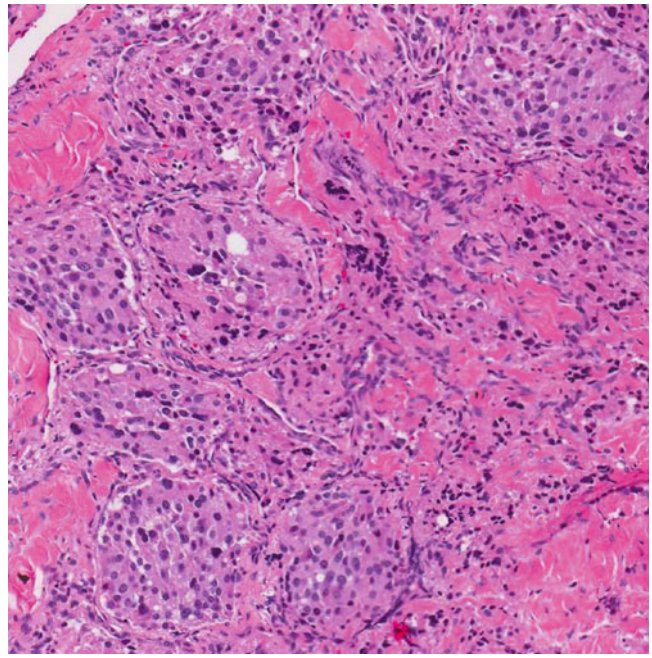

Fig. 12.57 Paraganglioma: Zellaballen formation of neuroendocrine cells with ample pink cytoplasm

Paraganglioma (Fig. 12.57):
- Classically organized into Zellballen pattern (balls of cells)
- Two-cell types idenfiable:
  - Chief cells:
    - Abundant, eosinophilic, vaguely granular cytoplasm. Eccentric nucleus, +/– hyperchromatic nuclei, +/– nuclear polymorphism
    - IHC: SYN/Chr+ (both neuroendocrine markers)
  - Sustentacular cells:
    - Form a delicate, inconspicuous peripheral framework around the zellballen
    - IHC: S100+

Acoustic Neuroma (Fig. 12.58):
- Clinical: In setting of bilateral tumors, exclude Neurofibromatosis-2
- Spindle cell tumor of neural origin, often with two coexisting histologic patterns
- Antoni A:
  - Cellular and compact, with nuclear palisading (Verocay bodies)
  - Palisading nuclei, pink cells
- Antoni B:
  - Hypocellular, myxoid areas, pale, patternless
- IHC:
  - Strong, diffuse S100+

ENDOCRINE

Thyroglossal Duct Cyst (Fig. 12.59):
- Majority located at or below level of hyoid bone
- Treatment of choice: Sistrunk procedure
- Cyst lined by squamous or respiratory epithelium
- Presence of thyroid tissue variably reported (25–60 %)
- Thyroid tissue may exhibit nodules, hyperplasia, or rarely neoplasia

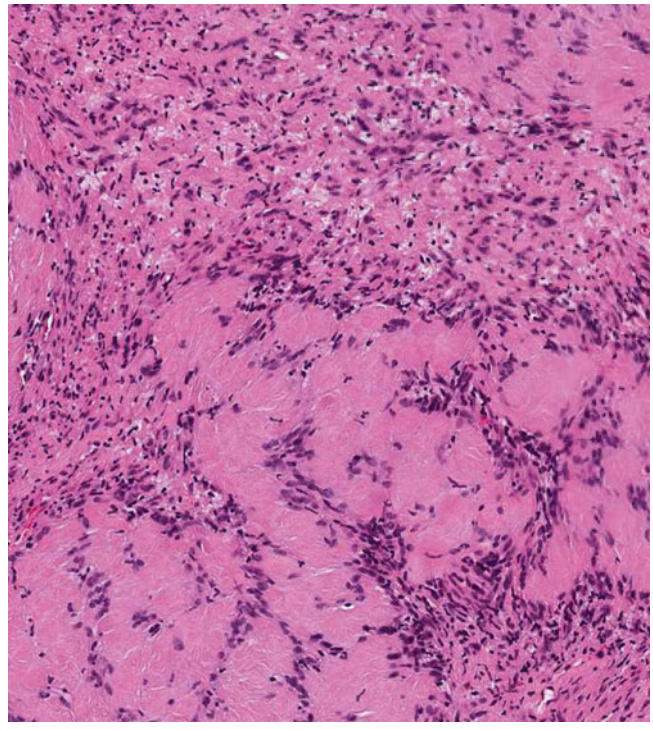

Fig. 12.58 Acoustic neuroma: Antoni A tissue with verocay body formation

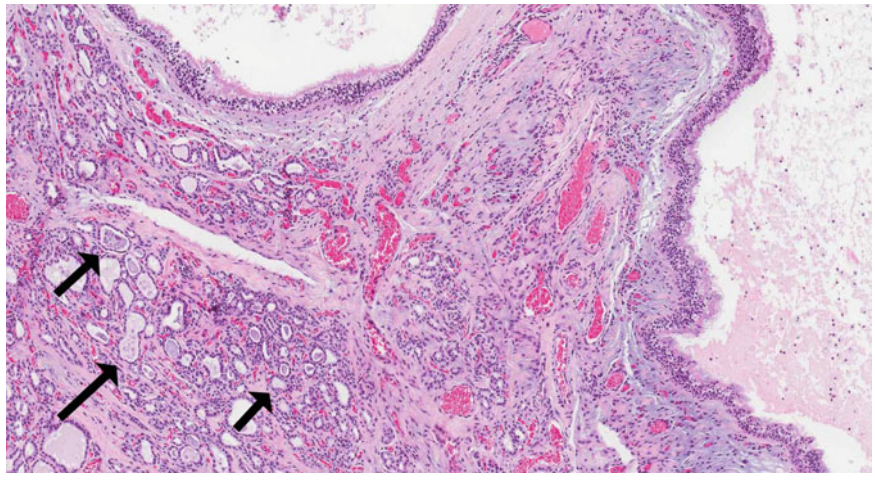

Fig. 12.59 Thyroglossal duct cyst: Thyroid tissue within wall of cyst (*arrows*)

Thyroid Tissue (Fig. 12.60):

- Delicate connective tissue septae divide gland into lobules
- Thyroid follicles lined by single layer of cells
- Normal lumen contents: Colloid (pink/eosinophilic), can also see calcium oxalate crystals
- Follicles vary in diameter

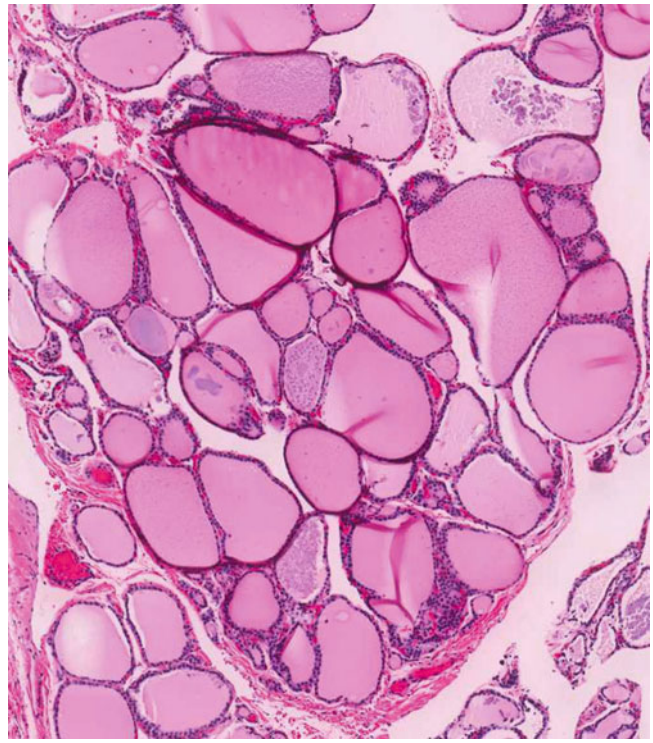

Fig. 12.60 Normal thyroid: Low magnification of thyroid follicles

Graves disease (Diffuse Hyperplasia) (Fig. 12.61):
- Diffuse toxic form of goiter; autoimmune hyperthyroidism
- Hyperplasia affecting entire gland, formation of simple papillary projections observed
- Scalloping phenomenon of colloid
- Colloid may be absent when disease untreated
- Lymphocytic infiltration not uncommon
- Ophthalmopathy:
  - Accumulation of chronic inflammatory cells, edema and glycosaminoglycans in extra-ocular muscles and contributes to proptosis

Multinodular Goiter (Fig. 12.62):
- Adenomatoid nodules with cystic degeneration
- Enlarged follicles with abundance of colloid
- No compression of surrounding gland, poor or no encapsulation of nodules
- Cells comprising nodule have similar morphology to cells adjacent to nodule

Amyloid (Fig. 12.63):
- Pale, eosinophilic, acellular, amorphous material with peculiar "cracking" artifact
- Can accumulate around blood vessels
- Minimal normal thyroid tissue remains, amyloid overtakes gland in systemic amyloidosis
- May see focal amyloid deposition in association with medullary thyroid carcinoma
- Special stains:
  - Congo red stain shows apple green birefringence under polarized light

Hashimoto's Thyroiditis (Fig. 12.64):
- Autoimmune disease
- Advanced: similar to Riedel's (extensive fibrosis) but localized to thyroid
- Lymphocytic thyroiditis: infiltration with germinal center formation
- Follicular acinar atrophy, degenerative phenomenon

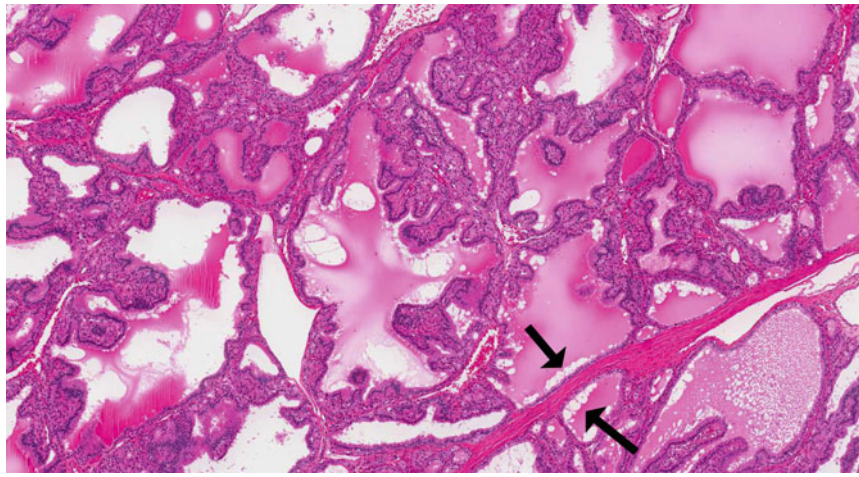

Fig. 12.61 Grave's disease: Hyperplastic papillary thyroid epithelium. Scalloping of colloid (*arrow*)

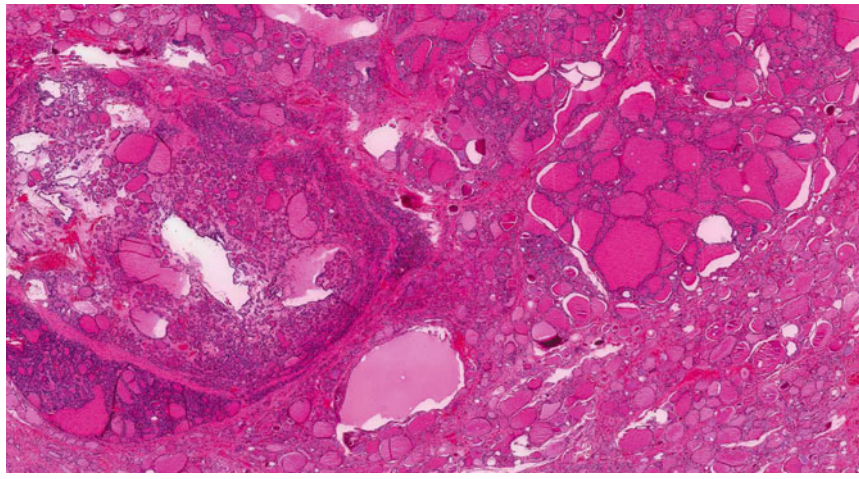

Fig. 12.62 Multinodular goiter: Low magnification view of multinodular appearance

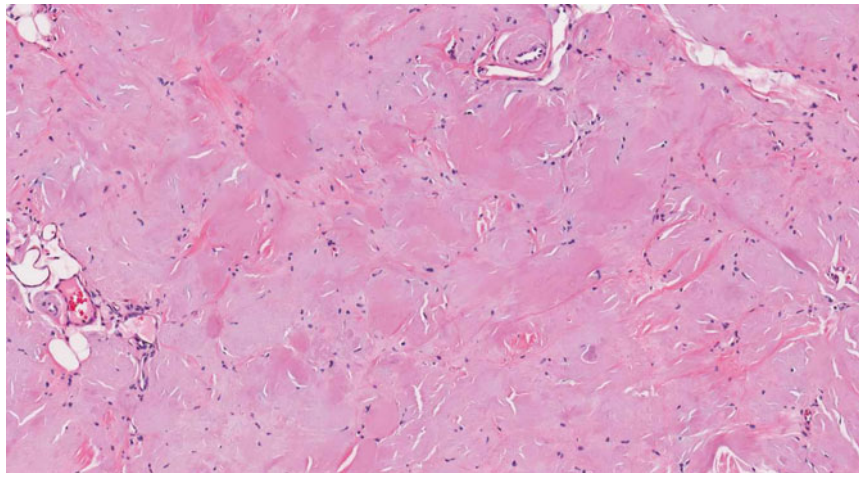

Fig. 12.63 Amyloid: acellular, eosinophilic amyloid. Present around blood vessel

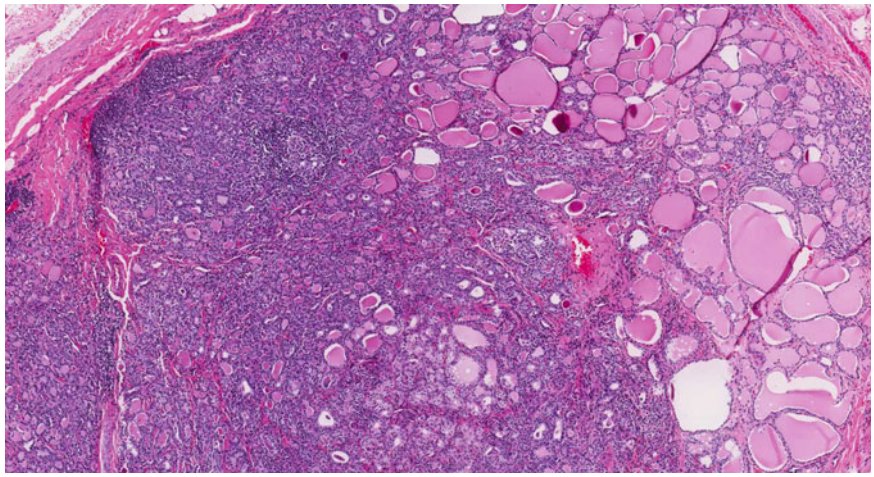

Fig. 12.64 Hashimoto's: Thyroid tissue with marked inflammation and germinal center formation

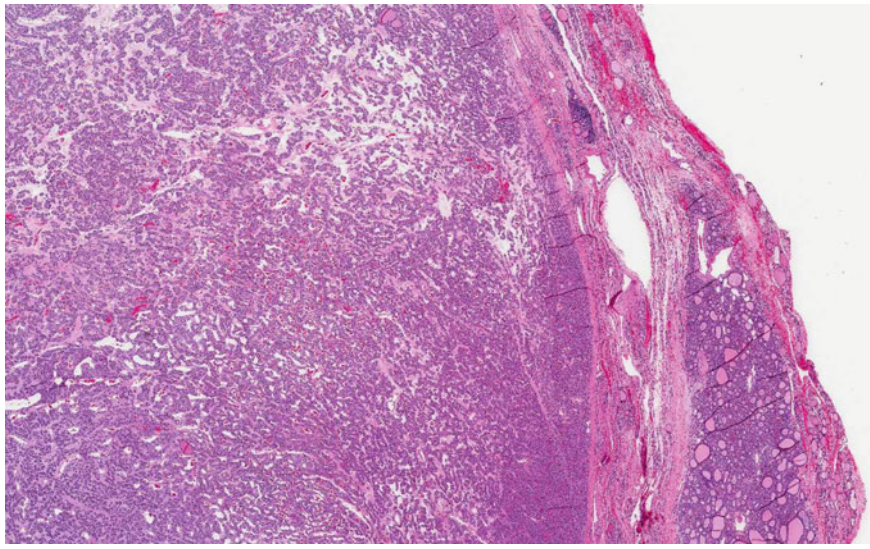

Fig. 12.65 Follicular adenoma: Encapsulated, cellular benign thyroid neoplasm

- Hurthle cell metaplasia
  - Oxyphilic/oncocytic cells
  - Extensive eosinophilia, large polygonal follicular cells with granular cytoplasm

Follicular Adenoma (Fig. 12.65):

- Adenoma cells different from normal gland: More cellular, +/– larger follicles
- Normal thyroid gland may appear compressed
- Capsule present around adenoma, no capsular invasion, no vascular invasion
- Nuclear atypia may be seen
- Hurthle cell/oxyphilic cells can be present

Follicular Carcinoma (Fig. 12.66):

- Variable microscopic patterns of tumor cells (solid, trabecular, microfollicles)
- Significant morphologic overlap with benign follicular adenoma

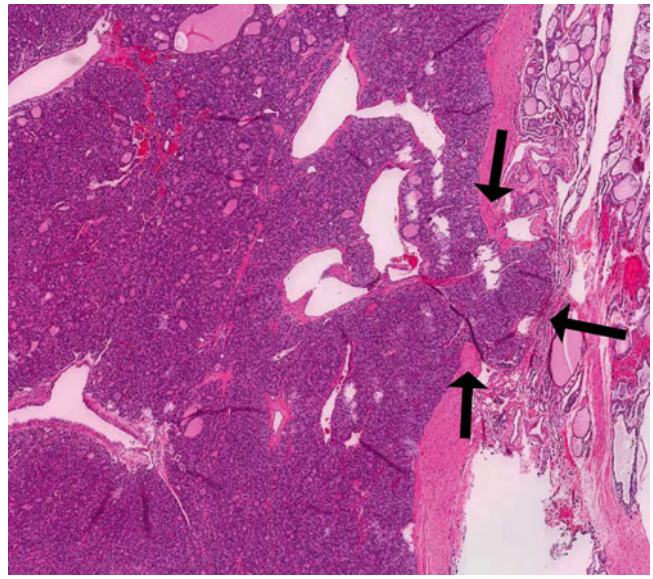

Fig. 12.66 Follicular carcinoma: Capsular invasion by malignant thyroid neoplasm (*arrows*)

- Hurthle cell subtype/oxyphilic type may have limited colloid
- Most reliable indication of malignancy: capsular and/or vascular invasion
  - Either is sufficient to assign malignant diagnosis

Papillary Thyroid Carcinoma (Fig. 12.67):
- Formation of papillae and unique nuclear features
- "Orphan Annie eye": nuclei of epithelium are large with nuclear margins folded or grooved with prominent nucleoli
- Psammoma body: round collection of calcium, concentric lamination, circular, acellular
- Unfavorable histologic forms: diffuse sclerosing, tall-cell, columnar cell variants

Medullary Carcinoma (Fig. 12.68):
- Malignancy arising from parafollicular C-cells
- Tumor cells organized into many patterns
  - Stippled "salt and pepper" nuclear chromatin present in individual cells
- Amyloid present as amorphous pink material in stroma
- C-cell hyperplasia with associated elevated calcitonin levels
- Familial inheritance and syndromic association (MEN2A and 2B)
- RET oncogene point missense germline mutation

Anaplastic Carcinoma (Fig. 12.69):
- High grade malignancy composed of undifferentiated cells
- Extrathyroidal extension common and rapid, lymphovascular invasion
- Significant cell pleomorphism, high mitotic rate, tumor necrosis
- Must identify origin from thyroid, otherwise appears to be soft tissue sarcoma

Parathyroid Gland (Fig. 12.70):
- Chief cells: round nuclei, pale eosinophilic cytoplasm
- Oxyphil cells: larger than chief cells, densely pink cytoplasm (oncocytic)
- Mature fat

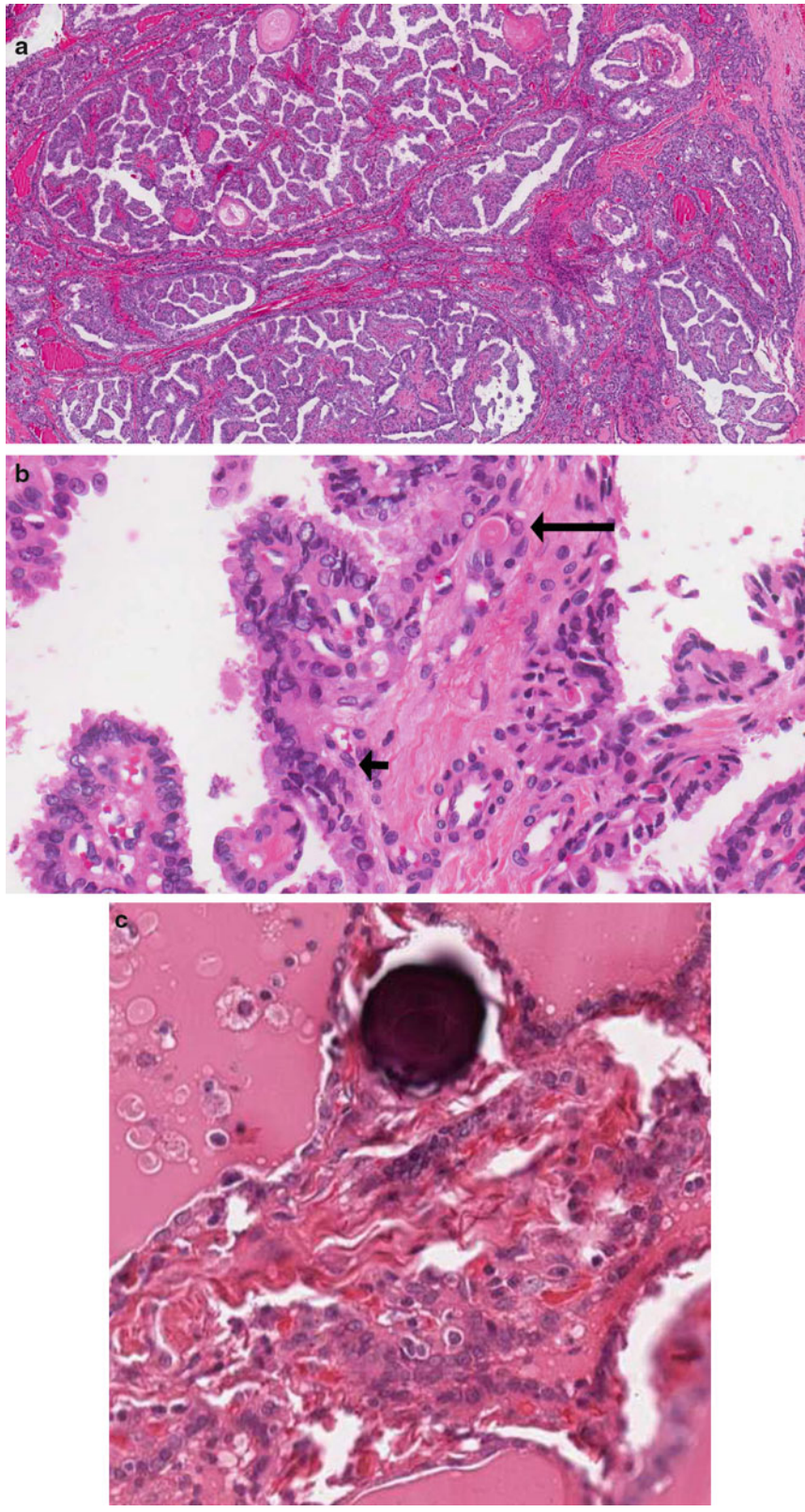

Fig. 12.67 Papillary thyroid carcinoma: (**a**) Papillary architecture of malignant neoplasm. (**b**) Nuclear pseudoinclusion (*long arrow*) and nuclear groove (*short arrow*). (**c**) Concentric lamination of psammoma body

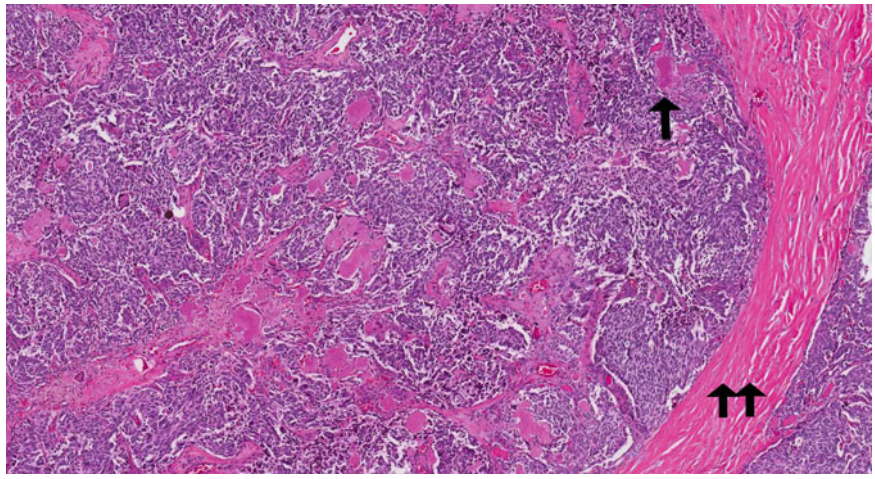

Fig. 12.68 Medullary carcinoma: Basophilic tumor cells, fibrous bands (*two arrows*) and amyloid deposits (*single arrow*)

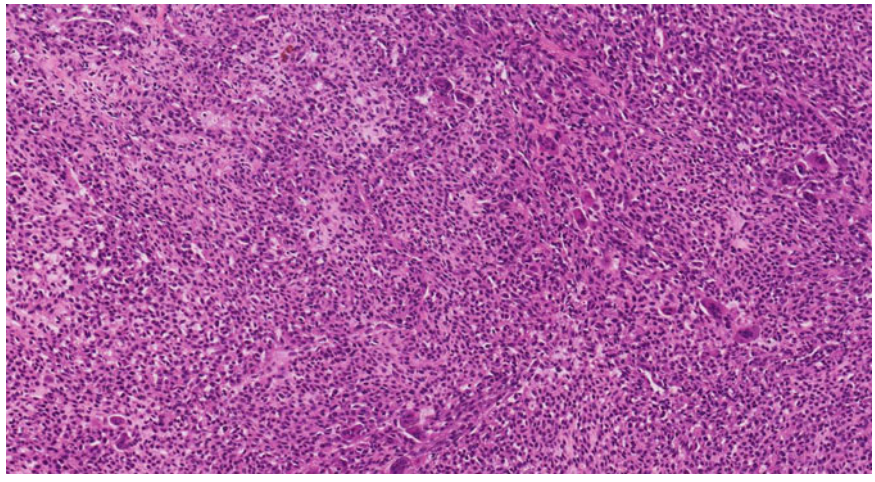

Fig. 12.69 Anaplastic carcinoma: Sheet of pleomorphic tumor cells and giant cells

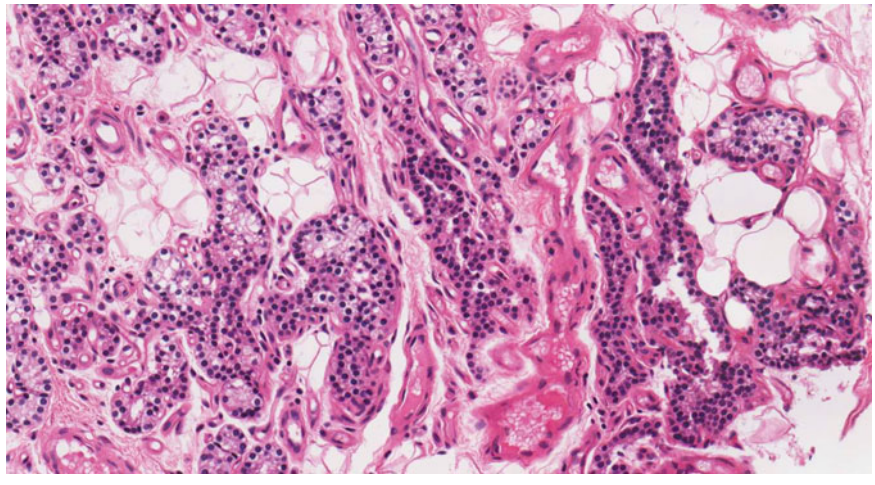

Fig. 12.70 Normal parathyroid: Chief (*pale*), oxyphilic (*densely pink*) and mature adipose tissue

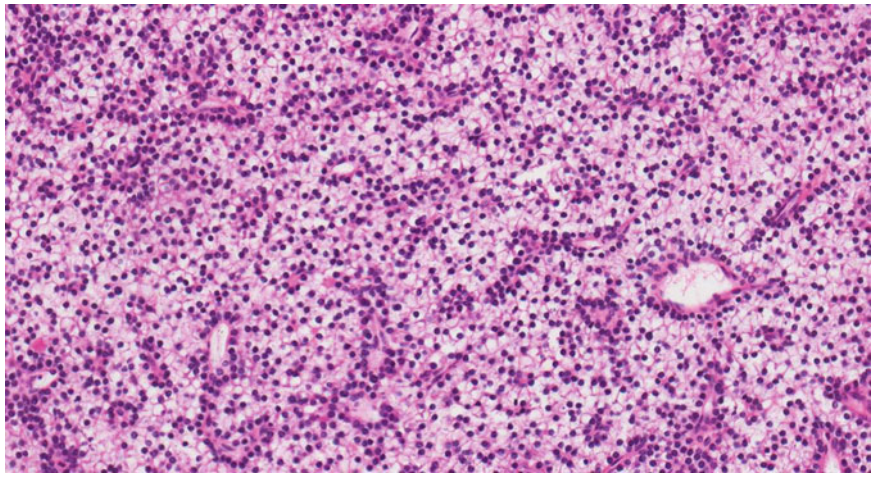

Fig. 12.71 Parathyroid hyperplasia

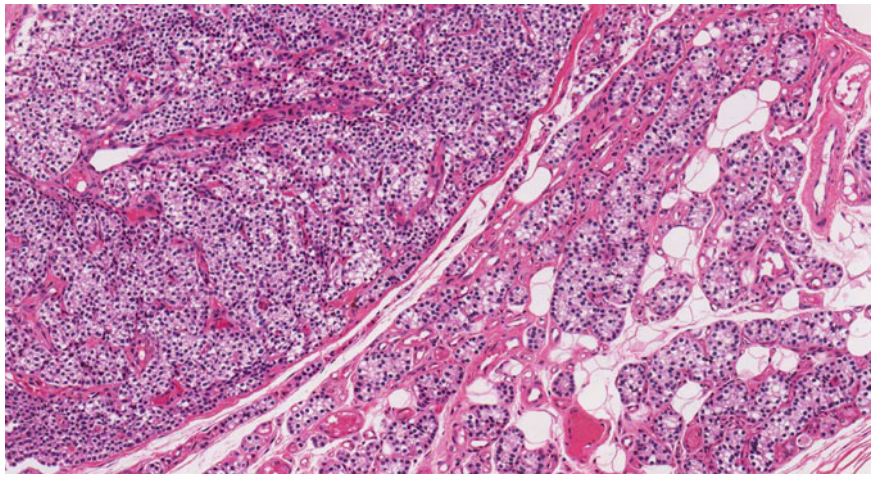

Fig. 12.72 Parathyroid adenoma

Parathyroid Hyperplasia (Fig. 12.71)
- Non-neoplastic
- Most commonly results of hyperparathyroidism, but can be idiopathic
- Increased number of chief and oncocytic cells in multiple parathyroid glands

Parathyroid Adenoma (Fig. 12.72)
- Benign neoplasm of gland parenchymal cells
- Single, enlarged, hypercellular gland
- Proliferation of parenchymal cells (oncocytic/chief cells) and absence of intraparenchymal fat

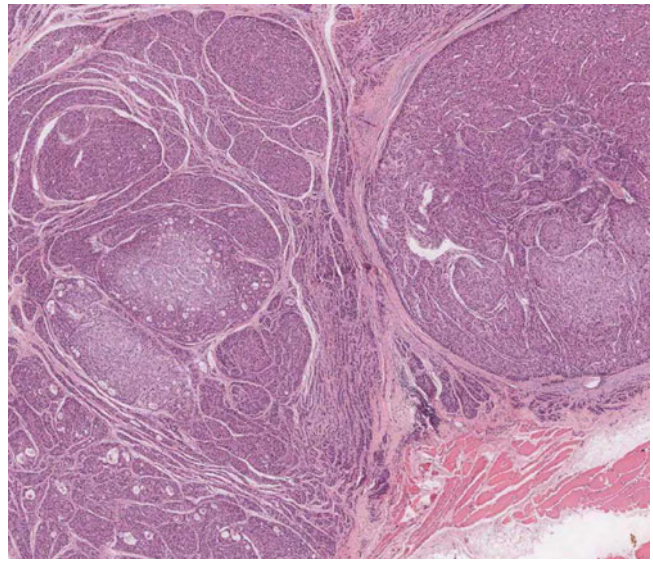

Fig. 12.73 Parathyroid carcinoma: Trabeculae and islands of parathyroid carcinoma metastatic to skeletal muscle

Parathyroid Carcinoma (Fig. 12.73)

- Malignant neoplasm of gland parenchymal cells
- Aggregate of microscopic features are suggestive of diagnosis
- Perineural invasion (not commonly seen)
- Adherence to thyroid, or soft tissue extension
- Formation of thick fibrous septae/bands
- Vascular invasion
- Trabecular growth

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PART IV
Otology
Section Editor: Stanley Pelosi, MD

Chapter 13
Otologic and Neurotologic Disorders

Stanley Pelosi and Matthew Luke Carlson

PEARLS

- The pure tone average (PTA) is the average of hearing sensitivity at 500, 1,000, and 2,000 Hz
- Otoacoustic emissions are useful for infant screening (transient evoked otoacoustic emissions have high sensitivity/specificity), disabled individuals who cannot participate in testing, diagnosis of auditory neuropathy, and malingerers

OTOLOGIC EMBRYOLOGY, ANATOMY, AND PHYSIOLOGY

- External/middle ear embryology
  - External ear
    - Begins development in fifth to sixth gestational week
    - Six hillocks of His are derived from first/second branchial arches
    - First arch → hillocks 1–3 → tragus, helicus crus, helix
    - Second arch → hillocks 4–6 → antihelical crus, antihelix, antitragus
  - External auditory canal, tympanic membrane, middle ear
    - EAC develops from first branchial groove (ectoderm, begins in sixth week)
    - Eustachian tube and middle ear develop from first branchial pouch (endoderm)
    - TM: first branchial groove ectoderm (epithelium), mesoderm (fibrous layer), first branchial pouch endoderm (mucosa)
    - Malleus: first arch—head and neck (epitympanic portions), second arch—manubrium
    - Incus: first arch—body and short process (epitympanic portions), second arch—long process
    - Stapes: second arch—superstructure and middle ear portion of footplate, otic capsule—otic portion of footplate, annular ligament
- Inner ear embryology
  - Ectodermal thickening → otic placode (third week) → otic pit (fourth week) → otic vesicle (end of fourth week)
  - Otic vesicle forms membranous labyrinth
  - Mesenchyme surrounding membranous labyrinth forms otic capsule (ninth week, initially cartilage, then ossifies later in gestation)
  - Vestibular side of stapes footplate develops from the otic placode and is one of the most common sites for development of otosclerosis (fissula ante fenestrum)
  - Differences in embryonic origin and timing of gestational development for inner ear means that disorders affecting inner ear are less likely to have coexisting external ear/middle ear abnormalities
- External auditory canal and temporal bone surface anatomy
  - External auditory canal
    - Lateral third is cartilage, medial two-thirds is bone
    - Multiple cranial nerves contribute to auricle/external auditory canal sensation including V3, VII, IX, X, greater auricular nerve, lesser occipital nerve

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- Tympanic bone forms incomplete ring, tympanomastoid suture (posteriorly) and tympanosquamous suture (superiorly/anteriorly)
- Fissures of Santorini: vertically oriented fissures in the anteroinferior cartilaginous canal that allow spread of infection or tumor between the EAC and parotid gland
- Persistent foramen tympanicum (foramen of Huschke) occurs in approximately 5 % of population, results from incomplete fusion of tympanic ring and provides a potential communication for spread of infection or tumor from the external auditory canal to the infratemporal fossa

- Tympanic membrane
  - Layers: squamous epithelium, radiating and circular fibrous layers, mucosal layer
  - ~1 cm diameter
  - Pars tensa: organized fibrous layer, stiff
  - Pars flaccida: disorganized fibrous layer, less stiff and therefore prone to retraction and primary cholesteatoma formation
  - Annulus fibrosus
  - Notch of Rivinus
- Temporal bone surface and mastoid
  - Temporal line: approximates level of tegmen
  - Spine of Henle: used to identify posterior wall of external auditory canal
  - Suprameatal (Macewen's) triangle: external landmark for antrum
  - Körner's septum: bony plate separating squamous and petrous air cells of temporal bone
  - Donaldson's line: imaginary line from lateral canal posteriorly through posterior canal to sigmoid, identifies endolymphatic sac just inferior to line
  - Facial recess: triangle formed by incudal buttress, facial nerve, and chorda tympani
  - Arcuate eminence: bony prominence in middle fossa suggesting location of superior semicircular canal
- Middle ear anatomy
  - Ossicles
    - Malleus: subunits include manubrium (handle), umbo (tip of handle), neck (attaches to tensor tympani), head (articulation with incus)
    - Tensor tympani muscle (innervated by V3), muscle is parallel to eustachian tube, muscle tendon attaches to malleus neck via cochleariform process
    - Incus: subunits include body (articulates with malleus), short process, long process, lenticular process (articulates with stapes head)
    - Stapes: head, neck (attaches to stapedial tendon), anterior/posterior crus, footplate
      - Stapedial muscle (innervated by CN VII) is parallel and medial to facial nerve
      - Stapes attaches to bony oval window via annular ligament
  - Eustachian tube: posterior third osseous, anterior two-thirds cartilage; tensor veli palatini (V3) dilates eustachian tube and tenses soft palate, levator veli palatini (CN X) attaches to eustachian tube and elevates soft palate, more horizontal in young children (predisposes to reflux)
  - Promontory: prominence of bone overlying cochlea on medial wall of middle ear, contains Jacobson's nerve (from glossopharyngeal nerve, contains salivary fibers to parotid gland)
  - Sinus tympani: portion of posterior middle ear medial to facial nerve between the subiculum and ponticulus, common site of residual cholesteatoma due to difficult visualization
  - Epitympanum: Prussak's space bordered laterally by pars flaccida (Shrapnell's membrane), medially by head of malleus, inferiorly by malleus lateral process, anteriorly by lateral malleal fold; most common site of primary acquired cholesteatoma
  - Ponticulus: bony ridge from pyramidal eminence to promontory
  - Subiculum: bony ridge bordering round window niche posteriorly
  - Iter chordae anterior (canal of Huguier) and posterior: anterior and posterior sites of chorda tympani entry to mesotympanum

- Inner ear anatomy
  - Labyrinth
    - Perilymph is similar to cerebrospinal fluid and extracellular fluid, high in sodium and positive for beta-2 transferrin
    - Endolymph is similar to intracellular fluid, high in potassium
    - Bony labyrinth encloses membranous labyrinth, separated by perilymph
    - Vestibular aqueduct: contains endolymphatic duct, which courses from medial wall of vestibule (inferior to otolithic organs) to region of thickened posterior fossa dura called endolymphatic sac
    - Cochlear aqueduct: contains periotic duct, which is continuous with subarachnoid space of posterior fossa; courses inferior and parallel to internal auditory canal and opens into inner ear at base of scala tympani
    - Cochlea and saccule joined by segment of membranous labyrinth called ductus reuniens
  - Cochlea
    - Has 2.5 turns
    - Modiolus is central cochlear nerve-containing region, osseous spiral lamina forms bony cochlear framework medially
    - Spiral ligament forms lateral wall of cochlea, contains stria vascularis that produces endolymph
    - Scala vestibuli and scala tympani contain perilymph, connected by helicotrema
    - Scala media contains endolymph and organ of corti, separated from scala vestibuli by Reissner's membrane
  - Organ of corti
    - Supported by basilar membrane (separates scala media and scala tympani)
    - Tectorial membrane: gelatinous structure which contacts with stereocilia of hair cells; vibration of basilar membrane → tectorial membrane displacement → hair cell stimulation
    - Inner hair cells: provide most afferent auditory information to brain (90 %), 15 neurons synapse on each inner hair cell
    - Outer hair cells: provide only 10 % of afferent auditory information to brain, source of otoacoustic emissions, one neuron synapses on ten outer hair cells, receive large efferent projection from superior olive in brainstem (cochlear amplifier)
- Semicircular canals
  - Three canals on each side, each are oriented 90° to one another (orthogonal)
  - Ampulla: expansion at one end of each semicircular canal near vestibular opening, contains cupula (gelatinous layer), crista ampullaris (hair cells at base of cupula)
  - Superior and posterior canals have common crus
- Otolith organs
  - Utricle: senses horizontal linear acceleration
  - Saccule: senses vertical linear acceleration, also has some sound sensitivity (basis of vestibulocollic reflex)
  - Maculae of utricle and saccule contain hair cells and are covered by a gelatinous otolithic membrane which contains calcium carbonate (otoliths)
  - Polarity of hair cells are oriented around a central line called the striola
- Vestibular nerve
  - Superior vestibular nerve: innervates utricle, superior/lateral semicircular canals
  - Inferior vestibular nerve: innervates saccule, posterior canal
  - Scarpa's ganglia: distal vestibular nerve cell bodies
- Conductive sound pathway
  - Sound energy from air transferred to inner ear via pinna, external auditory canal, tympanic membrane, and ossicles
  - Each conductive component has an inherent "resonant frequency," or natural vibrating frequency (pinna 5 kHz, external auditory canal 3 kHz, tympanic membrane/ossicles 500–2,000 Hz)

        - Gain in sound intensity from tympanic membrane to inner ear ~30 dB
        - Larger surface area of TM relative to footplate more important for intensity gain than lever action of ossicles
    - Neural sound transduction pathway
        - Displacement of stapes → endolymph movement → basilar membrane displacement → hair cell stereocilia deflected by shearing force of tectorial membrane → hair cell activation → auditory nerve stimulation
        - Cochlea is tonotopically organized with higher frequency sounds causing greater hair cell stimulation at base, and lower frequency sounds causing stimulation at the apex
        - Ipsilateral auditory nerve → ipsilateral cochlear nuclei → bilateral superior olive → lateral lemniscus → inferior colliculus → thalamus → temporal lobe auditory cortex

AUDIOLOGY

- Audiology definitions
- Decibel: logarithmic unit of measurement used to express sound intensity
    - dB SPL (sound pressure level): magnitude of displacement of sound molecules in air
    - dB HL (hearing level): difference in sound intensity compared to average dB SPL for normal-hearing listeners
    - dB SL (sensation level): difference in sound intensity compared to an individual patient's HL threshold
    - 10 dB difference changes sound intensity by factor of 10 (i.e.. 30 dB has 100× greater sound intensity than 10 dB)
- Pure-tone audiometry measures thresholds for pure tone stimuli, speech audiometry for speech stimuli
- Pure tone average (PTA): average of hearing sensitivity at 500, 1,000, and 2,000
- Speech reception threshold/speech recognition threshold (SRT): lowest level at which a given word can be repeated 50 % of the time
    - Uses two-syllable (spondee) words for testing
    - Good estimate of pure tone average to within 10 dB
- Speech awareness threshold/speech detection threshold (SAT/SDT): lowest level at which patient is aware that speech is present
    - Less difficult, used when speech reception threshold cannot be determined
- Word recognition score (WRS): percentage of words correctly repeated when presented with a 50 word list
    - Uses single-syllable, phonetically balanced words (e.g., NU-6)
    - Presented at ~40 dB greater than patient's speech reception threshold
- Interaural attenuation: reduction in sound energy when a signal introduced to the test ear is transmitted through the skull to the non-test ear
    - No sound energy reduction for bone conduction signal, 40 dB reduction for air conduction
- Crossover: sound energy that has exceeded interaural attenuation to stimulate non-test ear
- Masking: use of a noise source placed into the non-test ear to prevent the participation of the non-test ear in determining the patient's audiometric threshold in the test ear
    - Air conduction testing: mask if signal presented to test ear is 40 dB greater than bone conduction threshold of non-test ear
    - Bone conduction testing: mask if there is any suspected difference in bone conduction between test and non-test ears
    - Masking dilemma: occurs when there is a bilateral moderate to severe conductive hearing loss. The sound intensity for masking the non-test ear crosses over to the tested ear and interferes with testing

- Audiometric evaluation in young children
  - Behavioral observation audiometry (birth–6 months): present sound, look for bodily responses to sound (eye widening, eye opening, body movement)
  - Visual reinforcement audiometry (6 months–3 years): present sound, when child looks toward source of sound, visual reinforcement provided (flashing lights)
  - Conditioned play audiometry (3–5 years): present sound, child is taught to perform a repetitive play task (place peg in pegboard)
- Immitance audiometry
  - Tympanometry: evaluates eardrum mobility, measured with ear canal volume (normal 0.2–2 cm^3)
  - Type A: normal middle ear pressure, normal compliance
    - As (shallow or stiff): normal middle ear pressure, decreased compliance (otosclerosis, tympanosclerosis)
    - Ad (deep): normal middle ear pressure, increased compliance (ossicular discontinuity or flaccid tympanic membrane)
  - Type B: non-mobile tympanic membrane (normal external canal volume indicates effusion, large volume indicates perforation)
  - Type C: negative middle ear pressure, normal compliance (Eustachian tube dysfunction)
  - Stapedial reflex
    - Tests integrity of cranial nerve 8 and 7, normally occurs at 70–100 dB HL
    - Reflex arc: ipsilateral cochlea → ipsilateral CN 8 → ipsilateral cochlear nucleus → ipsilateral trapezoid body → bilateral superior olive → bilateral facial motor nucleus → bilateral CN 7 → bilateral nerve to stapedius
    - Absent reflexes:
      - Sensorineural hearing loss >65 dB, CN 8 cannot initiate reflex
      - Any level of conductive hearing loss
      - Facial nerve pathology impairs efferent limb of reflex
    - Reflex decay test: test stapedial reflex 10 dB above threshold, <50 % of original amplitude within 10 seconds suggests a retrocochlear lesion
- Otoacoustic emissions
  - Low-energy sounds produced by the cochlea, believed to be generated by outer hair cells
    - Spontaneous: present in 75 % of normal-hearing patients, but may not be present with >25 dB HL
    - Evoked
      - Transient evoked: most sensitive measure, elicited by clicks; response contains multiple frequencies (500–4,000 Hz); if present indicates a patient does not have a sensorineural hearing loss any worse than 20–40 dB at these frequencies
      - Distortion product: two pure tones presented simultaneously, response is a tone at a specific frequency; can test at higher frequencies, useful for testing for noise-induced hearing loss and medication ototoxicity
  - Useful for infant screening (transient evoked otoacoustic emissions have high sensitivity/specificity), disabled individuals who cannot participate in testing, diagnosis of auditory neuropathy, malingerers
  - Able to identify patients with cochlear hearing loss (loss of hair cells), but does not test for patients with auditory neuropathy or other retrocochlear pathology (in these cases auditory brainstem response testing is helpful)
  - Conductive hearing loss and sensorineural hearing loss worse than 20–40 dB can eliminate otoacoustic emission responses
- Auditory brainstem response/electrocochleography
  - Measure of neural response of cochlea, auditory nerve, and central auditory pathways to auditory stimulus
  - Auditory click allows an electrode placed in external auditory canal to measure changes in electrical potential; each wave represents neural activity of different parts of auditory pathway

- Electrocochleography (ECoG)
  - Comparison of waves that represent cochlear activity
  - Summating potential: electrical activity generated from hair cells/stria vascularis
  - Cochlear microphonic: electrical activity generated from outer hair cells, polarity of waveform inverts depending on polarity of acoustic signal (other waveforms have polarity which do not change)
  - Action potential: equivalent to wave I of the auditory brainstem response, represents neural activity from distal auditory nerve
  - Clinical utility
    - Traditionally used in diagnosis of Ménière's disease, although sensitivity/specificity is limited
    - Increased summating potential to action potential ratio (greater than 0.5, normal 0.2) suggests Ménière's disease (theory is that endolymphatic hydrops causes increased displacement of basilar membrane and increased summating potential)
- Auditory brainstem response
  - Waveforms + electrical activity representing central auditory pathways
  - Waveforms (Pneumonic "ECOLI")
    - I Distal *e*ighth nerve
    - II Proximal *e*ighth nerve
    - III *C*ochlear nuclei
    - IV Superior *o*live
    - V *L*ateral lemniscus
    - VI *I*nferior colliculus
  - Uses
    - Traditionally obtained in cases of asymmetric hearing loss/tinnitus or unilateral vestibular weakness to evaluate for vestibular schwannoma
    - Can also be used intraoperatively during vestibular schwannoma surgery in hearing preservation cases to measure integrity of auditory pathway
    - If patient has severe–profound hearing loss in ear to be tested, auditory brainstem response may not be measurable
    - Result interpretation
    - Prolonged wave I, normal I–V interwave latency may be caused by conductive hearing loss or cochlear sensorineural hearing loss
    - Retrocochlear pathology
      - Abnormal wave V latency relative to opposite ear
      - Abnormal I–V, I–III, III–V interwave latencies relative to opposite ear or established norms
      - Sensitivity not as high as MRI for diagnosing vestibular schwannoma

- Pseudohypoacusis
  - Suggestive audiometric findings
    - Discrepancy (>10 dB) between pure tone average and speech reception threshold/speech awareness threshold
    - Present acoustic reflexes but large air-bone gap suggestive of conductive hearing loss
    - Bone conduction thresholds worse than air conduction
    - Absence of crossover hearing in a patient with a unilateral loss
    - Stenger's test with example: patient suspected of malingering is complaining of a right HL, has measured 50 dB pure tone threshold at 2,000 Hz in right ear, 0 dB in left ear; for Stenger's test present two tones at same frequency to both ears that is slightly louder (30 dB) in right ear than left (10 dB), but still lower than their admitted 50 dB right ear threshold; if patient has a true 50 dB right sensorineural hearing loss, they will hear only the tone in the left ear; if they are malingering, they will only hear the tone in the right ear, and claim to hear nothing since they are feigning hearing loss in this ear
    - Lombard test with example: patient complaining of left hearing loss is asked to read a book; masking noise is then presented to the left ear; if patient increases the volume of

their voice above the masking sound, then malingering is suspected; if no change in their voice occurs, they likely have a true hearing loss

- Hearing aids
  - Definitions
    - Gain: ratio of output to input
    - Occlusion effect: larger hearing aids block external auditory canal which results in low-frequency amplification
    - Compression: adjusts the range of sound to fit the patient; often includes making quiet sounds louder and making very loud sounds quieter
    - Venting: allows low frequency sounds to escape, decreases occlusion effect but can increase feedback
    - Feedback: sound coming out of speaker travels back to microphone and is amplified again, worse with venting and smaller aids since less distance between microphone and speaker
  - Smaller hearing aids afford better cosmesis, decreased occlusion effect, limited gain due to feedback problems, can malfunction from moisture/cerumen
    - In-the-ear
    - In-the-canal
    - Completely-in-the-canal
  - Larger hearing aids provide better gain/amplification, longer battery life, decreased feedback, risk of occlusion effect
    - Behind-the-ear
    - Open-fit: behind the ear aid connected by thin tube to a non-occluding earmold; decreases occlusion effect
  - Digital hearing aids: better programming flexibility, can amplify specific frequencies while reducing gain of background noise, more expensive than analog hearing aids
  - Binaural hearing aid advantages: better sound localization, better hearing in noise
  - Bone anchored hearing aid (BAHA): indicated for (1) patients with conductive hearing loss and inability to wear hearing aids (external/middle ear malformations, chronic otorrhea/dermatitis) and (2) patients with unilateral sensorineural hearing loss
  - Contralateral routing of signal (CROS): microphone on deaf side routed to good side; Bi-CROS: microphone on deaf side routed to better side, which also requires a hearing aid
- Cochlear implants
  - Convert sound into an electrical signal to stimulate cochlear nerve directly
  - Components: microphone collects sound → speech processor analyzes sound and separates into different channels based on frequency/intensity → external transmitter → internal receiver/stimulator → electrode array
  - Implant criteria vary slightly depending on specific manufacturer; generally speaking, for adults should have bilateral pure tone average no better than 70, and bilateral aided speech discrimination scores no better than 60 %
  - Children should have profound hearing loss (assessed via otoacoustic emissions, auditory brainstem response) and failure of auditory skills development, with minimal to no benefit from hearing aids; being implanted as young as 1 year of age
  - Evaluation: CT shows presence of cochlear anomalies, evidence of ossification, suggests small/absent cochlear nerve (narrow internal auditory canal); MRI can confirm presence/absence of cochlear nerve, is more sensitive for detecting labyrinthitis ossificans (no inner ear fluid visible on T2 images)
  - Surgical approach using mastoidectomy with facial recess and cochleostomy or round window opening with electrode insertion

- Best outcomes with shorter duration of deafness (most important predictor), longer duration of implant use, increased level of residual hearing prior to implantation, post-lingual patients
- Complications:
  - Device exposure/extrusion
  - Device failure (hard failure—can be detected with testing of device integrity by audiologist, soft failure—device testing normal but decrease in patient's cochlear implant performance over time)
  - Wound infection
  - Meningitis: increased risk in all cochlear implant recipients of pneumococcal meningitis, both adult and pediatric patients require immunization
  - Facial paralysis and dysgeusia
  - Facial stimulation: more common in patients with inner ear otosclerosis
  - Perilymphatic gusher: increased risk in patients with congenital inner ear deformities, persistent leakage can increase meningitis risk, manage by limiting cochleostomy size, plugging with muscle

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Chapter 14
Vestibular System

Stanley Pelosi and Matthew Luke Carlson

PEARLS

- Ampullopetal endolymph flow in the semicircular canals causes excitatory response in lateral canal
- Multiple sclerosis can present as dizziness and is diagnosed with increased gamma globulin/oligoclonal bands and scattered white matter plaques on MRI

VESTIBULAR PHYSIOLOGY AND DIAGNOSTIC STUDIES

- Vestibular principles
  - Nystagmus: rapid involuntary to-and-fro-oscillatory motion of the eye
  - VOR (vestibuloocular reflex): causes eye movement equal but opposite in direction to head movement, stabilizes gaze during head motion
  - Ewald's three laws
    - Stimulation of the semicircular canal causes a movement of the eyes in the plane of the stimulated canal
    - In the horizontal semicircular canals, ampullopetal endolymph movement causes greater stimulation than ampullofugal one
    - In the vertical semicircular canals, the reverse is true
  - Alexander's law
    - The intensity of vestibular nystagmus increases when looking toward the direction of the fast-phase and slows when looking in the opposite direction
  - Otolithic organs
    - Linear acceleration or gravity causes otolith displacement, which in turn displaces hair cell cilia and results in hair cell stimulation
  - Semicircular canals
    - Deflection of cupula by rotational acceleration causes altered neuronal firing rate
      - Ampullopetal endolymph flow causes excitatory response in lateral canal
      - Ampullofugal flow causes excitatory response in superior and posterior canals
- Vestibular function evaluation
  - Office testing
  - Characterize "dizziness:" room-spinning vertigo, chronic imbalance, presyncope
  - Episodic (benign positional vertigo, Ménière's disease) or constant disequilibrium (migraine)
  - Associated symptoms: hearing loss, headache/photophobia, focal neurologic weakness

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- Test for nystagmus
  - Positioning testing (Dix-Hallpike, supine roll test): *see benign positional vertigo workup for details*
  - Spontaneous or gaze-induced: peripheral nystagmus always beats in same direction, looking in direction of the fast-phase increases rate of nystagmus; central nystagmus may be bidirectional, pure vertical nystagmus indicates brainstem disease
  - Head shake nystagmus: peripheral weakness will cause nystagmus with fast-phase toward ear with increased function; cerebellar disease can also cause positive response
  - Head thrust nystagmus: briskly move patient's head from one side to another; refixation "catch-up" saccade indicates impaired VOR (can be caused by peripheral or central weakness)
  - Hyperventilation nystagmus: decreased carbon dioxide can bring out an irritative nystagmus
  - Noise-induced nystagmus: audiometer at 110 dB to induce nystagmus; Tullio's phenomenon: sound-induced vertigo and/or nystagmus
  - Fistula test: pressure-induced nystagmus (perilymphatic fistula, superior canal dehiscence); low sensitivity; Hennebert's sign or symptom: pressure-induced nystagmus or dizziness
  - Fukuda test: patient steps in place for 20–30 s, patient rotates toward the side of a unilateral weakness
  - Frenzel lenses inhibit fixation and can bring out nystagmus due to peripheral cause
- Electronystagmography (ENG)/Videonystagmography (VNG)
  - Electronystagmography uses corneoretinal potential changes, videonystagmography uses video to track eye movements
  - Vestibulosuppressants (benzos, meclizine) can affect test results, should be discontinued at least 1 day prior
  - Tests performed
    - Spontaneous/Gaze nystagmus, positional testing, positioning testing (Dix-Hallpike)
    - Bithermal caloric testing: only test that evaluates peripheral function in isolation (lateral canal), abnormal results considered significant if >20 % weakness compared to other side, only tests low-frequency rotation
      - Cannot perform if ear tubes present
      - Relies on comparison of response between sides to determine unilateral weakness
      - To assess for bilateral weakness, absolute responses can be used and compared to norms, but may not be as accurate as rotary chair
    - Oculomotor testing: saccade, smooth pursuit, optokinetic tests
  - Findings suggestive of peripheral nystagmus: unilateral caloric weakness, direction-fixed nystagmus, positional nystagmus that fatigues, able to suppress nystagmus with fixation
  - Findings suggestive of central nystagmus: normal caloric results with spontaneous/gaze-evoked/positional nystagmus, normal caloric results with abnormal oculomotor tests, direction-changing nystagmus with gaze changes, no fixation suppression
- Rotary chair testing
  - Measures vestibular function at both high and low rotational frequencies
  - Useful for testing for bilateral vestibular impairment (i.e., aminoglycoside toxicity), may not be able to differentiate between unilateral and bilateral impairment
  - Rotary chair parameters
    - Gain: maximum slow phase eye velocity to chair velocity. Normal is 1; acutely will be decreased, may normalize over time if weakness is mild (indicates vestibular compensation)
    - Phase: eye velocity normally leads chair velocity (phase lead) at low frequencies; this is exaggerated in unilateral or bilateral peripheral vestibular weakness (loss of velocity storage mechanisms)

        - Symmetry: difference between maximum slow-wave eye velocity on left compared to right
        - Complete bilateral vestibular loss will show absent gain and phase (no response to measure)
      - Compensated vestibular loss will generally have normalized gain, but still with phase lead and unilateral caloric weakness; uncompensated loss will have abnormal gain, phase, asymmetry, and caloric weakness; these patients can benefit from vestibular rehabilitation
    - VEMP (vestibular evoked myogenic potentials)
      - Cervical VEMP measures the vestibulocollic reflex
      - Mechanism: sound → stapes → saccule (has some sound sensitivity) → inferior vestibular nerve, vestibular nucleus → media/lateral vestibulospinal tract → ipsilateral sternocleidomastoid muscle
      - Test interpretation
        - Unilateral decreased amplitude/absence: may suggest peripheral vestibular weakness
        - Unilateral decreased thresholds present with superior semicircular canal dehiscence, perilymph fistula
        - Bilateral absent may be a normal aging variant (20 %)
      - Ocular VEMP
        - Unclear utility: may test utricular and superior vestibular nerve function
    - Dynamic computerized posturography: systematically takes away one or more sensory components of balance (vestibular, visual, and somatosensory) to evaluate which component the patient is reliant on

VESTIBULAR DISORDERS

- Peripheral vestibular disorders
  - Benign positional vertigo characterized by vertigo for seconds
  - Ménière's disease characterized by vertigo for hours
  - Vestibular neuritis/viral neurolabyrinthitis characterized by vertigo for days
  - Superior semicircular canal dehiscence
  - Fistula (lateral canal, perilymphatic fistula)
    - Iatrogenic (postoperative stapedectomy)
    - Erosive middle ear disease: Chronic otitis media/cholesteatoma, otosyphilis
  - Vestibular schwannoma
  - Autoimmune disorders: Cogan syndrome, autoimmune inner ear disease
  - Medication vestibulotoxicity
- Benign positional vertigo
  - Most common cause of vertigo, usually affects posterior canal, less commonly lateral canal (superior canal rare)
  - Usually idiopathic, but can also occur after head trauma, vestibular neuritis or virtually any inner ear insult
  - Thought to be caused by displaced otoconia which stimulate the affected canal
  - Clinical
    - Vertigo that occurs with tilting head back (looking up, rolling over in bed)
    - Nystagmus begins after several seconds (latency), lasts less than 1 min, is fatiguable, does not change direction
    - Does not present with other otologic symptoms
  - Diagnosis
    - Posterior canal benign positional vertigo: Dix-Hallpike maneuver—bring patient from sitting with head tilted to left or right to supine position with head hanging; if present, patient will have vertical (upward) torsional nystagmus

        - Lateral canal benign positional vertigo: can usually see on Dix-Hallpike, but best way to observe is supine roll test: patient is supine and head inclined 30° (in plane of lateral canal), rapidly turn head from side to side; if present, patient will have horizontal nystagmus that changes direction depending on way head is turned; direction of nystagmus can be geotropic (toward ground, more common) or ageotropic (away from ground)
    - Treatment
        - Posterior canal benign positional vertigo: In-office treatments include Epley maneuver, Semont maneuver; Home treatment includes Brandt-Daroff exercises
        - Lateral canal benign positional vertigo: log roll maneuver, start with affected side down
        - Can recur in significant percentage of patients; lateral canal benign positional vertigo may develop after an Epley maneuver
        - Surgical intervention for recurrent intractable benign positional vertigo has been described (posterior canal occlusion, singular neurectomy); risk of sensorineural hearing loss with both, not commonly performed
- Ménière's disease
    - Symptoms consist of episodic vertigo, fluctuating hearing loss, tinnitus, aural fullness
    - Possible etiologies/triggers: viral, autoimmune, allergy, genetic
    - American Academy of Otolaryngology-Head and Neck Surgery diagnostic criteria
        - Certain: requires histologic confirmation of endolymphatic hydrops (postmortem)
        - Definite: recurrent vertigo episodes with documented hearing loss, tinnitus/aural fullness; episodes must last at least 20 min but typically several hours, often with nausea and vomiting
        - Probable: one episode of vertigo with hearing loss and tinnitus/aural fullness
        - Possible: episodic vertigo without hearing loss, or sensorineural hearing loss with dizziness but no episodic vertigo
    - Variants
        - Drops attacks (Tumarkin crisis): loss of lower extremity muscle tone, no loss of consciousness (6–7 %), thought to be caused by sudden stimulation of vestibular end organ
        - Lermoyez's syndrome: hearing loss/tinnitus precede vertigo by days/months, improve with onset of vertigo
        - Cochlear hydrops: hearing loss/aural fullness/tinnitus without vertigo
        - Vestibular hydrops: episodic vertigo without hearing loss/tinnitus
    - Workup
        - Audiogram: sensorineural hearing loss, classically low-frequency
        - Electronystagmography: 30–50 % with unilateral weakness
        - MRI to rule out vestibular schwannoma or central cause of dizziness
        - Electrocochleography: test compares summating potential to action potential of auditory nerve; Ménière's disease patients have increased summating potential/action potential ratio from altered basilar membrane function in endolymphatic hydrops, test not routinely performed because of limited sensitivity/specificity
    - Treatment
        - Medical (controls symptoms in 80 %)
            - Acute symptoms
                - Vestibular suppressants—diazepam for vertigo, promethazine for nausea/vomiting, meclizine
                - Oral steroids can be used for acute episode, especially if drop in hearing
                - Allergy management may help symptoms
            - Prophylaxis
            - Sodium restriction: counseled as initial first step, but little data to support
            - Dyazide shown to reduce vertigo episodes in randomized controlled trial, can also use acetazolamide

- Betahistine: vasodilator, shown to decrease dizziness/vertigo in two randomized controlled trials
- Intratympanic steroids: one nonrandomized study showed 70 % improvement at 18 months (but no difference from intratympanic gentamicin or endolymphatic sac decompression)

■ Intratympanic gentamicin (selectively vestibulotoxic) has been used to decrease vestibular symptoms; may give repeat doses if vestibular symptoms are present, but should stop if patient develops symptoms suggestive of cochlear injury (worsening tinnitus/hearing loss)

■ Surgical

- Endolymphatic sac surgery: first-line surgical intervention for patients with useful hearing, widely quoted success rates, decompress sac through transmastoid approach, some also open sac ± place silastic stent
- Vestibular nerve section: creates stable vestibular deficit through retrosigmoid or middle fossa approach, can preserve hearing, but requires craniotomy
- Chemical labyrinthectomy: gentamicin (selectively vestibulotoxic) administered to middle ear; injections continued until vertigo symptoms under control (do not need to ablate all vestibular function) or sensorineural hearing loss occurs (Minor—90 % vertigo control, 3 % profound hearing loss)
- Transmastoid labyrinthectomy: ablates unilateral residual hearing and vestibular function

- Vestibular neuritis/viral neurolabyrinthitis
  - Vestibular neuritis: Acute vertigo >1 day with recovery over weeks/months (prolonged compared to Ménière's disease, disequilibrium can persist for months
  - Viral neurolabyrinthitis: vestibular neuritis + sensorineural hearing loss/tinnitus
  - Clinical: fast-phase of nystagmus away from affected side, fall toward side of lesion
  - Electronystagmography: unilateral caloric weakness, spontaneous nystagmus (fast-phase away from weak ear), decreased vestibulo-ocular reflex gain on rotary chair, increased vestibulo-ocular reflex phase lead (loss of velocity storage)
  - Treatment: vestibular suppressants for acute symptoms, steroids if sensorineural hearing loss also present
- Superior semicircular canal dehiscence syndrome
  - Lack of bone covering superior canal that causes vestibular and/or otologic symptoms
  - Clinical
    - Dizziness: dizziness with loud noises (Tullio phenomenon, most common), dizziness with Valsalva, chronic dysequilibrium
    - Otologic: aural fullness, hearing loss, autophony ("hear my eyes move"), pulsatile tinnitus
    - Exam: Excitatory stimulus (loud noise or positive pressure to ear) induces nystagmus with slow phase up and away from affected ear; inhibitory stimulus (valsalva against closed glottis increases intracranial pressure) induces nystagmus down and toward affected ear
  - Workup
    - Audiogram: conductive hearing loss, can be due to suprathreshold bone conduction, present acoustic reflexes (in contrast to otosclerosis)
    - CT: look for dehiscence in coronal, Poschel (cuts oriented parallel to the plane of the canal), Stenver (cuts oriented perpendicular to the plane of the canal) views, CT may over-diagnose (false positive) or overestimate the size of the dehiscence
    - Vestibular function testing: decreased cervical VEMP/ocular VEMP thresholds
  - Management
    - Symptom avoidance
    - Surgical
      - Middle fossa plugging (low recurrence rate, risk of sensorineural hearing loss) or resurfacing (higher risk of persistent/recurrent symptoms)
      - Transmastoid occlusion avoids temporal lobe retraction; difficult access for low lying tegmen

- Perilymphatic fistula
  - Triad of hearing loss, vertigo, tinnitus
  - Etiologies include iatrogenic (post-stapedectomy, most common), trauma (t-bone fracture, explosive or implosive barotrauma), congenital/spontaneous (controversial), erosive (cholesteatoma, otosyphilis)
  - Clinical: sudden or progressive sensorineural hearing loss/vertigo/tinnitus, may fluctuate; may be associated with a positive Hennebert's sign, Tullio's phenomenon, or fistula test
  - Diagnosis: must be confirmed via middle ear exploration, CT may show pneumolabyrinth or middle ear anomalies; protein markers have been suggested (beta-2 transferrin, beta-trace protein)
  - Treatment:
    - Conservative: bed rest, head elevation, avoidance of straining, and stool softeners
    - Surgical: may be performed from the outset or in cases where progressive hearing loss and persistent vertigo develop following initial period of observation
      - Middle ear exploration with plugging of affected site consider plugging both oval and round windows even if no fistula is observed
- Other etiologies of peripheral vestibular disorders
  - Autoimmune
    - Cogan's syndrome: episodic vertigo lasting hours (similar to Ménière's disease), sensorineural hearing loss, non-syphilitic interstitial keratitis; steroid responsive
    - Vogt-Koyanagi-Harada Syndrome: hearing loss, vertigo, uveitis, vitiligo; also steroid responsive
    - Autoimmune inner ear disease: see below
  - Otosyphilis: episodic vertigo and sensorineural hearing loss, can mimic Ménière's disease, perilymphatic fistula, autoimmune inner ear disease; classically with positive Hennebert's sign, and positive Tullio's phenomenon; consider FTA-ABS in high-risk patients with vertigo
  - Inner ear decompression: vertigo, hearing loss, tinnitus seen in divers during ascent (nitrogen becomes more soluble in inner ear during descent because of increased pressure, on ascent solubility decreases and air bubbles form); treatment is hyperbaric oxygen
  - Medication ototoxicity
    - Aminoglycosides: gentamicin and streptomycin more vestibulotoxic; kanamycin, amikacin more cochleotoxic
    - 12S rRNA mutation increases susceptibility to aminoglycoside ototoxicity
    - Vancomycin, lasix, cisplatin, flagyl all potentiate aminoglycoside toxicity
    - Clinical: oscillopsia, ataxia
    - Diagnosis: rotary chair is most sensitive test for bilateral weakness (decreased gain, increased phase lead), may also have bilateral caloric weakness on electronystagmography
    - Can monitor for inner ear damage while using ototoxic medications with symptoms (tinnitus), otoacoustic emmisions, audiometry
- Etiologies of central vestibular disorders
  - Migraine: most common, variable duration of vertigo/dysequilibrium
  - Infarction/ischemia: Vertebrobasilar insufficiency, Wallenberg syndrome
  - Multiple sclerosis
  - Cerebellar ataxia syndromes
  - Neoplasms affecting brainstem/cerebellum
  - Craniovertebral junction disorders: can result in compression of basilar artery (basilar impression), cerebellum (Chiari malformation), vertebral artery (atlantoaxial dislocation)
  - Vascular loop compression syndrome: controversial cause of repeated brief spells of vertigo, thought to be caused by irritability of the vestibular nerve from a vascular loop

- Migrainous vertigo
  - Variety of dizziness/dysequilibrium symptoms associated with migraine headaches
  - Episodic vertigo occurs in 25–35 % of migraine patients; most common in women
  - Patients may have personal or family history of migraine
  - Clinical
    - Vestibular: episodic vertigo, constant imbalance, movement-associated disequilibrium, lightheadedness
    - Headache may occur before, during, or not at all; may have photophobia, phonophobia, visual aura
    - Motion intolerance, sensitivity to complex visual stimuli
    - Hearing loss uncommon, may have unilateral or bilateral tinnitus
  - Subtypes
    - Basilar migraine: more clearly defined subtype of migraine with aura, patients have two or more symptoms (vertigo, tinnitus, hearing loss, ataxia, dysarthria, visual symptoms, diplopia, parethesias, paresis, decreased consciousness) followed by a throbbing headache
    - Benign positioning vertigo of childhood: episodic vertigo in children lasting minutes–hours, may progress to migraine, strong migraine family history
  - Diagnosis: Electronystagmography normal
  - Treatment
    - Prophylactic: nortriptyline, verapamil, topiramate;
    - Diet: avoid migraine triggers (MSG, alcohol, aged cheese, chocolate, aspartame)
    - Vestibular rehabilitation
- Infarction/ischemia
  - Vertebrobasilar insufficiency: transient ischemic attacks in brainstem vasculature associated with atherosclerosis, may experience transient vertigo; can also have diplopia, dysphagia, drop attacks
    - Wallenberg Syndrome: posterior inferior cerebellar artery (PICA) thrombosis causing lateral medullary infarction manifesting with acute vertigo, ataxia, ipsilateral Horner syndrome, ipsilateral palatal paresis and vocal ford paralysis, ipsilateral face numbness, contralateral decreased pain sensation from body
- Multiple sclerosis
  - Demyelinating central nervous system disorder affecting multiple white matter regions
  - Dizziness is a common symptom, may have other neurologic symptoms caused by scattered plaques in different brain regions (spasticity, unilateral sensory disturbances, optic neuritis)
  - Electronystagmography: disconjugate eye movements (internuclear ophthalmoplegia), ocular dysmetria on saccade testing (undershoot, overshoot), impaired smooth pursuit
  - Diagnosis: Labs: increased gamma globulin/oligoclonal bands; MRI: scattered white matter plaques
- Cerebellar ataxia syndromes
  - Wide range of disorders which collectively cause inability to coordinate balance, gait, extremity, and eye movements
  - Some conditions include cerebellar atrophy, ataxia telangectasia, Friedrich's ataxia, Refsum's disease, paraneoplastic cerebellar degeneration, familial episodic ataxia
  - Clinical:
  - Symptoms: difficulty with fine motor control (writing, eating), walking with wide stance, may affect speech and swallowing
  - Exam: dysmetria, dysdiadochokinesia, dysarthria
    - Electronystagmography: abnormalities of oculomotor testing: ocular dysmetria on saccade testing (undershoot, overshoot), abnormal smooth pursuit, direction-changing nystagmus or periodic alternating nystagmus (changes direction every 2–6 min), rebound nystagmus (gaze-evoked nystagmus that fatigues and changes direction after a few seconds)
    - Treatment involves management of underlying cause

- Craniovertebral junction disorders
  - Can result in compression of basilar artery (basilar impression), cerebellum (Chiari malformation), vertebral artery (atlantoaxial dislocation)
  - Classically shows vertical down-beating nystagmus, more prominent with down gaze or lateral gaze

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Chapter 15
Ear Disorders

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PEARLS

- Sudden sensorineural hearing loss is classified as unilateral hearing loss of at least 30 dB in at least 3 frequencies occurring within 3 days
- Otosclerosis is an autosomal dominant metabolic bone disease with incomplete penetrance of the otic capsule and ossicles that causes stapes fixation, most commonly at the fissula ante fenestrum
- Acute coalescent mastoiditis is the most common intratemporal complication of otitis media

SENSORINEURAL HEARING LOSS

- Categories of sensorineural hearing loss
  - Congenital
    - Hereditary (50 %)
      - Syndromic (30 %): most common include Usher, Pendred syndromes (both autosomal recessive)
      - Non-syndromic (70 %) GJ2B mutation (autosomal recessive) coding for the protein gap junction beta 2 (also called connexin 26); results in impaired K + exchange
    - Nonhereditary (25 %)
      - Infectious: Cytomegalovirus (most common cause of congenital viral deafness), mumps (most common cause of acquired sensorineural hearing loss), rubella
      - Other perinatal factors: prematurity, maternal diabetes, hyperbilirubinemia
    - Idiopathic (25 %)
  - Acquired
    - Presbycusis (most common): progressive symmetric sensorineural hearing loss associated with aging, begins in high frequencies, treat with hearing aid or cochlear implant if advanced
    - Noise-induced hearing loss: often associated with a 4-kHz notch
    - Post-meningitis: may be associated with labyrinthitis ossificans
    - Cerebrovascular accident
    - Ototoxic medication exposure
    - Autoimmune inner ear disease: includes Cogan's syndrome, relapsing polychondritis, Wegener's granulomatosis, systemic lupus erythematosus, Sjogren's syndrome, and rheumatoid arthritis
    - Idiopathic, including sudden sensorineural hearing loss
    - Vestibular schwannoma or meningioma: usually asymmetric and displays retrocochlear pattern (disproportionately poor word recognition compared to pure tone losses)
    - Erosive inner ear disease (cholesteatoma, chronic otitis media without cholesteatoma)

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- Noise-induced hearing loss
  - Temporary threshold shift: brief period of hearing loss after noise exposure that returns to normal after rest
  - Permanent threshold shift: hearing loss that does not return to previous hearing level
  - Natural resonance of external auditory canal is 3 kHz which may be the reason for a "noise notch" at 4 kHz
  - Workplace restrictions
    - Must limit noise exposure at 90 dB to 8 h; with each 5 dB increase must cut exposure into half
    - Employers must provide protective hearing equipment for 8-h "time-weighted average" over 90 dB
    - Hearing conservation program must be implemented for average exposure 85 dB or greater over 8 h
- Sudden sensorineural hearing loss
  - Unilateral hearing loss of at least 30 dB in at least 3 frequencies occurring within 3 days
  - Unknown etiology, possible viral or vascular (ischemic) cause
  - Studies: audiogram, MRI to rule out vestibular schwannoma (incidence in general population 2/100,000, but as high as 4 % in sudden sensorineural hearing loss patients)
  - Treatment
    - Steroids: most recent clinical practice guidelines recommend oral or intratympanic steroids as first line
      - Oral prednisone typically given at 1 mg/kg/day (up to 60 mg) for 7–14 days, then taper
      - Intratympanic dexamethasone
        - Give 10, 24, or 40 mg/ml every 3–7 days for 3–4 doses
        - Can be given alone, as adjunct to oral steroids, or if oral steroid contraindication
    - Hyperbaric oxygen: more popular abroad, may offer as initial therapy
    - Antivirals: have been used, but not recommended in most recent guidelines
  - Prognosis worse with greater degree of hearing loss, if associated with vertigo, advanced age

- Auditory neuropathy/dyssynchrony
  - Defined as abnormal/absent auditory brainstem response but evidence of inner hair cell function (cochlear microphonic and otoacoustic emissions normal)
  - Thought to be caused by abnormal central auditory temporal processing in response to stimulus
  - Typically seen in young children, frequent association with other developmental delays
  - May have relatively good pure tone thresholds but poor speech understanding and auditory development
  - Exhibit variable response to amplification and/or cochlear implants
- Autoimmune inner ear disease (AIED)
  - Subacute progressive bilateral sensorineural hearing loss that responds to steroids (too slow to be sudden sensorineural hearing loss, too fast to be presbycusis)
  - Diagnostic criteria
    - Bilateral sensorineural hearing loss >30 dB at any frequency
    - Progression in at least one ear on two serial audiograms < 3 months apart
  - 15 % with other systemic autoimmune disease including multiple sclerosis, rheumatoid arthritis, inflammatory bowel disease
  - Studies
    - Audiogram, MRI internal auditory canal if asymmetric hearing
    - Labs: may consider anti-HSP-70 (= 68-kD antigen), although limited sensitivity/specificity, so not routinely ordered
    - If suspect other autoimmune disease (arthritis, ocular disease, skin lesions, kidney disease), order erythrocyte sedimentation rate, antinuclear antibody, rheumatoid factor

- Treatment
  - Trial of prednisone 60 mg daily for 4 weeks, repeat audio at 4 weeks
  - Nonsteroid responders taper immediately
  - Steroid responders continue until plateau is reached in hearing, then maintenance dose for at least 6 months
  - Methotrexate used for patients who cannot tolerate steroids, or in cases where weaning steroids cause a decline in hearing
  - Cyclophosphamide, etanercept second line

CONDUCTIVE HEARING LOSS

- Otosclerosis
  - Metabolic bone disease of otic capsule and ossicles that causes stapes fixation
  - Autosomal dominant with incomplete penetrance
  - 10 % prevalence in Caucasians, 1 % with clinical disease
  - Most common site is fissula ante fenestrum, other subtypes → bipolar (anterior/posterior involvement only), biscuit (footplate only), obliterative (footplate + annular ligament)
  - Clinical
    - Progressive conductive hearing loss beginning in 20s–30s, + tinnitus, typically without a history of chronic otitis media or prior ear surgery
    - Patients may have autophony, perceive voice as louder than it actually is
    - Paracusis of Willis: improved hearing in background noise—speaker is talking with increased volume to compensate for background noise (increased signal), and patient's conductive hearing loss causes decreased perception of background noise (decreased noise)
    - May have sensorineural hearing loss and/or vestibular symptoms (25 %); indicates inner ear involvement
    - Clinical exam usually normal, may occasionally see Schwartze's sign (10 % active disease foci in the region of oval window/promontory, appears hyperemic)
    - Tuning fork:
      - Negative Rinne at 250 Hz only in early disease, with worsening disease progresses to include 512 and 1,024 Hz (negative Rinne indicates conductive hearing loss of at least 15 dB at 250 Hz, 25–30 dB at 512 Hz, >35 dB at 1,024 Hz)
  - Diagnosis
    - Audiogram: conductive hearing loss or mixed loss, Carhart's notch, diphasic or absent stapedial reflex, advanced cases may show type As tympanogram
    - Carhart's notch is an artificial depression in the bone conduction line centered on 2 kHz; reverses after stapedectomy resulting in the phenomenon of overclosure
    - CT: focal areas of demineralization (indicating active "spongiosis" early in disease), later disease shows sclerotic regions; double-ring effect (halo sign)—active foci of demineralization around cochlea
  - Differential
    - Includes several diagnoses in which otologic exam may appear normal
      - Congenital stapes fixation: nonprogressive conductive hearing loss more likely to have other congenital anomalies
      - Superior canal dehiscence: often has suprathreshold hearing, no Carhart's notch, normal stapedial reflexes, and abnormal VEMP threshold
      - Malleus head fixation: may be congenital or acquired (tympanosclerosis)
      - Ossicular discontinuity: temporal bone trauma or erosive middle ear disease resulting in a maximal conductive hearing loss
      - Osteogenesis imperfecta: blue sclera, stapes footplate fixation but hypermobile tympanic membrane, may have stapes crura fracture, conductive hearing loss but no Carhart's notch, mottled otic capsule appearance from demineralization and sclerosis (similar to otosclerosis, may cause sensorineural hearing loss); can perform stapedectomy

- Osteitis deformans (Paget's disease): diffuse bilateral temporal bone demineralization starting at petrous apex (also affects other skull base bones), sensorineural hearing loss can result from cochlear or internal auditory canal involvement (sensorineural hearing loss more common in Paget's), conductive hearing loss from crowding of ossicles in epitympanum and ossicular chain fixation, elevated alkaline phosphatase, middle ear exploration generally not indicated

■ Chronic otitis media/cholesteatoma: usually apparent on exam

○ Treatment

■ Medical

- Hearing aid trial should be offered for all patients initially
- Fluoride, bisphosphonates have been met with mixed success

■ Surgical

- Middle ear exploration: raise tympanomeatal flap, curette scutum, create control hole in footplate (useful for footplate removal if becomes floating), separate incudostapedial joint, palpate ossicle mobility, cut stapes tendon, down-fracture suprastructure
- Open vestibule
  - Stapedotomy: make small hole in footplate with flexible laser (CO2, KTP, argon) and/or 0.7 mm drill, most common procedure currently performed
  - Stapedectomy: remove the entire footplate with right-angle hooks, cover with graft and place piston
- Place piston, seal hole with blood patch, fascia, perichondrium, vein graft

■ Intraoperative variations

- Facial nerve dehiscence/overhang: consider aborting procedure or gently displacing nerve
- Floating footplate: stapes footplate dislodges from oval window niche; use right-angle hook to remove the entire footplate (total stapedectomy) to prevent displacement into vestibule; can also perform laser stapedotomy
- Obliterative otosclerosis: usually cannot use laser because footplate is so thin; use drill to thin footplate until blue, then can perform stapedotomy or stapedectomy; may get floating footplate during drilling (manage as above)
- Perilymph gusher: increased risk with patent cochlear aqueduct, congenital stapes fixation; increases the risk of sensorineural hearing loss; can cover with graft and complete procedure, but should not perform total stapedectomy; manage postoperatively like cerebrospinal fluid leak (bedrest, head of bed elevation, avoidance of straining)
- Round window obliteration: may give poorer hearing outcomes; not recommended to drill out
- Persistent stapedial artery: arises from internal carotid artery instead of middle meningeal artery, runs between crura and then into fallopian canal to geniculate and then dura; often too large to bipolar, may have to abort

■ Complications: prosthesis displacement (most common), profound sensorineural hearing loss (1 %), facial paralysis (<1/1,000), postoperative vertigo (prosthesis too long), perilymph fistula (fluctuating vertigo, tinnitus, sensorineural hearing loss treat with re-exploration and patch), reparative granuloma (initial period of hearing improvement followed by decline in hearing, tinnitus, vertigo; exam shows reddish hue behind TM; treat with re-exploration and surgical removal)

● Chronic otitis media

○ Suppurative otitis media with perforation

■ Etiologies of tympanic membrane perforation: otitis media (acute or chronic), pressure equalization tube extrusion, traumatic (penetrating, temporal bone fracture, barotrauma), iatrogenic, systemic (Wegener's granulomatosis, tuberculosis)

■ Subtypes include central, marginal (involves annulus), subtotal

■ *Pseudomonas* most commonly involved for chronic draining perforation

■ Clinical: chronic draining ear, but no cholesteatoma present

- Audiogram: conductive hearing loss with type B tympanogram, degree of hearing loss dependent on the degree of tympanic membrane, ossicular disruption
  - If ossicular chain is intact, size of tympanic membrane perforation proportional to degree of hearing loss up to ~35 dB, also affected by location
  - Ossicular disruption results in conductive hearing loss of at least 35 dB
  - Total tympanic membrane perforation with ossicular disruption: 50 dB (still some direct conduction from sound waves hitting oval/round windows)
  - Intact tympanic membrane with ossicular disruption: maximal 60 dB conductive hearing loss (intact tympanic membrane prevents direct sound wave transmission to oval/round windows)
- Treatment
  - Medical: fluoroquinolone drops for acute otorrhea with perforation, avoid drops with ototoxic potential
  - Surgical: chronic otorrhea with perforation unresponsive to drops may require tympanomastoidectomy

- Cholesteatoma
  - Congenital: embryonic epithelial tissue, most commonly a white mass in anterosuperior middle ear with intact tympanic membrane
  - Primary acquired: tympanic membrane retraction and trapped epithelium result in skin debris formation; most common cholesteatoma type
    - Most common locations: posterior epitympanum (pars flaccida pockets invade Prussak's space, posterior mesotympanum, anterior epitympanum)
  - Secondary acquired: perforation with epithelium invading middle ear from margin of perforation; inadvertent surgical implantation from PE tubes, or middle ear surgery
  - Clinical: otorrhea, hearing loss, dizziness if labyrinthine fistula present
  - Diagnosis: exam shows retraction pocket extending beyond the limits of bony annulus, more advanced cholesteatomas accumulate squamous debris; CT can be obtained to evaluate the extent of disease, for complications (tegmen erosion, lateral canal erosion, ossicle status)
  - Management
  - Treatment is surgical
    - Canal-wall-up (CWU) versus canal-wall-down (CWD) mastoidectomy
      - CWU mastoidectomy preserves native ear anatomy, has faster healing, less otorrhea, better hearing if ossicles not removed
      - Modified CWD recreates a middle ear space whereas a radical CWD mastoidectomy is left completely unreconstructed
      - CWD has lower rates of residual/recurrent disease, allows for cleaning in office
      - Consider CWD from outset in posterior ear canal erosion, "unresectable" disease, labyrinthine fistula, patient unlikely to follow up consistently
      - Only hearing ear management controversial: traditionally CWD mastoidectomy recommended
  - Medical management with in-office debridement may be considered in patients with limited disease and advanced age and/or poor surgical candidates

- Complications of otitis media
  - Extracranial
    - Acute coalescent mastoiditis (most common intratemporal complication)
      - Mastoid opacification without bony destruction relatively common, does not always indicate acute infection
      - Opacification with loss of bony septations = coalescent mastoiditis, requires acute treatment
      - Most commonly caused by *S. pneumoniae*, also Group A *Strep*, *S. aureus*, coag-negative staph
      - Clinical: otalgia, fever, mastoid tenderness; otoscopy shows acute otitis media
      - CT: destruction of mastoid bony septations, cortical bone intact

  - Treat initially with intravenous antibiotics (AAO-HNS recommends vancomycin and ceftriaxone), consider pressure equalization tube and/or mastoidectomy if not responding to intravenous antibiotics alone
- Subperiosteal abscess: destruction of cortical bone overlying mastoid with auricle protrusion and loss of postauricular sulcus, generally requires pressure equalization tube and cortical mastoidectomy
- Bezold's abscess: abscess involving mastoid tip and sterncleidomastoid; treat with intravenous antibiotics and neck abscess drainage with pressure equalization tube placement ± mastoidectomy
- Facial nerve paresis/paralysis
  - Incidence with acute otitis media is 0.05 %; most common organism in one series shown to be *S. aureus*
  - For paralysis with acute otitis media, perform wide-field myringotomy ± pressure equalization tube insertion, followed by antiobiotic drops
  - For paralysis with chronic otitis media (i.e., cholesteatoma), need surgical decompression with mastoidectomy
- Labyrinthine fistula: risk of sensorineural hearing loss with removal of cholesteatoma sac; if small, can remove cholesteatoma and place fascia graft; if large, may want to leave cholesteatoma sac down and perform CWD procedure
- Labyrinthitis
  - Acute inner ear inflammation causing sensorineural hearing loss, vertigo, nausea, and vomiting; can be serous or suppurative
  - Suppurative infection can lead to labyrinthitis ossificans
  - Treatment for acute infection is intravenous antibiotics, mastoidectomy, give steroids if sensorineural hearing loss present
- Petrous apicitis
  - Suppurative bacterial infection causing destruction of bony septae of petrous apex air cells
  - Clinical: Gradenigo's syndrome: otorrhea, headache/retro-orbital pain (in distribution of trigeminal nerve), abducen's nerve weakness (sixth nerve travels adjacent to petrous apex in Dorello's canal)
  - Imaging: CT air cell coalescence; T1 intermediate signal, does not enhance; T2 high signal
  - Treatment is intravenous antibiotics, pressure equalization tube, mastoidectomy

■ Intracranial
- Meningitis (most common intracranial complication)
  - Most common pathogen is *S. pneumoniae, N. meningitis; H. influenzae* type B a risk in infants but vaccine has reduced incidence
  - Increased risk with congenital inner ear malformations (also increased risk of cerebrospinal fluid leak), cochlear implant recipients
    - Mondini dysplasia
    - Hyrtl's fissure: potential space present in infants between subarachnoid space and hypotympanum, persistent fissure increases meningitis risk
    - Enlarged petromastoid canal: normally contains subarcuate artery
  - Clinical: headache, fever, stiff neck, photophobia, seizures (especially in children)
    - Kernig's sign: extension of leg while supine causes pain
    - Brudzinski's sign: flexion of neck causes flexion at hips/knees due to pain
    - Limited sensitivity
  - Diagnosis
    - CT to ensure no impending brain herniation from increased intracranial pressure present
    - Lumbar puncture: suggestive findings include elevated nucleated cell count, increased protein, decreased glucose, elevated opening pressure

- Treat initially with intravenous antibiotics and dexamethasone (decrease inflammatory sequalae); consider surgical intervention if not responding to antibiotics alone (pressure equalization tube for acute otitis media, tympanomastoidectomy for chronic suppurative otitis media and cholesteatoma)
- Complications include sensorineural hearing loss (10–20 % of infants) and labyrinthitis ossificans (monitor with serial MRIs), ossification may prevent the ability to place cochlear implant

■ Intracranial abscess
- Typically polymicrobial; most common pathogens are *S. pneumoniae*, *S. aureus* (*H. influenzae* rare)
- Subtypes include epidural (pus between skull and dura), subdural (pus between dura and arachnoid), and brain (usually in temporal lobe or cerebellum)
  - Treat initially with intravenous antibiotics and neurosurgical drainage, tympanomastoidectomy may be performed at the time of abscess drainage or later once intracranial infection has resolved

■ Lateral sinus thrombosis
- Inflammation from neighboring otologic infection spreads to sigmoid sinus and causes infected thrombosis
- Clinical: spiking fevers ("picket fence"), headache
- Diagnosis: CT shows bony erosion over sigmoid, MRI/MRV will show filling defect/no flow through sinus
- May result in otitic hydrocephalus (intracranial hypertension from impaired venous sinus drainage which can cause chronic headache, lethargy, papilledema, abducens palsy; CSF studies normal aside from increased intracranial pressure)
- Management
  - Treatment based on small series: intravenous antibiotics, pressure equalization tube, and mastoidectomy with removal of infected thrombosis
  - Anticoagulants have been suggested if evidence or concern for septic emboli
  - Manage otitic hydrocephalus with acetazolamide, steroids

● Tinnitus

○ Subjective: perception of sound in the absence of any stimulus, more common than objective

■ Causes
- Any otologic disorder that causes sensorineural hearing loss can cause subjective tinnitus (most common is high-frequency ringing that is similar to the frequencies with hearing loss)
- Medications: aspirin (reversible), aminoglycosides, antihypertensives
- Neurologic disease (multiple sclerosis, brainstem ischemia/infarction)
- Psychiatric (depression/anxiety)

■ Management
- Avoidance of triggers (caffeine, nicotine, anxiety)
- Masking
  - Broadband noise (radio, static)
  - Hearing aids: amplify sound from environment to mask tinnitus
  - Commercial maskers: resemble hearing aids (worn in or behind ear), can be used concurrently with or without hearing aids
- Medications
  - Low-dose benzodiazepines
  - Nortriptyline, selective serotonin reuptake inhibitors in anxious/depressed patients
  - Intratympanic dexamethasone
- Sound treatments
  - Tinnitus retraining therapy: combination of broadband noise and psychologic counseling to cause habituation to tinnitus
  - Neuromonics: association of tinnitus with pleasurable musical stimulus

- Behavioral strategies
  - Biofeedback: relaxation strategies to decrease response to stress and reduce tinnitus perception
  - Cognitive behavioral therapy
- Cochlear implants: electrical stimulation from implant may mask tinnitus, or suppress neural activity that normally causes tinnitus
- Repetitive transcranial magnetic stimulation: investigational

○ Objective: perception of sound by an internal body sound or vibration
  ■ Pulsatile: hypertension, glomus tumors, dural arteriovenous malformations, aberrant carotid/jugular bulb, benign intracranial hypertension
  ■ Mechanical (clicking)
    - Palatal myoclonus: clicking caused by palatal muscle contraction, can treat with neurontin or botox
    - Stapedial/tensor tympani muscle hyperfunction: fluttering caused by spasm of stapedial/tensor tympani muscle, if severe can do middle ear exploration and cut tendon
    - Eustachian tube dysfunction/patulous eustachian tube
    - Temporomandibular joint disorder
    - Spontaneous otoacoustic emissions: unclear link between the presence of otoacoustic emissions and tinnitus perception

- Eustachian tube dysfunction
  ○ Chronic blockage of the eustachian tube when it should be open
  ○ Allergies can cause nasal mucosa edema that narrows the eustachian tube opening
  ○ Other causes include obesity, adenoid hypertrophy, polyps, tumors
  ○ Clinical: ear fullness, pain, popping/clicking with swallowing, symptoms may be worse when flying
  ○ Audiogram: type C tympanogram suggests diagnosis (type A does not exclude since eustachian tube dysfunction may be intermittent)
  ○ Treatment
    ■ Medical: oral/topical decongestants, oral/topical antihistamines, nasal steroids, auto-insufflation
    ■ Surgical: pressure equalization tube
- Patulous eustachian tube
  ○ Abnormally open eustachian tube causes "ocean roar" that is synchronous with respiration, worse when sitting up, improves when supine (more mucosal edema near eustachian tube opening); may also have autophony (most common symptom), sensation of "plugged" ear, hearing loss/vertigo (pressure changes transmitted to inner ear)
  ○ Associated with pregnancy, significant weight loss, post-radiation
  ○ May see mobility of the tympanic membrane that occurs with respiration
  ○ Treatment
    ■ Medical: regain weight, estrogen (premarin) nasal drops
    ■ Surgical
      - Pressure equalization tube: may worsen symptoms
      - Plugging of eustachian tube with fat or cartilage
      - Paraffin or gelfoam or calcium hydroxylapatite injection at Eustachian tube orifice
      - Eustachian tube occlusion with catheter (reversible, can be removed at any time)
- Temporomandibular joint syndrome
  ○ Common cause of otalgia, may also cause clicking/popping sensation in ear
  ○ May also have headache, symptoms worse with chewing
  ○ Bruxism (teeth grinding/clenching) a causal factor in most cases
  ○ Diagnosis usually clinical alone; MRI can evaluate for articular disk displacement or other pathology
  ○ Treatment: soft diet, warm compresses, nonsteroidal anti-inflammatories, muscle relaxants, occlusal splints (mouth guards) to reduce clenching at night

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Chapter 16
The Facial Nerve and Lateral Skull Base Disorders

Stanley Pelosi and Matthew Luke Carlson

PEARLS

- Electroneuronography (evoked electromyography (EMG)) to test the facial nerve is not useful until 2–3 days after injury when Wallerian degeneration occurs.
- Necrotizing otitis externa can be diagnosed with a Technetium-99 scan looking for osteomyelitis, and gallium scans are used to follow the resolution of disease during treatment
- Vestibular schwannomas histologically show Antoni A cells with parallel palisading nuclei and Antoni B cells with histologically less uniform appearances

The Facial Nerve

- Facial nerve anatomy
  - Segments: intracranial → meatal → fundus (narrowest portion, 0.68 mm) → labyrinthine → tympanic → mastoid → extratemporal
  - Extratemporal branches: temporal, zygomatic, buccal, marginal mandibular, cervical
  - Brainstem nuclei: facial motor (voluntary facial movement), superior salivatory (parasympathetic efferents for tearing, salivation), nucleus of the solitary tract (sensory afferents for taste)
  - Facial nerve most commonly dehiscent in tympanic segment > geniculate (middle fossa) > mastoid (adjacent to retrofacial cells)
- House–Brackmann classification
  - I: Normal function
  - II: Slight weakness but symmetric at rest, good forehead motion
  - III: Obvious weakness but symmetric at rest, impaired forehead motion, able to close eye, may have synkinesis, spasm, or contracture
  - IV: Symmetric at rest, incomplete eye closure, no forehead motion
  - V: Asymmetry at rest, barely perceptible movement
  - VI: Asymmetry at rest, no movement
- Sunderland classification of nerve injuries
  - Class I: Neuropraxia; compression of axon, no axonal disruption
  - Class II: Axonotmesis; disruption of axon; endoneurium, perineurium, and epineurium still intact
  - Class III: Neurotmesis; disruption of endoneurium surrounding axon; perineurium and endoneurium still intact, risk for synkinesis
  - Class IV: Neurotmesis; disruption of perineurium and endoneurium, epineurium still intact
  - Class V: Neurotmesis; complete nerve disruption (endoneurium, perineurium, epineurium)

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- Facial nerve function tests
  - Use to assess integrity of nerve in cases of paralysis (for paresis not used because nerve is intact)
    - Electroneuronography (evoked EMG)
      - Records facial muscle compound action potentials in response to transcutaneous stimulation (stimulating electrode placed at angle of mandible in the region of stylomastoid foramen)
      - Can provide an objective measure of action potential amplitudes from normal and paralyzed sides
      - Not useful until 2–3 days after injury; have to wait for Wallerian degeneration to occur
      - Has been used to predict prognosis and determine the criteria for surgical intervention in traumatic/idiopathic causes of paralysis
        - Bell's palsy: Middle fossa decompression suggested if > 90 % degeneration compared to normal side within 2 weeks
        - Temporal bone fracture
    - EMG: Determines the level of spontaneous muscle activity, useful in predicting prognosis for acute or long-standing paralysis
      - Fibrillation: Seen in denervated muscle ~2 weeks after injury
      - Silence: Muscle atrophy (long-standing denervation)
      - Polyphasic potentials → seen with muscle reinnervation ~6 weeks after injury
      - Normal voluntary action potentials indicate at least partial nerve continuity
    - Other tests (infrequently used)
      - Nerve excitability test: Compare the lowest current stimulation threshold required to cause minimal muscle contraction on each side of the face (difference > 3.5 mA considered significant); stimulation probe placed at angle of mandible; requires subjective observation by tester
      - Maximum stimulation test: Compare muscle movement on each side of face in response to suprathreshold current stimulation, stimulation probe placed in the region of nerve branch to be tested; requires subjective grading by tester
- Causes of unilateral facial nerve weakness/paralysis
  - Congenital
    - Mobius syndrome: Unilateral/bilateral CN VII/VI palsies, club foot, mental retardation
    - Congenital unilateral lower lip palsy: Hypoplasia of depressor anguli oris muscle, cardiac defects
  - Acute acquired
    - Infectious
      - Bell's palsy
      - Herpes zoster oticus/Ramsay Hunt syndrome
      - Lyme disease: 10 % develop ipsilateral or bilateral facial weakness/paralysis, consider ordering Lyme titer in any patient with acute facial palsy; treat with antibiotic
      - HIV
    - Traumatic: Temporal bone fracture
  - Chronic acquired
    - Neoplastic: Schwannoma, glomus, parotid tumor
    - Infectious: Cholesteatoma
  - Autoimmune/unknown: Melkerson–Rosenthal syndrome manifesting with recurrent facial edema, recurrent facial weakness (unilateral or bilateral), recurrent fissured tongue; begins in childhood, treat with steroids
- Bell's palsy
  - Most common cause of unilateral facial weakness/paralysis, idiopathic but viral etiology suspected
  - Risk factors: Diabetes, pregnancy, prior history (10 % recur)

- Clinical findings
  - Acute unilateral weakness or paralysis developing within 48 h
  - May have viral prodrome, hyperacusis, decreased tearing, numbness/pain of ear/face/neck, taste changes
- Work-up for unilateral facial nerve weakness/paralysis
  - MRI with contrast evaluates full course of facial nerve (brain/internal auditory canal/neck)
  - Audiogram
  - Lyme titer
  - Electroneuronography can be considered for patients who develop complete paralysis, can be used to determine candidacy for surgical intervention
- Treatment
  - Medical
    - High-dose steroids (prednisone 1 mg/kg) shown to increase the rate of recovery, antivirals may have a modest benefit
    - No evidence of improvement with addition of antivirals to steroids
    - Eye care if difficulty with eye closure to prevent exposure keratitis (saline drops, lacrilube ointment, eye bubble)
  - Surgical
    - Middle fossa decompression for patients under 65 with >90 % neuronal degeneration within 2 weeks of onset increased chances of good facial nerve recovery, surgery should ideally be performed within 2 weeks
- Prognosis
  - Poor prognosis with advanced age, complete paralysis

- Herpes zoster oticus/Ramsay Hunt syndrome
  - Herpes zoster oticus: Reactivation of herpes zoster virus (normally dormant in geniculate ganglion) with cutaneous lesions in distribution of nervus intermedius (CN VII)
  - Ramsay Hunt syndrome: Herpes zoster oticus + facial paralysis, 18 % of adult facial palsies
  - Increased risk of residual facial weakness compared to Bell's palsy
  - Clinical: Vesicular rash in distribution of tympanic membrane, external auditory canal, pinna, anterior 2/3s of tongue, soft palate; facial paresis/paralysis with Ramsey Hunt syndrome, may have associated hearing loss (50 % of patients, due to involvement of CN VIII), also tinnitus, vertigo/disequilibrium
  - Diagnosis: Audiogram may show sensorineural hearing loss; MRI to evaluate the course of facial nerve
  - Treatment
    - High-dose steroids, antivirals, eye care for difficulty with eye closure
    - Consider anticonvulsants (carbamazepine, gabapentin, lyrica) for post-herpetic neuralgia
- Temporal bone fractures
  - Caused by blunt trauma
  - Several different classification schemes
    - Longitudinal versus transverse
      - Longitudinal caused by lateral blow, fracture runs anteromedial to otic capsule; associated with external auditory canal laceration, tympanic membrane perforation, bloody otorrhea, ossicle disruption, conductive hearing loss
      - Transverse caused by occipital or frontal trauma, causes hemotympanum, sensorineural hearing loss, higher risk of facial nerve injury
      - Majority of fractures have mixed components of longitudinal and transverse fractures
      - Otic capsule sparing versus otic capsule involvement
  - Clinical: Hearing loss (conductive, sensorineural, or mixed), facial nerve weakness/paralysis (most commonly injured at perigeniculate region), cerebrospinal fluid leak (otorrhea with longitudinal fracture, rhinorrhea with transverse), dizziness (labyrinthine concussion or otic capsule fracture)

- Diagnosis: CT of the temporal bones, beta-2 transferrin if suspect cerebrospinal fluid leak
- Management
  - Hearing loss: Middle ear exploration at a later date for conductive hearing loss
  - Facial paralysis: Management analogous to Bell's palsy
    - Medical: High-dose steroids (prednisone 1 mg/kg)
    - Surgical
      - Consider decompression for patients with immediate complete paralysis and >90 % neuronal degeneration on electroneuronography within 2 weeks of onset (similar to Bell's palsy indications)
      - If no hearing, perform translabyrinthine exploration; if hearing still present, combined middle fossa/transmastoid exploration
    - Penetrating temporal bone trauma causing paralysis (gunshots, knives): High risk of nerve transection, should proceed with urgent surgical exploration and repair
    - Iatrogenic facial paralysis: Wait for local anesthetic to wear off, then explore surgically if still present
  - Cerebrospinal fluid leak
    - Temporal bone fractures are the most common cause of otogenic leaks; others include iatrogenic (mastoid surgery, often associated with encephalocele), erosive (cholesteatoma), congenital (inner ear malformations), spontaneous (risk in obese patients with intracranial hypertension)
    - Majority of leaks caused by t-bone fractures close within 1–2 weeks, initially bed rest, head of bed elevation, avoid straining, acetazolamide
    - Give prophylactic antibiotics if leak present > 1 week (increased meningitis risk); consider surgical closure if leak present beyond this time
    - Iatrogenic and spontaneous leaks unlikely to close, require surgical intervention
    - Surgical approaches
      - Single defect, <1 cm consider transmastoid repair
      - Large defects, multiple, involving tegmen tympani (difficult to plug from below due to the presence of ossicles) consider middle fossa or combined approach

- Causes of bilateral facial nerve weakness/paralysis
  - Guillain–Barré syndrome
  - Sarcoidosis
  - Infectious: Lyme disease (most common infectious cause), HIV, syphilis, meningitis/encephalitis
  - Melkersson–Rosenthal syndrome
  - Diabetes mellitus
  - Intrapontine/prepontine tumors
- Facial nerve reanimation strategies
  - < 1 year from the time of injury (EMG still shows evidence of muscle activity)
    - Primary anastamosis: Best outcome, involves microsurgical anastomosis of epineurium
    - Cable (interposition) graft
      - Greater auricular nerve if need < 10 cm, sural nerve if > 10 cm (graft multiple nerve branches)
    - CN 12-7 jump graft
      - End-to-end connection of hypoglossal nerve to distal segment of facial nerve
      - Indicated when proximal stump unavailable but distal segment intact
      - Sacrifices ipsilateral hypoglossal function
      - Requires physical therapy to reduce synkinesis
    - Facial nerve crossover graft: Use graft to connect branches of opposite facial nerve to distal segment of injured nerve
  - > 1–2 years from the time of injury (employ if EMG shows facial muscle atrophy)
    - Static procedures
      - Gold weight, lateral canthoplasty, brow lift
      - Alloderm or tensor fascia lata graft

- Dynamic procedures
  - Temporalis or masseter muscle transposition

The Lateral Skull Base

- Differential diagnosis of external auditory canal lesions
  - Cerumen impaction
  - Otitis externa (including necrotizing)
  - Osteoma/exostosis
  - Neoplasm: Cutaneous malignancy, glandular neoplasm
  - Canal cholesteatoma
  - Keratosis obturans
  - Diffuse temporal bone lesions: Eosinophilic granuloma, plasmacytoma
- Cerumen impaction
  - Accumulation of cerumen in external ear canal
  - Predisposing factors include narrowed external auditory canals (congenital, iatrogenic, or idiopathic stenosis), bony ear canal growths (osteoma, exostosis), dermatologic disease (eczema), blockage of epithelial migration (hearing aids, q-tips, excessive ear canal hair), aging (harder cerumen, migrates slower)
  - Clinical: Aural fullness, hearing loss (can be up to 10 dB conductive hearing loss), pruritis
  - Treatment: For symptomatic patients
    - Manual removal
    - Cerumenolytics (use for 3–5 days)
      - Hydrogen peroxide, carbamide peroxide (debrox); available over the counter
      - Mineral oil (over the counter), colace: Better for dry/eczematous skin
    - Irrigation: Less favored due to risk of external auditory canal and tympanic membrane injury, but accepted method
- Otitis externa
  - Acute inflammation of external ear canal
  - May be precipitated by swimming ("swimmer's ear"), ear trauma (q-tips, hearing aids, foreign body in external auditory canal), dermatologic conditions (eczema, psoriasis, contact dermatitis)
  - Most commonly caused by pseudomonas, also *S. aureus*
  - Clinical: Otalgia, otorrhea
  - Diagnosis: Purulent otorrhea with external auditory canal edema, may have surrounding cellulitis; consider CT if infection not resolving with conventional treatment and risk factors for necrotizing otitis externa (see below) are present
  - Treatment
    - Antibiotic drops
      - Fluoroquinolones: Ciprodex, floxin cover gram± organisms, twice-daily dosing, no systemic absorption (can use for peds), no ototoxicity risk
      - Neomycin/gentamicin; often combined with polymyxin (increases pseudomonas coverage) and steroid (decrease edema); ototoxic and not recommended if perforation present; aminoglycosides may cause skin rash/irritation; require four-times-per-day dosing
      - Antifungals: Clotrimazole otic, tolnaftate (tinactin)
    - Other topical treatments
      - Acids: Boric acid, acetic acid (vosol, domeboro), alcohol/vinegar (5 % acetic acid) mix
        - All work by creating acidic environment to limit bacterial and fungal growth (vosol often used for fungal infection)
        - Can be painful to use, may have ototoxicity potential
      - Gentian violet: Dye with antiseptic/antifungal properties

        - Give oral antibiotics if cellulitis/chrondritis are also present
        - Use temporary wick if cannot visualize tympanic membrane (remove after 2–3 days)
        - Maintain dry ear precautions
        - Frequent ear cleanings
- Necrotizing otitis externa
    - Risk factors: Diabetes, immunosuppression, advanced age
    - Clinical findings
        - Prolonged otalgia (>1 month), otorrhea with granulation
        - Cranial nerve involvement: CN 7 > CN 10 > CN 11
    - Diagnosis
        - Biopsy to exclude external auditory canal malignancy (symptoms overlap)
        - Imaging
            - Technetium-99 scan for diagnosis of osteomyelitis, high sensitivity
            - Gallium scan to follow resolution of disease during treatment
            - CT temporal bone with/without contrast: Can detect bony erosion, less sensitivity for early disease
    - Treatment
        - Initiate treatment with oral ciprofloxacin
        - Intravenous ceftazidime if fluoroquinolone resistant, progression on oral cipro
        - Gallium scan every 4–6 weeks, continue treatment until resolution (average length ~9 weeks)
        - Hyperbaric oxygen has been used as adjunct
    - Prognosis
        - Worse prognosis with cranial nerve involvement
- Canal cholesteatoma versus keratosis obturans
    - Canal cholesteatoma
        - Invasion of squamous tissue into localized area of canal wall with periostitis and focal bony erosion
        - Occurs in older patients, presents as dull chronic pain with purulent otorrhea
        - Treatment: Biopsy to rule out malignancy; office versus operating room debridement
    - Keratosis obturans
        - Accumulation of desquamated keratin in the external auditory canal
        - Keratin is shed from the entire surface of ear canal, can cause circumferential bony widening
        - Occurs in younger patients, presents as acute severe ear pain, may be bilateral
        - Treatment: Biopsy to rule out malignancy, topical steroids, office versus operating room debridement, canalplasty may help
- Osteoma versus exostosis
    - Osteoma: Solitary, pedunculated, related to suture lines; histology—lamellar bone around trabecular cancellous bone
    - Exostosis: Multiple, can be bilateral, broad-based, medial external auditory canal; associated with cold water exposure; histology—dense lamellar bone parallel to periosteum, poorly developed trabeculations
- Neoplasm
    - See Head and Neck section
- Differential diagnosis of middle ear masses
    - Cholesteatoma (acquired or congenital)
    - Glomus tympanicum/jugulare
    - Schwannoma (facial most common)
    - Middle ear adenoma: Range from epithelial (adenoma) to neuroendocrine (carcinoid) differentiation; presents as nonspecific middle ear soft tissue mass, difficult to differentiate from chronic otitis media until the time of surgery
    - Vascular: Hemangioma (facial), aberrant carotid artery, persistent stapedial artery, high-riding jugular bulb

- Paraganglioma
  - Most common types: Carotid body (65 %), glomus tympanicum, glomus jugulare, glomus vagale
  - Rule of 10s: 10 % familial, 5–10 % of patients have multiple lesions (in familial cases, this may be 25 %)
  - 1–3 % active secretors causing flushing, diarrhea, palpitations, hypertension, palpitations, headache
  - Malignant in 3–5 %
  - Clinical
    - Hearing loss, dizziness, cranial nerve deficits (IV–XII, 10 %), otorrhea
    - Brown's sign (10–30 %): Reddish-blue hue of glomus tympanicum behind intact eardrum, blanches on pneumatic otoscopy
  - Labs: If suspect secreting tumor, can obtain 24-h urine catecholamines (vanillylmandelic acid, metanephrine) or plasma-free metanephrines (most sensitive, but high false positives); order abdominal CT for positive lab tests to rule out pheochromocytoma
  - Histology: Neuroendocrine cells from parasympathetic ganglia; chief cells arranged in "zellballen"
  - Imaging
    - Temporal bone CT: Glomus tympanicum: enhancing mass in middle ear/mastoid/hypotymanum; for glomus jugulare look for destruction of bone overlying jugular bulb and/or carotid canal, can have "moth-eaten" appearance
    - MRI: T1 with contrast shows enhancement, "salt and pepper" appearance from flow voids, also perform neck imaging to look for multicentricity
    - Angiography: Not routinely employed preop for diagnosis, but may be used for preoperative embolization
  - Fisch and Mattox glomus staging system
    - Includes both glomus tympanicum and jugulare
    - Type A involves promontory only
    - Type B involves hypotympanum but no erosion over jugular bulb
    - Type C erodes bone over jugular bulb
      - C1 erodes carotid foramen, C2 involves vertical carotid canal, C3 extension to horizontal carotid canal but not through foramen lacerum, C4 involves entire petrous carotid with extension to cavernous sinus
    - Type D intracranial extension
      - De extradural, Di intradural
      - D1 <2 cm intracranial, D2 >2 cm intracranial, D3 unresectable
  - Glomus tympanicum
    - Glasscock–Jackson staging
      - I: Small mass on promontory
      - II: Completely fills middle ear
      - III: Fills middle ear and extends to mastoid
      - IV: Fills middle ear, extends to external auditory canal
    - Treatment: Transcanal for small tumors, tympanomastoidectomy with extended facial recess appropriate for larger tumors
  - Glomus jugulare
    - Glasscock–Jackson staging
      - I: Involves jugular bulb, middle ear, and mastoid
      - II: Extends under internal auditory canal
      - III: Extends to petrous apex
      - IV: Extends to clivus or infratemporal fossa
      - Types II–IV may have intracranial extension
    - Treatment
      - May observe if not growing, older patient
      - Surgery favored for younger patients with + cranial nerve deficits

- Primary radiotherapy (stereotactic or external beam radiotherapy) can arrest tumor growth
- Favorable control rates reported with primary surgery or radiation therapy
- Trend is subtotal resection to spare functioning cranial nerves, adjuvant radiation therapy if subsequent tumor progression
- Multiple approaches described
  - Transmastoid jugular foramen approach with extended facial recess
  - Add canal-wall-down mastoidectomy and external auditory canal overclosure to increase anterior exposure near carotid
  - Can anteriorly reroute facial nerve to further increase exposure (Fisch type A infratemporal fossa approach); causes some degree of permanent facial weakness, not all authors recommend
  - All approaches need neck dissection for proximal internal carotid artery and internal jugular vein control
  - Preoperative embolization may decrease tumor blood flow; embolize external carotid artery branches commonly including ascending pharyngeal artery

- Facial nerve tumors
  - Schwannoma: Most common facial nerve tumor; can affect any portion of nerve, some series have reported highest incidence in perigeniculate region
  - Hemangioma: Very rare, usually involves perigeniculate region
  - Clinical: Slowly progressive facial twitching and/or weakness; hearing loss in 50 %, can be conductive or sensorineural depending on tumor location
  - Imaging: CT shows smooth expansile fallopian canal mass, hemangioma may show bony spicules; MRI with enhancement on T1 with contrast for both schwannoma and hemangioma
  - Management
    - Observe until patient's facial nerve function reaches House–Brackmann grade 3 or 4, or if large cerebellopontine angle component that is compressing brainstem
    - Consider middle fossa decompression once House–Brackmann grade 3 to give tumor more room to grow into middle fossa and decrease facial nerve compression
    - Surgical resection with interpositional graft once worse than House–Brackmann grade 3
      - Translabyrinthine route can access the entire extent of facial nerve, but sacrifices hearing
      - Middle fossa approach for hemangioma involving perigeniculate region; occasionally can peel small hemangiomas off facial nerve
    - Stereotactic radiotherapy may be considered for growing tumor but still with good (House–Brackmann grade 1–3) facial function
- Differential diagnosis of cerebellopontine angle masses
  - Schwannoma: (Vestibular 80 %, facial 1 %) T1/T2 isointense, enhances on T1 with contrast, greater internal auditory canal involvement
  - Meningioma (3 %) T1/T2 isointense, enhances on T1 with contrast, dural tail, often eccentric to internal auditory canal, hyperostosis at base on CT
  - Epidermoid (2 %) T1 hypointense, T2 hyperintense (high fluid content), does not enhance with contrast, has a high signal (restricted diffusion) on diffusion-weighted imaging
  - Paraganglioma: T1/T2 heterogenous hyper/hypointense foci, enhances on T1 with gadolinium "salt and pepper" appearance from flow voids
  - Arachnoid cyst: T1 hypointense, T2 hyperintense, does not enhance, low signal (limited restriction) on diffusion-weighted imaging
  - Metastatic tumors: T1/T2 isointense focal meningeal thickening, T1 with contrast bilateral linear or nodular meningeal enhancement
  - Endolymphatic sac tumor: T1 and T2 hyperintense, centered in the retrolabyrinthine, presigmoid space; enhances with contrast
  - Lipoma: T1 hyperintense, T2 hypointense, does not enhance and has signal suppression with fat saturation technique

- Vestibular schwannoma
  - Most common cerebellopontine angle tumor
  - Very rare malignant degeneration, typically sporadic and unilateral except when associated with neurofibromatosis type 2
  - Neurofibromatosis type 2
    - Autosomal dominant
    - Diagnosis requires one of the following: Bilateral vestibular schwannomas, unilateral vestibular schwannoma with a family history of neurofibromatosis type 2, or multiple brain tumors (schwannoma, meningioma, glioma) with a family history of neurofibromatosis type 2
  - Clinical findings: Asymmetric hearing loss, tinnitus, dysequilibrium (less common since slow growth allows for vestibular compensation), headache if large tumor size
  - Audiometry: Asymmetric sensorineural hearing loss, word discrimination may be disproportionately worse than pure tone thresholds; rollover (increased sound intensity results in decreased word discrimination), tone decay (sustained signal with decreased perception)
  - Balance function testing: Unilateral caloric weakness
  - Auditory brainstem response: May have prolonged wave I–III, I–V, III–V latencies, not as sensitive as MRI
  - Imaging
    - MRI: T1 with contrast shows homogenous enhancing mass in internal auditory canal and cerebellopontine angle
    - CT with contrast may miss smaller tumors
  - Histology: Antoni A: cells with parallel palisading nuclei; Antoni B: histologically less uniform
  - Management
    - Observe non-growing tumors (~40–50 %)
    - For growing tumor, options include surgery or radiotherapy
    - Stereotactic radiotherapy
      - Gamma-knife: Single fraction (commonly 12–14 Gy at tumor margin) given using stereotactic frame rigidly fixed to patient's head
      - Linear accelerator (LINAC, includes cyber-knife): Nonrigid image-guided system used to give stereotactic radiotherapy in hypofractionated doses
      - Goal is to prevent tumor growth
      - Better for older patients with multiple comorbidities
      - Intensity-modulated radiotherapy (non-stereotactic) has also been used with hypofractionated treatment schedules
    - Surgery better for younger healthy patients, larger tumors
    - Approaches
      - Translabyrinthine: Most direct access route to internal auditory canal and provides consistent facial nerve identification distally, avoids cerebellar retraction, sacrifices hearing
      - Retrosigmoid: Potential for hearing preservation but increased cerebellar retraction, risk of headaches
      - Middle fossa: Potential for hearing preservation but limited to intracanalicular tumors; higher risk of facial nerve paresis
    - Outcomes
      - Increased tumor size associated with decreased rates of facial nerve function and hearing preservation
      - Cerebrospinal fluid leak risk 10 % (similar across approaches)
      - Stereotactic radiotherapy often results in delayed sensorineural hearing loss; overall long-term outcomes similar to surgery
    - Management in neurofibromatosis type 2 patient
      - Screen relatives with MRI
      - Remove larger tumor with less hearing first

- Consider placement of auditory brainstem implant at the time of initial surgery if cochlear nerve sacrificed (generally gives poor hearing results)
- If able to preserve cochlear nerve at the time of surgery, consider cochlear implant
- Observe the only-hearing ear with serial MRI

- Endolymphatic sac tumor
  - Association with von-Hippel–Lindau syndrome (seen in 10–30 % of VHL patients)
  - Locally destructive and capable of intracranial seeding but does not metastasize distantly
  - Imaging: Presigmoid retrolabyrinthine lesion, posterior to internal auditory canal; T1 hyperintense foci within tumor, T2 heterogenous signal, T1 with contrast reveals heterogenous enhancement
  - Histology shows papillary features
  - Management: Surgery with or without radiotherapy
- Differential diagnosis of petrous apex masses
  - Cholesterol granuloma: T1 and T2 hyperintense from both high fluid and fat (cholesterol crystal) content, does not enhance
  - Asymmetric marrow: T1 hyperintense, does not enhance
  - Effusion/trapped fluid: CT air cell septations present; T1 hypointense, does not enhance; T2 hyperintense
  - Petrous apicitis: CT air cell coalesence; T1 intermediate signal, may have enhancing ring with abscess; otherwise does not enhance; T2 high signal
  - Aneurysm (carotid): Smoothly marginated bone-eroding lesion in the region of carotid canal, may have thrombus making contrast-enhanced scans appear heterogenous
  - Chondrosarcoma: Presents with headache and diplopia; CT shows irregular bone destruction, may have "popcorn" calcifications; enhances on T1 with contrast; treatment is surgical resection; radiotherapy (proton beam) may be of benefit in cases of subtotal resection, recurrent tumor
  - Chordoma: Usually midline with extension from clivus to petrous apex; CT shows destructive lesion with calcification foci, enhances on T1 with contrast, may be difficult to differentiate from chondrosarcoma
  - Schwannoma (trigeminal): T1 with contrast demonstrates homogenous enhancement in the region of Gasserian ganglion
  - Metastasis
- Cholesterol granuloma
  - Pathogenesis: Obstruction of air cell drainage pathways resulting in inflammation/hemorrhage, red blood cell breakdown and foreign body reaction to cholesterol crystals
  - Slowly expansive
  - Clinical findings: Usually asymptomatic, may expand to compress brainstem or temporal bone structures
  - Imaging: MRI T1/T2 hyperintense, no enhancement with contrast
  - Management
    - Observe if not causing symptoms
    - Surgical decompression for cranial neuropathies, brainstem compression
      - Transnasal approaches provide the widest access for lesions with extension medial to carotid
      - Lateral approaches
        - Infracochlear and infralabyrinthine affords only narrow access, but provides route for aeration and drainage through connection with middle ear/mastoid
        - Middle fossa approach does not provide a route for drainage or aeration
        - Translabyrinthine approach provides the widest exposure, but does not preserve hearing

- Differential diagnosis of diffuse temporal bone/skull base lesions
  - Fibrous dysplasia: Usually monostotic, progressive external auditory canal occlusion with conductive hearing loss, rarely causes sensorineural hearing loss, temporal bone with uniform "ground glass" appearance; treatment is generally observation, may consider canalplasty for conductive hearing loss or cholesteatoma formation behind canal stenosis
  - Paget's disease (*see causes of conductive hearing loss*)
- Eosinophilic granuloma
  - Mildest form of Langerhans cell histiocytosis
  - Affects older children and young adults
  - Typically affects mastoid, external auditory canal, petrous apex; may involve entire temporal bone
  - Presents as painful postauricular swelling, or with granulation and otorrhea of external auditory canal
  - CT shows areas of bony destruction, MRI T1 with contrast shows enhancement
  - Treatment
    - Conservative surgical excision
    - Low-dose radiotherapy
  - Rhabdomyosarcoma: Most common temporal bone malignancy of children; affects middle ear/mastoid, presents with chronic otalgia/otorrhea; treat with chemotherapy + surgery/radiotherapy depending on group and stage
  - Osteopetrosis (Albers–Schonberg disease): Symmetrical increase in bone density, narrows internal auditory canal and causes sensorineural hearing loss, narrows fallopian canal and causes facial weakness/paralysis, spares otic capsule; middle fossa decompression of facial nerve may be of benefit

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PART V
Head and Neck
Section Editor: Brett A. Miles, DDS, MD

Chapter 17
Thyroid and Parathyroid Surgery

Anthony G. Del Signore and Brett A. Miles

PEARLS

- Multiple staging systems employed, stage affected by age (45)
- Cervical metastatic disease very common in papillary thyroid cancer, does not usually affect prognosis
- Thyroid malignancy is usually treated surgically
- Key to successful parathyroid adenoma is accurate preoperative localization
- Intraoperative parathyroid hormone (PTH) assay used at most centers to verify adequate treatment

THYROID

Embryology

- Development begins between the 2nd and 11th week of gestation
- Three pharyngeal bodies: the median anlage and two lateral bodies
- Median anlage is derived from invagination of endoderm at foramen cecum
- The descent occurs along the thyroglossal duct (TGD) to the anterior trachea at the level of the 2nd and 4th tracheal rings
  - Incomplete descent: Ectopic thyroid (lingual thyroid)
    - 70 % without cervical thyroid → establish functional thyroid tissue
  - Incomplete involution of TGD: Pyramidal lobe
- Calcitonin-secreting parafollicular C cells arise within the ultimobranchial bodies from neural crest cells

ANATOMY

Macroscopic

- The thyroid gland is a bilobed structure connected by central isthmus
- Enveloped by deep cervical fascia and covered by strap muscles → posterior condensation of fascia → suspensory ligament of Berry

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Microscopic

- Each lobe is contained within a fibrous capsule
- Within each capsule there are a collection of follicles, composed of thyroglobulin-producing cells surrounding manufactured colloid material
  - Each follicle is surrounded by a basement membrane with a fine capillary network
  - Parafollicular cells (C cells) can also be found within the basement membrane

VASCULAR

Arterial supply (2 vessels)

- Superior thyroid artery from external carotid artery
- Superficial to external branch of superior laryngeal nerve
- Inferior thyroid artery from thyrocervical trunk from subclavian artery

Venous drainage (3 vessels)

- Inferior, middle, and superior thyroid veins → internal jugular

Lymphatic drainage

- Dominant drainage to level VI
- Secondary drainage basins: precricoid, delphian, paratracheal, pretracheal, perithyroidal.

NERVES

- Recurrent laryngeal nerves → enter at cricothyroid joint
  - Left: around aorta → ascends in tracheoesophageal groove
  - Right: around subclavian artery→ ascends in tracheoesophageal groove
  - Relationship with inferior thyroid artery
    - Branching patterns highly variable
    - Nerve generally anterior to artery
    - Nerve posterior to artery (50 % of patients on left)
    - Nerve between branches of artery (50 % of patients on right)
  - Simon triangle → assists in triangulating the recurrent nerve intraoperatively
    - Common carotid artery laterally
    - Esophagus medially
    - Inferior thyroid artery superiorly
- Superior laryngeal nerve
  - Originates nodose ganglion→ divides at hyoid cornu
  - Internal branch: sensation to supraglottis and pyriform sinus
  - External branch: motor innervation to inferior constrictor and cricothyroid muscles

HISTOLOGY

- Composed of follicles (single layer of epithelial cells) surrounding a colloid matrix
- Iodine important for synthesis→ thyroid hormone stored bound to thyroglobulin → unbound and released into circulation
  - T3: potent form, half-life is 1 day, majority converted in periphery
  - T4: correlates with TSH levels, half-life 6 days

BENIGN THYROID DISEASE

Hyperthyroidism

- Grave's disease → autoimmune, TSH receptor antibody → stimulation
- Toxic nodule/multi-nodular goiter
- Thyroiditis
- Exogenous hyperthyroidism
- Thyrotropin

Treatment of hyperthyroidism
- Propylthiouracil/methimazole
- Iodides
- Beta blockers
- Radioactive iodine
- Thyroidectomy
- Graves: total thyroidectomy (thyroid storm precautions)
- Toxic nodules: ipsilateral lobectomy

Hypothyroidism
- Hashimoto's thyroiditis
- Iodine deficiency
- Radiation induced
- Iatrogenic/postsurgical
- Drug (lithium, iodine)
- Central hypothyroidism

MALIGNANT THYROID DISEASE

Epidemiology

- Incidence of thyroid malignancy is 5–15 %, with 90 % being papillary and follicular cancers

Risk Factors for Thyroid Malignancy	
History of radiation exposure	Family history of thyroid carcinoma
Single dominant nodule >4 cm	Male gender
Age <20 and >70	Cervical nodules
Vocal fold immobility	Firmness to palpation

CLASSIFICATION

Papillary thyroid carcinoma
- Most common well-differentiated carcinoma
- Derived from follicular cells, form papillae, "Orphan Annie eye" nucleus
- Typically multicentric both within ipsilateral and contralateral lobe
- Lymphatic spread → cervical node metastasis possible: rates of 62 % central nodes and 25 % lateral nodes
- Histologic subtypes with worse prognosis: tall cell, columnar cell, diffuse sclerosing
- Noted extensive invasion of vascular and extrathyroidal tissue

Follicular thyroid carcinoma
- May exhibit minimal or wide vascular invasion, which affects prognosis
- Primarily hematogenous or direct spread with little lymphatic invasion

Hurthle cell carcinoma
- Tend to be older patients (60s)
- Variant of follicular carcinoma, oxyphilic cells noted
- Aggressive in nature, spread via lymphatics or hematogenous
- Increased risk for distant metastasis (30 %), with 40 % bone and 30 % lung

Medullary thyroid carcinoma
- Carcinoma of parafollicular C cells: sporadic and familial type
- Genetic component → RET testing recommended → multiple endocrine neoplasia (MEN) IIa and IIb
- Typically multifocal and metastatic disease noted

Anaplastic thyroid carcinoma

- 2 % of all thyroid carcinomas, but 15–39 % of all deaths
- Aggressive rapidly growing infiltrative thyroid mass, vocal cord paralysis
- Tend to be older patients (50–60s)
- Metastasis possible to lungs, liver, bones within weeks
- FNA typically shows necrosis and degeneration
- Survival rates low (20 %) at 1 year

WORK-UP

- Laboratory studies
  - TSH levels with reflexive T3/4
  - Serum calcitonin levels if concerned about medullary thyroid cancer
- Imaging
  - Ultrasound: allows identification, characterization, and trending of nodules, central and lateral lymphadenopathy
    - Findings suggesting malignancy: solid/hypoechoic appearance, increased vascularity, microcalcifications, irregular margins, absence of "halo" sign
    - Sensitivity 80 % and specificity 83 %
  - Ultrasound-guided fine needle aspiration (FNA): improves diagnostic yield and selection of appropriate nodules to aspirate
    - Typically recommended for nodules > 1 cm unless high-risk factors
    - Reported as benign, malignant, indeterminate, non-diagnostic which categorizes risk of malignancy
- Fiber-optic laryngoscopy: all patients should have vocal cords assessed preoperatively

STAGING

The staging of papillary thyroid cancer is somewhat controversial with multiple staging systems utilized at many centers (see below). Important items which confer greater risk are age >45, male, distant metastasis, non-papillary pathology (i.e., tall cell, anaplastic), advanced local disease/extracapsular extension.

TNM staging for differentiated thyroid carcinoma	
T1	Tumor diameter 2 cm or smaller
T2	Primary tumor diameter >2 to 4 cm
T3	Primary tumor diameter > 4 cm limited to thyroid/minimal extracapsular extension
T4A	Tumor of any size extending beyond thyroid capsule, invading subcutaneous soft tissue, larynx, trachea, esophagus, recurrent laryngeal nerve
T4B	Tumor invades prevertebral fascia or encases carotid artery, mediastinal nerves
CT4A	Intrathyroidal anaplastic carcinoma
CT4B	Anaplastic carcinoma with gross extrathyroid extension
N0	No metastatic nodes
N1A	Metastasis to level VI (pretracheal, paratracheal, prelaryngeal)
N1B	Metastasis to unilateral or bilateral or contralateral cervical or superior mediastinum
NX	Nodes not assessed at surgery
M0	No distant metastasis
M1	Distant metastasis

	Patient < 45 years old	Patient > 45 years old
Stages for differentiated thyroid cancer		
Stage I	ANY T, ANY N, M0	T1, N0, M0
Stage II	ANY T, ANY N, M1	T2, N0, M0
Stage III		T3, N0, M0
		T1–3, N1A, M0
Stage IVA		T4A, N0-N1A, M0
		T1–3, N1B, M0
		T4A, N1B, M0
Stage IVB		T4B, ANY N, M0
Stage IVC		ANY T, ANY N, M1
Stages for anaplastic carcinoma		
Stage IVA	T4A, ANY N, M0	
Stage IVB	T4B, ANY N, M0	
Stage IVC	ANY T, ANY N, M1	

OTHER STAGING SYSTEMS

AMES—age, metastases, extent of primary cancer, tumor size
High-risk features:

- Age: males >41, females >51
- Metastases: distant metastases
- Extent: papillary with extrathryoidal spread or follicular with major capsule invasion
- Size: ≥5 cm

Risk groups:

- Low risk—not high risk
- High risk—(1) any patient with metastases, or (2) high-risk age and either high-risk extent or size

Overall survival:

- Low risk 98 % (95 % disease-free survival (DFS)). High risk—54 % (45 % DFS)

AGES—age, tumor grade, tumor extent, tumor size

- Prognostic score = $0.05 \times$ age in years (except in pts < 40, then $y = 0$) + 1 (grade 2) or +3 (grade 3 or 4) +1 (if extrathyroidal) or +3 (distant mets) + $0.2 \times$ tumor size in cm
- Risk categories—0–3.99, 4–4.99, 5–5.99, >6 (median is 2.6)

20-year survival:

- <4 (99 %), 4–5 (80 %), 5–6 (33 %), >6 (13 %)

MACIS—metastasis, age, completeness of resection, invasion, size

- Prognostic score = 3.1 (age < 39 years) or $0.08 \times$ age (if >40) + $0.3 \times$ tumor size in cm + 1 (if incompletely resected) +1 (if locally invasive) +3 (if distant mets)
- Risk categories—0–5.99, 6–6.99, 7–7.99, >8

20-year survival:

- <6 (99 %), 6–7 (89 %), 7–8 (56 %), >8 (24 %)

MANAGEMENT

Papillary thyroid carcinoma

- Some controversy—total thyroidectomy versus hemithyroidectomy
- High risk: distant disease, extrathyroidal papillary cancer, capsular invasion, age > 40 (men) and >50 (female)
- Hemithyroidectomy for incidental papillary microcarcinoma (<5 mm)
- Central compartment and paratracheal neck dissection with + nodal disease or in high-risk patients

Follicular thyroid carcinoma
- Partial thyroidectomy with pathologic evaluation, if carcinoma proceed to completion thyroidectomy
- Spread via hematogenous or direct extension, may eliminate the need for elective or prophylactic neck dissection

Hurthle cell carcinoma
- Total thyroidectomy
- Central neck dissection in the presence of + nodal disease

Medullary thyroid carcinoma
- Family RET genetic testing and counseling
- Total thyroidectomy with central neck dissection + selective neck dissection
- With + lateral disease, imperative to perform level II–V
- Postoperative neck ultrasound, calcitonin, and CEA testing

Anaplastic thyroid carcinoma
- Aggressive multimodal therapy in early stage: total thyroidectomy, intensity-modulated radiation therapy (IMRT), and adjuvant chemotherapy
- Palliative therapy (tracheostomy controversial due to poor prognosis) for advanced lesions

POSTSURGICAL MANAGEMENT

Radioactive iodine
- For differentiated thyroid cancer, indicated for remnant ablation, adjuvant therapy, treatment of residual or metastatic disease
- Facilitates monitoring of thyroglobulin levels
- Some controversy for routine use postoperatively regarding utility and dosage, some risk of associated hematologic malignancy

TSH suppression
- Used in intermediate- and high-risk patients, maintain TSH at or slightly below lower limit of normal with supraphysiologic doses of T4 to decrease recurrence
- External beam irradiation
  - Consider for patients over 45 with extrathyroidal extension and high likelihood of residual disease

Surveillance
- Serum thyroglobulin measured every 6–12 months
- Neck ultrasounds examining surgical bed, central and lateral lymph nodes

PARATHYROID

Embryology
- Development starts at 5th week of development
- Derived from endoderm of 3rd and 4th pharyngeal pouches
- Inferior glands arise from 3rd pouch and migrate with thymus
- Long descent → large area of possible ectopic placement
- Superior glands arise from 4th pouch
- Shorter descent→ much less variability

ANATOMY

- Paired superior and inferior glands (4) → typically 70–80 % are found to be symmetric
- Typically weigh 35–40 mg with average diameter of 3–8 mm
- Variability of location
- Inferior: large area from angle of mandible to pericardium
- Most common ectopic location anterior mediastinum
- Typically found with plane drawn along recurrent laryngeal nerve
- 1 cm inferior, lateral or posterior to inferior pole of thyroid

- Superior: little variation in descent
- 85 % can be found at posterior aspect of thyroid lobe in 1 cm above crossing of inferior thyroid artery and recurrent nerve

EPIDEMIOLOGY

- Adenoma prevalence in range of 0.1–0.4 %, with highest incidence at 50–60 years
- 80–85 % present with single adenomas, 10–15 % with multi-gland disease, 5 % with double adenoma, and 1 % with parathyroid cancer
- Higher frequency: women and history of neck irradiation
- Primary hyperparathyroidism most common cause of hypercalcemia in outpatient setting

PATHOPHYSIOLOGY

- Parathyroid glands detect changes in serum calcium via calcium-sensing receptor
  - Regulation of calcium levels via production of PTH
  - PTH in turn acts on several receptors systemically up or down regulating calcium metabolism
- Primary hyperparathyroidism from an adenoma results in uninhibited production of PTH→ elevated serum calcium
- Must rule out other causes of hyperparathyroidism: chronic renal disease, thiazide diuretic use, lithium use, familial hypocalciuric hypercalcemia (FHH), MEN I, MEN IIa, hyperparathyroidism-jaw tumor syndrome, neonatal severe primary hyperparathyroidism, parathyroid cancer

PRIMARY HYPERPARATHYROIDISM

Presentation

- Primary presenting sign: hypercalcemia with 80 % asymptomatic or vague sx
  - Neurologic sx: fatigue, depression, memory loss, decreased concentration, sleep changes
  - Renal sx: nephrolithiasis (20 % present with sx), hypercalciuria
  - Bone sx: bony pain, osteitis, osteopenia, osteoporosis, fractures, muscle weakness

DIAGNOSIS/WORK-UP

- Serum calcium levels, PTH levels, vitamin D, phosphorus, creatinine clearance, 24-h urine calcium
- Bone densitometry
- Neck imaging not indicated for diagnosis, but helpful for localization
- High-resolution ultrasound: inexpensive and allows concurrent study of the thyroid gland as 18 % may have synchronous thyroid disease
- Sensitivity 72–85 %
- Technetium 99 Sestamibi: avid uptake by adenomatous and hyperplastic parathyroid glands
- Sensitivity 76–88 %
- Combination of techniques helps to increase sensitivity to 95 %

2008 NIH Guidelines for Surgical Treatment of Asymptomatic Primary Hyperparathyroidism

- Serum Ca > 1 mg/dl above upper limit of normal
- CrCl <30 % of age-matched normal subjects
- Diminished bone density (T score < –2.5 or fragility fracture
- Age < 50 years
- Difficult follow-up

- Newer MRI and 4-D CT functional imaging have improved localization of adenomas especially for ectopic locations
- Multi-glandular disease difficult to image accurately

TREATMENT

- Intraoperative parathyroid hormone assay: allows the determination of continued disease and helps to prevent missed adenoma
- Utilize the Miami criteria: 50 % or greater drop from highest PTH level to PTH level measured 10 min post gland excision
- Accuracy of 97 %
- Minimally invasive parathyroid surgery: 2.5 cm incision over anterior neck
- 97 % success rate → preoperative localization is key
- Unilateral neck exploration if needed to explore and converted to bilateral if gland cannot be located
- Complications
  - Persistent hyperparathyroidism
  - Recurrent laryngeal nerve injury
  - Transient postoperative hypocalcemia

PARATHYROID CARCINOMA

- Frequency of 1 % of patients with primary hyperparathyroidism, prevalence of 0.005 % of all cancers, with typical age of onset 40–50s
- Majority of tumors are functional (secrete PTH), nonfunctional tumors present as expanding neck mass with late diagnosis and typically have poorer prognosis
- Elevated calcium and PTH levels markedly elevated compared to adenomas
- Intraoperative appearance typically hard lobulated fibrous mass
- En bloc resection is key with resection of ipsilateral thyroid lobe with isthmus, and paratracheal and central neck dissection, as adjuvant therapy has been disappointing
- Tendency for spread to local lymph nodes but can also metastasize to lung, liver, and bone
- 5- and 10-year survival are 85 and 50–75 %, respectively

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Chapter 18
Salivary Gland Diseases

Fred Y. Lin

PEARLS

- Saliva is antibacterial via secretory IgA, lactoferrin, salivary peroxidase, and lysozymes.
- Necrotizing sialometaplasia is commonly mistaken as malignancy histopathologically (pseudoepitheliomatous hyperplasia) and resolves without intervention.
- The tubular form for adenoid cystic carcinoma has the best prognosis and the solid form has the worst prognosis.

ANATOMY

Parotid Gland

- Largest salivary gland.
- Derived from first pharyngeal pouch.
- Overlies the masseter muscle and sternocleidomastoid muscle.
- The facial nerve divides the gland into a deep lobe and a superficial lobe.
- The parotid gland fascia consists of the superficial layer of the deep cervical fascia.
- Consists of basophilic and serous cells.
- Stensen's duct runs 1 cm inferior to the zygoma and opens opposite to the upper second molar.
- Venous drainage to the retromandibular vein.
- Parasympathetics.
  - Mediate secretion of saliva.
  - Nucleus—inferior salivatory.
  - Preganglionics—CN IX, Jacobsen's nerve, lesser superficial petrosal nerve.
  - Ganglion-otic.
  - Postganglionic—auriculotemporal nerve (V3).
- Sympathetics.
  - Modulates composition of saliva.
  - Nucleus—superior salivatory.
  - Preganglionics—sympathetic chain.
  - Ganglion—superior cervical.
  - Postganglionic—runs with blood vessel supplying the gland.
    - External carotid artery.

Submandibular gland

- Lies within the submandibular triangle and below the mylohyoid muscle.
- Second largest salivary gland.
- Gland is enveloped by the superficial layer of the deep cervical fascia.
- The facial artery hooks over the posterior belly of the digastric to enter the gland. It runs medial to the digastric muscle.

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- The lingual artery runs deep into the digastric muscle along the lateral surface of the constrictors and then goes medial and anterior to the hyoglossus.
- CN XII (hypoglossal) runs deep into the digastric tendon and the mylohyoid along the hyoglossus.
- Consists of serous and mucinous cells (mixed).
- Parasympathetics (same for sublingual glands).
  - Nucleus—superior salivatory.
  - Preganglionics—nervus intermedius, chorda tympani.
  - Ganglion—submandibular.
  - Postganglionics—lingual nerve.
- Sympathetics.
  - Same as parotid gland.
  - Postganglionics—facial artery (submandibular) and lingual artery (sublingual).
- Marginal mandibular nerve within the superficial layer of the deep cervical fascia.
  - Muscles innervated—depressor of anguli oris, depressor of labii inferioris, orbicularis oris, and mentalis.

Sublingual gland

- Smallest named salivary glands.
- Mucinous cell type.
- Opens into ducts of Rivinus.

Saliva

- Lubricates and moistens food.
- Protects mucosa from desiccation and chemical irritation.
- Antibacterial via secretory IgA, lactoferrin, salivary peroxidase, and lysozymes.
- Prevention of dental caries.
- 1–1.5 L in 24-h period.
- Non-stimulated flow primarily from submandibular gland.
  - Mixed serous and mucinous saliva.
- Parotid gland supplies the majority of stimulated salivary flow.
  - Serous saliva.

DIAGNOSTICS

- Sialography.
  - Low-viscosity contrast study of a salivary gland.
  - May trigger acute sialoadenitis.
  - Indications:
    - Suspicion of chronic, recurrent, or nonspecific sialoadenitis.
    - Autoimmune disease (Sjogren's).
    - Sialolithiasis.
    - Postoperative or post-trauma.
  - Contraindications:
    - Iodine allergy.
    - Acute sialoadenitis.
  - Findings:
    - Chronic inflammation.
      - Saccular dilatation of terminal ducts and acini.
      - Segmental strictures and dilatation.
      - Pseudocyst formation.
- Computed tomography (CT).
- Magnetic resonance imaging (MRI).
- Ultrasound.
- Sialoendoscopy.
- Fine needle aspiration (FNA).

SALIVARY GLAND DISEASES

- Acute sialoadenitis
  - Secondary to salivary obstruction or stasis.
  - Mumps virus is the most common cause of acute parotid enlargement.
    - Peak incidence at 4–6 years.
    - Unilateral or bilateral.
    - Symptoms—fever, malaise, headache.
    - Associated sudden sensorineural hearing loss, pancreatitis, meningitis, and orchitis.
    - Dx—antibodies to hemagluttinin, mumps antigens, and viral isolation from urine.
  - *S. aureus* most common bacterial cause.
  - Parotid most commonly infected due to stasis in serous secretions which are less bacteriostatic than mucinous secretion.
  - Treatment—rehydration, warm compresses, antibiotics, sialogogues.
- Sialolithiasis
  - More common in submandibular gland.
    - High mucin content.
    - Alkaline pH.
    - Higher percentage of organic matter.
    - Low carbon dioxide level.
    - High concentration of calcium and phosphate salts.
    - High phosphatase enzyme content.
    - Length and irregular course of Wharton's duct.
    - Dependent position of gland and ducts.
    - Duct orifice smaller than lumen.
  - 90 % of submandibular calculi are radiopaque.
  - 90 % of parotid calculi are radiolucent.
  - Treatment—gland massage, incision and drainage (not commonly performed in relation to parotid gland due to possible damage to facial nerve from direct incision), gland excision, sialoendoscopy.
- Uveoparotid fever (Heerfordt's disease)
  - Variant of sarcoidosis (third to fourth decade).
  - Parotitis, uveitis, CN VII paralysis in 50 % of patients.
  - Diagnosis confirmed with ACE levels.
  - Treatment—steroids and ocular care.
- Sjogren's syndrome
  - See Systemic/Inflammatory chapter.
- Recurrent parotitis
  - Secondary to sialectasis, autoimmune disease (Mikulicz's disease, Sjogren's) or non-autoimmune (Mikulicz's syndrome—recurrent sialoadenitis, sialosis, multi-nodular gland).
- Benign lymphoepithelial cysts
  - Associated with HIV.
  - Differential diagnosis—branchial cleft cyst, epidermoid cyst, dermoid cyst, mucocele, sialocele (pseudocyst).
  - Treatment—aspiration or excision.
- Necrotizing sialometaplasia
  - Inflammatory process that mimics malignancy.
  - Presents as ulceration or nodular lesion of the minor salivary glands.
  - Easy to mistake as malignancy histopathologically (pseudoepitheliomatous hyperplasia).
  - Treatment—self-resolution.

BENIGN MASSES

- Common salivary gland tumors in children:
  - Hemangioma.
  - Pleomorphic adenoma (most common).

  - Lymphangioma.
  - Neurogenic.
- Risk factors for salivary gland neoplasms:
  - Low-dose radiation.
  - Tobacco—associated with Warthin's.
  - Occupational exposure to wood dust.
- Cellular origin of parotid tumors:
  - Acinic cell carcinoma—acinar cells.
  - Adenoid cystic—myoepithelial cells.
  - Pleomorphic adenoma—myoepithelial and intercalated cells.
  - Adenocarcinoma—intercalated cells or striated duct.
  - Warthin's tumor—striated duct.
  - Oncocytoma—striated duct.
  - Squamous cell carcinoma—excretory duct.
  - Mucoepidermoid carcinoma—excretory duct and intercalated ducts.
- Pleomorphic adenoma
  - Most common in parotid gland and most common salivary gland tumor.
  - Epithelial and mesenchymal elements with mucoid, chondroid, myxoid, and osteoid components.
  - Treatment—surgical resection.
- Warthin's tumor (papillary cystadenoma lymphomatosum)
  - Most commonly in the parotid gland.
  - 10 % bilateral, 10 % multicentric.
  - FNA with thick turbid fluid.
  - High mitochondrial content with biphasic composition (abundant lymphoid sheets and lining epithelium with bilayer of oncocytic papillary cells).
  - Treatment—surgical resection.
- Oncocytoma
  - Most commonly in the parotid gland.
  - Slow growing, well circumscribed, but not encapsulated.
  - High density of mitochondria with sheets of oncocytic cells.
  - Treatment—surgical resection.
- Monomorphic adenoma
  - Most commonly in minor salivary glands.
  - No mesenchymal stromal component (unlike pleomorphic adenomas).
  - Basal cell is the most common type.
  - Other types: Clear cell, membranous, canalicular, myoepithelioma adenoma, glycogen-rich.

SALIVARY GLAND MALIGNANCIES

- Mucoepidermoid carcinoma
  - Located in the parotid most commonly, then minor salivary gland, and submandibular gland.
  - Associated with radiation exposure.
  - Low grade vs. high grade depends on mucinous-to-epidermoid cell ratio.
  - Low grade
    - Higher amount of mucinous cells.
    - Similar to benign lesion but capable of local invasion and metastasis.
    - Treatment—surgical excision.
  - High grade
    - Low ratio of mucinous to epidermoid cells with high content of solid nests of cells.
    - Behaves similar to squamous cell carcinoma.
    - Treatment—surgical excision with elective neck dissection (possible adjuvant radiation).

- Adenoid cystic carcinoma
  - Most common malignancy of submandibular gland and minor salivary glands.
  - High-grade tumor with perineural spread.
  - Infiltrates surrounding tissue with partial encapsulation or no capsule.
  - Types:
    - Solid—worst prognosis.
    - Tubular—best prognosis.
    - Cribriform—most common subtype and intermediate prognosis (Swiss cheese histopathology).
  - Treatment—surgical resection with consideration for adjunctive therapy.
  - Prognosis—typical course is relatively good 5-year survival, much poorer 10–15-year survival due to late metastasis.
- Acinic cell carcinoma
  - Most commonly in parotid gland.
  - Derived from serous cells.
  - Amyloid, a common finding histologically.
  - Low-grade tumor.
  - Treatment—surgical resection.
- Adenocarcinoma
  - High grade and aggressive.
  - Most commonly in minor salivary glands.
  - Treatment—surgical resection with elective neck dissection (possible adjuvant radiation).
- Polymorphous low-grade adenocarcinoma
  - Low grade.
  - Second most common malignancy of the minor salivary gland (palate and buccal mucosa).
  - Treatment—surgical resection.
- Others
  - Carcinoma, e.g., pleomorphic.
  - Squamous cell carcinoma.
  - Malignant oncocytoma.
  - Salivary duct carcinoma.
  - Lymphoma.
  - Metastases.
  - Malignant lymphoepithelial lesion.
- Signs suggesting malignancy
  - Facial nerve involvement.
  - Fixation to underlying or overlying structures.
  - Overlying ulceration.
  - Cervical adenopathy.
  - Metastatic disease.
  - Large size (>5 cm).
- Indications for neck dissection
  - Cervical metastases.
  - Tumors >4 cm.
  - High-grade malignancies.
- Indications for adjuvant radiotherapy
  - High-grade malignancies.
  - Unresectable disease.
  - Ulceration.
  - Tumors >4 cm.
  - Multiple tumor nodules.
  - Facial nerve involvement.
  - Extension to extraglandular tissue.

- Frey's syndrome
  - Gustatory sweating from aberrant reinnervation of post-ganglionic parasympathetic nerves to the sweat glands.
  - Diagnosis with starch iodine test.
  - Treat with scopolamine cream, antiperspirant, Jacobsen nerve section, SCM muscle flap, or grafting between skin and parotid bed.

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Chapter 19
Head and Neck Lymphoma and Sarcoma

Brett A. Miles

PEARLS

- The treatment of lymphoma is quite complex (multimodal) and requires accurate diagnosis including open lymph node biopsy with flow cytometry analysis and architecture
- Unfavorable sarcoma histology—angiosarcomas, rhabdomyosarcomas especially of the alveolar morphological type, and osteosarcomas are devastatingly aggressive tumors with an extremely high incidence of distant metastasis
- Chondrosarcoma may present as a slowly expanding mass of the laryngeal or the cricoid cartilages; treatment is surgical resection
- Angiosarcoma is an aggressive vascular malignancy that often presents in the cutaneous scalp of older Caucasian males; prognosis is poor

LYMPHOMA

Epidemiology

- Lymphoma can be nodal or extranodal
- Hodgkin lymphoma (HL) or non-Hodgkin lymphoma (NHL)
- 25 % extranodal lymphomas occur in the head and neck, and 8 % of findings on supraclavicular fine-needle aspirate biopsy yield a diagnosis of lymphoma
- Typically present as one or more slowly enlarging rubbery lymph nodes in the neck
- Chromosomal abnormalities
  - Aneuploidy occurs in HL
  - Translocations and deletions in NHL (*c-myc* translocation of Burkitt lymphoma and the *bcl-2* translocation in follicular lymphomas)
- Infectious agents implicated
  - Epstein–Barr virus
  - HIV-1
  - *Helicobacter pylori*
  - Human T-cell lymphotropic virus-1 (HTLV-1)
  - Hepatitis B and C viruses
  - Human herpes virus 8
  - *Borrelia burgdorferi*
  - *Chlamydia psittaci*
  - *Campylobacter jejuni*
- Chronic inflammation increases the risk of lymphoma, i.e., MALT lymphoma and Sjögren's syndrome

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- Hashimoto disease increases a patient's risk of thyroid lymphoma approximately 70×, usually aggressive NHL
- Immunosuppression following organ transplantation increases the risk of lymphoma and may regress after cessation of immune suppression (EBV-associated NHL)
- HIV infection significantly increases the incidence of lymphoma. The risk is increased approximately 1,000-fold for Burkitt lymphoma and 400-fold for aggressive lymphoma

Hodgkin lymphoma

- Extends by means of contiguous nodal spread; therefore, it is often localized and frequently occurs in the mediastinum
- Incidence of HL is increased tenfold in same-sex siblings

Non-Hodgkin lymphoma

- Tends to spread hematogenously and is often systemic at diagnosis
- NHL may present as a mass in the oropharynx or nasopharynx (Waldeyer's ring) or parotid
- Primary lymphoma of the oral cavity usually arises in the tongue base and is more rare than a cervical presentation
- Lymphoma masses tend to be rubbery, firm, and nonulcerating
- Worse prognosis relative to HL

Extranodal NK/T-cell lymphoma

- Ulcerative destructive lesion of the nose, sinuses, and face
- Associated with Epstein–Barr virus and worse prognosis compared with that of patients with B-cell lymphoma
- Presents as a nasal mass, epistaxis, and/or nasal obstruction and pain

Burkitt lymphoma

- Endemic (African form) manifests as a jaw or an abdominal tumor that spreads to extranodal sites
- Nonendemic (North American form) has an abdominal presentation with massive disease

Imaging

- Standard protocol is CT scanning of the chest, abdomen, and/or pelvis
- CT/MRI often indicated for head and neck lymphoma for accurate staging and therapy
- Positron emission tomography (PET) scanning indicated for staging of disease, detection of recurrence, and monitoring treatment response

Evaluation and Histology

- Initial evaluation is generally fine-needle aspiration cytology to differentiate from other malignancies
- Biopsy should be considered when a firm lymph node is larger than 1 cm and is not associated with infection and persists longer than 4 weeks
- May also have painless or mildly tender peripheral adenopathy in cervical, axillary, inguinal, and femoral regions
- Flow cytometry may be utilized for preliminary classification; however often excisional lymph-node biopsy is warranted for architecture for HL and NHL, submitted fresh for analysis
  - Immunohistochemical analysis identifies monoclonal antibody targets such as CD20 (rituximab) or CD52 (alemtuzumab)
  - Diffuse large B-cell lymphoma, fluorescent in situ hybridization (FISH) for t(8;14)/*MYC* translocation which is associated with a poor prognosis
- Bone marrow aspiration and lumbar puncture are also frequently indicated to detect disseminated disease in the bone marrow or CSF via flow cytometry
- Diagnostic tonsillectomy may be indicated if lymphoma of the tonsils is suspected in the setting of tonsillar asymmetry

Staging

Ann Arbor staging system

Stage I—Involvement of a single lymph node region or lymphoid structure.

Stage II—Involvement of two or more lymph node regions on the same side of the diaphragm or localized contiguous involvement of only one extralymphatic site and lymph node region.

Stage III—Involvement of lymph node regions or lymphoid structures on both sides of the diaphragm and possibly the spleen.

Stage IV—Disseminated involvement of one or more extralymphatic organs with or without lymph node involvement and/or involvement of the bone marrow or the liver. Bone involvement is distinct from bone marrow involvement as frank bone involvement is defined as disseminated disease.

Letter designations

A—Asymptomatic.

B—Constitutional symptoms: Persistent or recurrent fever with temperature higher than 38 °C or by recurrent and drenching night sweats within 1 month, or by unexplained loss of more than 10 % the person's body weight within 6 months.

E—Extranodal: Direct extension into extralymphatic organ from an adjacent lymph node.

X—Bulky disease: Width of the mediastinal tumor is greater than one-third the transthoracic diameter at T5/6, or the diameter of the tumor diameter is larger than 10 cm.

Management

- Generally treated with chemotherapy ± radiotherapy
- Occasionally with early local disease radiotherapy alone may be an option
- Radiotherapy is the primary treatment modality in early-stage NK/T-cell lymphomas

Hodgkin Lymphoma

- ABVD is a regimen of doxorubicin (Adriamycin), bleomycin, vinblastine, and dacarbazine now considered the standard of care in HL (70 % event-free survival in favorable stages)
- BEACOPP (i.e., cyclophosphamide, doxorubicin, etoposide, procarbazine, prednisolone, vincristine, and bleomycin with granulocyte colony-stimulating factor) are being used for advanced HL
- Stanford V regimen (mechlorethamine, doxorubicin, vinblastine, vincristine, bleomycin, etoposide, and prednisone) with consolidative radiotherapy to bulky sites produces a progression-free survival of over 80 %

Non-Hodgkin Lymphoma

Indolent B-cell lymphoma:

- Multiple subtypes are generally considered incurable with conventional therapy
- Characterized by an indolent course, patients may remain stable for several years without therapy
- Watch-and-wait strategy is often used
- Chemotherapy for symptomatic disease, hypersplenism, or bone marrow infiltration causing cytopenia

Aggressive B-cell lymphomas:

- These include diffuse large BCL, Burkitt lymphoma, mantle-cell lymphoma, and lymphoblastic lymphoma
- Potentially curable
  - Chemotherapy and consolidation radiotherapy has 5-year survival rates of up to 80 % depending on stage
  - Role of radiation is questionable with newer immunochemotherapy regimens (i.e., rituximab (DA-EPOCH-R)) but may be useful in certain situations

- Burkitt lymphoma is a highly aggressive B-cell lymphoma and is curable and treated with systemic and intrathecal chemotherapy
- Lymphoblastic lymphoma is usually of the T-cell phenotype and usually affects the mediastinum; this is curable with aggressive chemotherapy
- Mantle-cell lymphoma is a B-cell lymphoma that has a moderately aggressive clinical course, rarely curable
- Patients with HIV infection have a significantly increased incidence of lymphoma. The risk is increased approximately 1,000-fold for Burkitt lymphoma and 400-fold for aggressive lymphoma

T-cell lymphomas:

- Rare in the head and neck region relative to B-cell lymphomas
- Associated with HTLV-1
- Extranodal NK/T-cell lymphoma, nasal type
  - Nasal cavity, nasopharynx, and palate
  - Diagnosis difficult due to diffuse thickening
  - Localized disease treated with radiation
  - The prognosis for those with disseminated disease is poor
  - Common in East Asia and Latin America
- Anaplastic large-cell lymphoma (ALCL) tends to occur in young patients; long-term survival rate is approximately 70 % with chemotherapy
- Angioimmunoblastic T-cell lymphoma is usually associated with immunodeficiency. It tends to be aggressive with poor outcomes

HEAD AND NECK SARCOMA

Epidemiology

- Less than 10 % of all sarcomas occur in the head and neck and account for 1 % of all head and neck tumors
- Most head and neck sarcomas arise sporadically with no identifiable causative factor
- Sarcomas can be divided into those arising in the soft tissue and those arising in bone and classified based on their histological cell of origin
- Malignant fibrous histiocytoma (MFH) and liposarcoma are the most common of all adult sarcomas in soft tissue
- Exposure to radiation can cause late-onset radiation-induced sarcoma of the head and neck
- There may be an association between sun exposure and cutaneous angiosarcoma of the head and neck in Caucasians
- The most common site of distant metastatic disease is the lungs

Staging

AJCC soft tissue sarcoma

Primary tumor
TX Primary tumor cannot be assessed.
T0 No evidence of primary tumor.
T1—<5 cm in greatest dimension, T1a—superficial tumor, T1b—deep tumor.
T2—>5 cm in greatest dimension, T2a—superficial tumor, T2b—deep tumor.

Grade (differentiation, mitotic count, tumor necrosis).
GX—grade cannot be assessed.
G1—grade 1
G2—grade 2
G3—grade 3

Regional Lymph Nodes
NX cannot be assessed.
N0—no regional lymph node metastasis.
N1—regional lymph node metastasis.

Distant metastases
M0—no distant metastases.
M1—distant metastases.

Stage grouping:
Stage IA—T1aN0M0 G1,GX; T1bN0M0 G1,GX.
Stage IB—T2aN0M0 G1,GX; T2bN0M0 G1,GX.
Stage IIA—T1aN0M0 G2,G3; T1bN0M0 G2,G3.
Stage IIB—T2aN0M0 G2; T2bN0M0 G2.
Stage III—T2aN0M0 G3; T2bN0M0 G3; Any T,N1,M0, Any G.
Stage IV—Any T Any N M1 Any G.

AJCC osteosarcoma/chondrosarcoma

Primary Tumor
TX Primary tumor cannot be assessed.
T0 No evidence of primary tumor.
T1—<8 cm in greatest dimension.
T2—>8 cm in greatest dimension.
T3—Discontinuous tumor in primary site.

Grade (differentiation, mitotic count, tumor necrosis).
GX—grade cannot be assessed.
G1—grade 1
G2—grade 2
G3—grade 3

Regional lymph nodes
NX cannot be assessed.
N0—no regional lymph node metastasis.
N1—regional lymph node metastasis.

Distant metastases
M0—no distant metastases.
M1—distant metastases.
    M1a—lung.
    M1b—other distant sites.

Stage grouping
Stage IA—T1aN0M0 G1,GX; T1bN0M0 G1,GX.
Stage IB—T2aN0M0 G1,GX; T2bN0M0 G1,GX.
Stage IIA——T1aN0M0 G2,G3; T1bN0M0 G2,G3.
Stage IIB—T2aN0M0 G2; T2bN0M0 G2.
Stage III—T2aN0M0 G3; T2bN0M0 G3; Any T,N1,M0, Any G.
Stage IVA—Any T N0 M1a Any G.
Stage IVB—Any T N1 M1b Any G.

Malignant Fibrous Histiocytoma

Epidemiology

- Heterogeneous group of sarcomas without a specific line of differentiation
- Exposure to radiation is a very common etiology for malignant fibrous histiocytoma (MFH), grave prognosis
- 3–10 % occur in head and neck

Presentation
- Present as a mass in the scalp, neck, parotid, skull base, or orbit
- May have associated pain, compression
- Skin involvement common

Histology
- Very difficult, diagnosis of exclusion
- Most lesions of high grade
- Two more common types:
  - Undifferentiated high grade
  - Pleomorphic sarcoma and myxofibrosarcoma

Imaging
- CT and MRI to evaluate bone and soft tissue involvement, respectively

Treatment
- Surgery is the mainstay of treatment
- Adjuvant chemotherapy and radiotherapy may improve outcomes but this is not clear due to lack of data

Rhabdomyosarcoma

Epidemiology
- Fifth most common cancer in the pediatric age group
- Worse outcome in adults
- Rare aggressive variant spindle cell rhabdomyosarcoma (RMS) found in adults has a propensity for the head and neck

Presentation
- May involve orbit (most common), nasopharynx, nasal cavity, paranasal sinuses, and temporal bone (most common primary temporal bone malignancy in children)
- High incidence of lymph node and distant metastasis

Histology
- Four subtypes:
  - Embryonal (70 %) early age, better prognosis
  - Alveolar (20 %), poor prognosis
  - Botryoid, and pleomorphic (10 %)

Imaging
- CT and MRI to evaluate bone and soft tissue involvement, respectively
- PET/CT useful to rule out metastatic disease

Treatment
- Multimodal approach consisting of multi-agent chemotherapy, surgery, and radiation therapy
- Nonsurgical approach if unresectable due to critical structure involvement
- 5-year survival 60 %
- Orbital subsite is favorable compared to parameningeal sites

Angiosarcoma

Epidemiology
- Typically occurs in elderly male
- Arise in the dermal layers of the scalp and facial skin and spread in a radial fashion with multifocal pattern
- Raised purplish-red papule, classically multifocal
- Difficult to achieve clear surgical margins, high risk of local recurrence
- May arise spontaneously or secondary to external radiation, exogenous toxins, or immunosuppression
- 5-year survival rates of 10–30 % for high-grade angiosarcoma

Presentation
- Aggressive disease with a 10–20 % reported rate of lymph node metastases
- Typically spread hematogenously with lungs most common metastatic site

Histology
- Pleomorphic, multilayered malignant endothelial cells with aberrant and chaotic architecture and abnormal vascular channels
- Distinguished from hemangiomas by the presence of "collagen dissection pattern" and formation of papillae

Imaging
- CT and MRI to evaluate bone and soft tissue involvement, respectively
- PET/CT useful to rule out metastatic disease

Treatment
- Combination of wide surgical excision and neck dissection with postoperative radiation ± chemotherapy
- Chemotherapy and radiation for metastatic or unresectable disease
- Targeted vascular therapy (bevacizumab) with monoclonal antibodies is promising

Liposarcoma

Epidemiology
- Only 2–4 % of liposarcomas arise in the head and neck
- The neck is the most common location
- Different from other sarcomas in their propensity to metastasize to bone

Presentation
- Deep soft tissue expanding mass
- Rarely painful until large or compressive

Histology
- Lipoblasts often present; these are cells with an abundant clear multi-vacuolated cytoplasm and an eccentric darkly staining nucleus that is indented by the vacuoles
- Round-cell or pleomorphic tumors associated with poor prognosis
- Myxoid liposarcomas have a unique molecular signature characterized by the presence of the t(12; 16)(q13; p12)
  - Late-onset soft tissue or late-onset bone metastases
  - High radiosensitivity

Imaging
- CT and MRI to evaluate bone and soft tissue involvement, respectively
- PET/CT useful to rule out metastatic disease

Treatment
- Radical surgical excision and adjuvant radiotherapy

Synovial Sarcoma

Epidemiology
- Aggressive slowly growing tumor of young adults
- Very rare in head and neck subsites
- Synovial sarcomas are tumors of pluripotent mesenchymal cells that do not arise in the synovium but microscopically bear resemblance to normal synovium (name is a misnomer)
- High-grade sarcoma with poor survival

Presentation
- Hypopharynx (most common), orbit, larynx, oropharynx
- Dyphagia, pain, and hoarseness may occur
- May present as a painless mass in the neck or the upper aerodigestive tract

Histology
- Uniform spindle cells with high nuclear-to-cytoplasmic ratio
- Two types of SS:
  - Monophasic which consists of spindle cells
  - Biphasic includes epithelial cells with spindle cells
- Chromosomal alterations between X and 18

Imaging
- CT and MRI to evaluate bone and soft tissue involvement, respectively
- PET/CT useful to rule out metastatic disease

Treatment
- Treatment is surgical resection
- Adjuvant radiation and chemotherapy may be helpful but remain unproven due to small number of cases in the head and neck

Dermatofibrosarcoma Protruberans (DFSP)

Epidemiology
- Low-grade tumor with a predilection for local recurrence
- Can undergo fibrosarcomatous transformation after a span of many years
- Predominantly adult presentation

Presentation
- Commonly cutaneous presentation seen in the scalp, neck
- Distant metastasis rare but may develop in up to 5 % of patients
- Cutaneous pink to red-bluish painless trophic and/or sclerotic plaque-like mass that develops into lumpy nodular protuberant tumor.

Histology
- Unclear origin may be fibroblastic, neuroectodermal, and histiocytic or from pluripotential progenitor cells
- Characterized by the arrangement of spindle-shaped tumor cells in a "cartwheel" pattern
- Honeycomb pattern of infiltration into the subcutaneous fat may project up to 3 cm peripherally

Imaging
- CT and MRI to evaluate bone and soft tissue involvement, respectively

Treatment
- Surgical resection with wide margins although this can be challenging due to invasion of local tissue planes (villous pattern of extension)
- Adjuvant radiotherapy provides local control of up to 85 %
- Imatinib is offered in patients with positive platelet-derived growth factor receptor (PDGF-r) or unresectable local or metastatic disease
- Excellent 5-year survival despite tendency to recur

Osteosarcoma

Epidemiology
- Maxilla and mandible are the predominant sites
- Highly malignant tumor with equal sex distribution but occurs in the third and fourth decades (extremity sarcomas occur earlier)
- May be radiation induced
- Genetic link with retinoblastoma 13q14 chromosomal abnormality
- Distinct from Ewing's sarcoma, an aggressive sarcoma of bone treated with chemotherapy and surgery, considered a systemic disease

Presentation
- Rapidly enlarging mass lesion of facial bones
- May present with paresis or neuropathy, pain depending on location

Histology
- Histological hallmark is the deposition of osteoid
- Majority are high-grade lesions
- Chondroblastic, osteoblastic, fibroblastic, telangiectatic depending on the cell type observed

Imaging
- CT and MRI to evaluate bone and soft tissue involvement, respectively
- PET/CT useful to rule out metastatic disease

Treatment
- Surgery is the mainstay of treatment; negative margins are critical for improved outcomes
- Current literature indicates that radiotherapy is controversial and should be reserved for palliation, or occasionally adjuvant therapy with close or positive margins
- Postoperative chemotherapy
- 60–70 % overall survival

Chondrosarcoma

Epidemiology
- 10 % of malignant bone tumors and are the second most common sarcoma arising in bone after osteosarcoma
- Predilection for the larynx
- Can also arise in the petrous temporal bone or in the clivus, maxilla, mandible
- Mean age around 30–40

Presentation
- Low incidence of regional metastasis of <5 %
- Swelling and mild pain, slowly enlarging mass

Histology
- Low-grade chondrosarcomas—few mitotic figures with a bland enlarged chondrocytes
- High-grade chondrosarcomas show hypercellular stroma consisting of characteristic "blue-balls of cartilage" lesion which permeate the trabeculae
- Rare clear cell variant is more aggressive, most common in larynx

Imaging
- CT and MRI to evaluate bone and soft tissue involvement, respectively
- PET/CT useful to rule out metastatic disease

Treatment
- Surgical resection, the mainstay of treatment, with wide excision is required to achieve clear margins
- May have microscopic fingerlike extensions and risk of seeding the wound with late nodular recurrence

Radiation-Induced Sarcoma

Epidemiology
- Lesions with different histological features to those of the sarcomas arising in radiation naïve tissues
- Must meet the following criteria:
  - Histological or radiological proof that there was no previous tumor in the involved area
  - Development of sarcoma in an irradiated area
  - Sufficiently long interval between irradiation and the development of sarcoma
  - Histological proof of sarcoma

Presentation
- Occur after previous radiotherapy for benign or malignant disease
- Arise after a median latent period of 9–12 years

Histology
- High-grade malignant fibrous histiocytoma is the most common
- Osteosarcoma second most common

Imaging

- CT and MRI to evaluate bone and soft tissue involvement, respectively
- PET/CT useful to rule out metastatic disease

Treatment

- Prognosis is generally poor but a proportion of these patients can be cured
- 25–30 % 5-year survival
- Irradiation is contraindicated and chemotherapy responses are poor
- Surgical resection is the treatment of choice but margins are difficult to ascertain due to radiation fibrosis

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Chapter 20
Laryngeal Squamous Cell Carcinoma

Victor J. Schorn and Brett A. Miles

PEARLS

- Early-stage laryngeal SCC can be treated surgically via a variety of transoral techniques or non-surgically with radiation therapy; both have excellent oncologic outcomes.
- Transoral surgical techniques have improved swallowing outcomes but slightly worse voice quality when compared to radiation therapy for early disease.
- Endolaryngeal SCC rarely exhibits cervical metastasis, unless disease is advanced.
- Supraglottic SCC often exhibits cervical metastasis and has a poor prognosis compared to laryngeal SCC.
- Salvage laryngectomy is a highly effective therapy when the disease is contained within the larynx.
- Chondrosarcoma of the larynx most commonly involves the cricoid; in early lesions the cricoid is resected; for later-stage lesions total laryngectomy is required.

ANATOMY

- Supraglottis
  - Epiglottis, aryepiglottic folds, arytenoids, false vocal cords.
  - Bilateral lymphatic drainage, levels II, III, IV.
    - Tendency for early lymphatic metastasis.
      - T1—10 %
      - T2—29 %
      - T3—38 %
      - T4—57 %
  - Predominantly pseudostratified columnar epithelium.
  - Derived from third to fourth branchial arches.
- Glottis
  - True vocal cords, including the anterior and posterior commissures.
  - Stratified squamous epithelium.
  - Unilateral lymphatic drainage, levels II, III, IV, and VI.
    - Infrequent lymphatic metastasis.
      - T1—0.1 %
      - T2—5 %
      - T3—18 %
      - T4—32 %
  - Derived from sixth branchial arch.

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- Subglottis
  - Lower border of glottis to inferior border of cricoid cartilage.
  - Pseudostratified columnar epithelium.
  - Paratracheal nodes most common site of regional metastases.
  - Derived from sixth branchial arch.
- Pre-epiglottic space (PES)
  - Potential for spread through fenestrations in the epiglottis, with resultant T3 lesion.
  - Superior boundaries.
    - Hyoepiglottic ligament.
    - Vallecula.
  - Anterior
    - Thyrohyoid ligament.
    - Thyroid cartilage.
    - Hyoid.
  - Posterior
    - Epiglottis.
    - Thyroepiglottic ligament.
- Paraglottic space (PGS)
  - Provides route of vertical spread, continuous with PES.
  - Lateral boundaries.
    - Thyroid cartilage.
    - Pyriform sinus.
    - Cricothyroid membrane.
  - Medial boundaries
    - Quadrangular membrane.
    - Laryngeal ventricle.
    - Conus elasticus.

EPIDEMIOLOGY

- SCCA accounts for 85–95 % of laryngeal CA.
- Male to female 3.8:1 due to increased exposure to risk factors.
- Peak in sixth and seventh decades of life.
- Tobacco, alcohol usage main environmental causes, synergistic.
  - Tobacco more commonly associated with glottic SCCA.
  - Alcohol more commonly associated with supraglottic SCCA.
- Laryngopharyngeal reflux moderately increases risk.
- Glottic SCCA slightly more common than supraglottic SCCA in the United States.
- Subglottic rare, 1 % of laryngeal SCC.
- Presentation dependent on site.
  - Supraglottic SCCA commonly presents in advanced stage with neck disease.
    - Dysphonia, dysphagia, odynophagia, otalgia, dyspnea, stridor.
  - Glottic SCCA more commonly presents at early stage.
    - Dysphonia, dyspnea, stridor.
  - Subglottic SCCA often presents at late stage, with frequent distant metastases.
    - Dyspnea, stridor.

WORK-UP AND STAGING

- Complete head and neck history and physical.
  - Particular attention to risk factor exposure.
  - Comorbidities, particularly COPD and lung disease.
- Fiber-optic laryngoscopic examination, with particular attention to vocal fold mobility.

- Imaging
  - CT with contrast or MRI of head and neck.
  - Important to assess invasion of the pre-epiglottic space, paraglottic space, laryngeal cartilages.
  - PET/CT to assess for regional and distant metastases, and synchronous primary.
  - Chest CT or chest radiograph, given frequency of synchronous primary lung CA and lung metastases.
- Labs
  - Standard preoperative labs, with particular attention to nutritional status.
- Direct laryngoscopy with biopsy and esophagoscopy.
  - Palpation of vocal folds.
  - Use of angled endoscopes to evaluate ventricles, underside of vocal cords.
  - Significant airway compromise may require awake tracheostomy under local anesthesia prior to laryngoscopy.
    - Tracheostomy should be done as high as possible to preserve trachea for subsequent laryngectomy.
- Pulmonary function tests indicated in case of partial laryngectomy surgery.

TNM staging as per AJCC

Primary tumor (T): Supraglottis

TX	Primary tumor cannot be assessed
T0	No evidence of primary tumor
Tis	Carcinoma in situ
T1	Tumor limited to one subsite of supraglottis with normal vocal cord mobility
T2	Tumor involving more than adjacent subsite of supraglottis or glottis or region outside supraglottis (base of tongue, vallecula, medial wall pyriform sinus), without fixation of larynx
T3	Tumor limited to larynx with vocal cord fixation and/or invades postcricoid area, pre-epiglottic tissue, paraglottic space, and/or inner cortex of thyroid cartilage
T4a	Tumor invades through thyroid cartilage and/or invades tissue beyond the larynx (e.g., trachea, soft tissue of neck including deep extrinsic muscle of the tongue, strap muscles, thyroid, esophagus)
T4b	Tumor invades prevertebral space, encases carotid artery, or invades mediastinal structures

Primary tumor (T): Glottis

TX	Primary tumor cannot be assessed
T0	No evidence of primary tumor
Tis	Carcinoma in situ
T1	Tumor limited to the vocal cord(s) with normal mobility (may involve anterior/posterior commissure)
T1a	Tumor limited to one vocal cord
T1b	Tumor involves both vocal cords
T2	Tumor extends to supraglottis and/or subglottis, and/or with impaired mobility
T3	Tumor limited to larynx with vocal cord fixation and/or invades paraglottic space, and/or inner cortex of thyroid cartilage
T4a	Tumor invades through thyroid cartilage and/or invades tissues beyond larynx
T4b	Tumor invades prevertebral space, encases carotid artery, or invades mediastinal structures

Primary tumor (T): Subglottis

TX	Primary tumor cannot be assessed
T0	No evidence of primary tumor
Tis	Carcinoma in situ
T1	Tumor limited to the subglottis
T2	Tumor extends to the vocal cord(s) with normal or impaired mobility
T3	Tumor limited to larynx with vocal cord fixation
T4a	Tumor invades the cricoid or thyroid cartilage and/or invades tissues beyond the larynx
T4b	Tumor invades prevertebral space, encases carotid artery, or invades mediastinal structures

Regional lymph nodes (N)	
N	Regional lymph nodes cannot be assessed
N0	No evidence of regional lymph node metastasis
N1	Metastasis to a single ipsilateral lymph node ≤3 cm in greatest dimension
N2a	Metastasis in a single ipsilateral lymph node >3 cm but ≤6 cm in greatest dimension
N2b	Metastasis in multiple ipsilateral lymph nodes ≤6 cm in greatest dimension
N2c	Metastasis in bilateral or contralateral lymph nodes ≤6 cm in greatest dimension
N3	Metastasis in a lymph node >6 cm in greatest dimension
Distant metastasis (M)	
Mx	Distant metastasis cannot be assessed
M0	No distant metastasis
M1	Distant metastasis

American Joint Committee Staging	
Stage 0	Tis, N0, M0
Stage I	T1, N0, M0
Stage II	T2, N0, M0
Stage III	
	T3, N1, M0
	T3, N0, M0
	T1, N1, M0
	T2, N1, M0
	T3, N1, M0
Stage IVA	
	T4a, N0, M0
	T4a, N1, M0
	T1, N2, M0
	T2, N2, M0
	T3, N2, M0
	T4a, N2, M0
Stage IVB	
	Any T, N3, M0
	T4b, any N, M0
Stage IVC	
	Any T, any N, M1

MANAGEMENT

- Goals of treatment are cure and laryngeal preservation.
- Premalignant lesions.
  - Hyperplasia
  - Keratosis
  - Dysplasia
    - Mild
    - Moderate
    - Severe
  - Carcinoma in situ.
  - Treated with microsurgical excision or radiation therapy.
    - Radiation therapy.
      - Apx 90 % local control rate.
      - Preferred for diffuse or recurrent lesions, unreliable patients.
      - Voice outcomes not significantly different from surgical excision.

    - Microsurgical excision.
      - Apx 80 % local control rate.
      - Preferred for reliable patients.
      - May need to be repeated multiple times.
    - Vocal fold stripping.
      - Apx 75 % local control rate.
      - Higher risk of vocal fold scarring, adverse voice outcomes.
- Supraglottic SCCA
  - Early primary (T1, T2, select T3).
    - Open supraglottic laryngectomy (OSL)
      - Resection of upper half of thyroid cartilage, false vocal cords, epiglottis, pre-epiglottic space, aryepiglottic folds.
      - Indications
        - T1, T2, select T3 with pre-epiglottic involvement but without glottic involvement
      - Contraindications
        - Poor pulmonary reserve or medical condition.
        - Vocal cord fixation
        - Thyroid or cricoid cartilage invasion.
        - Tumor in deep muscles of tongue or within 1 cm of circumvallate papilla.
      - Local control ~90 %.
    - Transoral laser microsurgery
      - Similar indications and contraindications as OSL.
      - Comparable oncologic outcomes.
      - Less morbidity, shorter hospital stays, less frequent need for temporary tracheostomy, equivalent voice outcomes.
      - May be limited by exposure.
    - Adjuvant RT recommended for positive margins, lymphovascular or perineural invasion, extracapsular spread, or N2+ disease.
    - Primary radiation therapy.
      - Slightly lower initial local control rate, but surgical salvage gives an ultimate local control rate comparable to primary surgical treatment.
      - Useful in patients with contraindications to surgical procedure, poor pulmonary function.
    - Total laryngectomy for salvage.
  - Advanced primary
    - Concurrent chemotherapy and radiation (CCRT).
      - Department of Veterans Affairs (VA) Laryngeal Cancer Study.
        - Induction chemotherapy with RT had equivalent survival to total laryngectomy with RT.
        - 64 % rate of laryngeal preservation in nonsurgical arm.
      - RTOG 91-11
        - CCRT higher rates of locoregional control and laryngeal preservation compared to induction chemotherapy, then RT, and RT alone.
        - Increased acute toxicity with CCRT.
    - Total laryngectomy with adjuvant RT.
      - Primary treatment in patients not amenable to SCPL or concurrent chemoradiotherapy.
        - Generally patients with significant cartilage destruction or extralaryngeal spread.
      - Used for salvage in recurrent disease, or in cases of nonfunctional larynx after CCRT.
  - Neck treated surgically with a bilateral selective II–IV dissection in case of N0 or N1 neck, comprehensive level I–V in case of N2 or N3 disease.

- Glottic SCCA
  - Early primary (T1, T2)
    - All treatment methods generally have very high local control, laryngeal preservation, and disease-free survival.
    - Elective treatment of the N0 neck is not indicated.
    - Radiotherapy
      - T2 with impaired mobility significantly lower rates of local control (76.1 % vs. 51.1 %) and 5-year survival (86.8 % vs. 75.2 %).
    - Transoral laser surgery
      - Anterior commissure involvement increases recurrence rate.
      - Similar voice outcomes with RT for T1 lesions.
    - Vertical partial laryngectomy (VPL)
      - Removal of ipsilateral false and true cord.
      - Superior rates of local control for patients with T2 lesions.
      - Relatively poor voice outcomes compared to RT, laser cordectomy.
      - Supracricoid partial laryngectomy (SCPL) more extensive with poorer voice quality, but improved local control when anterior commissure is involved.
  - Advanced primary
    - Concurrent chemoradiotherapy and total laryngectomy with postoperative RT (see discussion of RTOG and VA trials above).
    - Total laryngectomy indicated for T4a tumors with extensive cartilage destruction and as surgical salvage after CCRT.
- Subglottic SCCA
  - Treatment guidelines limited by rarity of disease.
    - Early-stage disease amenable to treatment with primary radiotherapy.
    - Advanced disease treated with laryngectomy, neck dissection, adjuvant radiotherapy.
    - Generally grim prognosis (25 % 3-year DFS in one series) given propensity to present in advanced stage and with distant metastases.

OTHER LARYNGEAL MALIGNANCIES

- Spindle cell carcinoma
  - Has both squamous and spindle cell elements.
    - Some debate about biological behavior, but most accepted theory is that of an epithelial origin with metaplastic transformation.
  - Tobacco and alcohol most common etiologic factors.
  - Male predominance.
  - Most commonly glottic.
    - Supraglottic and subglottic tumors associated with lower survival and more regional metastases, similar to SCCA.
  - Commonly polypoid and exophytic.
  - Treatment and prognosis similar to SCCA.
    - Traditionally treated primarily surgically, data for treatment with primary radiation very limited but case reports support its possible use in early-stage lesions.
- Chrondrosarcoma
  - Uncommon laryngeal malignancy, less than 1 %.
  - Male predominance.
  - Typically arise in cricoid cartilage.
  - Most commonly low grade, with good prognosis.
    - 5-year survival 90 %.
    - High-grade tumors, though uncommon, have worse prognosis and higher tendency to metastasize.
  - Treated with partial or total cricoid resection.
    - High-grade tumors may require total laryngectomy.
  - Radiation experience is very limited, but may be an option if conservation laryngeal surgery not feasible or as salvage prior to total laryngectomy.

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Chapter 21

Oral Cavity and Oropharyngeal Squamous Cell Carcinoma

Abib A. Agbetoba and Brett A. Miles

PEARLS

- Erythroplakia>leukoplakia are premalignant conditions which require monitoring/biopsy.
- Bone invasion (mandible or maxilla) portends poor prognosis and represents T4 disease (see TNM staging below).
- Cervical metastasis is the most influential prognostic factor and confers a 50 % decrease in survival.
- Tumors >5 mm thickness have higher (20 %>) risk of cervical metastasis.
- Cervical metastasis (neck mass) is a common presenting sign of oropharyngeal malignancy.
- HPV viral induced oropharyngeal SCCA has dramatically improved prognosis when compared with HPV– cancers and has shifted treatment paradigms and research protocols.

ORAL CAVITY SQUAMOUS CELL CARCINOMA

ANATOMY

- Boundaries—vermilion border of lip anteriorly to junction of hard and soft palate superiorly and to circumvallate papillae (linea terminalis) inferiorly
- Echelon of lymph node metastasis
  - First—facial, submental, submandibular gland (SMG), I–III of jugulodigastric LN
  - Second—parotid LN, IV–V LN
  - Increased bilateral metastasis for midline tumors
  - Can also have drainage to retropharyngeal lymph node
- Premalignant lesion
  - Leukoplakia—(white lesion)
  - Erythroplakia—(red lesion)
  - Dysplasia—histopathologic distinction—mild, moderate, or severe
  - Carcinoma in situ (present in 20–45 % of leukoplakia and 90 % of erythroplakia)
  - Field cancer effect due to environmental factors (tobacco, EtOH)

EPIDEMIOLOGY

- Risk factors
  - Tobacco and alcohol (synergistic)
  - Immunosuppression in transplant and HIV patients
  - Betel nut chewing (India, Hong Kong, Taiwan, Asia)

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  - HPV (less data than oropharyngeal sub-sites)
  - Poor dentition and chronic inflammation, mechanical irritation (controversial)
- 95 % oral cavity malignancy is SCCA

PRESENTATION

- Presenting signs and symptoms include:
  - Pain, dysphagia, bleeding, otalgia, loose dentition, numbness to chin, lip, trismus, pathological fractures of the mandible, and neck mass

WORK-UP AND STAGING

- Physical exam—tumor size and location (thickness), deep muscle invasion, trismus, mandibular and bony involvement, pathologic fracture, cranial nerve examination (sensory disturbances), dermal invasion, cervical nodal disease, assessment of adequate airway
- Tissue diagnosis
  - Biopsy of lesion
  - FNA of clinical and radiographic apparent LN (incisional or excisional biopsy should be avoided)
  - Operative panendoscopy
    - Rule out synchronous neoplasm of H&N
- Imaging
  - CT with contrast H&N to determine local invasion/extent
  - PET/CT (to evaluate metastatic disease)
  - PET/CT higher sensitivity than CT for detecting occult nodal disease
  - MRI (adjunct to assess PNI and soft tissue involvement)
  - Panoramic radiograph or Dentascan (adjunct to evaluate mandibular involvement)
- Lab
  - Peri-operative assessment and screening for metastatic disease to lung, liver, and/or bone
  - Include CBC, PT/PTT, BMP, liver-function tests, alkaline phosphates, and serum calcium, pre-albumin (poor nutritional status associated with adverse outcomes)
- Staging TNM
  - AJCC staging system

Primary tumor (T)

TX	Primary tumor cannot be assessed
T0	No evidence of primary tumor
Tis	Carcinoma in situ
T1	Tumor ≤2 cm in greatest dimension
T2	Tumor >2 cm and ≤4 cm in greatest dimension
T3	Tumor >4 cm in greatest dimension
T4a	Tumor involves cortical bone, deep musculature of tongue (genioglossus, hyoglossus, palatoglossus, styloglossus, maxillary sinus, and skin of face)
T4b	Tumor involves masticator space, pterygoid plates, skull base, or internal carotid artery encasement

Regional lymph nodes (N)

N	Regional lymph nodes cannot be assessed
N0	No evidence of regional lymph node metastasis
N1	Metastasis to a single ipsilateral lymph node ≤3 cm in greatest dimension
N2a	Metastasis in a single ipsilateral lymph node >3 cm but ≤6 cm in greatest dimension
N2b	Metastasis in multiple ipsilateral lymph nodes ≤6 cm in greatest dimension
N2c	Metastasis in bilateral or contralateral lymph nodes ≤6 cm in greatest dimension
N3	Metastasis in a lymph node >6 cm in greatest dimension

continued

Distant metastasis (M)	
Mx	Distant metastasis cannot be assessed
M0	No distant metastasis
M1	Distant metastasis

American Joint Committee Staging for Oral Cavity Squamous Cell Cancer	
Stage 0	Tis, N0, M0
Stage I	T1, N0, M0
Stage II	T2, N0, M0
Stage III	
	T3, N1, M0
	T3, N0, M0
	T1, N1, M0
	T2, N1, M0
	T3, N1, M0
Stage IVA	
	T4a, N0, M0
	T4a, N1, M0
	T1, N2, M0
	T2, N2, M0
	T3, N2, M0
	T4a, N2, M0
Stage IVB	
	Any T, N3, M0
	T4b, any N, M0
Stage IVC	
	Any T, any N, M1

- Sub-sites of oral cavity (including 1st echelon of LN drainage)
  - Mucosal lip (LN: level I)
    - Junction of skin–vermilion border
    - Most common site for oral cavity SCCA
    - Lower lip 93 %, upper lip 8 %, oral commissure 2 %
    - SCCA (involves lower lip most commonly) > BCC (involves upper lip most commonly)
    - Risk factors
      - Fair skinned, excessive sun exposure, tobacco and excessive alcohol use
    - Treatment and management
      - Single modality for early-stage lesion: surgery or XRT
      - Multimodality treatment for advanced-stage disease with surgery and XRT ± chemotherapy. Definitive chemoradiotherapy alternatively, less favorable
    - Treatment of cervical nodal disease
      - Regional neck involvement uncommon
      - Level I–III neck dissection for advanced-T-stage disease or clinical evidence of nodal disease (I–IV)
      - Factors with increased risk of cervical metastasis:
        - Large tumors, PNI, oral commissure involvement, high histological grade
    - Reconstruction can be complex, clear surgical margins paramount, oral competence, and facial aesthetics. Options for surgical treatment:
      - Wedge rsxn with primary closure<advancement flaps/melolabial flaps<Abbe and Estlander flap<Karapandzic flap<Bernard–Burrow's flap and Fan-Flap<vascularized free flap

- 5-year survival:
  - 70–99 % in the absence of cervical lymph node disease
  - 40–80 % with cervical lymph node disease

- Buccal mucosa (LN: parotid, level II)
  - Aggressive oral cavity cancer with high rates of regional recurrence
    - Lacks a strong anatomic barrier to protect against local tumor spread
  - Increased incidence in Southeast Asia secondary to betel nut use
  - Treatment of cervical nodal disease
    - Recommended for at least T2 lesions or greater
    - Ipsilateral SND I–IV should be performed
    - Recurrence rate for patients undergoing prophylaxis neck dissection has been reported as 29 % versus 48 % for those who did not
  - Treatment of primary site
    - Very-early-stage lesion treated with single modality: surgery and XRT equally effective
    - Advanced-stage lesions treated with multimodality: surgery with postoperative radiation ± chemotherapy or definitive chemoradiation with surgery reserved for salvage treatment
  - 5-year survival
    - Stage I, II, III, and IV disease, 78, 66, 62, and 50 %, respectively
  - Postoperative trismus is generally severe if multimodality therapy is utilized
- Anterior 2/3 of tongue (tip—level IA, lateral—2/3 level IB, level II LN, medial—level III)
  - Most common intraoral site SCCA
  - Sub-sites include tip, paired lateral, dorsal, and undersurface of tongue
  - Treatment of neck
    - Risk of occult nodal disease T1—17 %, T2—45 %, T3/4—86 %
    - Level I–III recommended for all tongue carcinomas with exception of T1 lesions with <4 mm depth of invasion, no PNI, LVI
    - Consider bilateral neck dissections for tumors close to or involving the midline
  - Treatment of primary site
    - Early-stage lesion treated with single modality: surgery and XRT equally effective
    - Advanced-stage lesion treated with multimodality: surgery with postoperative radiation ± chemotherapy (preferred) or alternatively definitive chemoradiation with surgery reserved for salvage treatment
  - 5-year overall survival
    - Stage I and II lesions range from 80 to 90 %, stages III and IV lesions range from 30 to 50 %
    - When compared stage for stage with posterior 1/3 of tongue there is no difference in survival
- Mandibular alveolar ridge (level IA, IB, II, lateral RP LN) and maxillary alveolar ridge (level IA, IB, II, lateral RP LN)
  - 80 % involve mandibular alveolar ridge
  - Rare occurrence with ominous disease given proximity to underlying bone
  - Evaluation of underlying periosteum and bone of critical importance
    - Once periosteum and bone invaded survival rates are reduced
  - Treatment primarily surgical
    - Marginal mandibulectomy is an acceptable approach in the absence of cortical bone invasion
    - Gross mandible invasion requires segmental mandibulectomy
  - Chemoradiation reserved for adjuvant therapy in advanced-stage disease or as definitive modality for those not candidates for surgical therapy
  - N0 neck may be observed in early-stage disease; however late stage and presence of nodal metastasis require treatment with SND I–III or XRT

- 5-year overall survival
  - Stage I—73 %, stage II—41 %, stage III—17 %
- Retromolar trigone (level II)
  - Triangular region of posterior oral cavity (posterior mandibular alveolus distal to last molar represents floor of triangle, coronoid process represents lateral superior aspect, maxillary tuberosity represents apex)
    - Represents confluence between buccal mucosa, soft palate, tonsillar pillar, BOT, floor of mouth
    - As a result, involvement usually represents extension from adjacent sites rather than isolated RMT tumors
    - Mucosa tightly adherent to underlying periosteum allowing for early osseous invasion
  - Treatment of primary site
    - Early-stage lesion treated with single modality: surgery and XRT equally effective
    - Advanced-stage lesion treated with multimodality: surgery with postoperative radiation ± chemotherapy or definitive chemoradiation with surgery reserved for salvage treatment
  - 5-year overall survival rates 20–60 %
    - Stage I—100 %, stage II—74.1 %, stage III—75 %, stage IV—43.6 %
- Hard palate (posterior HP—level II or RP LN, primary palate—level Ib LN)
  - Formed by palatine process of maxilla and horizontal plate of palatine bone
    - Mucosa tightly adherent to underlying hard palate (Sharpey's fibers)
    - Greater and lesser palatine foramina posterolaterally and incisive foramen anteriorly act as potential routes of direct spread and PNI
  - Higher incidence of salivary gland tumors given rich supply of minor salivary glands
  - Treatment of neck
    - Treatment of bilateral necks recommended for lesion >T2 and with soft palate invasion, or gross maxillary bone invasion
      - Treatment with surgery or XRT
    - 40 % incidence of nodal metastasis and 26 % rate of regional recurrence
  - Treatment of primary site
    - Treatment for early-stage lesion with single modality: surgery (preferred) and XRT are equally effective
    - Advanced-stage lesion treated with multimodality: surgery with postoperative radiation ± chemotherapy or definitive chemoradiation with surgery reserved for salvage treatment
    - Wide surgical margin required to improve locoregional recurrence
    - Reconstruction dependent on size of resection and defect
      - Goals: separation of nasal and oral cavity, cosmesis, restoration of speech and swallowing function
      - Palatal island flap, free buccal mucosal graft, for small lesions
        - Microvascular free flap for large composite resection
        - Obturator if patient not a candidate for reconstruction
  - 5-year overall survival 24–80 %
    - Decreased disease-free survival with soft palate invasion, close or involved margins
- Floor of mouth (level II)
  - Area between oral tongue and lingual surface of mandibular alveolus and extends posteriorly to anterior tonsillar pillar
  - Treatment of neck
    - Observation appropriate for N0 neck, unless depth of lesion is >1.5 mm
  - Treatment and management
    - Single modality for early-stage lesion: surgery and XRT equivocal survival outcomes
    - Multimodality treatment for advanced-stage disease with surgery and XRT ± chemotherapy or definitive chemoradiotherapy

- High locoregional recurrence rate (41 % locally, 19 % regionally)
- 5-year overall survival—45.7 %
  - Stage I and II 88–51 %, stage III–IV 66–38 %

MANAGEMENT

- Multidisciplinary approach (H&N surgical team, medical oncology, radiation oncology, dental team, nutritionist, speech and swallow, social work)
- Surgical treatment preferred primary modality over radiation or chemoradiation at most centers
- Early stage I and II cancers of oral cavity
  - Single modality
    - Surgical treatment preferred method over primary XRT
  - Advanced stage III and IV
    - Multimodality
    - Chemoradiation vs. surgery and adjuvant radiation ± chemotherapy
      - Higher rates of osteoradionecrosis (ORN), xerostomia, dental caries, and swallowing dysfunction with combined radiation and chemotherapy treatment
  - Osseous cortical invasion
    - Histological invasion exhibits two types: erosive and infiltrative
      - Infiltrative pattern more aggressive than erosive pattern
      - 3-year disease-free survival rates for the erosive and infiltrative patterns are 30 and 73 %, respectively
    - Treatment primarily surgical with adjuvant XRT or chemoXRT
      - Increased risk of ORN, orocutaneous fistula, wound dehiscence, and infection with use of chemoradiation
      - Periosteum invasion requires at least marginal mandibular resection
      - Gross cortical involvement requires segmental mandibulectomy
  - Neck dissection
    - Prevalence for occult nodal disease
      - 18–30 % for T1 lesions
      - 24–53 % for T2 tumors
    - Recommended neck observation in clinically negative neck only with
      - T1/T2 mucosal lip carcinomas
      - T1/T2 oral tongue carcinomas less than 4 mm thick
      - T1/T2 floor of mouth cancer 1.5 mm thick or less
    - Treatment of contralateral neck
      - Bilateral tumors
      - Tumors that approach, cross, or involve midline
      - Advanced-stage disease with >20 % risk of contralateral neck involvement
  - Radiation
    - Approximately 6-week course
    - Techniques include EBRT, brachytherapy, IMRT
    - Indications:
      - Primary single modality
      - Adjuvant treatment
      - Patients with surgical contraindications
      - Advanced-stage tumors
      - Unresectable tumors
  - Chemotherapy
    - Given as induction or concurrently with XRT
    - Associated with improved overall survival (oropharynx)
    - Key role in palliation treatment

- Reconstructive methods—provide wound closure, functional stability, cosmesis, introduce healthy tissue in a previously irradiated bed:
  - Oral prosthetic
  - Healing by secondary intention
  - Primary closure
  - Split thickness skin graft
  - Locoregional flaps
  - Myocutaneous pedicle flaps
  - Microvascular free flaps
- Palliation
  - Metastatic or unresectable disease
  - Involve XRT, chemo, or both
  - Tracheostomy, PEG if indicated
  - Consider tumor debulking, radio-frequency ablation for large painful ulcerative lesions
- Prognostic factors
  - Tumor thickness of >4 mm in oral tongue associated with worse outcomes in T1–T2 lesions
  - Additional poor prognostic factors include ECS, perineural, vascular, and lymphatic invasion

- 5-year overall survival for OC SCCA
  - All stages: 46–59 %
    - Stage I: 53–90 %
    - Stage II: 54–100 %
    - Stage III: 37–71 %
    - Stage IV: 15–50 %
- 20 % chance of developing second primary cancer (H&N, esophagus, lung)
  - Increased risk and poor survival outcomes with continued tobacco and alcohol intake

OROPHARYNGEAL SQUAMOUS CELL CARCINOMA

ANATOMY

- Boundaries
  - Superior boundary—soft palate
  - Anterior boundary—junction of soft and hard palate and circumvallate papillae of posterior 1/3 tongue
  - Posterior and posterior lateral boundary—muscular pharyngeal wall
  - Inferior boundary—hyoid bone
- Function
  - Deglutition and prevention of aspiration
  - Speech production
  - Respiration
  - Prevention of nasophayrngeal reflux
- Echelon of lymph node (LN) metastasis
  - 1st—Level II–III of jugulodigastric LN
  - 2nd—Level I, level IV, V, retropharyngeal
  - Increased b/l metastasis for midline tumors
- Sub-sites of oropharynx (including 1st echelon of LN drainage)
  - Soft palate (level II)
  - Base of tongue (level II, III, and IV)
  - Tonsillar fossa and pillars (level II, III, IV)
  - Posterior and lateral pharyngeal wall (between level of velopharynx and hyoid bone)

EPIDEMIOLOGY

- SCCA represents 90 % of all OP cancers
- Risk factors
  - Tobacco and alcohol (work in synergy)
  - HPV—improved overall survival when compared to non-HPV tumors
    - Reported to be present in 40–80 % of OP SCCA
    - Most common in tonsillar SCCA
    - Associated with HPV types 16 and 18, which express the E6 and E7 oncogenes
    - Strong correlation with nuclear and cytoplasmic p16 overexpression
    - Incidence of HPV(+) OPC has increased by 225 % between 1988 and 2004, whereas the incidence of HPV(–) OPC has decreased by 50 %
    - HPV(+) OPC
      - Younger age, frequently white males, nonsmokers or infrequent smokers, and moderate or non-alcohol drinkers
      - Associated with high-risk sexual practice
    - HPV(–) OPC
      - Older age, heavy smokers, and experience a synergistic increase in risk with alcohol consumption.
  - Immunosuppression in transplant and HIV patients
  - Betel chewing (India, Hong Kong, Taiwan, Asia)
- Presenting symptoms: odynophagia, dysphagia, globus, otalgia, trismus, dysarthria, bleeding, history of unexplained weight loss, and airway obstruction
  - Early stage usually asymptomatic
  - Initial presentation with cervical nodal mass is common
    - 45–78 % present with cervical lymphadenopathy

Base of tongue

- Poor prognosis secondary to late disease presentation, high risk of nodal metastasis
- Can spread to involve retromolar trigone, buccal mucosa, and tongue base
  - Extension posteriorly onto the pharyngeal wall less common
- Treatment of cervical nodal disease
  - Cervical lymph node metastasis present in 60 % of patients at the time of presentation
  - Treatment of bilateral necks recommended in all patients, either with surgery or radiation with salvage neck dissection
- Treatment options for primary site and reconstruction discussed below
- High incidence of HPV-positive cancers
- 5-year overall survival
  - Stage I–II 80–43 %, stage III–IV 38–20 %
  - Survival markedly improved for HPV+ vs. HPV– disease

Tonsil and tonsillar pillars

- Most common site of involvement in OP SCCA
- Highest prevalence of HPV-positive cancers in head and neck
- Most patients initially asymptomatic and as a result present with advanced-stage disease
- Treatment of cervical nodal disease
  - Cervical lymph node metastasis present in 66–76 % of patients at the time of presentation
  - T1 tumors with no clinical nodal disease may be candidates for observation of the neck
  - Contralateral neck treatment recommended in tumors with >T2 staging, involving midline, or the presence of ipsilateral neck disease
- Treatment options for primary site and reconstruction discussed below
- 5-year overall survival rates range from 43 to 47 %

Soft palate SCCA

- Uncommon, represent 5–12 % of OP SCCA
- Present earlier than other sites of H&N cancer secondary to gross appearance on exam and symptoms of odynophagia and dysphagia
  - Incidence of T stage presentation: T1—21 %, T2—34 %, T3—25 %, T4—13 % (all with N0 disease)

- Surgical treatment can be accomplished through transoral approach
  - Surgery preferred for lateral or very-early-stage disease
  - Surgery and radiation offer similar overall survival rates
  - Surgery associated with higher morbidity compared to radiotherapy for lesions involving significant portions of the soft palate (velopharyngeal insufficiency, nasal regurgitation, speech disturbance)
- Treatment of cervical nodal disease
  - Treatment of cervical neck controversial
    - Observation vs. treatment (surgery or XRT) in early-stage disease
    - Consider treatment of contralateral neck in advance tumors or lesions that cross midline
  - 20 % of T1/T2 lesions present with regional metastasis
  - 60–70 % of T3/T4 lesions present with regional metastasis
- Treatment options for primary site and reconstruction discussed below
- Higher incidence of second primary tumors compared to other sub-sites in H&N
- 5-year overall survival
  - Stage I—60 %, stage II—55 %, stage III—55 %, stage IV—37 %

Posterior oropharyngeal wall

- Usually presents in advanced stage
- Dysphagia and odynophagia are most common symptoms
- Can extend superiorly to nasopharynx and inferiorly to hypopharynx
- Extension posteriorly to retropharyngeal and prevertebral space more common than extension laterally
- Treatment of cervical nodal disease
  - Given anatomic site, most present with bilaterally cervical lymph node metastasis
  - Involves treatment of bilateral necks as well as addressing retropharyngeal nodal basin
- Treatment and management
  - Early-stage lesion treated with single modality XRT
  - Advanced lesion treated with combined modality: chemo/XRT with surgical salvage
- 5-year overall survival
  - Stage I—56 %, stage II—52 %, stage III—24 %, stage IV—22 % (includes pooled data of posterior pharyngeal wall of HP)
    - Improved DFS when comparing posterior pharyngeal wall of OP compared with posterior pharyngeal wall of HP

WORK-UP AND STAGING

- Physical exam—tumor size, deep muscle invasion, trismus, decreased tongue mobility, cervical nodal disease, assessment of adequate airway
- Tissue diagnosis
  - Biopsy of lesion
  - FNA of clinical and radiographic apparent LN (incisional or excisional bx should be avoided)
  - Panendoscopy (laryngoscopy, bronchoscopy, esophagoscopy)
    - Rule out synchronous neoplasm of H&N
- Imaging
  - CT with contrast H&N
  - PET/CT (to evaluate metastatic disease and diagnosis unknown primary)
  - MRI (adjunct to assess PNI and soft tissue involvement)
- Lab
  - Perioperative assessment and screening for metastatic disease to lung, liver, and/or bone
  - Include CBC, PT/PTT, BMP, liver-function tests, alkaline phosphates, and serum calcium, pre-albumin (poor nutritional status associated with adverse outcomes)
- Staging TNM
  - AJCC staging system

Primary tumor (T)	
TX	Primary tumor cannot be assessed
T0	No evidence of primary tumor
Tis	Carcinoma in situ
T1	Tumor ≤2 cm in greatest dimension
T2	Tumor >2 cm and ≤4 cm in greatest dimension
T3	Tumor >4 cm in greatest dimension
T4a	Tumor involves mandible, hard palate, deep musculature of tongue, medial pterygoid muscle, and/or larynx
T4b	Tumor invades lateral pterygoid muscle, pterygoid plates, lateral nasopharynx, skull base, or carotid artery encasement

Regional lymph nodes (N)	
N	Regional lymph nodes cannot be assessed
N0	No evidence of regional lymph node metastasis
N1	Metastasis to a single ipsilateral lymph node ≤3 cm in greatest dimension
N2a	Metastasis in a single ipsilateral lymph node >3 cm but ≤6 cm in greatest dimension
N2b	Metastasis in multiple ipsilateral lymph nodes ≤6 cm in greatest dimension
N2c	Metastasis in bilateral or contralateral lymph nodes ≤6 cm in greatest dimension
N3	Metastasis in a lymph node >6 cm in greatest dimension

Distant metastasis (M)	
Mx	Distant metastasis cannot be assessed
M0	No distant metastasis
M1	Distant metastasis

American Joint Committee Staging for Oral Cavity Squamous Cell Cancer	
Stage 0	Tis, N0, M0
Stage I	T1, N0, M0
Stage II	T2, N0, M0
Stage III	
	T3, N1, M0
	T3, N0, M0
	T1, N1, M0
	T2, N1, M0
	T3, N1, M0
Stage IVA	
	T4a, N0, M0
	T4a, N1, M0
	T1, N2, M0
	T2, N2, M0
	T3, N2, M0
	T4a, N2, M0
Stage IVB	
	Any T, N3, M0
	T4b, any N, M0
Stage IVC	
	Any T, any N, M1

MANAGEMENT

- Multidisciplinary approach (H&N surgical team, medical oncology, radiation oncology, dental team, nutritionist, speech and swallow, social work)
- Early stage I and II cancers of oropharynx
  - Single modality (XRT vs. surgical)
    - Similar locoregional recurrence rates

        - XRT may offer decreased morbidity and treatment of retropharyngeal and parapharyngeal LN
    - Surgical treatment
        - Transoral robotic surgery/transoral laser surgery—improved exposure with minimally invasive technique
            - Comparable oncologic outcomes for T1 and T2 OP SCCA
            - Potential for de-escalation adjuvant XRT and chemotherapy (under investigation)
        - ± Ipsilateral SND
        - Indications for postoperative XRT
            - +LN
            - ECS
            - PNI
- Advanced stage III and IV
    - Multimodality
        - Chemoradiation vs. surgery and adjuvant radiation ±chemotherapy
    - Surgical approaches
        - Transoral—simplest, optimal exposure may be an issue with robotic/laser techniques
        - Mandibular swing—wide exposure of entire oropharynx
        - Transcervical transpharyngeal approaches—exposure of posterior OP tumors
            - Suprahyoid approach—access to midline BOT
            - Lateral pharyngotomy approach—poor exposure of superior lesions of tonsillar fossa or RMT region
        - Reconstructive methods—provide wound closure, functional stability, and cosmesis, introduce healthy tissue in a previously irradiated bed:
            - Oral prosthetic
            - Healing by secondary intention
            - Primary closure
            - Split-thickness skin graft
            - Locoregional flaps
            - Myocutaneous pedicle flaps
            - Microvascular free flaps
    - Radiotherapy
        - Approximately 6-week course
        - Techniques include EBRT, brachytherapy, IMRT
        - Indications:
            - Primary single modality
            - Adjuvant treatment
            - Patients with surgical contraindications
            - Advanced-stage tumors
            - Unresectable tumors
    - Chemotherapy associated with improved overall survival in advanced OP SCCA
        - Given concurrently with XRT
        - Primary chemotherapy reserved for palliation without curative intent
    - Treatment of cervical nodal disease
        - N0 neck managed with regional radiotherapy or planned neck dissection
            - Consider primary surgical treatment of cutaneous involvement
            - Consider adjuvant neck irradiation for the presence of ECS
            - Consider post-XRT surgical salvage for bulky nodal disease
        - 15–30 % of OP SCCA with initial N0 neck present with cervical nodal metastasis
- Palliation
    - Metastatic or unresectable disease
    - Involve XRT, chemo, or both
    - Tracheostomy, PEG if indicated
    - Consider tumor debulking, radio-frequency ablation for large painful ulcerative lesions
- 5-year cause-specific survival 60–65 %
    - Primary surgical vs. radiotherapy with equivocal survival outcomes

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Chapter 22
Nasal Cavity and Paranasal Sinus Carcinoma

Alfred M. Iloreta and Brett A. Miles

PEARLS

- Nasal cavity and sinus anatomy in close proximity to many vital structures.
- Lymph drainage:
  - Nasal cavity → larger vessels pass posterior to the tonsillar region and directly to the upper deep cervical nodes.
- Most drain into pharyngeal plexus → retropharyngeal nodes.
  - Anterior nose via nares connect with lymphatic vessels of the face.
  - Maxillary → submandibular gland (SMG).
  - Ethmoid cells have few lymph capillaries that pass via ostia to connect with nasal mucosa → SMG.
  - Sphenoid—retropharyngeal nodes.
- Ohngren's line (the malignant plane) runs from medial canthus to angle of the mandible—tumors located superoposterior to this plane have poorer prognosis.
- Thin bone of fovea ethmoidalis, cribriform, and lamina are not a strong anatomical barrier to adjacent spread and local invasion.
- Incidence less than 1 per 100,000 persons worldwide, 3–5 % of all upper aerodigestive tract tumors and 0.2 % of all cancers.

ANATOMY

- Nasal cavity (see Rhinology section for further detail)
  - Boundaries
    - Anterior roof: nasal bone, nasal spine of frontal bone
    - Medial roof: cribriform plate from ethmoid bone
    - Posterior roof: anterior wall of sphenoid sinus and sphenoid bone
    - Medial: septum
    - Anterior floor: palatal process of maxillary bone
    - Posterior floor: horizontal process of palatine bone
    - Lateral
      - Uncinate process, ethmoid infundibulum, inferior turbinate, and lateral nasal wall

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EPIDEMIOLOGY

- Risk factors:
  - Adenocarcinoma: woodworkers, shoe workers, furniture workers because of exposure to wood dust, preservatives, stains, and paints
  - SCC: chromium, nickel, mustard gas, organic fibers
- Exposure of epithelial cells to wood dust show overexpression of p53
- Tobacco increased relative risk by 1.5–2.5
- HPV, radiation exposure

PRESENTATION

- Patients may present with pain, headaches, unexplained epistaxis, recurrent epistaxis, nasal obstruction, loss of sense of smell, visual changes, proptosis, sensory and motor disturbances due to cranial nerve involvement

WORK-UP AND STAGING

- Physical exam—tumor size and location, deep muscle invasion, trismus, bony involvement, office nasal endoscopy, cranial nerve examination (sensory and motor disturbances), ocular examination, cervical nodal disease
- Tissue diagnosis
  - Appropriate imaging prior to biopsy to rule out vascular lesion or meningoencephalocele
  - Biopsy of lesion
  - FNA of clinical and radiographic apparent LN (incisional or excisional biopsy should be avoided)
- MRI
  - Better for soft tissue involvement
  - Assess perineural invasion, cranial neuropathies
  - Dural invasion, extension into infratemporal fossa
  - Differentiate from sinus filled with fluid secretions vs. soft tissue lesion (tumor hyper intense on T1)
- CT
  - Visualize bone invasion/erosion
  - Navigation
  - Angiography: for extension into infratemporal fossa or near carotid arteries
- PET
  - Less accurate for primary site evaluation
  - Very sensitive for regional or distant disease

Histopathologic Markers

- ENB: cytokeratin negative (not a carcinoma), +EMA, CHR, SYN
- SNEC: normal neuronal differentiation though cytokeratin positive—express one or more of these markers diffusely: chromogranin, synaptophysin
- SNUC: undifferentiated small round blue cells, CK, epithelial membrane antigen, neuron-specific enolase

Inverted Papilloma (IP)

- EGFT and TGF-alpha expression associated in IP carcinogenesis included with EBV and HPV
- Approximately 10 % of IP harbor SCC
- Hyperplastic stratified squamous-to-columnar epithelium w/without atypia
- Unilateral polyp red-to-tan mass nasal cavity
- Most commonly arises from the lateral nasal wall
- CT imaging: bony dehiscence, hyperostotic bone at the site of attachment

- Mucocutaneous junction: squamous papilloma found anterior, inverted papilloma posterior
- MR: T2-weighted images with convoluted cerebriform appearance T1 enhancement (secretions bright on T2)
- No role for PET scanning unless malignant changes occur
- Krouse staging to describe the extent of involvement

Krouse Staging System for Inverted Papilloma

T1	Tumor totally confined to the nasal cavity, without extension into the sinuses. The tumor can be localized to one wall or region of the nasal cavity, or can be bulky and extensive within the nasal cavity, but must not extend into the sinuses or into any extra nasal compartment. There must be no concurrent malignancy
T2	Tumor involving the ostiomeatal complex, and ethmoid sinuses, and/or the medial portion of the maxillary sinus, with or without involvement of the nasal cavity. There must be no concurrent malignancy
T3	Tumor involving the lateral, inferior, superior, anterior, or posterior walls of the maxillary sinus, the sphenoid sinus, and/or the frontal sinus, with or without involvement of the medial portion of the maxillary sinus, the ethmoid sinuses, or the nasal cavity. There must be no concurrent malignancy
T4	All tumors with any extra nasal/extra sinus extension to involve adjacent, contiguous structures such as the orbit, the intracranial compartment, or the pterygomaxillary space. All tumors associated with malignancy

- Meta-analysis of 32 retrospective studies indicate that endoscopic and open approaches have similar recurrence rates.
- Depends on expertise and experience of surgeon whether tumor can be approached endoscopically alone or if there is a need for adjuvant external approach. Decision should be based on the ability to completely access and excise IP with drilling of bony attachment site, regardless of the approach.

SCCA

AJCC 7th ed., 2010: Nasal Cavity and Paranasal Sinus Cancer

Primary tumor (T)	
TX	Primary tumor cannot be assessed
T0	No evidence of primary tumor
Tis	Carcinoma in situ
T1	Tumor limited to maxillary sinus mucosa with no erosion or destruction of bone
T2	Tumor causing bone erosion or destruction including extension into the hard palate and/or middle nasal meatus, except extension to posterior wall of maxillary sinus and pterygoid plates
T3	Tumor invades any of the following: bone of the posterior wall of maxillary sinus, subcutaneous tissues, floor or medial wall of orbit, pterygoid fossa, ethmoid sinuses
T4a	Moderately advanced local disease. Tumor invades anterior orbital contents, skin of cheek, pterygoid plates, infratemporal fossa, cribriform plate, sphenoid or frontal sinus
T4b	Very advanced local disease. Tumor invades any of the following: orbital apex, dura, brain, middle cranial fossa, cranial nerves other than maxillary division of trigeminal nerve (V2), nasopharynx, or clivus
Nasal cavity and ethmoid sinus	
T1	Tumor restricted to any one subsite, with or without bone invasion
T2	Tumor invading two subsites in a single region or extending to involve an adjacent region within the nasoethmoidal complex, with or without bony invasion
T3	Tumor extends to invade the medial wall or floor of the orbit, maxillary sinus, palate, or cribriform plate
T4a	Moderately advanced local disease. Tumor invades any of the following: anterior orbital contents, skin of nose or cheek, minimal extension to anterior cranial fossa, pterygoid plates, sphenoid or frontal sinus
T4b	Very advanced local disease. Tumor invades any of the following: orbital apex, dura, brain, middle cranial fossa, cranial nerves other than maxillary division of trigeminal nerve (V2), nasopharynx, or clivus

continued

Regional lymph nodes (N)

N	Regional lymph nodes cannot be assessed
N0	No evidence of regional lymph node metastasis
N1	Metastasis to a single ipsilateral lymph node ≤3 cm in greatest dimension
N2a	Metastasis in a single ipsilateral lymph node >3 cm but ≤6 cm in greatest dimension
N2b	Metastasis in multiple ipsilateral lymph nodes ≤6 cm in greatest dimension
N2c	Metastasis in bilateral or contralateral lymph nodes ≤6 cm in greatest dimension
N3	Metastasis in a lymph node >6 cm in greatest dimension

Distant metastasis (M)

Mx	Distant metastasis cannot be assessed
M0	No distant metastasis
M1	Distant metastasis

Anatomic stage/prognostic groups

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

- 80 % of malignancy in nasal cavity and PNS
  - Maxillary 70 %
  - Intranasal—turbinates 20 %
  - Ethmoid, sphenoid, frontal
- Verrucous, basaloid, spindle, transitional variants
- Regional spread to neck is rare and elective neck dissection is not recommended
- Overall 5-year OS estimated at 60–64 % recurrence rate approx. 30 % recurrence, stage III, IV disease 25–30 %
- 18 % of patients present with distant mets with LR spread in 17–30 % of patients
- Early stage I and II disease—surgery ± radiation, either pre- or postsurgical resection
- Advanced stage III and IV disease = surgery ± radiation/chemotherapy, either pre- or post-surgical resection, or concurrent chemoradiation (CRT) considered in unresectable tumor
- Tx nodal disease with RT or surgery, depending on initial approach to tumor
- SCC (T4b) involving orbit, brain, dura = induction chemo followed by concomitant CRT or surgery with post op RT +/- chemo

- Clinical outcomes:
  - Advanced local stage tumors treated with induction chemo (taxane + platinum) trend towards organ preservation of globe and critical neurovascular structures
  - Locally advanced tumors (T3/T4) associated with higher incidence of nodal involvement and nodal relapse
  - Postoperative radiotherapy can reduce skull base failure and nodal recurrence in patients with high-risk features

Lymphoreticular

- B and T cell lymphoma
  - Most patients present with locally advanced disease (50 % at T4)
- Need sufficient, fresh biopsy for flow cytometry and immunohistochemical analysis
  - CRT and RT alone for TX
- Extramedullary plasmacytoma
  - Involvement of nose PNS, NP in 60 % of cases
  - Wide local excision with or without CRT
  - 5-year control rates for early lesions 78 to 48 % for T4 lesions

Adenoid Cystic

AJCC 7th ed., 2010 Salivary Gland Cancer

Primary tumor (T)	
TX	Primary tumor cannot be assessed
T0	No evidence of primary tumor
Tis	Carcinoma in situ
T1	Tumor ≤2 cm in greatest dimension without extraparenchymal extension
T2	Tumor >2 cm but ≤4 cm in greatest dimension without extraparenchymal extension
T3	Tumor >4 cm and/or tumor having extraparenchymal extension
T4a	Moderately advanced disease. Tumor invades skin, mandible, ear canal, and/or facial nerve
T4b	Very advanced disease. Tumor invades skull base and/or pterygoid plates and/or encases carotid artery
Regional lymph nodes (N)	
N	Regional lymph nodes cannot be assessed
N0	No evidence of regional lymph node metastasis
N1	Metastasis to a single ipsilateral lymph node ≤3 cm in greatest dimension
N2a	Metastasis in a single ipsilateral lymph node >3 cm but ≤6 cm in greatest dimension
N2b	Metastasis in multiple ipsilateral lymph nodes ≤6 cm in greatest dimension
N2c	Metastasis in bilateral or contralateral lymph nodes ≤6 cm in greatest dimension
N3	Metastasis in a lymph node >6 cm in greatest dimension
Distant metastasis (M)	
Mx	Distant metastasis cannot be assessed
M0	No distant metastasis
M1	Distant metastasis
Stage 0	Tis, N0, M0
Stage I	T1, N0, M0
Stage II	T2, N0, M0
Stage III	
	T3, N1, M0
	T3, N0, M0
	T1, N1, M0
	T2, N1, M0
	T3, N1, M0

continued

Stage IVA	
	T4a, N0, M0
	T4a, N1, M0
	T1, N2, M0
	T2, N2, M0
	T3, N2, M0
	T4a, N2, M0
Stage IVB	
	Any T, N3, M0
	T4b, any N, M0
Stage IVC	
	Any T, any N, M1

- Most common salivary gland tumor of nose and PNS
- **Skip Lesions** due to perineural spread
- Propensity to recur locally and distally even several years after tx
- Even with aggressive surgery 64 % of cases with + margins
- 5-year OS is 65 %, 15-year OS is 28 %
- Distant spread to lung, liver, bone
- Primary therapy with surgery (adjuvant RT ± chemotherapy for positive margins, PNI, extensive disease)
- RT for palliation in unresectable cases
- Combined modality therapy with chemoradiation with 5-year OS of 65 % and 10-year OS of 55 %
- Neutron beams have shown an increase in local control rates; however no conferred overall survival benefit

Adenocarcinoma

See Paranasal Sinus and Nasal Cavity Staging Table

- Can mimic mucoepidermoid or adenocarcinoma of the colon
- Histologic grade affects prognosis and LR metastatic rates
- High-grade AC—OS <35 % at 3 years
- Low-grade AC—OS at 80 % at 5 years
- Associated with exposure to wood dust, lacquers
- Surgical excision with wide margins (post op RT ± chemo for advanced disease or positive margins)
- Surgical treatment includes open approaches, endoscopic approaches, or combined open/endoscopic
- Similar survival rates endoscopic vs. open, when patients are well selected for appropriate approaches

Sarcoma

AJCC 7th ed., 2010: Sarcoma

Primary tumor (*T*)	
TX	Primary tumor cannot be assessed
T0	No evidence of primary tumor
T1	Tumor ≤5 cm in greatest dimension
T1a	Superficial tumor
T1b	Deep tumor
T2	Tumor >5 cm in greatest dimension

continued

T2a	Superficial tumor
T2b	Deep tumor
Regional lymph nodes (*N*)	
NX	Regional lymph nodes cannot be assessed
N0	No regional lymph node metastasis
N1	Regional lymph node metastasis[a]
[a]The presence of positive nodes (N1) in M0 tumors is considered stage III.	
Distant metastasis (*M*)	
M0	No distant metastasis
M1	Distant metastasis

- Rare
- Rhabdomyosarcoma frequently found in children
  - Embryologic, alveolar, and pleomorphic
  - Children most often treated with radiation and chemotherapy
  - Adults wide surgical excision and post op radiation and chemotherapy
- Advanced stage at presentation with bone and extensive soft-tissue destruction
- 50 % Survival
- Optimal treatment is complete resection with margins
- Even with low-grade tumors most patients receive combined modality treatment with radiation and chemotherapy
- No proven efficacy for adjuvant chemotherapy but should be considered for high-grade lesions
- Pediatric tumors have higher response rate to treatment

Hemangiopericytoma

- Capillary origin
- Rare, very vascular
- Arise from pericytes of Zimmerman
- Nasal cavity > sphenoethmoid > maxilla/NP
- High recurrence rate >50 % within 5 years
- Surgery is the primary treatment modality; may be combined with adjuvant radiation ± chemotherapy
- High recurrence rate >50 % within 5 years
- Need for long-term follow-up
- Preoperative embolization for large tumors

Metastatic Tumors

- Renal carcinoma most common

Chordoma

AJCC 7th ed., 2010: Chordoma Staging System

Primary tumor (*T*)	
TX	Primary tumor cannot be assessed
T0	No evidence of primary tumor
T1	Tumor ≤5 cm in greatest dimension*
T2	Tumor >5 cm in greatest dimension*

Regional lymph nodes (*N*)	
NX	Regional lymph nodes cannot be assessed
N0	No histologically verified regional node metastasis
N1	Histologically verified regional node metastasis
Distant metastasis (*M*)	
M0	No distant metastasis
M1	Distant metastasis
Histologic grade of malignancy	
G1	Well differentiated
G2	Moderately differentiated
G3	Poorly differentiated
G4	Undifferentiated

- Malignant, slow growing, from clivus, extra-axial notochord remnant, *physaliferous cells*
- Diagnosed on imaging CT, MRI
- Can metastasize usually to skin, bone, lung, lymph nodes or also recur

Chondrosarcoma

- Rare, Dx usually by radiographic findings
- Chondromas usually <3 cm, chondrosarcomas usually >3 cm
- Grade I–III, well to poor differentiation
  - Differentiation dependent on chondroid-to-myxoid ratio, presence of mitosis, nuclear appearance
- High-grade lesions (II–III) confer worse prognosis
- Lesions at the skull base have worse prognosis due to proximity to critical neurovascular structures
- Wide surgical resection
- Recurrence rate of up to 85 %

Olfactory Neuroblastoma (Esthesioneuroblastoma)

Kadish Staging for Esthesioneuroblastoma

Kadish staging for esthesioneuroblastoma	
Stage A	Tumor limited to the nasal cavity
Stage B	Tumor extends to paranasal sinuses
Stage C	Tumor extends beyond paranasal sinuses

- Olfactory epithelium of cribriform plate, septum, or superior turbinate.
- Differentiation from other small blue-cell tumors with staining.
- Staging.
  - Kadish = extent of disease within and beyond nasal cavity and PNS.
- Grading.
  - Hyams = includes tissue architecture, mitosis, nuclear polymorphism, fibrillary matrix, rosettes, and necrosis.
- Locally aggressive with lymphatic and hematogenous spread.
  - LR metastatic disease in 10–30 % of patients.
- Cervical involvement portends an exceptionally unfavorable prognosis.
- Multimodality therapy offers optimal survival rate, especially for advanced disease: Surgery w/post op RT or CRT followed with planned or salvage surgical therapy.
- Multimodality therapy resulted in 8-year disease-free survival of 80 % of patients.

- Long-term survival with late recurrence.
- Surgical approach (endoscopic vs. craniofacial) dependent on the extent of disease.
- Early case series have shown that endoscopic resection is an effective method of management.

Radiation Therapy

- Early-stage disease can be treated with single-modality therapy with radiation
- Brachytherapy can be used in nasal septum tumors, although not common
- Dose limitations
  - Lens <10 Gy
  - Retina <45 Gy
  - Brain <60 Gy
  - Lacrimal gland <30–40 Gy
  - Optic chiasm <54 Gy
  - Pituitary and hypothalamus <40 Gy

Surgical Treatment

- Open craniofacial resection carries a 4.7 % mortality
  - Morbidity 33–36 %—wound 20 %, systemic 5 %, and orbital 1.5 %
  - Overall 5-year survival is approximately 50 %
- Endoscopic endonasal approach (EEA)
  - Traditionally indicated for low-stage disease; however newer series are showing that advances in endoscopic instrumentation and technique have allowed for resection of higher stage with similar survival.
  - Overall mortality 0.9 %
  - Intracranial infection 2 %
  - Overall morbidity 2.6 %
  - CSF leak rate between 4 and 6 %
- Early-stage disease treated with single-modality therapy, usually surgical resection with some exceptions (rhabdomyosarcoma, lymphoma, small-cell carcinoma, SNUC, metastasis)
  - Role of surgery can be for palliation for pain or tumor debulking
- Advanced-stage disease
  - Multimodality therapy: (±induction chemotx) surgical resection and postoperative radiation ± chemotx
- Unresectable disease: primary RT, CRT, or chemotx alone
- N0 Neck:
  - Usually not indicated because drainage goes to retropharyngeal nodes
- N1–3 Neck
  - Treat for clinical neck disease
  - Parotid nodes will require superficial parotidectomy
- Consider craniofacial resection when tumor is extending very far laterally or posteriorly intracranially
- Craniofacial resection—contraindications
  - Absolute
    - Distant metastasis
    - Cavernous sinus invasion
    - Carotid artery invasion
    - Prevertebral fascia involvement
    - Involvement of optic chiasm or both optic nerves
  - Relative
    - Dural invasion
    - Intracranial nerve involved by adenoid cystic

- Orbital exenteration
  - Not necessarily indicated with bone erosion alone, but once periorbita is violated and orbital fat involved, this is good indication
  - Tumor within the orbital apex
  - Spread via direct extension, perineural, nasolacrimal, perivascular, or orbital fissures
- External approaches
  - Midface degloving:
    - Lesions inferior and medial maxillary walls, difficult superior exposure
    - No facial incisions
  - Lateral rhinotomy
    - Standard incision for open medial maxillectomy
    - Exposure for ethmoid, sphenoid, nasal cavity, medial orbital wall, maxillary wall
  - Fascial translocation
    - Wide exposure of middle cranial base, pterygopalatine fossa, nasopharynx
  - Weber-Fergusson
    - Lateral rhinotomy + lip split to connect with sublabial incision
    - Exposure for total maxillectomy
  - Transpalatal approach
    - Floor of nose or inferior maxilla
  - Infratemporal fossa
    - Preauricular with extension via hemicoronal and cervical incisions
- Resections
  - Medial maxillectomy
    - Lateral nasal wall + medial maxilla
  - Inferior maxillectomy
    - Maxillary sinus inferior to the infraorbital nerve
  - Total maxillectomy
    - Includes entire bone of the maxilla, up to its articulations with the frontal, sphenoid, and ethmoid bones.
  - Radical maxillectomy
    - Total maxillectomy + orbital exenteration
- Reconstruction of skull base defects/CSF leaks (watertight closure of skull base and dural defect is the goal)
  - Endoscopic
    - Vascularized pedicled
      - Nasoseptal flap—based on posterior septal branch of sphenopalatine artery (introduction reduced recurrent CSF leaks from 30 to 3 % with endoscopic resection)
      - Inferior turbinate flap—inferior turbinate branch of sphenopalatine artery
      - Middle turbinate flap—middle turbinate branch of sphenopalatine artery
    - Nonvascularized
      - Tensor fascia lata
      - Fat
      - Temporalis fascia
      - Bone grafts
      - Cadaveric bone or tissue
      - Synthetic implants (e.g., Medpore, Duraform, etc.)
  - Transfacial
    - Regional flaps
      - Temporoparietal fascial flap—superficial temporal artery
      - Pericranial flap—supraorbital and supratrochlear artery
    - Free flaps: De-epithelialized anterolateral thigh, rectus myofascial flap, radial forearm free flap fibula, iliac crest, or scapula for reconstruction of maxilla. Obturator in cases where reconstruction is contraindicated

- Complications
  - CSF leak
  - Intracranial infection
  - Osteitis
  - Epiphora
  - Orbital complications
  - Cerebrovascular occlusion
  - Hemorrhage
  - Tension pneumocephalus
  - Cranial nerve injury

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Chapter 23
Vascular Tumors

Eitan Prisman and Brett A. Miles

PEARLS

- Imaging of vascular tumors with ultrasound, MR, or CTA techniques can determine the extent of lesion and flow rate PRIOR to biopsy.
- Hemangiomas are generally treated conservatively with medical therapy and often spontaneously regress.
- Sclerotherapy may be utilized for lymphatic malformations and is more effective for macrocystic lesions; microcystic lesions often require surgical excision if feasible.
- Angiosarcoma is commonly seen in elderly white patients involving the scalp and has an extremely poor (20 % 5-year) survival; excision is frequently associated with dermal spread and positive margins.
- Carotid body tumors are the most common head and neck paraganglioma.
- Paragangliomas are biochemically active in 1–3 % of head and neck lesions; however biochemical work-up is required in all cases of suspected paraganglioma.
- Hereditary hemorrhagic telangiectasia is an autosomal dominant (AD) disease of small vessels presenting with recurrent nasal or nasopharyngeal bleeding, often treated with laser coagulation combined with endoscopic techniques.

CLASSIFICATION

- Vascular tumors can be classified as
  - Benign
    - Hemangioma
    - Vascular malformations
    - Juvenile nasopharyngeal angiofibroma (JNA)
    - Inflammatory
    - Telangectasia
    - Paraganglioma (97 %)
  - Malignant
    - Angiosarcoma
    - Hemangiopericytoma
    - Kaposi sarcoma
    - Paraganglioma (3 %)

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- Associated with syndromes
  - PHACES
  - Osler–Weber–Rendu
  - Sturge–Weber
  - Maffucci
  - Von Hippel-Lindau

Hemangioma

Epidemiology
- Most common benign vascular tumor of the H&N
- Mainly affects cutaneous surface of H&N but mucosal surfaces also affected
  - Must rule out subglottic hemangioma in pediatric patient with stridor and cutaneous hemangioma
  - 50 % of pediatric subglottic hemangiomas associated with cutaneous hemangioma
  - Most common adult laryngeal hemangioma is in supraglottis
- Either present at birth (30 %) or a few weeks later
- Male:female of 1:6

Presentation
- Clinical course
  - Rapid proliferation in first year
    - Histologically: endothelial hyperplasia
  - Followed by spontaneous involution over several months
    - 50 % involute by 5 years
    - 70 % involute by 7 years
- Pediatric subglottic hemangioma presents with failure to thrive or stridor
- Adult supraglottic hemangioma most commonly presents with hoarseness; with bleeding and respiratory distress less commonly

Imaging
- Well-circumscribed, high-flow, contrast-enhancing vascular tumor
- MRI: high intensity on T2-weighted images
- Flow voids on T1 and T2

Histology
- Gross: well circumscribed
- Low power: submucosal endothelial hyperplasia and presence of mast cells
- High power: frequent mitosis
- Two phases
  - Proliferative phase: increased angiogenesis-stimulating proteins
  - Involuting phase: mast cells and tissue inhibitor metalloproteinases

Management
- Observation is strongly recommended unless
  - Very large disfiguring ulcerative lesions
  - Lesion affecting function
    - Vision, hearing, deglutition, airway compromise, lumbosacral
  - Associated with high-output cardiac failure
- Medication
  - Propranolol
    - Must have baseline cardiac evaluation
    - Severe complications including bradycardia, hypoglycemia, and bronchoconstriction have been reported
  - Intralesional or systemic corticosteroids, interferon alpha-2a
- Surgical
  - Superficial hemangioma
    - Treated successfully with pulse dye laser (PDL)

- Subglottic hemangioma
  - CO_2 laser resection, laryngotracheoplasty, tracheotomy
- Wide excision and reconstruction may be indicated in rare cases

Vascular Malformation

Epidemiology
- Always present at birth, although may not be realized for months to years later
- Generally grows proportionally with patient
- May increase with trauma, infection, and hormonal changes

Classification
- Low flow—capillary, lymphatic, venous combinations
- High flow—arterial, combination (arteriovenous)

Histology
- Not associated with cellular hyperplasia but rather hypertrophy of existing cells
- Normal endothelial cell turnover and mast cells

Low flow—capillary malformation (CM)
- AKA port wine stain
- Present at birth and become darker with age and may be associated with soft tissue hypertrophy
- Arise from cutaneous superficial vascular plexus
- Equal M:F
- Associated with Sturge–Weber syndrome
  - Capillary malformation involving eye, skin, and leptomeninges
- Treated with 585 nm PDL

Low flow—lymphatic malformation (LM)
- Epidemiology
  - Most common pediatric head and neck vascular malformation
  - 90 % detected prior to 2 years of age
  - Soft and non-tender on palpation
- Categorized as
  - Macrocystic (cyst >2 cm)
  - Microcystic (cyst <2 cm)
  - Mixed (>50 % of lesion is macrocystic)
- Imaging
  - Low intensity on T1-weighted MRI
  - High intensity on T2-weighted MRI
  - Absence of flow voids
- Staging system based on anatomic position
  - I—unilateral infrahyoid
  - II—unilateral suprahyoid
  - III—unilateral suprahyoid and infrahyoid
  - IV—bilateral suprahyoid
  - V—bilateral suprahyoid and infrahyoid
- Histologically
  - Aberrant collections of lymphatic vessels and sacs
- Treatment
  - Microcystic disease as well as stage II–V are less responsive to treatment
  - Medical
    - Sclerotherapy
      - OK-432—lyophilized, low virulence strain of *Streptococcus pyogenes*, first line due to lack of associated fibrosis
      - EtOH
      - Bleomycin/tetracycline

    - Surgical excision
        - Usually delayed until 5 years of age
        - At least 3 months following infection
            - Macrocystic LM

Low flow—venous malformation (VM)

- Collection of dilated vascular channels with normal endothelium
- Presentation
    - Commonly at lips and cheeks
    - Can be isolated superficial skin lesions that appear in bluish color; or complex lesions spanning various tissue planes with otherwise normal-appearing skin
    - Increase in size in dependent positions
    - May be associated with pain if VM develops phleboliths
    - May be complicated by a consumptive coagulopathy
        - Diagnosed by elevated D-dimers, low fibrinogen
        - Treated with antiplatelet and anti-inflammatory ± heparin
- Imaging
    - Calcification representing phleboliths (because low flow)
- Treatment
    - Mostly observation
    - Surgical resection or sclerotherapy reserved for symptomatic lesions or significant cosmetic deformity

High flow—arteriovenous malformation (AVM)

- Aberrant communication between arteries and veins bypassing capillary bed
- Possible complications
    - Heart failure, ulceration, skin necrosis
- Presentation
    - Commonly presents in 20s and 30s
    - Red, warm pulsatile mass with a thrill or a bruit
    - Associated with pain, pulsation, or tinnitus
- Imaging
    - No enhancement on T2-weighted images
    - Flow voids on T1- and T2-weighted images
    - Angiography shows dilation of veins and early shunting
- Four clinical stages
    - Dormancy, expansion, destruction, heart failure
- Treatment
    - Observation
    - Preoperative embolization and surgical resection reserved for AVM complications

Juvenile Nasopharyngeal Angiofibroma

Epidemiology

- Typically in adolescent males
- Most common tumor in the nasopharynx
- Presents with epistaxis or nasal obstruction
- Less commonly with OME, proptosis, diplopia, recurrent sinusitis
- Originates at basisphenoid suture, at the level of pterygopalatine fossa
- Both spontaneous resolution and malignant transformation have been reported but are uncommon

Chandler classification

- Stage I—confined to nasopharynx
- Stage II—extending into nasal cavity and/or sphenoid
- Stage III—extending into one or more of the following: antrum, ethmoid, pterygomaxillary and infratemporal fossae, orbit and/or cheek
- Stage IV—extending into cranial cavity

Histology
- Gross: Reddish smooth polypoid mass
- Multiple staghorn-shaped vessels of varied sizes in a rich fibrous connective tissue stroma with little or no smooth muscle or elastic fibers around vessels

Imaging
- CT: soft tissue contrast-enhancing mass with enlarged sphenopalatine foramen
- *Holman-Miller sign*—anterior bowing of posterior maxillary sinus wall
- MRI: multiple flow voids on T1 and T2. Should be ordered to rule out intracranial, infratemporal, or intraorbital extension

Investigation
- Biopsy is not indicated unless evidence of rapid growth or atypical pattern of extension; if undertaken before complete excision, should be done in controlled OR setting where hemostatic control is possible.
- Imaging CT and MRI

Treatment
- Surgical therapy is gold standard
  - Historically approached via lateral rhinotomy, midfacial degloving, infratemporal fossa, transpalatal approaches
  - Standard approach is now endoscopic transnasal, transmaxillary
  - Combined endonasal–external approach in rare circumstances
- Preoperative embolization (within 24 h) is controversial but commonly done
  - Pro: decreased bleeding
  - Con: inadvertent cerebral embolization
- Radiation therapy reserved for unresectable tumors or non-operable recurrences
- Hormonal therapy (flutamide, estrogen) lacks sufficient evidence

Angiosarcoma

Epidemiology
- Aggressive malignant endothelial soft tissue sarcoma most commonly present in head and neck; scalp subsite most common
- Commonly in elderly white males
- 2 % of soft tissue sarcomas, 4 % of cutaneous sarcoma
- Overall 5-year survival of ~20 %
- May arise spontaneously or secondary to external radiation, exogenous toxins, or immunosuppression
- May be associated with syndromes
  - NF-1, Mafucci syndrome, Klippel–Trenaunay syndrome

Presentation
- Raised purplish-red papule, classically multifocal
- Aggressive disease with a 10–20 % reported rate of lymph node metastases
- Hematogenous spread typical with lungs most common metastatic site

Histology
- Pleomorphic, multilayered malignant endothelial cells with aberrant and chaotic architecture and abnormal vascular channels
- Distinguished from hemangiomas by the presence of "collagen dissection pattern" and formation of papillae

Imaging
- CT and MRI to evaluate bone and soft tissue involvement, respectively
- PET/CT useful to rule out metastatic disease

Staging (AJCC soft tissue sarcoma)

TX—primary tumor cannot be assessed
T0—no evidence of primary tumor
T1—<5 cm in greatest dimension, T1a—superficial tumor, T1b—deep tumor
T2—>5 cm in greatest dimension, T2a—superficial tumor, T2b—deep tumor
N0—no regional LN metastases
N1—regional LN metastases
M0—no distant metastases; M1—distant metastases
GX—grade cannot be assessed; G1—grade 1; G2—grade 2; G3—grade 3

Stage IA—T1aN0M0 G1,GX; T1bN0M0 G1,GX
Stage IB—T2aN0M0 G1,GX; T2bN0M0 G1,GX
Stage IIA—T1aN0M0 G2,G3; T1bN0M0 G2,G3
Stage IB—T2aN0M0 G2; T2bN0M0 G2
Stage III—T2aN0M0 G3; T2bN0M0 G3; any T, N1, M0; any G
Stage IV—Any T, any N M1, any G

Treatment
- Combination of wide surgical excision and neck dissection with postoperative radiation ± chemotherapy
- Induction chemotherapy can be considered in metastatic or unresectable disease

Hemangiopericytoma

Epidemiology
- Rare perivascular tumor most common in extremities
- Presents in the head and neck in 15 % of cases
- Originates from the pericapillary pericytic cells
- <1 % of all sarcomas are hemangiopericytoma

Presentation
- Normally hemangiopericytoma has an indolent growth pattern but may be locally aggressive and has distant metastases
- Uncommonly involve lymph nodes
- Metastatic disease most commonly to the lungs via hematogenous dissemination
- May present with oncogenic osteomalacia
  - Muscle and bone pain
  - Electrolyte abnormalities including hypophosphatemia

Histology
- Spindle or ovoid tumor cells in compacted nests or sheets between vascular channels with "pericytes of Zimmerman"
- Single layer of flattened endothelial cells
- Immunohistochemistry stains for vimentin but not desmin or factor VIII.

Treatment
- Even in the setting of complete excision, local recurrence is as high as 20 %, at an average of 46-month follow-up
- Complete surgical excision is the mainstay of therapy
- The role of radiotherapy remains to be clarified, and is applied in the setting of positive margins or unresectable disease

Kaposi Sarcoma (KS)

Epidemiology
- Spindle cell tumor derived from endothelial cell lineage
- Four types

- AIDS related
  - Most common malignancy in HIV-positive patients
  - Seroconversion to human herpes virus 8 (HHV-8) predates KS by 5–10 years
- Immunocompromised
  - KS 100-fold more likely in solid transplant recipients, with an incidence of 1/200
  - Average time to develop KS post transplant is 15–30 months
- Classic
  - Elderly men of Mediterranean or Eastern European origin
- Endemic (Africa)
  - African men and women who are HIV seronegative

Presentation
- Mucocutaneous lesions of skin, oral mucosa, and viscera
- Cutaneous lesions can be nodular, papular or plaques
- Typically of violaceous color, but may be pink or gray

Histology
- HHV-8 genomic sequences are identified in 90 % of KS
- Spindle cell proliferation with numerous and narrow vascular spaces and extravasated red blood cells

Investigation
- Must rule out underlying HIV, CD4 counts
- Punch biopsy to confirm diagnosis

Treatment
- HAART therapy for HIV positive
- Radiation therapy for larger lesion
- Surgical excisions for small lesions
- Intralesional therapy with vinca alkaloids

Paraganglioma

Epidemiology
- Aka glomus tumors, chromaffin and non-chromaffin cells, and chemodectoma
- Derived from neural crest cells
- Morphologically and cytochemically neuroectodermal derived neurosecretory cells
- Two types of paraganglia
  - Sympathetic—along prevertebral and paravertebral chain
  - Parasympathetic—along parasympathetic cervical and thoracic branches of IX and X
- Paraganglioma (PG) are hyperplastic or hypertrophied paraganglia with capacity to produce neuropeptides
- PG in general population is 1:50,000
  - 90 % in adrenal gland termed pheochromocytoma
  - 10 % extra-adrenal site
    - 85 % in abdomen
    - 12 % in thorax
    - 3 % in head and neck in decreasing order of frequency
      - Carotid body PG (most common)
      - Jugulotympanic PG
      - Vagal PG from nodosa ganglia of vagus
- More common in hypoxic environment
  - Particularly high-altitude population
  - Females, COPD

Presentation
- PG is biochemically active in 1–3 % of cases and may present with hypertension refractory to medical therapy, headaches, palpitations, and flushing
- Symptoms
  - Pulsatile tinnitus, neck mass, conductive hearing loss, cranial neuropathies of IX–XII

- Signs
  - Cartoid body (CB) PG
    - Fontaine sign: can palpate to illicit lateral displacement of neck mass but not in a cranio/caudal direction
    - Bruits on auscultation of mass
  - Jugulotympanic PG (see Otology section)
  - Vagal PG
    - Vagal paralysis → dysphagia, dysphonia

Etiological classification
- Familial paraganglioma syndrome (PGL)
  - Associated with mutations in succinate dehydrogenase (SDH) genes
- Sporadic mutations in SDH
- Associated with syndromes
  - VHL, MEN type 2, NF2

Shamblin classification of carotid body PG
- I—localized and small tumors that are minimally attached to the carotid vessels
- II—tumors adherent to and partially surrounding the carotid vessels
- III—tumors completely encasing the carotid

Histology
- Gross pathology: well demarcated and rubbery
- Nested growth pattern of tumor cells with an intervening stromal component of delicate fibrovascular stroma termed "Zellballen"
- Type 1 chief cells with hyperchromatic nuclei and granular cytoplasm
  - Stain for neuroendocrine differentiation
    - Chromogranin, synaptophysin, CD56, neuron-specific enolase
- Type 2 sustentacular supporting cells
  - Stain for S-100
- Malignant PG is reported in 6 % of cases and defined by spread to lymph node or distant spread (most commonly lung and bones)

Imaging
- Salt and pepper on MRI
- Carotid body PG
  - Lyre sign—splaying of internal and external carotid artery on CT/MRI
- Vagal PG
  - Displace the internal carotid artery anteromedially

Investigation
- CT with contrast, MRI with contrast, MRA
- Angiography ± preoperative embolization
- $Indium_{111}$ pentatreotide scanning to detect familial PG
- Biochemical testing to rule out secretory PG
  - 24 h urinary catecholamine (norepinephrine, VMA, normetanephrine)
  - Or plasma metanephrines
- CT abdomen to r/o pheochromocytoma

Treatment
- Carotid body PG
  - Observation for stable tumor and elderly or unstable patient
  - Surgical excision in young patients, or growing tumors
    - Preoperative embolization may be considered
    - Preparation for saphenous graft if vascular reconstruction necessary
  - Must stage bilateral CB PG because of labile blood pressure postoperatively
- Vagal PG
  - Surgical therapy is the mainstay of treatment
  - Results in vagal paralysis requiring laryngoplasty

PHACES syndrome

Hemangioma associated with the following:

- Posterior fossa malformation
- Hemangioma
- Arterial abnormality, and coarctation of the aorta
- Cardiac defects
- Eye abnormality

Symptoms

- Developmental delay, seizure, congenital stroke

Investigation

- Ophthalmology, cardiac and neurologic investigation

Kasabach–Merritt phenomenon

- Thrombocytopenia and Kaposiform hemangioendothelioma (KH) or tufted angioma (TA)
- KH
  - Unlike infantile hemangioma, they do not spontaneously involute
  - Blue red mass in superficial/deep extremity soft tissue, less common in head and neck
  - 42 % present with KMP
  - Small capillaries arising directly from large vessels → turbulent flow → platelet activation
- Treated with chemotherapy to decrease the risk of bleeding, and may require transfusion to treat active bleeding

Hereditary hemorrhagic telangiectasia (HHT)

- Osler–Weber–Rendu syndrome
- Autosomal dominant syndrome affecting blood vessels
- Presentation
  - Ectatic vessels of skin, mucous membranes, and viscera
  - Epistaxis usually presenting symptom at puberty/early adulthood
  - Skin telangiectasia can be punctate, linear, or spider like
  - Mucous membranes of oral cavity, naso/oropharynx, and GI tract
  - Associated with pulmonary, cerebral, and hepatic arteriovenous malformations
- Diagnosis
  - Hemorrhagic episodes (nasal cavity/nasopharynx, GI)
  - Vascular ectasia
  - Family history
- Investigation
  - Genetic testing available
  - Must rule out cerebral and pulmonary AVM with imaging in children with family history
- Treatment
  - Supportive
  - Electrocoagulation, photocoagulation (pulse-dye, Nd:YAG, argon beam)

Mafucci syndrome

- Cavernous hemangiomas
- Chondrosarcoma (25 % of cases)
- Dyschondroplasia
- Visceral vascular lesions

Sturge–Weber syndrome (SWS)

- Capillary malformation involving eye, skin, and leptomeninges
- Nevus Flammeus (port wine stain) is a cutaneous facial venous dilation: is the hallmark of SWS, and present at birth
- Seizure in up to 85 % of patients, mental retardation in 60 %
- Requires ophthalmology and neurology work-up

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Chapter 24
Cutaneous and Temporal Bone Malignancies

Hailun Wang and Brett A. Miles

PEARLS

- Basal cell carcinoma (BCC) body distribution = 85 % head and neck (most commonly nasal tip and alae of nose)
- BCC 4× more common on embryonic fusion planes than other regions of midface
- Cutaneous SCC most common index lesion site: the lateral aspect of head and the ear
- Cutaneous SCC most common met site: parotid (75 %) and upper cervical nodes
- Prognostic factors for melanoma include the number of metastatic lymph nodes, tumor burden and primary tumor ulceration, satellite and in-transit metastasis
- High-dose interferon-a 2b is the only FDA-approved adjuvant therapy for stage III melanoma

ANATOMY

- Layers of skin (superficial to deep)
  - Epidermis
    - Stratum corneum
    - Stratum granulosum
    - Stratum spinosum
    - Stratum germinativum/basale
  - Dermis
    - Papillary dermis
    - Reticular dermis
- Melanocytes = melanin-producing cells located in stratum basale; primarily responsible for skin color
- Basal cells = small, round, epithelial cells found in stratum basale
- Temporal bone
  - Squamosa
  - Mastoid
  - Petrous
  - Tympanic
- Posterior surface temporal bone
  - Boundaries
    - Superior = superior petrosal sinuses
    - Inferior = inferior petrosal sinuses

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    - Contents
        - Internal auditory canal, CN VII, CN VIII
        - Endolymphatic duct
        - Vestibular aqueduct
- Inferior surface of temporal bone
    - Contents
        - Mastoid tip
        - Styloid process (anterior to stylomastoid foramen)
        - Stylomastoid foramen
        - Temporomandibular fossa (anterior to styloid process)
        - Jugular foramen
        - Jugular bulb
        - Cochlear aqueduct
        - Jacobson's nerve (CN IX)
        - Carotid canal (anterior to jugular foramen, medial to styloid process)
        - Hypoglossal canal (medial, inferior to jugular foramen)
- Anterosuperior surface of temporal bone
    - Arcuate eminence (superior surface of petrous bone, overlying superior semicircular canal)
    - Facial hiatus = transmits greater superficial petrosal nerve
- Extenal auditory canal (EAC)
    - Lateral 1/3 = cartilaginous, cerumen glands (modified sweat glands, sebaceous glands)
    - Medial 2/3 = bony, epithelium closely adherent to periosteum, resistant to radial spread of cancers
    - Huschke foramen = developmental defect in tympanic ring → anterior extension of EAC malignancy to parotid.
    - Fissures of Santorini = small dehiscences in anterior cartilage → direct radial EAC tumor extension
- Middle ear (points of spread)
    - Anterior: Eustachian tube
    - Medial: round window, oval window
    - Posterior: mastoid cavity
    - Superior: tegmen tympani
- Lymphatic drainage
    - Auricle and EAC = periparotid lymph nodes (LN), parotid gland, jugular chain, LN overlying mastoid
    - Medial EAC, middle ear = retropharyngeal nodes, deep jugular nodes

EPIDEMIOLOGY

- Skin cancer = most common cancer in the United States
    - >1 million new cases/year
    - >10,000 deaths
    - ~2 % all cancer deaths
- BCC
    - 80 % of non-melanotic skin cancers, most common skin cancer
    - Locally destructive but least likely to metastasize (0.1 %)
    - Lifetime risk = 33–39 % men, 23–28 % women
    - Age of diagnosis = 20–90 y/o (mean 64.4 ± 5.6)
- Squamous cell carcinoma (SCC)
    - 20 % of non-melanotic skin ca (second most common skin ca), 90 % of cancers of H&N

- Malignant melanoma
  - 5 % skin cancers, 3× as many deaths as non-melanotic skin cancer
  - Lifetime risk = 0.4 %
  - M:F ratio = 1.2:1
  - 25 % of cutaneous melanomas arise in head and neck region
  - Median age of diagnosis 55 y/o

BASAL CELL CARCINOMA

Presentation

- Primary
  - Slowly enlarging lesion, non-healing, bleeds
  - Chronic sun exposure
- Fair skin 10- to 20-fold higher rates than dark skin
- Incidence lowest in blacks, Asians, and Hispanics.
- Recurrence

  Non-healing ulcer, tissue destruction, red/scaled/crusted scar, scar enlargement, papule/nodule within scar

Etiology/Pathogenesis

- Ultraviolet radiation
  - Sunlight (most frequently associated with development of BCC), tanning booths, UV light therapy
    - Latency period 20–50 years
  - UV radiation → modify nucleic acids → mutations leading to activation of oncogenes or inactivation of tumor-suppressor genes
  - Other radiation = X-ray, Grenz-ray
- Gene mutations
  - TP53 (tumor protein p53)
  - *Patched* (*PTCH*) = tumor-suppressor gene, Gorlin syndrome
  - *Patched homologue 1* (*PTCH1*) = loss-of-function mutation, sporadic and familial cases of BCC
  - Sonic hedgehog (*SHH*), smoothened (*SMO*), *Gli* = gain-of-function mutations, sporadic and familial cases of BCC
- Immunosuppression
  - Tenfold higher incidence of skin cancer in transplant patients
- Other causes:
  - Arsenic ingestion (Fowler solution, water contaminant)
  - Sites of trauma
  - Xeroderma pigmentosum
  - Epidermodysplastic verruciformis = autosomal recessive (AR)
    - BCC, SCC, and warts
  - Nevoid basal cell carcinoma syndrome = autosomal dominant (AD), *PTCH* gene
    - BCC, odontogenic keratocysts, intracranial calcifications, brain tumors, rib anomalies
  - Bazex syndrome = follicular atrophoderma, BCCs, local anhidrosis
  - Rombo syndrome = AD
    - BCC, atrophoderma vermiculatum, trichoepitheliomas, hypotrichosis milia, peripheral vasodilation with cyanosis
  - Alcohol consumption → link between excessive ETOH and higher incidence of sunburn

Work-Up/Staging

- Shave or punch biopsy
- Dermatoscopy: arborizing telangiectasia, blue-grey globules, blue-grey ovoid nests, spoke wheel areas
- Histopathology
  - Undifferentiated (solid type): basaloid cell proliferation with extension into papillary dermis, palisading peripheral columnar cells
  - Differentiated: keratotic (hairlike structures), cystic (sebaceous, gland-like structures), adenoid (tubular structures, lacelike pattern)
- High-risk BCCs: >2 cm, high-risk anatomical locations (centrofacial, periocular, embryological fusion zones), poorly defined edges, morpheaform or aggressive subtypes, perineural invasion (PNI), perivascular invasion (PVI), recurrence, immunosuppression
- Types
  - Nodular: most common, pearly/translucent, rolled edges, telangiectasia, central depression, ± ulceration
  - Superficial: scaly, pink, patch or plaque, more common on trunk/extremities
  - Morpheaform: flat or depressed, whitish scar; aggressive, worst prognosis
  - Pigmented: similar to nodular type, more pigmented, resembles a melanoma or a benign nevus
  - Fibroepithelioma: raised, firm, pedunculated, or sessile, red with smooth skin surface

Staging

Stage 0	Only epidermis, no spread to dermis
Stage 1	<2 cm, no mets to LN or other organs
Stage 2	>2 cm, no mets to LN or other organs
Stage 3	Spread beneath skin (e.g., muscle, bone, cartilage) and/or LN but not other organs
Stage 4	Any size, spread to other organs

TREATMENT RECOMMENDATIONS

- Prognosis excellent, 100 % survival if no spread to other sites
- Most common sites of metastasis (rare) = lymph nodes, lungs, bones
- 5-year risk of new primary = 50 %
- 5-year recurrence = 5 % (depending on treatment modality)
- Local excision
  - Small well-defined lesions (<20 mm) are cleared 95 % of cases with 4–5 mm margins
  - Morphoeic and large BCC require wider margins for complete histological resection
    - Morphoeic: 82 % cleared with 5 mm margins, >95 % with 13–15 mm margins
  - Recurrent lesions: 5–10 mm margin
- Mohs micrographic surgery (MMS)
  - Indications: tumor location in cosmetically sensitive area (e.g., central face, eyes, nose, lips, ears), size (esp >2 cm), poorly defined tumor margins clinically, recurrent lesions, perineural or perivascular involvement
- Radiotherapy: higher recurrence rate than surgery, less acceptable cosmetic outcomes
- Photodynamic therapy
  - Methyl aminolevulinate → cancer cell uptake → protoporphyrin IX → visible red light → create free radicals and singlet oxygen species → cytotoxic
  - Higher recurrence rate than surgery, better cosmesis

- Curettage and cautery: high recurrence rate; not generally used
  - Consider in small nodular or superficial BCC lesions
  - Poor outcomes for high-risk and recurrent BCC lesions
- Cryotherapy: liquid nitrogen
  - Not recommended first line, poor cosmesis, high recurrence rate (2-year estimated recurrence rate 20.6 %)
- Laser: carbon dioxide, Erb:YAG
  - Limited data, risk of more aggressive histological pattern, need for subsequent surgery

CUTANEOUS SQUAMOUS CELL CARCINOMA OF THE HEAD AND NECK

Presentation

- History
  - Presents in the middle- and older-aged individual with change in existing lesion, now present as non-healing ulcer or abnormal growth in sun-exposed area
  - Sun exposure, occupational exposures, previous cutaneous squamous cell carcinoma (cSCC), HPV infection (16, 18)
  - Actinic keratosis is often the precursor lesion to cSCC, but <1 % of actinic keratosis progresses to cSCC annually
  - Medical conditions—associated with xeroderma pigmentosum, previous cutaneous nonmelanoma malignancies, and lymphocytic leukemia
- Cutaneous squamous cell carcinoma of the head and neck (CSCCHN) represents 25 % of all nonmelanoma skin ca
- Directly related to proximity to equator
- Risk factors: Caucasian, M > F 3:1, >65 y/o, sun-exposed, immunocompromised
- 60 % arise out of actinic keratoses, 40 % de novo
- Signs and symptoms
  - Flesh tone, reddish-brown, or erythematous opaque papule or nodule with hyperkeratotic center, borders may be diffuse or distinct based on the degree of differentiation, often palpable
  - Cutaneous horn, ulceration, or erosion may be present
  - Mets to affected LN may be palpable, namely, the parotid and upper cervical LN

Etiology/Pathogenesis

- Ultraviolet radiation
  - Sunlight (most frequently associated with cSCC), tanning booths, UV light therapy
  - UV radiation → modify nucleic acids → mutations leading to activation of oncogenes or inactivation of tumor-suppressor genes
- Gene mutations
  - Telomerase gene
  - p53 tumor suppressor
  - p16 tumor suppressor
- Allogenic transplant patients with subsequent immunosuppression
  - Population most at-risk for cSCC
- Other causes
  - HPV or EBV infection
  - Occupational exposures
  - Dermatoses—genodermatoses, scarring dermatoses, chronic wounds, burn scars

Work-Up/Staging

- Punch/wedge biopsy with histopathologic diagnosis, fine-needle aspiration (FNA) often uncovers secondary cSCC lesions
- Histopathology

- Solar keratosis—atypical squamous cells infiltrating papillary dermis
- Spindle cell—commonly presents in previous wound, burn, or trauma as whorled cluster of cells with stretched nuclei
- Adenoid—glandular-like histology, more common in elderly, periauricular
- Verrucous—wart-like, less malignant than other types
- Bowen's disease—in situ form of cSCC presenting as erythematous scaly plaque with well-defined edges, may progress to invasive cSCC if left untreated

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Stage 0	Only epidermis, no spread to dermis (Tis)
Stage I	≤2 cm plus ≤1 high-risk feature (T1), no mets to LN (N0) or distantly (M0)
Stage II	>2 cm plus ≤1 high-risk feature (T2), no mets to LN (N0) or distantly (M0)
Stage III	Tumor invasion of regional bone (T3) plus ≤1 ipsilateral LN ≤3 cm, *or* T1/2 plus met in single ipsilateral LN ≤3 cm (N1)
Stage IV	T1/2/3 plus met in single ipsilateral LN >3 cm or multiple LN, but ≤6 cm (N2), *or* Any met in LN >6 cm (N3), no mets distantly (M0), *or* Tumor invasion of distant bones (T4), no mets distantly (M0), *or* Any met distantly (M1)

- Perineural invasion associated with up to 47 % metastasis rate with standard treatment, but as low as 8 % metastasis rate with MMS

TREATMENT RECOMMENDATIONS

- Good prognosis, 95 % cure rate with complete excision
- Recurrence risk of 5 %, met risk of 5 %, disease-specific death in 1 %
- High-risk (metastatic) cSCC: >2 cm in size, >6 mm (or ≥5 mm or >4 mm) in depth, in scars/wounds, in embryonic fusion zones, in non-sun-exposed areas, on ear or lip, in poorly differentiated lesions, bullous lesions, where there is vessel invasion, with an immunocompromised host, with EGFR expression, conveys ≥20 % risk for mets, possesses lower overall 5-year survival rate of 46–70 %
- Wide local surgical excision, 4 mm margins for well-defined lesions, 6 mm margins for poorly defined lesions
- Cryotherapy, curettage, and electrodessication therapies have been utilized for isolated, low-grade, primary lesions
- MMS for lesions with indiscreet margins, large size, or central facial location
  - Mohs with histologically clear borders can result in up to 97 % cure rates
  - cSCC with perineural invasion may be successfully cleared by MMS
- In metastatic disease, local excision plus adjuvant radiotherapy with appropriate parotidectomy
- Radiotherapy may be used as adjuvant or preoperative therapy, and as sole therapy only in unresectable cases
- Chemotherapy as a postsurgical adjuvant benefit not well established

MALIGNANT MELANOMA

Presentation

- History: changes in color/size/shape, bleeding, ulceration, pain, or pruritus; family or personal h/o skin cancer, h/o excessive tanning, and sunburns
- Physical exam:
  - ABCD checklist: asymmetry, border irregularity, color variation, diameter >6 mm
  - Evolving changes in lesion
  - Total body exam, lymph node exam
- Risk factors: fair complexion, freckling, h/o sunburning, immunosuppresion, tanning booth exposure, prior h/o melanoma (8 % concurrent multiple melanomas, 5–10 % develop second primary)

- Unknown primary
  - 2–8 % of melanoma cases
  - 2/3 with regional metastasis in the absence of primary lesion or h/o melanoma, 1/3 distant mets.

Etiology/Pathogenesis

- Gene mutations
  - p16 is most common mutation, however only seen in 0.2 % of melanoma cases
  - Ras–Raf–Erk pathway: pathway in cell proliferation, gain-of-function mutations in BRAF (50–70 % of melanomas)
  - PI2K/PTEN: activating mutation PI3K, loss of PTEN, amplification of AKT
  - c-kit (tyrosine kinase receptor): activating mutations → constitutive activation of proliferation pathways
- Hereditary causes
  - B-K mole syndrome, xeroderma pigmentosa, familial atypical multiple mole-melanoma (FAMMM) syndrome (aka atypical mole syndrome; 100 % with melanoma by mid 70s)
- Premalignant lesions:
  - Congenital melanocytic nevi: Appear between birth and 6 months; increased risk for melanoma (5–20 %) associated with large CMN
  - Dysplastic nevus/atypical mole: irregular/indistinct borders, heterogeneous coloration
  - Lentigo maligna (aka Hutchinson's melanotic freckle): In situ melanoma, precursor to lentigo malignant melanoma
- Growth phases: radial (outward spread, through epidermis), vertical (invasion deep into dermis, risk for metastasis)
- Histological subtypes
  - Superficial spreading: 70 %, arise from dysplastic nevus
  - Nodular
  - Lentigo maligna
  - Acral lentiginous
  - Mucosal lentiginous

Work-Up/Staging

- Biopsy
  - Excisional biopsy with 1–2 mm margin, including dermis and subcutaneous fat
  - Consider incisional or punch biopsy in case of large lesions or those in cosmetically important areas (e.g., face)
- Histopathology
  - Reports should include the following:
    - Thickness (see Breslow classification below), ulceration, mitotic rate, margin status, level of invasion, microsatellites
    - Angiolymphatic invasion, neurotropism, regression, vertical growth phase, lymphocytic infiltration
- Imaging
  - CXR
    - Cost-ineffective, high false-positive rate
    - Obtain in stage III disease, may consider as baseline in earlier stages
  - PET
    - Best imaging modality for detecting sites of metastasis
    - Low sensitivity in detection of occult regional nodal metastasis compared with sentinel lymph node biopsy
    - Helpful in evaluating response of metastatic disease to therapy
    - Not indicated in early-stage disease (i.e., I and II)
  - CT
    - Chest: staging w/u in patient with known metastatic disease (stage IV)

    - Abdomen: obtain in patients with stage III, locally recurrent or in transit disease
      - Low yield but provides baseline
    - Pelvis: obtain in patients with h/o primary tumors below waist or local recurrence below waist
  - Ultrasound
  - Surveillance imaging in asymptomatic melanoma patients: low yield, high false-positive rates
- Sentinel lymph node biopsy
  - Most sensitive and specific staging test, important prognosticator for disease-specific survival (melanomas >1 mm thick)
- Clark staging
  - Level I: All tumor cells above basement membrane (in situ)
  - Level II: Tumor extends into papillary dermis
  - Level III: Tumor extends to junction between papillary and reticular dermis
  - Level IV: Tumor extends into reticular dermis
  - Level V: Tumor invasion into subcutaneous tissue
- Breslow classification
  - ≤0.75 mm
  - 0.76–1.5 mm
  - 1.51–4 mm
  - ≥4 mm

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T classification	(Thickness)
Tx	Tumor cannot be assessed
Tis	Melanoma in situ
T1	≤1.0 mm (a) Without ulceration and <1 mitosis/mm^2 (b) With ulceration or ≥1 mitosis/mm^2
T2	1.01–2.0 mm (a: with ulceration; b: with ulceration)
T3	2.01–4.0 mm (a: w/o ulceration; b: with ulceration)
T4	>4.0 mm (a: w/o ulceration; b: with ulceration)
N classification	
NX	Regional lymph nodes cannot be assessed
N0	No regional metastasis detected
N1	1 lymph node (a: micrometastasis; b: macrometastasis)
N2	2–3 lymph nodes (a: micrometastasis; b: macrometastasis; c: in-transit or satellite w/o metastatic nodes)
N3	≥4 metastatic nodes, matted nodes, in-transit mets or satellites with metastatic nodes
M classification	
M1a	Distant skin, subcutaneous, or nodal mets; normal LDH
M1b	Lung mets
M1c	All other visceral mets or any distant mets and elevated LDH
AJCC staging	
Stage 0	Tis, N0, M0
Stage I	A: T1aN0M0 B: T1bN0M0
Stage II	A: T2bN0M0, T3aN0M0 B: T3bN0M0, T4aM0M0 C: T4bN0M0
Stage III	(Any T, N1-3, M0) A: pT1-4aN1aM0, pT1-4aN2aM0 B: pT1-4bN1aM0, pT1-4bN2aM0, pT1-4aN1bM0, pT1-4aN2bM0, pT1-4a/bN2cM0 C: pT1-4bN1bM0, pT1-4bN2bM0; any TN3M0
Stage IV	Any T, any N, any M

TREATMENT RECOMMENDATIONS

- Surgical resection
  - Wide excision with 1–2 cm margins around primary tumor; 2 cm margins for tumors >2 mm in thickness
    - (No evidence of improved survival or local recurrence rates with margins >2 cm)
- Adjuvant therapy
  - Interferon alpha-2b
    - Immunomodulatory cytokine → increase phagocyte and lymphocyte activity
    - FDA approval based on large multicenter study showing improved disease-free survival using high-dose IFN, delayed time to progression (8 months), and 1-year survival benefit
    - Subsequent prospective randomized trials have not shown significant differences in overall survival or relapse-free survival
    - One-year treatment regimen, significant toxicity
  - Vemurafenib
    - Inhibits mutated forms of BRAF serine–threonine kinase
    - Indications: unresectable or metastatic melanoma with BRAF-V600 mutation
- Stage IV melanoma
  - Poor therapeutic options, no significant prolongation of survival
  - Dacarbazine (DTIC): 10–15 % response rate
  - Combination regimens commonly used (no significant improvement compared with DTIC alone)
    - Cisplatin, vinblastine, DTIC
    - Cisplatin, DTIC, carmustine, tamoxifen
- Lentigo maligna subtype associated with broader superficial subclinical extension, requiring wider surgical margins
- Therapeutic LND acceptable for proven neck disease but prophylactic LND does not demonstrate overall survival benefit
- Melanoma of unknown primary prognosis: survival similar to stage III disease (55 and 44 %, 5- and 10-year survival). Treatment should include aggressive surgical approach and consider for adjuvant therapy.

TEMPORAL BONE MALIGNANCIES

Presentation

- Presenting symptoms:
  - Chronic otalgia (80–85 %), otorrhea (40–75 %)
  - Hearing loss (45–80 %), tinnitus (8–10 %)
    - CHL from canal obstruction
    - SNHL and vertigo → labyrinthine involvement, aggressive lesions
  - Cranial nerve paresis (30 %)
    - CN V, IX, XI
  - Parotid mass (19 %)
  - Others: vertigo, auricular lesion, external canal mass, skin lesions
- Rare, <0.2 % of all H&N tumors
- Most commonly arise from pinna and lateral concha (BCC, SCC) with medial spread to EAC
- SCC = most common primary EAC tumor; "meaty" or polypoid lesions

Etiology/Pathogenesis

- Difficult to measure given rarity of temporal bone (TB) cancers
- Chronic otitis media and cholesteatoma common
- Chronic suppurative otitis media → squamous metaplasia

- HPV
- History of radiotherapy
- Other TB carcinomas
  - Basal cell carcinoma = second most common, ulceration, absence of pearly edges (thin, adherent canal epithelium)
  - Melanoma = third most common, arising from auricle or EAC
  - Rhabdomyosarcoma = most common pediatric TB malignancy; 10 % of all rhabdomyosarcomas occur in ear
  - Adenoid cystic: rare in TB; epithelium-covered, "small pimple," significant pain
  - Endolymphatic sac papillary tumor (aka Heffner's tumor): hearing loss, cranial nerve deficits
    - Usually isolated, 11–30 % associated with von Hippel-Lindau disease
  - Adenocarcinoma (ceruminous), giant cell tumor, chondrosarcoma, osteosarcoma, verrucous carcinoma

Work-Up/Staging

- History: prolonged otalgia, recurrent/persistent ear infections, h/o cholesteatoma
- Physical exam:
  - Complete H&N exam
  - Inspection of pinna, EAC, middle ear
  - Cranial nerve exam
- Audiology
- Thin-slice CT temporal bone with contrast
  - Soft tissue detail, bony erosion, medial extension
- Metastatic work-up: CT C/A/P, PET/CT (r/o lung mets in cases of SCC)
- Carotid angiography
  - If carotid involvement suspected
  - Balloon occlusion test

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Primary tumor (T)

T1: limited to EAC w/o bony erosion or soft tissue involvement

T2: limited to EAC bone erosion (not full thickness), limited soft tissue involvement (<0.5 cm)

T3: eroding osseous EAC (full thickness), limited (<0.5 cm) soft tissue involvement, or involving middle ear, mastoid, or both

T4: eroding cochlea, petrous apex, medial wall of middle ear, carotid canal, jugular foramen of dura, extensive (>0.5 cm) soft tissue involvement (e.g., TMJ, stylomastoid foramen), or facial paresis

Regional lymph nodes (*N*)

N1: Single ipsilateral lymph node ≤3 cm in greatest dimension

N2: Single ipsilateral lymph node >3 cm but ≤6 cm in greatest dimension

N2b: Multiple ipsilateral lymph nodes, ≤ 6 cm in greatest dimension

N2c: Bilateral or contralateral lymph nodes ≤6 cm in greatest dimension

N3: Lymph node >6 cm in greatest dimension

Distant metastasis (*M*)

Distant metastasis cannot be assessed

No distant metastasis

Distant metastasis

Stage 0	Tis, N0, M0
Stage I	T1, N0, M0
Stage II	T2, N0, M0
Stage III	
	T3, N0, M0
	T1, N1, M0
	T2, N1, M0
	T3, N1, M0
Stage IV	
	T4, N0, M0
	T4, N1, M0
	Any T, N2, M0
	Any T, N3, M0
	Any T, any N, M1
	T4a, N2, M0
Stage IVB	
	Any T, N3, M0
	T4b, any N, M0
Stage IVC	
	Any T, any N, M1

TREATMENT RECOMMENDATIONS

- Dependent on location of carcinoma: cartilaginous vs. bony
- Late findings/poor prognosis = parotid mass, CN palsies, lymphadenopathy (LAD)
- Sleeve resection
  - T1 tumors, limited to cartilaginous canal, adjunct radiotherapy if bony, cartilaginous, or soft tissue invasion
- Lateral temporal bone (LTB) resection
  - T1/T2 tumors, involving or abutting osseous EAC; adjunct XRT if bony, cartilaginous, or soft tissue invasion
- Subtotal temporal bone (STTB) resection
  - Involving or abutting osseous EAC with mesotympanic extension, <1 cm dural involvement; can also consider LTB with subtotal petrosectomy
- Total temporal bone (TTB) resection
  - Extending beyond labyrinth and cochlea, extension into petrous apex (extremely rare)
- Palliative radiation
  - ICA encasement, petrous apex extension, >1 cm dural involvement, intraparenchymal invasion
- Adjunctive radiation
  - All T3 and T4, or if indicated by pathologic behavior (perineural invasion, LN mets, extracapsular spread)
  - 50–60 Gy (T3 and T4, consider for T2)
- Perioperative chemotherapy
  - Consider pre-op in borderline resectable tumors
  - Post-op given concurrently as radiosensitizer during adjuvant radiotherapy
  - Retrospective series
    - Four of eight pts treated with 5-FU or fluoropyrimidine complex during external beam radiation (40 Gy) → disease free at 24–47 months

- Outcomes of radical surgery and postoperative XRT for SCC of TB
  - Stage I–II: 100 %
  - Stage III: 100 %
  - Stage IV: 34.3 %
  - Overall for entire series: 43.2 %
  - Node positive, poorly differentiated, brain involvement, and salvage surgery = poorer outcome
    - Improved survival in de novo therapy vs. salvage surgery

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Chapter 25
Odontogenic Cysts and Tumors

Robert N. Sharobiem and Brett A. Miles

PEARLS

- Dentigerous cysts are the most common odontongenic cysts and arise from the dental follicle.
- Keratocysts have a high rate of recurrence and most commonly occur in the mandible.
- Ameloblastomas are the most common of odontogenic tumors.

ODONTOGENIC CYSTS

- All odontogenic cysts consist of a central lumen, an epithelial lining of odontogenic origin, and a connective tissue wall.

DENTIGEROUS CYST

- Clinical features
  - Most common developmental odontogenic cyst.
  - Peak incidence during the teenage years and 20s, male predilection of 1.6:1.
  - Most common in posterior mandible or maxilla and usually associated with third molars. Other common teeth are maxillary canines and mandibular second premolars.
  - Arises from the dental follicle of an unerupted tooth.
  - May present as an incidental finding or as an asymptomatic bony expansion as these can be as large as 15 cm causing facial asymmetry. These cysts are thought to enlarge due to increased osmotic pressure in their lumen.
  - Asymptomatic unless secondarily infected, no paresthesia, pain.
- Radiographic features
  - Well-defined, unilocular radiolucency associated with the crown of an unerupted tooth. The tooth may be significantly displaced by cyst expansion.
- Histopathologic features
  - Surrounds the crown of a tooth and is attached at the cemento-enamel junction. Grossly there may brownish fluid or semisolid cystic material.
  - The epithelial cyst lining resembles reduced enamel epithelium and has two to three rows of cuboidal or flattened nonkeratinizing cells.
  - Cholesterol clefts may be seen.

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- Treatment and prognosis
  - Enucleation is the treatment of choice and no recurrence is expected.
  - Marsupialization is an option for larger cysts. Consider marsupialization when it will allow the tooth to erupt or when surgical removal presents a risk to damaging developing teeth, the inferior alveolar (IA) nerve, or other structures.
  - Prognosis excellent, but malignant transformation of lining has been reported 1–2 %.

ODONTOGENIC KERATOCYST (KERATOCYSTIC ODONTOGENIC TUMOR)

- Clinical features
  - Twice as common in the mandible and more common in posterior body/ramus region.
  - Most aggressive of all odontogenic cysts with high rates of recurrence.
  - Primordial origin—60 % arise from dental lamina rests or from the basal cells of oral epithelium.
  - Dentigerous origin—40 % arise from reduced enamel epithelium of the follicle.
  - Tumors extend anteroposteriorly as they progress through medullary bone although cortical expansion and perforation may be observed. Usually does not infiltrate soft tissues.
  - Associated with the nevoid basal cell carcinoma (Gorlin) syndrome—multiple basal cell carcinomas of the skin, multiple odontogenic keratocysts, intracranial calcifications, epidermal cysts of the skin, palmar/plantar pits, enlarged head circumference, hypertelorism, and rib and vertebral anomalies. Prevalence is 1:60,000.
- Radiographic features
  - May present as a well-defined, small or large unilocular radiolucency or as a multilocular radiolucency. Those of dentigerous origin are associated with a tooth.
- Histopathologic features
  - Epithelial lining is 6–8 cells thick of stratified squamous epithelium.
  - Fibrous wall is thin and may have epithelial islands, cysts, or cords with central keratinization and cyst formation. These are daughter or satellite cysts. Present in 7–26 % of cases. Some authors regard these as the source of recurrence.
  - The cyst lumen contains varied amount of keratinaceous debris that grossly appears as a caseous/cheesy material.
- Treatment and prognosis
  - Treatment options include enucleation and curettage, marsupialization, and resection.
  - Enucleation is the best option for small lesions, especially if cyst can be removed without rupturing the lining. If unable, then curettage of bony cavity is necessary. Curettage may be physical with a rotary bur (peripheral ostectomy), hypothermal with cryotherapy, or chemical with Carnoy's solution (fixative composed of 60 % ethanol, 30 % chloroform, and 10 % glacial acetic acid, also can include ferric chloride).
  - Marsupialization can bring an associated tooth into functional position or when surgical removal presents a risk to damaging developing teeth, the IA nerve, or other vital structures. This is also thought to thicken the cyst lining making subsequent removal easier.
  - Resection is indicated if there have been multiple recurrences after enucleation and curettage. Resection can be subperiosteal as there is no soft tissue invasion and osseous margin should be 1.0 cm.
  - Recurrences occur in 5–62 % of cases and are either due to failure to remove all original cyst lining or a new primary cyst formation from activated rests or oral basal epithelium. Most recur within 5 years, but may recur later than 10 years.

CALCIFYING ODONTOGENIC CYST

- Clinical features
  - Also known as a Gorlin's cyst, 2005 WHO Classification includes it as a tumor.
  - Asymptomatic jaw expansion and usually an incidental radiographic finding.
  - Average size is about 3.0 cm, but can be as large as 12.0 cm.
  - The more infiltrative or even malignant neoplasms are referred to as dentinogenic ghost cell tumors and occur in older patients.
  - Extraosseous calcifying odontogenic cysts (COCs)—25 % of all COCs, occur anterior to first molar in people older than 50 years. Appear on interdental papilla or alveolar mucosa as a firm, soft tissue mass. Also may show calcifications on radiographs.
- Radiographic features
  - Early on, the cysts are completely radiolucent, but as they mature develop calcifications and are well-defined, mixed radiolucent-radiopaque lesions.
  - Three patterns of radiopacity: salt-and-pepper pattern of flecks, fluffy cloud appearance, and a crescent-shaped pattern on one side of the radiolucency appearing moon-shaped. Radiopacities are present in 33–50 % of cases.
  - 1/3 of cases are associated with an unerupted tooth, with the canine being most common and root resorption or divergence commonly seen.
- Histopathologic features
  - Unilocular cysts with a distinct odontogenic, ameloblast-like basal cell lining consisting of cuboidal to columnar cells with hyperchromatic nuclei, which may show reverse polarization away from the basal membrane. These cells are loose in arrangement (similar to stellate reticulum) and include the presence of *ghost cells*, which are eosinophilic cells with degenerated nuclei (only a clear space remains).
- Treatment and prognosis
  - Enucleation and curettage are curative and they rarely recur.
  - Ameloblastomas may have ghost cell differentiation and should be treated as an ameloblastoma and shows no relation to the COC.
  - Malignant odontogenic ghost cell carcinomas although rare can occur and have a 5-year survival rate of 73 %.

GLANDULAR ODONTOGENIC CYST

- Clinical features
  - Middle-aged adults with a mean age of 48 years, 75 % occur in the mandible.
    - Predilection for anterior region of jaws and may cross the midline.
  - May present as a small asymptomatic lesion or a large destructive lesion with clinical expansion, pain, and paresthesia.
- Radiographic features
  - Well-defined, unilocular or multilocular, radiolucent lesions especially in the anterior mandible.
- Histopathologic features
  - Multilocular with stratified squamous epithelial lining of varying thickness and a flat epithelium-connective tissue interface. The epithelium has a distinctive surface layer of cuboidal to columnar cells with eosinophilic cytoplasm and cystic spaces.
- Treatment and prognosis
  - Enucleation and curettage is treatment, but recurrence rates are as high as 30 %.
  - Higher recurrences in multilocular lesions and some authors advocate for en bloc resection, especially of multilocular lesions.
  - Surveillance is recommended to follow up for malignancy including low-grade mucoepidermoid carcinoma, which has been misdiagnosed as a glandular odontogenic cyst (GOC).

ODONTOGENIC TUMORS: ODONTOGENIC EPITHELIUM

- Ameloblastoma
  - Most common true odontogenic benign neoplasm.

INVASIVE AMELOBLASTOMA: CONVENTIONAL SOLID/MULTICYSTIC AMELOBLASTOMA (86 %)

- Clinical features
  - Asymptomatic expansion of the jaw—mandible 75–80 %, maxilla 20–25 %.
    - Posterior third molar-ascending ramus region most common.
  - Locally aggressive, slow-growing, destructive lesion.
  - Root resorption of adjacent teeth is common.
- Radiographic features
  - Unilocular or multilocular expansile radiolucency with well-defined borders and possibly displacement of surrounding structures.
  - May have "soap bubble" or "honeycombed" appearance with scalloping borders.
- Histopathologic features
  - Follicular pattern—most common. Islands of odontogenic epithelium with palisaded columnar cells at the periphery.
  - Plexiform pattern—second most common type. Odontogenic epithelial cells proliferate in a network of connecting strands.
  - Desmoplastic ameloblastoma—thickened bony trabeculae in a dense fibroblastic collagenized stroma. Islands and cords of odontogenic epithelium.
  - Basal cell pattern—least common type. Tumors in which the hyperchromatic basaloid cells form islands and connecting strands in a fibrous stroma.
- Treatment and prognosis
  - Bony resection with 1.0–1.5 cm margins and anatomic barrier margins of one uninvolved anatomic barrier. For both primary and recurrences.
  - Enucleation and curettage will have a 70–85 % recurrence rate in 5 years.
  - Ameloblastomas treated by resection have a 98 % cure rate.

UNICYSTIC AMELOBLASTOMAS/AMELOBLASTOMAS ASSOCIATED WITH CYSTS (13 %)

- Unicystic ameloblastoma is a term used to describe an ameloblastoma arising in the lining, lumen, or wall of a cyst.
- Clinical features
  - 90 % occur in the mandible, especially posterior region.
  - In situ and microinvasive lesions are normally discovered histopathologically after removal of a dentigerous cyst.
- Radiographic features
  - Well-defined, unilocular radiolucency extending from the crown of a tooth. Has the typical appearance of a dentigerous cyst.
- Histopathologic features
  - Similar features of ameloblastoma, but in situ, intraluminal, and mural components are histological diagnoses depending on the relationship to the cyst lining.
- Treatment and prognosis
  - Enucleation vs. resection depending on the invasive component.

PERIPHERAL AMELOBLASTOMA (1 %)

- Clinical features
  - Firm and painless, single or polypoid exophytic mass arising from the gingiva or alveolar mucosa. Normally non-ulcerated and may be sessile or pedunculated.
  - Most occur in posterior regions of the jaws and mandible more common.

- Radiographic features
  - Does not invade bone, but may show saucerization of alveolar bone.
- Histopathologic features
  - Similar to intraosseous form with follicular, plexiform, and basilar forms.
- Treatment and prognosis
  - Soft tissue mass excision with 2–3 mm margins.

MALIGNANT AMELOBLASTOMA (MA) AND AMELOBLASTIC CARCINOMA (AC)

- Clinical features
  - MA may metastasize to lymph nodes, long bones, vertebrae, etc. Lungs most common. MA requires metastasis to be a diagnosis, as it is otherwise a benign process.
  - Metastasis is normally noticed 10 years after treatment of the primary jaw tumor.
  - Ameloblastic carcinoma may be locally aggressive and metastasize, as well.
  - ACs are usually large masses with ulcerations, bone resorption, and tooth mobility.
  - AC behaves similar to SCC.
- Radiographic features
  - MA will appear as a typical benign ameloblastoma, but with concomitant metastasis.
  - AC will normally have ill-defined margins and cortical destruction.
- Histopathologic features
  - MA is a benign ameloblastoma histopathologically, but with local or distant metastasis. The lesions show no cellular atypia or pleomorphism.
  - AC differs from MA, because the epithelial cells are atypical and consistent with a malignancy.
- Treatment and prognosis
  - Treatment requires surgical resection with 2–3 cm margins and neck dissection.
  - Postoperative radiation therapy also must be considered.
  - Prognosis is guarded with 5-year survival rates less than 40 %.
  - Distant metastasis is associated with poor prognosis, and palliative chemoradiotherapy may be indicated.
  - Recurrence rate >60 %.

CLEAR CELL ODONTOGENIC CARCINOMA

- Clinical features
  - Symptomatic central expansion of the jaws—mandible 84 %.
  - Expansion may displace teeth or resorb roots.
  - Locally aggressive and may invade local soft tissues ~60 % of cases.
  - 20–25 % will have metastasis, mostly to lymph nodes or lungs.
- Radiographic features
  - Large, unilocular, expansile radiolucency. Can have defined or irregular margins.
- Histopathologic features
  - Negative staining for mucin unlike clear cells of the mucoepidermoid carcinomas.
  - Grows in a lobular pattern with a surrounding capsule.
  - Demonstrate little pleomorphism, but are infiltrative and have capsular invasion.
- Treatment and prognosis
  - Treatment is bony resection with a 1.5 cm margin including periosteum. Soft tissue excision if there is invasion.
  - Selective neck dissection if lymph nodes involved on CT scan or clinical suspicion from aggressive behavior such as pain, paresthesia, rapid growth, or large size.
  - Postoperative radiation therapy also must be considered for close/positive margins.

ADENOMATOID ODONTOGENIC TUMOR/CYST

- Clinical features
  - Two-thirds tumor/cyst—2/3 occur in maxilla, 2/3 occur in young women (preteen and teenage years), 2/3 associated with unerupted tooth, and 2/3 of those teeth are canines.
  - Displaces rather than resorbs roots.
- Radiographic features
  - Well-defined, radiolucency usually associated with an impacted tooth (follicular type). May also appear as a unilocular radiolucency not related to an unerupted tooth (extrafollicular type).
- Histopathologic features
  - Grossly has a thick connective tissue capsule, which makes separation from bone easy and an exophytic epithelial lining, sometimes filling the entire lumen. Aspiration will return a straw-colored fluid.
- Treatment and prognosis
  - Enucleation and curettage are curative without recurrence.
  - The associated tooth must be removed as it is entirely within the cystic lumen and not surrounded by bone.

CALCIFYING EPITHELIAL ODONTOGENIC TUMOR

- Clinical features
  - Described by Pindborg in 1956 and frequently termed a "Pindborg Tumor."
  - Asymptomatic expansion of the jaw—mandible two to three times more than maxilla.
  - Invasiveness varies from mild to moderate.
  - Slow-growing, benign neoplasm.
- Radiographic features
  - Early tumors are radiolucent, while larger more mature tumors are mixed radiolucent-radiopaque. May be unilocular or multilocular with "soap bubble" appearance. May have a distinct sclerotic border with surrounding bone or an ill-defined border with no clear demarcation (20 %). Margins often scalloped.
  - Most are associated with crown of an impacted tooth mostly mandibular third molar.
- Histopathologic features
  - Infiltrating and unencapsulated tumors.
  - Epithelial components are sheets and islands of eosinophilic polygonal/polyhedral cells with intercellular bridges. Nuclei are central with prominent nucleoli and may have pleomorphism.
- Treatment and prognosis
  - Less aggressive and invasive than either the ameloblastoma or myxoma.
  - Enucleation and curettage show recurrence rates of 15–30 % after 2–4 years.
  - Best treated with bony resection using 1.0–1.5 cm margins and one uninvolved anatomic barrier (similar to ameloblastoma).
  - Calcifying epithelial odontogenic tumor (CEOT) is curable with resection.

SQUAMOUS ODONTOGENIC TUMOR

- Clinical features
  - Rare, hamartomatous proliferation.
  - Painless expansion of alveolar process that may displace teeth or resorb roots.
    - Premolar-canine region of maxilla and molar region of mandible.
- Radiographic features
  - Well-defined, unilocular radiolucencies less than 3.0 cm and confined to alveolar bone.
  - May appear as a triangular radiolucent defect lateral to the root or the roots of teeth.

- Histopathologic features
  - Islands of well-differentiated squamous epithelium without peripheral columnar cells, which are benign in appearance. Vacuolation and formation of microcysts may occur.
- Treatment and prognosis
  - Enucleation and curettage are curative with no recurrence.
  - 20 % of patients will have new lesions, which form in a different location.

ODONTOGENIC CARCINOMAS

- Clinical features
  - Residual odontogenic epithelium may undergo genetic alterations resulting in malignancy.
  - Pain and swelling are the most common complaints; paresthesias are also likely.
- Radiographic features
  - May appear as a typical dentigerous or odontogenic cyst. The radiolucency may also show irregular demarcation and a ragged border to the adjacent bone.
- Histopathologic features
  - Odontogenic cyst with an invasive carcinoma arising from the cystic lining. The carcinoma is usually well-differentiated squamous in nature and invades the surrounding tissue.
- Treatment and prognosis
  - Same regional lymph node and distant metastatic potential as a mucosal SCC and should be treated the same way.
  - Radical resection with or without radiation or adjuvant chemotherapy.

ODONTOGENIC TUMORS: MIXED TUMORS

Ameloblastic Fibroma

- Clinical features
  - Asymptomatic expansion of the jaws.
    - Mandibular molar is preferred site (70 %), but may occur anywhere.
  - Behaves as either a hamartomatous proliferation or a true neoplasm.
  - Thought of as aborted attempt at tooth formation, without the formation of calcified structures.
- Radiographic features
  - Unilocular or multilocular complete radiolucency with well-defined borders.
- Histopathologic features
  - Consists of both active epithelial and mesenchymal components without calcified structures. Well circumscribed and encapsulated.
- Treatment and prognosis
  - Enucleation and curettage is curative as it is noninvasive beyond its capsule, but with recurrence rates reported from 0 to 18 %.
  - Resection is reasonable in extremely large lesions.

AMELOBLASTIC FIBRO-ODONTOMA

- Clinical features
  - Asymptomatic expansion of the jaws—mandibular molar area most common.
- Radiographic features
  - Well-defined, mixed radiolucent-radiopaque appearance with irregular calcifications denser than the surrounding bone and similar to teeth.
- Histopathologic features
  - Grossly and macroscopically it has components of an odontoma and ameloblastic fibroma, so it will have soft and hard tissues.

- Treatment and prognosis
  - Enucleation and curettage are curative without recurrence.

AMELOBLASTIC FIBROSARCOMA

- Clinical features
  - Most common malignant odontogenic tumor.
  - Asymptomatic jaw expansion—80 % of cases in mandible.
  - Locally aggressive, infiltrative similar to ameloblastoma or myxoma.
- Radiographic features
  - Multilocular, ill-defined, radiolucent, expansile lesion, which is destructive.
- Histopathologic features
  - Similar to ameloblastic fibroma, but with cellular atypia. The epithelial component remains benign, but the mesenchymal component is malignant with hypercellularity, pleomorphism, and mitoses.
- Treatment and prognosis
  - Best treated with bony resection using 1.0–1.5 cm margins and one uninvolved anatomic barrier (similar to ameloblastoma and myxoma).
  - Radiation therapy is of little value to this tumor, but chemotherapy protocols have been used for more aggressive tumors.

ODONTOAMELOBLASTOMA

- Clinical features
  - Posterior molar/ramus region most common in either jaw.
  - These are two separate entities that are co-existing in the same space.
- Radiographic features
  - Features of both ameloblastomas and odontomas. Mostly multilocular mixed radiolucent-radiopaque lesions with complex odontomas.
- Histopathologic features
  - Epithelial components are identical to those of ameloblastoma with either plexiform or follicular pattern.
- Treatment and prognosis
  - Treatment and prognosis are the same as for invasive ameloblastoma, which are bony resection with 1.0–1.5 cm margins and one uninvolved anatomic barrier.

ODONTOMA

- Clinical features
  - Hamartoma of aborted tooth formation with calcified structures.
  - Compound odontoma—multiple small toothlike structures. Common anterior to mental foramen.
  - Complex odontoma—amorphous calcified mass. Common posterior to mental foramen.
- Radiographic features
  - Compound odontoma—gravel-like appearance with outline of miniature teeth.
  - Complex odontoma—dense, amorphous irregularly shaped mass.
  - Both are well defined with a radiolucent rim surrounding the radiopacities.
- Histopathologic features
  - Composed of mature dental tissues including enamel, dentin, cementum, and pulp arranged in toothlike arrangements (compound) or unstructured sheets (complex).
- Treatment and prognosis
  - Enucleation and curettage are curable without recurrence.

ODONTOGENIC TUMORS—ODONTOGENIC ECTOMESENCHYME

Central Odontogenic Fibroma

- Clinical features
  - Extremely rare, painless expansion that may displace teeth or resorb roots.
  - Maxillary lesions are anterior to first molar, while mandibular lesions are posterior.
- Radiographic features
  - Unilocular or multilocular, radiolucency with well-defined borders, sometimes sclerotic. Root resorption is common and divergence may also be seen.
- Histopathologic features
  - Pattern 1—simple type. Stellate fibroblasts in a delicate loose fibrous tissue, with various amounts of collagen and some rests of odontogenic epithelium.
  - Pattern 2—WHO type. Well-demarcated or encapsulated type with cellular fibrous tissue and myxoid areas.
  - Granular cell odontogenic fibroma—sheets of large granular cells with interspersing round islands of odontogenic epithelium.
- Treatment and prognosis
  - Enucleation and curettage are curative and recurrence should not develop.

PERIPHERAL ODONTOGENIC FIBROMA

- Clinical features
  - Firm, sessile, painless soft tissue mass of the gingiva.
  - Emerges from the gingival crevice or periodontal membrane.
  - Nondestructive and noninvasive.
- Radiographic features
  - No radiographic findings unless underlying alveolar surface erosion/saucerization.
- Histopathologic features
  - Similar to central counterpart (WHO type) with interwoven fascicles of cellular fibrous tissue mixed with myxoid areas.
- Treatment and prognosis
  - Local soft tissue excision with 1–2 mm margins and base of the fibroma.
  - Recurrences are rare, especially if base of emergence is excised.

GRANULAR CELL ODONTOGENIC TUMOR

- Clinical features
  - Most are asymptomatic expansions of the premolar-molar regions.
- Radiographic features
  - Well-defined radiolucency, which can be unilocular or multilocular.
- Histopathologic features
  - Sheets of large eosinophilic granular mesenchymal cells with small nests, cords, or islands of odontogenic epithelium.
- Treatment and prognosis
  - Enucleation and curettage are curative without recurrence.

ODONTOGENIC MYXOMA

- Clinical features
  - Asymptomatic jaw expansion—evenly distributed in the jaws and maxilla.
  - Growth characteristics and clinical presentation similar to ameloblastoma.
  - Benign neoplasm with infiltrative growth.
  - May see tooth displacement, root resorption, and displacement of IA nerve canal and soft tissue involvement.

- Radiographic features
  - Unilocular or multilocular radiolucency with "honeycombed" appearance and rarely as a unilocular radiolucency. Margins are often irregular or scalloped.
  - "Stepladder" or the "soap bubble" appearance.
- Histopathologic features
  - Unencapsulated, infiltrating, gelatinous tumors with sparse cells that are spindle shaped, round, or stellate with long cytoplasmic processes.
- Treatment and prognosis
  - Bony resection with 1.0–1.5 cm margins and one uninvolved anatomic barrier is curative. Overall prognosis is good and metastasis does not occur.

CEMENTOBLASTOMA

- Clinical features
  - Symptomatic hard expansion in the premolar-molar region—mandible 75 %.
    - About 50 % involve the first permanent molar.
  - Hamartomatous proliferation of cementoblasts forming disorganized cementum around the apical ½ of a tooth root.
  - May be locally aggressive causing cortical erosion, displacement of teeth, and infiltration.
- Radiographic features
  - Spherical, radiopaque mass encompassing and replacing the apical half of tooth root.
- Histopathologic features
  - Sheets of cementum-like material in continuity with the tooth root, which is usually resorbed and replaced by this cementum.
- Treatment and prognosis
  - Treatment is removal of the tooth with associated lesion. Lesion is normally encapsulated and separates easily from surrounding bone.

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PART VI
Laryngology
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Chapter 26
Deep Neck Space Infections

C. Kwang Sung

PEARLS

- In the parapharyngeal space, the prestyloid compartment contains the internal maxillary artery, maxillary nerve, deep lobe of the parotid, adipose tissue and the poststyloid compartment contains the carotid artery, internal jugular vein, sympathetic chain, and cranial nerves IX, X, XI, and XII
- Lemierre's syndrome is internal jugular vein (IJV) thrombophlebitis from pharyngitis typically due to *Fusobacterium necrophorum*

ANATOMY

Fascia of the Neck

- Superficial cervical fascia
  - Envelops platysma and muscles of facial expression
  - Incorporates the superficial musculoaponeurotic system (SMAS)
  - Extends from zygoma to the clavicles
- Potential space between superficial and deep cervical fascia
  - Contains adipose tissue, nerves, and blood vessels (anterior and external jugular veins)
- Deep cervical fascia
  - Superficial (investing) layer:
    - Envelops parotid, submandibular gland, sternocleidomastoid, and trapezius
    - Extends from nuchal line, mastoid, and mandible to the clavicles
  - Middle (visceral) layer:
    - Muscular division: envelops the infrahyoid strap muscles
    - Visceral division: envelops the buccinator, pharyngeal constrictor muscles, thyroid, larynx, trachea, and esophagus, and forms pre-tracheal fascia
      - Contributes the buccopharyngeal fascia posterior to the esophagus
      - Forms buccopharyngeal and pterygomandibular raphe
  - Deep layer (prevertebral fascia):
    - Prevertebral layer—ensheaths the paraspinous muscles and cervical vertebrae. Skull base to coccyx
    - Alar layer—lies between prevertebral and visceral layer of middle cervical fascia. Skull base to T2

DEEP NECK SPACES

The neck spaces can be organized into groups by location: suprahyoid neck (peritonsillar, submandibular, parapharyngeal, masticator, buccal, and parotid spaces), infrahyoid neck (anterior visceral), and the length of the neck (retropharyngeal, danger, prevertebral, and carotid spaces).

- Peritonsillar space
  - Loose connective tissue between capsule of the palatine tonsil and the superior constrictor muscle
  - May connect to parapharyngeal and retropharyngeal spaces

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- Submandibular space
  - Mylohyoid muscle divides the submandibular space into the superior sublingual compartment and the inferior submaxillary compartment
  - Tooth apices anterior to the second molar lie superior to the mylohyoid and involve the sublingual compartment when odontogenic infections occur
  - Second and third molars affect the submaxillary compartment
- Parapharyngeal space
  - Inverted pyramid extending from skull base down to the hyoid
  - Prestyloid compartment—contains internal maxillary artery, maxillary nerve, deep lobe of the parotid, adipose tissue
  - Poststyloid compartment—contains carotid artery, internal jugular vein, sympathetic chain, and cranial nerves IX, X, XI, and XII
- Masticator space
  - Lies between masseter and medial pterygoid
  - Contains masseter, temporalis, pterygoids, ramus of the mandible, divisions of the mandibular nerve (V3), and the internal maxillary artery
  - Infections typically from posterior molars
    - Present with severe trismus, sore throat, dysphagia
- Buccal space
  - Between the buccopharyngeal fascia and the skin of the cheek
  - Contains buccal fat pad, the parotid duct, and the facial artery
- Parotid space
  - Formed by the superficial layer of the deep cervical fascia ensheathing the parotid gland.
  - Contains facial nerve, external carotid artery, retromandibular vein, auriculotemporal nerve, and superficial temporal artery
  - Infection can spread medially to the parapharyngeal space
- Anterior visceral space
  - Enclosed by the visceral division of the middle layer of the deep cervical fascia anterior to the trachea
  - Extends from hyoid to superior mediastinum
  - Infections caused by traumatic perforation of anterior esophagus
- Retropharyngeal space
  - Between the visceral division (buccopharyngeal) of the middle layer and the alar fascia of the deep layer
  - Extends from skull base to the mediastinum at the tracheal bifurcation
  - The space is fused down the midline—abscesses are unilateral and primarily seen in children
- Danger space
  - Posterior to retropharyngeal space between alar and prevertebral fascia
  - Extends from skull base to diaphragm
  - High tendency for rapid inferior spread of infection to the posterior mediastinum through loose areolar tissue
- Prevertebral space
  - Between the prevertebral fascia and the vertebral bodies
  - Extends from skull base to coccyx
  - Minimal longitudinal extension of abscess due to dense areolar tissue and fibrous attachments
- Carotid space
  - Within the carotid sheath
  - Contains carotid artery, internal jugular vein, vagus nerve, and sympathetic chain

DIAGNOSTIC IMAGING

- Computed tomography (CT) scan with intravenous contrast is mainstay for neck infections
- Magnetic resonance imaging (MRI) better for assessing intracranial extension

- Ultrasound is often preferred for pediatric population
  - More accurate than CT scan in differentiating a drainable abscess from cellulitis
  - Cross-sectional imaging preferred for presurgical anatomic localization and planning

MICROBIOLOGY

- Commonly polymicrobial from oropharyngeal flora or odontogenic source:
  - Aerobes: *Strep* (*viridans,* beta-hemolytic [*pyogenes*]), *Staph* (*aureus, epidermidis*), *Neisseria*, *Klebsiella*, *Haemophilus*
  - Anaerobes: *Bacteroides*, *Peptostreptococcus*, *Peptococcus*, *Fusobacterium*, *Eikenella*, *Veionella*
- Antibiotics
  - Empiric therapy with a penicillin in combination with a beta-lactamase inhibitor (e.g., amoxicillin or ticarcillin with clavulanic acid) or a beta-lactamase-resistant penicillin (e.g., cefoxitin, cefuroxime, imipenem, or meropenem)
  - +/– antibiotic effective for anaerobes (e.g., clindamycin or metronidazole)

SURGICAL MANAGEMENT

- Needle aspiration with 16 or 18 gauge needle for small abscesses
- Transoral incision and drainage—peritonsillar or retropharyngeal abscesses
- Transcervical incision and drainage
  - Secure airway with awake fiber-optic intubation or tracheostomy
  - Pre-auricular parotid incision—parotid and temporal spaces
  - Horizontal neck incision—masticator, parapharyngeal, pterygoid, submandibular, prevertebral, retropharyngeal, and carotid spaces
  - Submental incision—submandibular space

COMPLICATIONS OF NECK SPACE INFECTIONS

- Ludwig's angina
  - Rapidly spreading, firmly indurated cellulitis that originates intraorally
  - Presentation: edema within sublingual, submandibular, or submental space displaces tongue superiorly and posteriorly causing airway obstruction
  - Treatment: awake fiber-optic intubation or tracheostomy, broad-spectrum antibiotics, submental incision and drainage
- Lemierre's syndrome
  - Internal jugular vein (IJV) thrombophlebitis from pharyngitis
  - Typically due to *F. necrophorum*
  - Presentation: spiking fevers, engorged optic disks, increased intracranial pressure, swelling and tenderness at angle of mandible, sternocleidomastoid tenderness, septic pulmonary emboli
  - Treatment: IV antibiotics, anticoagulation is controversial, possible excision of IJV
- Carotid artery pseudoaneurysm or rupture
  - Presentation: pulsatile neck mass
  - Sentinel hemorrhage from mouth or nose, protracted course, neck hematoma, cranial nerve palsies, Horner's syndrome, and hemodynamic collapse
- Mediastinitis
  - Caused by descent of infection from neck
  - Increasing chest pain, dyspnea, and widened mediastinum on chest X-ray
  - Mortality rate 30–40 %
- Necrotizing cervical fasciitis
  - Fulminant infection that spreads along fascial planes and causes extensive necrosis
  - Occurs in immunocompromised patients, especially poorly controlled diabetics

- Polymicrobial and odontogenic—*Strep pyogenes* and *Clostridium perfringens*, MRSA, mixed aerobic and anaerobic flora
- Presentation: rapidly progressive cellulitis, pitting neck edema with orange-peel appearance, subcutaneous crepitus
- CT scan shows tissue gas accumulation in >50 %
- Treatment: critical care with treatment of immunocompromising condition, broad-spectrum antibiotics, surgical drainage, and frequent debridement

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Chapter 27
Laryngology

Arash Shahangian and C. Kwang Sung

PEARLS

- The larynx has three main functions: to produce voice, to act as a conduit of air to the lungs, and to protect the airway from aspiration
- The superior laryngeal nerve (SLN) has an internal branch (sensory to mucosa of the TVFs, supraglottis, and hypopharynx) and an external branch (innervates cricothyroid muscle)

ANATOMY

Microscopic Anatomy

- True vocal folds (TVFs)—five layers
  - Stratified squamous epithelium—no mucin glands
  - Lamina propria—three layers
    - Superficial (Reinke's space)
      - consists of loose fibers and matrix
      - lowest concentrations of collagen and elastin
      - most important for vocalization
    - Intermediate layer
      - higher concentration of elastin and collagen
      - together with deep layer forms the vocal ligament
      - high concentration of macrophages; ready to fight pathogens translocating across the basement membrane
    - Deep layer
      - highest concentration of collagen and elastin
  - Thyroarytenoid muscle
- Vocal ligament
  - Intermediate and deep layers of lamina propria
  - Forms the upper most portion of conus elasticus
  - Some fibers insert into the vocalis muscle
- Broyle's ligament (anterior commissure ligament)
  - Condensation of fibers with insertion into perichondrium of the laryngeal cartilages
- Macula flava
  - Thickened lamina propria along anterior and posterior membranous vocal folds
  - Serves as transition zone between pliable vocal fold and tougher anchoring structures

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Gross Anatomy

- Intrinsic Muscles
  - Associated with quadrangular membrane
    - Thyroarytenoid (TA, vocalis)—shortens, tenses and adducts the TVF
    - Aryepiglottic—folds epiglottis posteriorly
    - Thyroepiglottic
  - Associated with the arytenoid cartilages
    - Lateral cricoarytenoid (LCA)—adducts TVF
    - Posterior cricoarytenoid (PCA)—sole abductor
    - Interarytenoid (IA)—adduct arytenoids. Unpaired, has bilateral innervation
- Extrinsic muscles
  - Cricothyroid (CT)—lengthens TVF, increases tension and changes pitch
- Accessory muscles
  - Sternohyoid, sternothyroid, and omohyoid—depressor of larynx
  - Stylohyoid, thyrohyoid, digastric, mylohyoid, and geniohyoid—main elevators of larynx
- Laryngeal cartilages
  - Thyroid, cricoid, and arytenoid cartilages are hyaline
  - Corniculate—sits above arytenoids. fibroelastic cartilage
  - Cuneiform—sits within aryepiglottic (AE) folds
- Laryngeal joints
  - Cricothyroid—synnovial (diarthrosis)
  - Cricoarytenoid—synnovial (diarthrosis)

Innervation of Larynx

- Recurrent laryngeal nerve (RLN)
  - Innervates all intrinsic muscles
  - Sensory to mucosa of subglottis and trachea
  - Loops around subclavian artery on the right and aorta on the left
  - Nonrecurrent in 0.5 % of cases on the right and less frequently on the left
- Superior laryngeal nerve (SLN)
  - Internal branch—sensory to mucosa of the TVFs, supraglottis, and hypopharynx
    - Pierces through thyrohyoid membrane
  - External branch—innervates cricothyroid muscle

PHYSIOLOGY OF VOICE (VOICE PRODUCTION)

Required Factors for Production of Voice

- Adequate intrathoracic pressure to generate air pressure
- Pliable membrane covering the vocal fold
- Vocal fold closure
- Favorable vocal fold shape
- Control of tension and length of vocal cord

Glottal Cycle

- Closed vocal folds and increased intrathoracic pressure
- Vocal folds separate starting at inferior lip progressing superiorly
- Air flows through glottis
- TVF is pulled medially due to air flow (Bernoulli's effect) and elastic recoil of the vocal fold
- Inferior lips of TVF close first as wave of contact moves from inferior to superior
- Inferior–superior wave transmission is known as the mucosal wave
- Increase pitch and rate of vocal fold vibration
  - Lengthening the vocal folds, increasing intrathoracic pressure, increased air flow and contraction of laryngeal muscles → increase in fundamental frequency

Vocal Fold Patterns

- Falsetto or light voice—vibration only at the upper edge of the vocal folds. Incomplete glottic closure
- Modal voice—mid range frequencies. Mucosa vibrates independently of the underlying muscle
- Vocal (glottal) fry—closed phase of the vocal folds is longer compared to open phase. Mucosa and muscle vibrate together. Low frequency voice

Normal Fundamental Frequency

- Men 100–125 Hz; increases with age
- Women 200–250 Hz; decreases with age

Variables That Affect Voice Frequency (Pitch)

- Vocal fold length
- Vocal fold tension
- Vocal fold mass
- Subglottic air pressure

CLINICAL VOICE ASSESSMENT

Components of Speech

- Prosody—inflection of speech consisting of putting the stress on syllables
- Phonation—production of voice dependent on VF closure, tension, pliable mucosa, and adequate intrathoracic pressure
- Resonance—modification of sound generated from the VFs by the supraglottis, pharynx, oral and nasal cavities and sinuses
- Articulation—production of speech sounds dependent on musculature of the tongue, lips, and teeth
- Pitch—subjective perception of VF frequency
- Fundamental frequency—measured in vocal analysis
  - Longer, thicker VFs in males yield an average fundamental frequency of 128 Hz
  - Thinner shorter VFs in females yield a fundamental frequency of 256 Hz
- Presbylarynx (aging of the VFs)—leads to increase in fundamental frequency in males and decrease in females
- Timbre (quality)—relates to color and quality of a voice that makes it distinctive

Voice Assessment Instruments

- Used for subjective self-reporting of severity of vocal symptoms
- Voice Handicap Index (VHI)—measures impact of functional, physical, and emotional aspects of vocal shortcomings
- Voice Related Quality of Life (VRQOL)—questionnaire of physical and social/emotional functioning subscales combined to give a voice-related quality of life assessment
- Reflux Symptoms Index (RSI)—documents contribution of laryngopharyngeal reflux to symptoms

Vocal Examination

- Auditory Evaluation
  - GRBAS—4 point scale scored by the clinician with 0 denoting no deficit and 3 indicating a severe deficit
    - Grade (quality)
    - Roughness

- Breathiness
- Asthenia
- Strain

Objective Voice Measures

- Maximum phonation time (MPT)—longest of three trials measured
  - Normal range (varies by source): females 15–25 s; males 25–35 s
- Subglottal air pressure
- Airflow
- Laryngeal airway resistance

Acoustic Measures

- Frequency—fundamental frequency and frequency range
- Intensity—loudness
- Variability Measures
  - Jitter—cycle to cycle variation in frequency
  - Shimmer—cycle to cycle variation in amplitude (intensity)

INFECTIOUS AND INFLAMMATORY DISEASES OF THE LARYNX

Acute Laryngitis

- Phonotrauma
  - Vocal fold edema and possibly hemorrhage due to vocal misuse, overuse, or abuse
- Viral—most common cause of acute laryngitis
  - Supportive care—rehydration, voice rest, +/– steroids
  - Croup—children <3 year, most commonly parainfluenza virus
- Bacterial
  - Epiglottitis due to *Haemophilus influenzae*
    - Decreased incidence with *H. influenzae* B vaccine
    - Intubation in controlled setting or awake tracheostomy if respiratory distress
- Fungal—most commonly *Candida albicans*
  - Dysphonia with white plaques or speckles and erythema on the TVFs
  - Immunocompromised patients
  - Immunocompetent patients with use of recent use of broad-spectrum antibiotics or inhaled corticosteroids
- Angioedema
  - Inflammatory reaction with vascular dilation and increased vascular permeability
  - Causes
    - Hereditary: C1 esterase inhibitor deficiency
    - Nonhereditary causes: medications (ACE-I most commonly), food, insect bites, transfusions, infections
  - Treatment: oxygenation, epinephrine, steroids, antihistamines

Chronic Laryngitis

- Bacterial—superinfection of injured larynx; commonly *Staphylococcus aureus*
- Fungal
  - Blastomycosis—endemic to southern USA
  - Coccidioidomycosis—endemic to southwestern USA and Central and South America
  - Histoplasmosis—endemic to Ohio and Mississippi River valleys
    - pseudoepitheliomatous hyperplasia can mimic carcinoma

- Mycobacterial
  - Tuberculosis (TB)—interarytenoid fold is most common site
    - Highly associated with active pulmonary TB
    - Granulomatous or ulcerative lesions
  - Leprosy (Hansen's Disease)—*Mycobacterium leprae*
- Laryngopharyngeal reflux (LPR) laryngitis—chronic inflammation secondary to back-flow of gastric contents
  - Symptoms: hoarseness (92 %), throat clearing (50 %), cough (44 %), globus (33 %), dysphagia (27 %). Over 50 % deny heartburn.
  - Laryngeal findings:
    - Diffuse laryngeal edema
    - VF edema
    - Subglottic edema
    - Erythema or hyperemia
    - Ventricular obliteration
    - Posterior commissure hypertrophy (pachydermia)
    - Granuloma
    - Thick endolaryngeal secretions
  - Diagnosis:
    - Gold standard is 24-h dual-probe pH-metry and impedance
    - Reflux Finding Score (RFS) > 8 suggestive
    - Reflux Symptom Index (RSI) > 13 suggestive
  - Treatment:
    - Twice daily dosage of proton pump inhibitor (PPI) for minimum 6 months
    - Laparoscopic Nissen fundoplication in refractory cases
- Immune diseases:
  - Sarcoid—non-caseating granulomas usually of the supraglottis
    - 5 % of patients with pulmonary sarcoid have laryngeal disease
  - Amyloidosis—firm, non-ulcerated, orange-yellow to gray submucosal nodules
  - Granulomatosis with polyangiitis (GPA or Wegner's granulomatosis)
    - Diagnosis is confirmed on histology—necrotizing granulomatous inflammation, multinucleated giant cells and small vessel vasculitis
    - C-ANCA positive in active disease
    - Subglottic stenosis in 16 % of patients

VOCAL FOLD PARALYSIS

- Etiologies:
  - Trauma—iatrogenic (thyroid and anterior cervical spine surgery, carotid endarterectomy, neck dissection, cardiothoracic surgery, intubation), non-iatrogenic
  - Neoplasm
    - Malignant—thyroid cancer, lung cancer, CNS tumors
    - Benign—vagal schwannoma, carotid body tumor, glomus jugulare
  - Neurologic—stroke, multiple sclerosis, ALS, myasthenia gravis, Parkinson's, Guillain-Barre´
  - Idiopathic—suspected to be viral neuropathy
- Evaluation:
  - History—breathy voice, diplophonia, aspiration, dysphagia
  - Flexible laryngoscopy and stroboscopy—assess symmetry, VF motion, VF position, glottic gap, pooled secretions in pyriform sinus
  - Classic VF positions in VF palsy
    - Lateral VF position
      - Suggests SLN and RLN injury, loss of cricothyroid with SLN injury causes increased abduction
      - Treated with type I thyroplasty and arytenoid adduction

        - Paramedian VF position
            - Suggests RLN injury only, implies a lesion below the take-off of the SLN
            - Treated with type I thyroplasty
    - Guttman's test
        - Test for SLN paralysis; normally, anterior thyroid cartilage pressure lowers pitch, lateral thyroid cartilage pressure raises pitch; with SLN paralysis this is reversed
    - Laryngeal electromyography (LEMG)
        - Most useful 3 weeks to 6 months after nerve injury
        - Because of synkinesis, LEMG is more reliable for predicting poor prognosis
- Medical management
    - Voice and swallowing therapy
- Surgical management
    - Injection laryngoplasty—awake or under general anesthesia
        - Gelfoam
        - Carboxymethylcellulose
        - Collagen
        - Hyaluronic acid
        - Micronized dermis
        - Calcium hydroxylapatite (CaHA)
        - Fat
        - Teflon is no longer used due to granuloma formation
    - Laryngeal framework surgery
        - Medialization laryngoplasty (Isshiki type I thyroplasty)
        - Carved silastic block, pre-formed implants, Gore-Tex
        - Arytenoid adduction or adduction arytenopexy
        - Cricothyroid subluxation
    - Laryngeal reinnervation
        - RLN direct reanastomosis or cable graft
        - Ansa cervicalis to RLN
- Bilateral vocal fold immobility
    - Surgical management
        - Tracheostomy
        - Endoscopic approach:
            - transverse cordotomy
            - arytenoidectomy (partial or total)
            - VF lateralization
        - Open arytenoidectomy

NEUROLARYNGOLOGY

- Signs suggestive of neurologic laryngeal disorder:
    - Vocal fatigue
    - Vocal tremor
    - Weak or breathy voice
    - Vocal strain
    - Dysarthria
    - Dysphagia
- Parkinsonism
    - Weak breathy voice, sluggish articulation, dysphagia, drooling
    - Thin, bowed TVFs due to atrophy
    - Lee Silverman Voice Treatment (LSVT)—intensive voice therapy stimulating loud voice with maximum effort
    - Injection laryngoplasty may be considered

- Essential tremor
  - Characteristic hand and voice tremor at 6–8 Hz
  - Muscles of the larynx, pharynx, soft palate and strap muscles involved
  - Treatment
    - Propranolol, primidone
    - Botox (botulinum toxin A) can be considered, but may lead to excessive breathiness
    - Injection laryngoplasty may be considered
- Spasmodic dysphonia (SD)
  - Idiopathic focal dystonia of the larynx
  - Adductor SD (ADSD)—85 to 90 % of SD
    - Intermittent voice breaks in the middle of vowels, strangled voice
    - Test sentences: "We eat eels every day." "We mow our lawn all year."
    - Treatment:
      - Botox injection to the TA muscles with or without EMG guidance
        - Dosage varies: 0.1–3.5 units bilaterally
      - Surgical: RLN sectioning; selective laryngeal adductor denervation-reinervation; type II thyroplasty.
  - Abductor SD (ABSD)—~15 % of SD
    - Prolonged voiceless consonants, occasional breathy voice
    - Test sentences: "The puppy bit the tape." "Harry's happy hat."
    - Treatment
      - Botox injection to the PCA muscle 0.5–5 units
  - Mixed SD—combination of ADSD and ABSD
    - Difficult to treat with Botox due to side effects
- Muscle tension dysphonia (MTD)
  - Voice with constant strain, but no discernible voice breaks
  - Anterior–posterior squeezing of the supraglottis, hyperconstriction of the false VFs
  - Treatment: voice therapy

MISCELLANEOUS LARYNGOLOGY

- Classification of laryngeal framework (Isshiki thyroplasty) procedures
  - Type I: vocal fold medialization
  - Type II: vocal fold lateralization
  - Type III: vocal fold shortening
  - Type IV: vocal fold lengthening

SUBGLOTTIC AND TRACHEAL STENOSIS

- Etiologies:
  - Trauma—blunt or penetrating; burns
  - Iatrogenic—prolonged intubation, tracheostomy, radiation, surgical trauma
  - Inflammatory disease/collagen vascular disease
    - Granulomatosis with polyangiitis (Wegener's)
    - Sarcoidosis
    - Amyloidosis
    - Relapsing polychondritis
  - Idiopathic
- Cotton-Meyers Classification
  - Grade I: 0–50 % obstruction
  - Grade II: 51–70 % obstruction
  - Grade III: 71–99 % obstruction
  - Grade IV: 100 % obstruction
- Preoperative assessment:
  - Flexible laryngoscopy and bronchoscopy

        - Identify location, dimension, quality of stenosis, vocal fold movement
    - High-resolution CT scan
    - Pulmonary function test
        - Objective testing of impairment
        - Flattened inspiratory and expiratory curves on flow-volume loop
- Endoscopic management:
    - Microdirect laryngoscopy with:
        - CO_2 laser and dilation
            - Indications: Cotton-Meyers Grade I–II, stenosis length <1.5 cm
            - Risks: Airway fire, laser smoke plume, thermal injury, perioperative edema
        - Balloon dilation—for soft tissue stenosis
        - Microdebrider
            - Indications: bulky, exophytic lesions, fibrous scar, granulation tissue
            - Benefits: no risk of airway fire, shorter operative time
        - Application of Mitomycin C
            - Antineoplastic, antibiotic, alkylating agent
            - Inhibits fibroblast proliferation, allowing re-epithelialization before scar formation
- Open surgical management:
    - Indications: high-grade stenosis, failed endoscopic treatment, circumferential scarring, loss of cartilaginous support, exposure of cartilage, long segment stenosis, combined laryngotracheal stenosis
    - Laryngotracheal reconstruction (LTR)
        - With anterior cartilage graft +/– posterior cartilage graft
    - Cricotracheal resection and primary anastomosis
    - Segmental tracheal resection and primary anastomosis
    - Stents: silicon roll, Montgomery stent, T-tube, finger cot
        - Provide support for cartilage grafts
        - Approximate skin or mucosal grafts to a recipient site
        - Separate opposing raw surfaces during healing
        - Maintain lumen in a reconstructed area that lacks adequate cartilaginous support

TRACHEAL NEOPLASMS

Benign

- Epithelial
    - Squamous papilloma
        - In children caused by HPV 6 and 11. Vertical transmission during childbirth
    - Mucoepidermoid adenoma
- Mesynchemal
    - Chondroma
        - Covered with normal mucosa
        - Found commonly on posterior trachea/cricoid region but can be anywhere
        - Affects elderly men
        - Can recur after resection
    - Leiomyoma
        - Typically arise from the distal third
        - Can be pedunculated
        - Significant bleeding with bronchoscopic excision of non-pedunculated lesions
    - Hemangioma
    - Lymphangioma (cystic hygroma)
        - Soft solitary compressible mass
        - >60 % present at birth and the rest declare themselves by 3 years
        - increased mast cells during proliferation
    - Granular cell tumor
    - Others include Schwannoma, neurofibroma, fibrous histiocytoma, chondroblastoma, lipoma, pseudosarcoma

Malignant

- See Chapter 20. Head and Neck Section

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Chapter 28
Benign Lesions of the Larynx

Melynda Barnes and C. Kwang Sung

PEARLS

- The mucosal wave is the most important parameter in differentiating cysts from polyps (diminished or absent in cysts compared to present in 80 % of polyps)
- Respiratory papillomas are most common at the transition between columnar and squamous epithelium

BENIGN LESION OF THE VOCAL FOLDS

Differential diagnosis of benign vocal fold lesions

- Polyp (most common): mucoid and angiomatous
- Nodules
- Cyst: mucus retention and dermoid
- Vocal process granuloma
- Scar
- Sulcus vocalis
- Recurrent respiratory papilloma
- Polypoid corditis (Reinke's edema)
- Leukoplakia/keratosis

(Note: two systemic diseases that should be considered in the differential of a vocal cord lesion are hypothyroidism and acromegaly)

- Polyps
  - Unilateral, broad-based vs. pedunculated, hemorrhagic vs. nonhemorrhagic outpouching of inflamed and organized Reinke's space of true vocal fold
  - Seen mostly in males, after intense intermittent voice abuse, aspirin use, anticoagulant use, vocal trauma or endotracheal intubation
  - Pathophysiology: breakage of capillaries in Reinke's space (SLP) with extravasation of blood → edema → blood organization with hyalinized stroma
  - Histology: acellular with thickened epithelium, increased vascularity, clustered fibronectin, disruption of laminar pattern
  - Symptoms: breathy voice, vocal fatigue, frequent voice breaks, worsening hoarseness with high-pitched soft phonation
  - Stroboscopy: small polyps have intact mucosal waves but phase asymmetry because of impaired phase closure and mass effect of the polyp; large polyps have prominent decreased amplitude
  - Treatment options: usually microsurgical or lasers for hemorrhagic polyps

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- Nodules
  - Bilateral, symmetric epithelial swelling of the anterior/mid third of the true vocal folds
  - Seen mostly in children, adolescents, women, professionals with high voice demands
  - Pathophysiology: mid-membranous (junction of anterior and middle third) vocal fold undergoing maximal shearing and repeated collision forces resulting in localized vascular congestion and edema. Reinke's space hyalinization and thickened overlying epithelium occurs with epithelial hyperplasia
  - Histology: acellular with thickening of epithelium over matrix of fibrin and collagen
  - Symptoms: chronic hoarseness and repeated episodes of progressively severe voice loss. Professional singers have inability to sing high notes softly, frequent voice breaks, increased breathiness, vocal fatigue
  - Stroboscopy: symmetric superficial swelling of vocal folds at strike zone (junction of anterior and middle cord) with decreased amplitude, hour-glass glottal closure and open phase dominance
  - Treatment options: voice rest, speech therapy, microsurgery
  - Microsurgical indications: longstanding nodules, speech therapy failure, reactive callus with primary lesion on opposite vocal fold
- Cysts
  - Subepidermal epithelial-lined sacs within lamina propria
    - Mucus retention—obstructed mucous gland duct (usually during URI or voice overuse)
    - Epidermoid—congenital cell rests in subepithelium from fourth or sixth branchial arch or buried epithelium from healing injured mucosa
  - Ruptured cyst may result in scar within lamina propria or a sulcus
  - The cyst can also irritate the contralateral vocal fold, producing a reactive lesion on the opposite vocal fold
  - Occurs in similar population as polyps and nodules, slight female predominance
  - Exam: diplophonic voice, pitch instability, splitting of frequency overtones, vocal hyperfunction
  - Stroboscopy: vocal fold asymmetry, significantly decreased or absent mucosal wave, phase closure depends on cyst size and whether there is a contralateral reactive callus
    - Mucosal wave is the most important parameter in differentiating cysts from polyps (diminished or absent in cysts compared to present in 80 % of polyps)
  - Treatment: Multidisciplinary approach but usually needs microsurgery
  - Cyst recurs if epithelium left behind during surgical excision
- Vocal process granulomas
  - Occur at vocal process of the arytenoid, not on the membranous vocal fold. May or may not cause dysphonia
  - Male predominance
  - Etiology: prolonged or repetitive contact trauma leads to mucosal ulceration, cartilage exposure and inflammation
  - Risk factors: trauma, laryngopharyngeal reflux (LPR), chronic cough, throat clearing, post endotracheal intubation (contact ulceration), forceful glottal closure (compensation for vocal fold paresis or presbylaryngis)
  - Stroboscopy: granuloma appears solitary or bilobed, normal mucosal wave, glottic closure may be impeded by large granuloma
    - If abnormal mucosal wave or phase closure rule out underlying vocal paresis, presbylaryngis or sulcus
  - Conservative treatment: treat LPR, cough, underlying condition, speech therapy, Botox to thyroarytenoid muscle, intralesional corticosteroids
  - Indications for surgery (CO_2 laser excision or cold knife): enlarging granuloma, compromised voice, breathing or swallowing or rule out malignancy
- Scar
  - Repeated inflammation, vocal trauma, vocal hemorrhage, presence of intracordal cyst (ruputered epidermoid) leads to intracordal scar

- May occur after vocal surgery involving lamina propria, use of CO_2 laser, repeated epithelial procedures
- Stroboscopy: markedly reduced or absent mucosal wave (asymmetric)
- Treatment: excision vs. steroid injections

- Sulcus vocalis
  - Epithelial scar with loss of superficial lamina propria
  - Etiology: unknown but usually acquired by vocal trauma
  - Vocal impairment usually due to stiffness of vocal fold and glottic insufficiency
  - Symptoms: hoarseness with strained, breathy voice
  - Stroboscopy: restriction of mucosal wave
  - Treatment: difficult to treat with unreliable outcomes. Options include:
    - Excision, collagen or steroid injection, mucosal "slicing" technique, elevation with submucosal grafting, endoscopic fat injection, Gray's minithyrotomy

- Recurrent respiratory papilloma
  - One of the most common laryngeal neoplasms—cauliflower exophytic. Mostly common at transition between columnar and squamous epithelium
  - Second most common cause of hoarseness in children
    - 2/3 present before age 15, usually regress by puberty
  - Risk factors: first-time mother (longer second stage of delivery in birth canal), lower socioeconomic status, 50 % born from mothers with maternal condyloma acuminata, oral sex, multiple sexual partners
  - Etiology: Human papilloma virus (HPV) infection (subtypes 6 and 11); 2 % likelihood of malignant degeneration (subtypes 16 and 18)
  - 10 % likelihood of tracheal spread, depending on the number of surgical procedures
  - Types:
    - Juvenile-onset—children, multiple sites of involvements, more aggressive, rapid recurrence
    - Adult-onset—single sites, recurrence less likely
  - Symptoms: hoarseness, stridor (inspiratory or biphasic), dyspnea, dysphagia
  - Stroboscopy: vascular stippling on the mass, decreased mucosal wave due to mass effect
  - Treatment: surgical—microdebrider, CO_2 laser (greater depth of penetration increases risk of scarring and implantation of virus into deeper tissues), pulsed dye laser, KTP laser. Avoid tracheostomy.
    - Adjuvant therapy—HPV vaccine (preventative), cidofovir injections, bevacizumab, indole-3-carbinol (I3C)

- Ectasias
  - Vascular lesion of the true vocal fold distinguished by a coalescent hemangiomatous appearance
  - Seen in voice professionals, post-radiotherapy
  - Etiology: vocal use, vocal abuse, trauma
    - Repeated trauma leads to new blood vessel formation and weakened blood vessel walls
  - Symptoms: hoarseness; can be episodic in menstruating women and patients with recurrent trauma
  - Treatment: treat underlying trauma-LPR, cough. Stop anticoagulation if possible. Speech therapy
  - Surgical indications: enlarging lesion, recurrent hemorrhage, development of a mass
    - Pulse dye laser or KTP laser, or surgical excision

- Polypoid corditis (aka Reinke's edema or vocal polyposis)
  - Proliferation or redundancy of SLP
  - More common in peri-menopausal female smokers
  - Seen in chronic irritant exposure (smoking, LPR, occupational exposures)

- Outpouching of membranous vocal folds with edematous appearance
- Stroboscopy: decreased mucosal wave (mass effect of the edema), phase asymmetry
- Treatment: surgical—reduce airway obstruction, preserve epithelium and some SLP to preserve mucosal wave
  - Stage procedures if bilateral disease
  - Medical treatment—smoking cessation, control LPR

- Rheumatoid nodules
  - Rheumatoid arthritis can cause inflammatory fixation of cricoarytenoid joint or inflammatory nodules on vocal fold
  - Symptoms: hoarseness, pain, globus, referred otalgia
    - Bilateral disease can lead to dyspnea and stridor
    - Serology: elevated ESR, RF, decreased complement level, abnormal lupus panel
  - Laryngoscopy: immobile arytenoid with erythema and edema (CA joint fixation). RA nodules have "bamboo larynx" appearance with bilateral white stripes perpendicular to the free edge of the vocal fold
  - Treatment: medical—steroids, anti-inflammatory medication; surgical—excision of nodule, severe airway obstruction may necessitate tracheotomy

- Leukoplakia
  - Spectrum of diseases affecting vocal fold epithelium (hyperkeratosis, dysplasia, early verrucous changes)
  - 8–14 % likelihood of malignant degeneration
  - Pathophysiology: unknown however, hypothesis is chronic irritation and genetic predisposition
  - Laryngoscopy/Stroboscopy: subtle hyperkeratotic epithelium, decreased or sluggish mucosal wave; progression of disease may be exophytic with a bed of erythema
  - Treatment: surgical—eradicate disease but preserve surrounding normal anatomy and voice quality. Treat severe dysplasia and carcinoma in situ aggressively

PHONOMICROSURGERY

- Cold instruments
  - 400 mm focal length operating microscope
  - laryngeal extended length instruments
  - small endotracheal tube
  - include sickle knife, endoscopic scissors, cup forceps
  - Two handed technique with an instrument in each hand
- CO_2 laser
  - Most commonly used laser in otolaryngology
  - Invisible (need aiming beam); wavelength of 10.6 μm
  - Absorbed by water and glass and reflected by mirrors or metallic substances
  - Must wear protective glasses
  - Used in conjunction with operating microscope or a hand piece

OTHER BENIGN LESION OF THE LARYNX

- Schwannoma
  - Benign, encapsulated, slow growing
  - Rare malignant sarcomatous degeneration
  - Symptoms: voice change, throat clearing, globus, cough
- Neurofibroma
  - Proliferation of sheath cells and fibers, non-encapsulated
  - Can appear nodular or diffuse on laryngoscopy
  - Can be multiple in Von Recklinghausen disease
  - Symptoms: voice change, throat clearing, globus, cough

- Paraganglioma
  - Rare in the larynx; most common subsite is supraglottis
  - Three times as common in women than men
  - Immunohistochemistry used to distinguish from other neuroendocrine tumors
  - Treatment: surgical excision; preoperative CT scan and possible embolization are important
- Granular cell tumor
  - Pathophysiology: Arise from Schwann cells in posterior aspect of true vocal fold or arytenoids
    - Mucosal granular cell tumor and gingival giant cell tumor
  - Slow, painless growth, well circumscribed mass that can be solitary, polypoid, sessile, papillary or cystic
  - Symptoms: subtle hoarseness
  - Histology: large polygonal cells in nests, strands, sheet. Infiltrative, non-encapsulated. Look for abundant eosinophilic cytoplasm filled with granules, keratin pearl formation
  - Treatment: surgical excision—endoscopic or open via laryngofissure
  - Recurrence rate 8 %, malignant transformation 5 %

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Chapter 29
Dysphagia

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PEARLS

- Total laryngectomy remains the procedure of choice for definitive treatment of life-threatening aspirations
- A Zenker's diverticulum is located above the upper esophageal sphincter at Killian's triangle (between cricophargyngeal sphincter and inferior pharyngeal constrictor muscle)

ANATOMY

- Pharyngoesophageal junction to gastroesophageal junction
  - Upper esophageal "Sphincter" (UES): Junction of inferior pharyngeal constrictor with cricopharyngeus
  - Lower esophageal sphincter: True sphincter with circular smooth muscle
  - 18- to 25-cm length with cervical, thoracic, and abdominal components
- Four layers
  - Mucosa: three sublayers
    - Stratified squamous epithelium
    - Lamina propria
    - Muscularis mucosa
  - Submucosa: Location of Meissner's plexus
  - Muscularis propria
    - Proximal skeletal muscle, distal smooth muscle
    - Inner circular, outer longitudinal muscle fibers
  - Adventitia
  - Diaphragmatal hiatus at T10, end of gastroesophageal junction T11
- Innervation
  - Myenteric (AKA Auerbach's plexus): Smooth muscle peristalsis controlled by vagus found between muscle layers
  - Meissner's complex: Afferent sensory input found in submucosa
- Arterial supply: Inferior thyroid arteries, bronchial arteries (off aorta, or off phrenic), left gastric artery
- Venous drainage: Azygous (to superior vena cava), left gastric vein (to portal vein) → form portal-systemic anastomosis → form esophageal varices in setting of portal hypertension
- Normal impressions seen on esophagram: Aortic arch, left mainstem bronchus, left atrium
- Normal sites of narrowing: Origin, aortic arch, left mainstem bronchus, diaphragm. These are sites proximal to which swallowed objects may lodge.

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PHYSIOLOGY OF SWALLOWING

Six Valves for Deglutition

- Lips
- Tongue
- Glossopalatal (soft palate to BOT)
- Velopharynx (soft palate to posterior pharyngeal wall)
- Larynx
- Upper esophageal sphincter

PHASES OF SWALLOWING

- Oral
  - Preparatory: Mastication, lubrication with saliva, bolus formation
  - Transit: To posterior tongue
- Pharyngeal
  - Velopharyngeal closure
  - Tongue movement posteriorly and superiorly
  - Pharyngeal constrictor contraction
  - Hyoid, laryngeal elevation
  - Laryngeal closure
  - Epiglottis inverts to contact arytenoids
  - False vocal folds close
  - True vocal folds adduct
  - Opening of UES
- Esophageal
  - Primary peristalsis: Associated with swallow reflex
  - Secondary peristalsis: Thoracic esophageal peristalsis without associated pharyngeal contraction; triggered by esophageal distention to clear residual food or gastroesophageal reflux
  - Nonperistaltic contractions, aka tertiary contractions, are dysfunctional, isolated contractions, prevalence increases with age

CAUSES OF DYSPHAGIA

Localization Based on Phase of Swallowing

- Oral: Symptoms start before initiation of swallow
  - Xerostomia, poor muscular control, lack of oral competence, cough before swallow
- Pharyngeal: Symptoms during swallow
  - Difficult to initiate, cough during swallow, nasal regurgitations, increased effort required for swallow, repeated swallows
- Esophageal: symptoms several seconds after swallow
  - Retrosternal discomfort, regurgitation

Classification Based on Type of Defect

- Physiologic
  - Xerostomia (medication, rheumatologic disease, radiation)
- Structural
  - Zenker's diverticulum, hypopharyngeal stricture, pharyngocele, osteophytes, head and neck cancer, soft palate abnormality, reduced hyolaryngeal elevation, reduced base of tongue volume
- Neurologic
  - CN IX, X, OR XII paralysis/paresis, stroke

- Neuromuscular
  - Parkinson's, amyotrophic lateral sclerosis, multiple sclerosis, myasthenia gravis, oculopharyngeal muscular dystrophy, inclusion body myositis, inflammatory myopathy, cricopharyngeal dysfunction
- Psychogenic

EVALUATION OF DYSPHAGIA

Swallow Specific History

- Localize deficit to:
  - Oral phase (before swallow): dry mouth complaint, tongue movement limitations
  - Oropharyngeal phase (during swallow): inability to initiate, nasal regurgitation, sensation of bolus stuck in upper throat
  - Esophageal phases (several seconds after swallow): forceful regurgitation, liquids backing up, retrosternal discomfort
- Signs of aspiration, history of pneumonia
- Validated dysphagia scales: MD Anderson Dysphagia Inventory, SWAL-QOL, Eating Assessment Tool
- Patient's overall health status: including weight loss, dehydration, indications of neuromuscular disorders, cardiopulmonary function

Physical Examination

- Communication (dysphonia, dysarthria, hypernasal speech)
- H&N exam: lesion tethering tongue, neck mass, fibrosis, CN abnormalities
- SLP swallow evaluation: oral motor competence, non-instrumented laryngeal evaluation, oral bolus trial
- Flexible laryngoscopy with or without stroboscopy if suspected glottic incompetence

Diagnostic Testing

- Videofluoroscopy
  - Also called "modified barium swallow" or MBS
  - Different from standard barium swallow with:
    - varying ingested consistencies
    - primarily oropharyngeal fluoroscopy
  - Evaluation of transit time, residues in pharyngeal recesses, penetration, presence and timing of aspirations, structural lesions, peristalsis, improvement with postural adjustments or swallowing maneuvers
    - Penetration=entrance of liquid or solid past the aryepiglottic fold into the larynx itself
    - Aspiration=entrance of liquid or solid past the vocal folds into the subglottis or trachea
- Barium swallow
  - Large barium bolus distends esophagus and reveals structural abnormalities, dysmotility, and gastroesophageal reflux under videoradiography
- Flexible endoscopic evaluation of swallowing (FEES)
  - Visualization of laryngopharynx before and after pharyngeal phase of swallowing with dyed boluses of varying consistencies
  - Optimal for evaluation of glottic competence, tolerance of secretions, vallecular stasis
  - Inability to assess pharyngeal swallow and PES function
- Flexible endoscopic evaluation of swallowing with sensory testing (FEEST)
  - FEES + sensory testing of laryngopharynx with pulsed air to prognosticate penetration and aspiration
  - Unilateral or bilateral sensory deficits classified from mild to severe based on pressure of air required for laryngeal adductor reflex

- Transnasal esophagoscopy
  - In-office procedure, working channels with ports for biopsy
  - Diagnosis of structural abnormalities, screening of Barrett's, neoplasm, eosinophilic esophagitis, hiatal hernia
- High-resolution manometry
  - Esophageal intraluminal pressure graph vs. time, using circumferential pressure transducers
  - Gold standard for diagnosis of esophageal motility disorder
- Multichannel intraluminal impedance and pH testing (MII-pH)
  - Impedance measurements detect non-acid and acid, anterograde and retrograde, gas and liquid reflux, as opposed to standard pH testing
- Cricopharyngeal electromyography (CP-EMG)
  - EMG measurements of cricopharyngeus activity allowing diagnosis of neuropathy (increased amplitude, polyphasic waveforms), myopathy (decreased amplitude, shorter duration), and central causes of dysphagia (normal motor unit)

CHRONIC ASPIRATION

Medical Management

- Swallow posture adjustment
  - Chin tuck: Touch chin to chest while swallowing, thus narrowing laryngeal entrance
  - Head rotation: Rotate head towards weak side, thus closing pharynx on that side and directing the bolus towards normal side
  - Head tilt: Tilt head towards normal side to direct bolus down with gravity away from weak side
- Swallowing maneuvers
  - Supraglottic swallow maneuver: Breath hold during swallow, allowing earlier CP opening and prolonged airway closure
  - Super-supraglottic swallow maneuver: Breath hold and Valsalva maneuver during swallow
  - Effortful swallow maneuver: Maximally contract all muscles of swallowing
  - Mendelsohn maneuver: Manually elevate larynx for 2 s at mid-swallow
- Bolus size and diet modification
  - Thickened liquids, smaller bolus sizes if single bolus difficult to clear, larger bolus volumes to improve sensory awareness
- Nasogastric feeding tubes, percutaneous endoscopic gastrostomy (PEG)

Surgical Management

- Tracheostomy
  - Does not prevent aspiration, but improves pulmonary toilet
  - May perturb laryngeal elevation during swallow
- Vocal fold medialization
  - In cases of glottic insufficiency secondary to unilateral vocal fold paralysis, especially with laryngeal sensory deficit
- Placement of endolaryngeal stent
  - Reversible glottis obturation with silicon stent (with or without slit for phonation)
  - Inserted endoscopically and secured with transcervical sutures
  - Requires tracheostomy
- Narrow field laryngectomy
  - Removal of laryngeal skeleton with sparing of hyoid bone and strap muscles, high tracheotomy and maximal preservation of pharyngeal mucosa, including aryepiglottic folds and vallecula
  - Irreversible. Requires tracheostomy and eliminates phonation

- Subperichondrial cricoidectomy
  - Removal of cricoid cartilage, with preservation of posterior cricoid lamina, and closure of inner cricoid perichondrium with subglottic mucosa
  - Irreversible. Requires tracheostomy and eliminates phonation
- Vertical laryngoplasty or tubed laryngoplasty
  - After tracheotomy, mucosal flap elevated from edge of epiglottis down to interarytenoid area, then closed and plicated into vertical tube
  - Irreversible. Requires tracheostomy. Allows phonation
- Epiglottopexy
  - Epiglottic flap used to close laryngeal inlet. Speech is allowed via small posterior laryngeal inlet
  - Reversible. Allows phonation. Requires tracheostomy. High risk of dehiscence
- Glottic closure
  - Via transthyrotomy, true and false vocal folds are closed after stripping their mucosa. Supraglottis may be further covered with sternohyoid muscle flap rotation
  - Irreversible. Requires tracheostomy and eliminates phonation
- Tracheoesophageal diversion (Lindeman procedure) and laryngotracheal separation
  - Separation of upper respiratory and digestive tract
  - Proximal trachea anastomosis with esophagus, thus diverting aspirated secretions into esophagus
  - Distal trachea sutured to skin to create a tracheostoma
  - Laryngotracheal separation is similar, except proximal tracheal stump is over-sewn as blind pouch. Used in patients with preexisting tracheostomy
  - Reversible. Eliminates phonation. Requires tracheostomy
- Total laryngectomy
  - Remains procedure of choice for definitive treatment of life-threatening aspirations.

BENIGN DISORDERS OF THE ESOPHAGUS

- Achalasia
  - Primary esophageal motility disorder of unknown etiology
  - Selective loss of postganglionic inhibitory neurons leading to insufficient LES relaxation and loss of esophageal peristalsis
  - Symptoms: dysphagia for solids and liquids, regurgitation, chest pain
  - Diagnosis
    - Barium swallow: bird's beak with dilated esophagus and closed LES, loss of peristalsis in distal 2/3 of esophagus
    - Manometry: aperistalsis with incomplete LES relaxation
    - Upper endoscopy: must be performed to rule out pseudoachalasia, from GEJ tumor mimicking achalasia
  - Treatment
    - Graded pneumatic dilation, followed by gastrografin study to rule out esophageal perforation (2–5 % of all dilations)
    - Heller's myotomy: anterior myotomy across LES
    - Botox injection and pharmacologic treatment (Ca channel blockers, long acting nitrates) when surgery is not possible
- Esophageal diverticulum
  - Sac protruding from esophageal wall. False diverticulum if only mucosa and submucosa have herniated through muscle layers
  - Zenker's diverticulum:
    - Located above UES, at Killian's triangle (between cricophargyngeal sphincter and inferior pharyngeal constrictor muscle)
    - Presents with dysphagia, regurgitation, halitosis, aspirations
    - Treatment when symptomatic: open division of CP muscle, diverticulopexy, caudal suspension of diverticulum, endoscopic diverticulotomy with stapler or CO_2 laser

- Midesophageal diverticula: usually asymptomatic, only true diverticulum
- Epiphrenic diverticula: near diaphragmatic hiatus and LES, secondary to motility disorders, such as achalasia, and occasionally symptomatic
- Intramural pseudodiverticula: multiple outpoutchings representing dilated submucosal glands. Associated with reflux and cancer

- Eosinophilic esophagitis
  - Defined as eosinophilic esophagitis with >15 eosinophils per high power field
  - Symptoms: dysphagia
  - Endoscopic finding: multiple esophageal rings
  - Treatment: bougienage +/– acid suppression, food elimination, oral or topical corticosteroids, leukotriene receptor antagonists
- GERD—gastroesophageal reflux disease
  - Chronic symptoms or mucosal damage due to reflex of gastric contents in esophagus
  - Associated with LES incompetence, hiatal hernias, delayed gastric emptying
  - Symptoms: retrosternal burning, acid regurgitation
  - Diagnosis: clinical response to acid suppression, endoscopic findings of reflux esophagitis, 24 h pH monitoring
  - Treatment
    - Lifestyle modification (avoidance of alcohol, caffeine, avoidance of recumbence postprandially, weight loss, smoking cessation)
    - Prokinetic agents, such as metoclopramide
    - Acid suppression therapy with histamine receptor antagonists, proton pump inhibitors for severe disease
    - Laparoscopic fundoplication: in patients with good response to PPI
- Barrett's esophagus
  - Complication of longstanding GERD
  - Squamous epithelium of distal esophagus replaced by intestinal columnar metaplasia, with mucin-containing goblet cells
  - Predisposes to esophageal adenocarcinoma
  - 6–12 % patients with GERD are found to have Barrett's
  - Requires endoscopic surveillance with biopsy every 3 years
- Hiatal hernia
  - Herniation of abdominal cavity through esophageal hiatus of diaphragm
  - Type I, sliding hernia (95 %): portion of gastric cardia herniates upwards through widened muscular hiatus
  - Type II–IV are paraesophageal hernias
  - Symptoms of GERD, postprandial fullness, nausea, retching
  - Treatment: medical management of GERD, Nissen fundoplication in case of type I hiatal hernia. Paraesophageal hernia repair has mortality rate of 1.4 %.
- Strictures
  - Loss of lumen within esophagus (~20 mm in diameter), presenting with dysphagia
  - Intrinsic strictures more common than extrinsic ones, most commonly acid causes
  - Treatment: esophageal dilation with
    - Maloney bougies for uncomplicated short strictures
    - Savary-Gilliard dilators and through the scope balloons for long strictures
    - Goal is to Dilate >15 mm Diameter
- Webs and rings
  - Webs: always mucosal, involve part of lumen, usually proximal
  - Rings: mucosa or muscle, circumferential, usually distal
    - Schatzki's ring (B ring): occurs at GEJ, the most common cause of solid food dysphagia
  - Present with dysphagia
  - Plummer–Vinson syndrome: triad of webs, iron deficiency anemia, dysphagia
  - Treatment: mechanical disruption with bougie or dilator

- Benign neoplasms of the esophagus
  - Lymphangioma, hemangioma, fibrovascular polyps, inflammatory fibroid polyps, and papilloma (unclear if HPV related): rarely symptomatic and resection is not necessary if asymptomatic
  - Granular cell tumors have malignant potential and should be resected
  - Adenomas are dysplastic lesions arising within Barrett's esophagus and should be resected

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Chapter 30
Lasers

Paula Borges and C. Kwang Sung

PEARLS

- Laser beams are monochromatic, collimated, coherent, and intense.
- A pulsed dye or KTP laser can be used for selective photoangiolysis of laryngeal lesions, hemangiomas, and port-wine stains.

LASER PHYSICS

Laser Components

- Active medium: (e.g., CO_2 [Carbon dioxide], Argon). Solid, liquid, or gas substance whose atoms can be excited to support stimulated emission.
- Power source: Acts on the active medium to energize atoms into an excited state (e.g., electric current).
- Optical chamber: Resonating chamber with mirrors (one reflective and one partially transmissive)—feedback mechanism.

Stimulated Emission

- Step 1: Excitation of atoms in the active medium by a power source.
- Step 2: As excited atoms return to a lower state of energy, they release photons which in turn excite other atoms, eliciting a chain reaction.
- Step 3: Photons of identical wavelengths are reflected by mirrors in the optical chamber and transmitted out in a beam.
- Step 4: Emitted beam passes through a lens that focuses the energy.
- Step 5: The mirrors continue to provide positive feedback to keep the emission going.

Laser Beam Characteristics

- Monochromatic: comprised of one wavelength
- Collimated: unidirectional
- Coherent: waves are in phase, equal and parallel
- Intense

Laser Operating Modes

- Continuous mode: Active medium is continuously stimulated producing constant energy.
- Pulsed mode: Active medium is activated for short bursts. This allows tissue to cool between pulses so thermal damage is minimized.
- Q-switched mode: Very short, intense, and quick pulses.

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Laser Settings

- Power (in Watts): Relationship of power and depth of tissue effect is highly dependent on spot size and exposure time.
- Spot size: Determined by focal length and focus.
- Exposure time
- Irradiance (in Watts/cm^2): Power/Area of the focal spot, determines tissue effects.
- Fluence (in J/cm^2): Total amount of laser energy per unit area of target tissue.

Delivery Systems

- Articulated arm
- Optical fibers
- Micromanipulator
- Hand piece: connection between the laser and the operation microscope.

TYPES OF LASERS

There are several lasers used in otolaryngology. Laser type is characterized by the active medium and its wavelength, which determines the tissue interaction, and thus its uses. The following are the most commonly used lasers in otolaryngology (Table 30.1)

TABLE 30.1 Summary of laser types

Laser type	Wavelength (nm)	Uses	Depth of penetration	Chromophore	Delivery system
Argon	514 (Visible)	Photocoagulation of pigmented lesions (Hemangiomas, telangiectasias), middle ear surgery (stapes, lysis of adhesions)	0.8 mm	Hemoglobin (Hg), melanin, myoglobin	Fiber-optic
KTP	532 (Visible)	Vascular lesions, turbinate reduction	0.9 mm	Oxyhemoglobin	Fiber-optic, contact quartz
Pulsed dye laser (PDL)	585 (Visible)	Vascular lesions	0.8 mm	Oxyhemoglobin	Fiber-optic
Nd:YAG	1,060 (Near infrared)	Tracheobronchial lesions, esophageal lesions, vascular lesions, lymphatic malformations, skin resurfacing, hair removal	4.0 mm	Pigmented tissues	Fiber-optic
Ho:YAG	2,100 (Infrared)	Sinus surgery (not widely adopted)	0.4 mm	Water	Fiber-optic
Er:YAG	2,940 (Infrared)	Skin resurfacing, stapes surgery	3.0 μm	Water	Fiber-optic
CO_2	10,600 (Infrared)	Laryngeal lesions, bronchial and esophageal lesions, stapes, deep skin resurfacing	30.0 μm	Water	Handpiece, wave guide, fiber-optic, articulating arm, micromanipulator

KTP Potassium titanyl phosphate, *Nd:YAG* Neodymium:Yttrium–Aluminum–Garnet, *Ho:YAG* Holmium:YAG, *Er:YAG* Erbium:YAG

Argon

- Transmits through clear tissue, absorbed by pigmented tissues, partially absorbed and reflected by white tissues (bone, fat, skin).
- Destroys upper dermis and epidermis—can scar skin.
- Small focal spot leads to high power density causing vaporization of tissue.
- Useful for stapedotomy, but must use a drop of blood on the stapes or the bone will reflect the laser.

KTP: Potassium Titanyl Phosphate

- Works by passing an Nd:YAG laser through a KTP crystal changing the wavelength to 532 nm.
- Delivery via fiber-optic carrier for vaporizing and coagulation or a contact quartz tip for cutting.
- May be used in the office setting through flexible channeled endoscopes.
- Used for selective photoangiolysis of laryngeal lesions such as papilloma and dysplastic lesions, also in otologic (stapes, chronic ear) and rhinologic (functional endoscopic sinus) surgery, and for tonsillectomy and pigmented dermal lesions.

PDL: Pulsed Dye Laser

- Used for selective photoangiolysis of laryngeal lesions, hemangiomas, and port-wine stains.
- Minimal thermal injury in the surrounding tissue.
- Dark skin types respond poorly, but lighter skin types show significant results.

Nd:YAG: Neodymium:Yttrium–Aluminum–Garnet

- Requires aiming beam (helium–neon laser) since it is invisible.
- Imprecise due to deep penetration of tissue—4 mm.
- Excellent for coagulation (requires high power).
- Treatment of tracheobronchial lesions.

Ho:YAG: Holmium:YAG

- Good hemostasis.
- Minimal thermal damage.

Er:YAG: Erbium:YAG

- Precise tissue ablation with minimal surrounding thermal damage.
- Poor hemostasis.
- Primarily for superficial skin resurfacing for fine wrinkles, brown spots, and acne scars.

CO_2

- Requires aiming beam (helium–neon laser).
- Very versatile with many applications (laryngeal lesions, stapedotomy, skin resurfacing).
- Minimal postoperative edema.
- Little reflection and scattering, very precise.
- For cutting, use a small (focused) spot size with a high power density.
- For vaporization and coagulation (limited to vessels <0.5 mm) use a low power density with a large (defocused) spot size.

Other Lasers

- Argon tunable dye: Used for photodynamic therapy, a treatment for malignant tumors (e.g., nasopharyngeal carcinoma, but still considered experimental and investigational in this application). The argon laser is coupled to a dye laser that can be varied to a desired wavelength.
- Thulium:YAG: Introduced as a possible alternative to the CO_2 laser because it can easily be applied through a flexible endoscope in an office setting. It has a wavelength of 2,013 nm and has water as its main target chromophore.

LASER TISSUE INTERACTION

Laser Tissue Interaction Types

- Absorption: Main determinant of tissue effect.
- Scattering: Energy is spread over a larger area but with less tissue penetration. Shorter wavelengths lead to more scattering.
- Transmission: Light travels through tissue. No effect on tissue.
- Reflection: Light does not enter tissue. No effect on tissue.

Interaction Determinants

- Wavelength: Shorter wavelengths have greater effect on tissue (wavelengths between 0.1 and 0.8 μm cause minimal water absorption but considerable hemoglobin–melanin absorption and wavelengths >3 μm are absorbed water).
- Operation mode.
- Amount of energy delivered.
- Tissue characteristics.

Tissue Effects

- Heating.
- Photodissociation of chemical bonds.

Temperature Dependent Laser Tissue Interactions

- Temperatures over 50 °C: Decrease in enzymatic activity.
- Over 60 °C: proteins denature (blanching of tissue).
- Over 100 °C: Vaporization of intracellular water (vacuole formation and shrinking of tissue).
- Several hundred °C: Carbonization, disintegration, smoke, and gas generation with destruction of the laser-radiated tissue.
- Collateral heat damage is reduced with infrared lasers.

Laser Wound Characteristics (Zones of Injury from Closest to Furthest from Beam)

- Center: Tissue vaporization.
- Thermal necrosis: (small vessels sealed in this area).
- Thermal conductivity and repair.
- Normal tissue.

LASER SAFETY

Laser Injury Mechanisms

- Direct exposure
- Reflected beam

Laser Safety Equipment

- Laser safety glasses for personnel and patient (or moist eye pads covered with moist towels or metallic eye protectors to patient)
- Operating room (OR) window covers (opaque material of the same wavelength as the laser)
- Laser warning signs posted at the entrances of the OR
- Surgical mask
- Smoke evacuation device/suction

Laser Hazards

- Beam: May cause eye injury. Avoid with eye protection.
- Plume (Smoke and radiation): Smoke from heat effect of laser on tissue. Radiation from beam contacting smoke. Plume content may be toxic. Prevent with smoke evacuation.
- Fire: Airway burns may result from endotracheal tube (ETT) fire if the beam strikes the flammable ETT. Minimize with tubes wrapped in reflective tape or laser safe tubes made of reflective metals, flame retardant surgical drapes, surgical field covered in saline-soaked towels.

Anesthetic Precautions During Laser Use

- Closed ventilatory system if possible to avoid anesthetic gas leak.
- ETT cuff filled with methylene blue.
- Minimal oxygen and nitrous oxide.
- Jet ventilation for some lesions.
- Managing ETT fire during laser laryngoscopy: Stop laser, turn off oxygen, remove tube, irrigate with saline, re-intubate, give IV steroids and antibiotics, bronchoscopy, delayed extubation, and second look laryngoscopy and bronchoscopy.

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PART VII

Facial Plastics and Reconstruction

Section Editor: Joshua D. Rosenberg, MD

Chapter 31
Facial Plastics

Chaz L. Stucken and Joshua D. Rosenberg

PEARLS

- The major tip support mechanisms of the nose include: The intrinsic size, shape, and strength of the lower lateral cartilages. The attachments of the medial crura of lower lateral cartilages with the caudal septum. And the attachments of the lower lateral cartilages with the upper lateral cartilages (scroll region)
- Pollybeak deformity is a soft-tissue or cartilage fullness of the supratip that can be caused by inadequate tip support and decreased tip projection, inadequate reduction of dorsal hump, inadequate reduction of anterior septal angle/reduce additional anterior septal angle, excessive reduction of columella/columellar strut, or supratip dead space scar formation

AESTHETIC FACIAL ANALYSIS

- Landmarks in the midsagittal plane
  - Trichion—the lowest point of hairline
  - Glabella—the most prominent projection of frontal bone just above the nasofrontal suture
  - Nasion—the deepest point of the forehead at the nasofrontal suture line
  - Radix—soft tissue correlate of the deepest point of the forehead at the nasal root (nasion)
  - Sellion—junction of the bony and cartilaginous nasal dorsum
  - Rhinion—soft tissue correlate of the bony–cartilaginous junction of nasal dorsum (sellion)
  - Supratip—point cephalic to the tip
  - Tip—the most prominent anterior projection of the domes
  - Columella point—most anterior point of the columella
  - Subnasale—junction of the columella and the cutaneous upper lip
  - Superior sulcus—the deepest point of the cutaneous upper lip between the subnasale and labrale superius
  - Labrale superius—mucocutaneous junction of the upper lip
  - Stomion—midpoint of the interlabial gap
  - Labrale inferius—mucocutaneous junction of the lower lip
  - Mentolabial sulcus—the most posterior point between the lower lip and the menton
  - Pogonion—the most prominent anterior projection of the chin
  - Menton—the most inferior point of the chin
  - Cervical point—point of intersection between (1) a line tangent to the neck and (2) a line tangent to the submentum
  - Gnathion—point of intersection between (1) a line from the subnasale to the pogonion and (2) a line from the cervical point to the menton

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- Landmarks outside of the midsagittal plane
  - Porion—the midpoint of the superior external auditory canal at the most lateral edge of the canal
  - Tragion—the most anterior point of the supratragal notch
  - Orbitale—the most inferior point of the infraorbital rim
  - Gonion—the most inferior, posterior, and lateral point of the mandibular angle
  - Frankfort Plane—the horizontal plane as defined by a line from the porion to the orbitale
- Evaluate the entire face as a whole by systematically examining aesthetic subunits
- Facial aesthetic units: (1) forehead/brow, (2) periorbital region, (3) maxilla/zygoma, (4) nose, (5) ears, (6) mouth and chin, and (7) neck
- Five vertical segments of equal width
  - Lateral border of helix → lateral canthus; lateral canthus → medial canthus; medial canthus → medial canthus; medial canthus → lateral canthus; lateral canthus → lateral border of helix
- Three horizontal segments of equal height
  - Upper third: trichion → glabella
  - Middle third: glabella → subnasale
  - Lower third: subnasale → mentum
- Fitzpatrick skin type
  - I—white, very fair—always burns, never tans
  - II—white, fair—usually burns, tans with difficulty
  - III—white, beige—sometimes mild burn, tans moderately and gradually
  - IV—light brown—burns minimally, tans well
  - V—brown—rarely burns, tans deeply
  - VI—dark brown/black—never burns, tans deeply
- Glogau photoaging scale
  - I—no rhytids, keratoses, or acne scaring—wears minimal or no make-up
  - II—early rhytids in motion, mild keratosis, brown spots, and scarring—wears some foundation
  - III—rhytids at rest, visible telangiectasias, keratosis, and discoloring—wears heavy makeup
  - IV—severe rhytids, significant skin discoloration, previous skin malignancies, skin laxity—cakes on makeup, makeup may crack

RHINOPLASTY

- Anatomy
  - Upper lateral cartilage—paired triangular cartilages connected medially to the middle third of the dorsal septum at a 10–15° angle. Bordered superiorly by the nasal bones, laterally by the maxillary pyriform aperture, and inferiorly by the lower lateral cartilages (scroll)
  - Lower lateral cartilage—paired C-shape cartilages with three segments (medial crus, intermediate crus, and lateral crus) that form the domes and nasal tip
  - Accessory cartilage—small cartilages and soft tissues located between the lateral edge of the lateral crus and the pyriform aperture
  - Sesamoid cartilage—small cartilages that are not always present, located between the caudal upper lateral cartilage and the cephalic lower lateral cartilages
  - Dome—the junction between the medial and lateral crura that creates the most anterior and angulated segment of the lower lateral cartilages
  - Scroll region—attachment of the upper and lower lateral cartilages
  - Alae—lateral nostril walls that extend from the nasal tip to the alar crease and nasal base
  - Alar crease—crease where the ala meets the cheek
  - Alar groove—groove on the lateral nose at the caudal edge of the lateral crus that defines the alae below it
  - Anterior septal angle—angle between the dorsal and caudal septum
  - Columellar break—a break-point created by the curvature of the intermediate crus that demarcates the transition from the columella to the infratip lobule

- External nasal valve—the nasal aperture bordered medially by the membranous septum, superiorly and laterally by the nasal ala, and inferiorly by the nasal sill
- Internal nasal valve—the internal nasal aperture bordered medially by the caudal septum, superiorly by the upper lateral cartilage, laterally by the lateral nasal side wall and inferior turbinate, and inferiorly by the rim of the pyriform aperture
- Keystone—location on the nasal dorsum that is the intersection of the nasal bones, cartilaginous septum, upper lateral cartilages, and the perpendicular plate of the ethmoid bone
- Lobule—the lower third of the nose is the lobule or tip
  - Alar lobule—fibrofatty tissue overlying the lateral crus
  - Infratip lobule—on basal view, the portion of the lobule between the columellar point and the nasal tip

- Rhinofacial analysis
  - Functional Analysis
    - Septum—cartilaginous and/or bony deviation, dislocation, or spur
      - Perform nasal endoscopy
    - External nasal valve—collapse
      - Examine from basal view during nasal inspiration
    - Internal nasal valve—narrowing, scarring, displaced upper lateral cartilages, hypertrophic inferior turbinates, septal deviation, maxillary spine bone spurs
      - Cottle Maneuver—examiner places thumbs on patient's cheeks and retracts the cheek soft tissue and nasal walls laterally during inspiration
      - Modified Cottle Maneuver—examiner places a Freer (or other blunt instrument) into the nose to push the lateral nasal wall laterally
    - Nasal bones—fractures, narrowing
      - Palpate bones and pyriform aperture
    - Columella—deflection, scarring
    - Tip—twisted, collapsed, boxy/bifid, scarred alae
      - Evaluate tip support by palpation
      - Prior surgery or injury; bossae
      - Tip defining points
  - Aesthetic Analysis
    - Photography
      - always obtain consent, dSLR camera, 90–105 mm "macro" lens, two umbrella flashes, light blue or green background
      - Frontal, R/L lateral, right and left oblique (3/4 view), and basal
    - Upper third
      - Bony pyramid—fractures, deviation, narrowing, depth of radix
    - Middle third
      - Cartilaginous dorsum—deflection, "twisted nose," asymmetry, dorsal hump
    - Lower third
      - Nasal tip—asymmetry, projection, rotation, alar collapse, columellar show, alar width
    - Nasofrontal angle—angle formed by (1) a line drawn from the nasal tip to the nasion and (2) a line drawn from the glabella to the nasion; Caucasian "ideal": 115–130°
    - Nasofacial angle—angle formed by (1) a vertical line drawn from the glabella to the pogonion and (2) a line drawn from the nasal tip to the nasion; Caucasian "ideal": 30–40°
    - Nasomental angle—angle formed by (1) a line drawn from the nasion to the nasal tip and (2) a line drawn from the nasal tip to the pogonion; Caucasian "ideal": 120–130°
    - Nasolabial angle—angle formed by (1) a line drawn from the columella point to the subnasale and (2) a line drawn from the subnasale and the labrale superius; males: 90–95°; females: 95–105°
    - Columellar show—amount of columella visualized caudal to the ala on lateral view; "ideal" is 2–4 mm

        - Alar lobule ratio—on lateral view, the distance from nasal tip to posterior lobule divided by the distance from the posterior lobule to the alar crease. "Ideal" ratio is 1:1
        - Columellar lobule ratio—on basal view, the distance from the subnasale to the columellar point divided by the distance from the columellar point to the nasal tip. "Ideal" ratio is 2:1 (columella twice as long as lobule)
    - Projection
        - Crumley's method
            - On lateral view, a vertical line is drawn from the nasion to the alar crease
            - A horizontal line is drawn perpendicular to the first line, from the nasal tip to the alar crease
            - A line is drawn from the nasion to the nasal tip
            - In a nose with "normal" projection, these three lines form a 3:4:5 triangle
        - Goode method
            - The same lines are drawn as described by the Crumley method
            - The length of the nasal tip-alar crease line divided by the length of the nasion–nasal tip line is "ideally" 0.55–0.60, creating a nasofacial angle of 36–40°
    - Skin
        - The thickest point—Nasion
        - The thinnest point—Rhinion
        - Thick skin
            - Advantages: hides imperfections in underlying nasal skeleton framework
            - Disadvantages: increased scarring (increased risk of pollybeak deformity)
        - Thin Skin
            - Advantages: allows for improved definition of underlying nasal skeleton
            - Disadvantages: contour imperfections and irregularities are easily visible
- Patient factors
    - smoking, systemic diseases (granulomatous disease), patient's motivation and expectations, psychiatric disorders, cocaine abuse, chronic sinusitis, nasal obstruction, anticoagulation medications, ethnicity
- Major tip support mechanisms
    - Intrinsic size, shape, and strength of the lower lateral cartilages
    - Attachments of medial crura of lower lateral cartilages with the caudal septum
    - Attachments of the lower lateral cartilages with the upper lateral cartilages (scroll region)
- Minor tip support mechanisms
    - Interdomal attachments between the lower lateral cartilages
    - Soft tissues of membranous septum
    - Nasal dorsum including the dorsal septum and upper lateral cartilages
    - Skin-soft tissue envelope—attachments of overlying skin and muscle to the alar cartilages
    - Sesamoid cartilage attachments of lower lateral cartilages to lateral nasal sidewall
    - Nasal spine
- Incisions
    - Marginal—an incision along the caudal edge of the lower lateral cartilage
    - Intercartilaginous—an incision between the caudal edge of the upper lateral cartilage and the cephalic edge of the lower lateral cartilage
    - Intracartilaginous (cartilage-splitting)—an incision through the lower lateral cartilage just caudal to the cephalic edge of the lateral crus.
    - Transcolumellar—a W-shaped or inverted V-shaped incision through the columella that extends to the posterior edges of the medial crura to meet the marginal incisions
    - Transfixion
        - Full transfixion—a through-and-through incision made through the membranous septum caudal to the cartilaginous septum, separating the medial crura from the caudal septum
        - Hemitransfixion—an incision through one side of the membranous septum just caudal to the cartilaginous septum without separating the medial crus from the septum

- Alar base—an incision made through the nasal vestibule, nasal sill, and nasal crease to release the ala

- Surgical Approach (Closed or Open)
  - Closed
    - Non-delivery—minor tip work performed through intracartilaginous incision or an intercartilaginous incision with retrograde dissection
    - Delivery—extensive tip work performed after delivering the lower lateral cartilages through marginal and intercartilaginous incisions.
      - Advantages—provides full access to the lower lateral cartilages to perform extensive tip work, no external scar
      - Disadvantages—intercartilaginous incision disrupts a major tip support mechanism
  - Open
    - Performed through transcolumellar and marginal incisions
    - Advantages—provides complete access to the lower lateral cartilages, septum, and upper lateral cartilages for extensive tip work, major reconstruction, revision rhinoplasty, dorsal septal deviations, easier placement of sutures/grafts/implants, and academic teaching/learning
    - Disadvantages—may disrupt major tip support mechanism if medial crura are separated from the caudal septum, external scar, increased post-operative edema, more time-consuming, nasal tip anesthesia
- Tip Modifications
  - Complete Strip—leaves the lower lateral cartilage *completely* intact after trimming of the cephalic edge; important to preserve ~8 mm caudal strip of alar cartilages to reduce risk of alar collapse
  - Interrupted Strip—interrupts the continuity of the lower lateral cartilage to obtain major changes in tip projection, rotation, and narrowing. Vertical dome division or Goldman tip technique is useful for extremely boxy or bulbous tips with resilient intrinsic cartilage strength
  - Dome binding suture
    - Single dome-binding suture—one horizontal mattress suture between the two domes used to correct a boxy or bifid tip
    - Double dome-binding suture—three different sutures: one suture in each dome and one suture to bring the two domes together. Useful for more severely bifid or boxy tips, results in more narrowing than single-dome binding suture
- Techniques to increase projection
  - Tripod concept: lengthen all three legs → increase projection
    - Augment medial and lateral crura
  - Suture techniques can create small increases in projection
    - Suturing together the medial crura
    - Septocolumellar sutures
    - Transdomal and/or interdomal sutures
  - Extensive tip modification can create major increases in projection
    - Goldman tip or interrupted strip techniques with augmentation of medial crura and lateral crural steal combined with transdomal and interdomal sutures
  - Augmentation of tip (shield graft)
  - Columellar strut
  - Augmentation of nasolabial angle and premaxilla (plumping grafts)
- Techniques to increase rotation
  - Most techniques that increase tip projection will also increase tip rotation. Increasing tip projection involves more extensive tip modification than achieving improvements in tip rotation. All of the above methods to increase projection will also increase rotation.
  - Complete strip technique with single dome-binding suture will increase rotation without major changes in projection
  - Lateral crural steal
  - Reduction of dorsal hump

- Techniques to decrease projection
  - Tripod concept: shorten all three legs → decrease projection
  - Reduction of medial and lateral crura
  - Complete transfixion incision
  - Reduction of caudal septum
  - Tip grafting
- Techniques to decrease rotation
  - The aforementioned techniques to decrease tip projection typically result in an apparent decrease in rotation
  - Augmentation of nasal dorsum
  - Augmentation of lateral crura with overlay grafts
  - Augmentation of infratip lobule
- Functional Considerations
  - Septal Deviation
    - Standard septoplasty if rhinoplasty is being performed through closed technique
    - Open septoplasty if rhinoplasty is being performed through open technique
    - Open rhinoplasty technique offers good access to correct deviation of the dorsocaudal L-strut. Extracorporeal septoplasty involves complete removal of the dorsocaudal strut and reforming/modifying it on a back table using cartilage grafts or synthetic grafts as necessary
  - Alar collapse—place batten grafts caudal to the lateral crura at the point of nasal valve collapse. Use cartilage graft with convex side facing outward. Alternatives: lateral crural strut graft, suspension suture, rim graft
  - Upper lateral cartilage collapse—spreader grafts placed between upper lateral cartilage and septum to widen nasal valve
  - Turbinate hypertrophy—perform outfracturing and reduction of inferior turbinates
- Dorsal hump
  - Dorsal hump is composed of caudal anterior nasal bones and superior dorsal septal cartilage
  - Elevate skin soft-tissue envelope, then use combination of osteotome, rasp, scissors, and blades to reduce hump
  - Skin is thinnest at rhinion, so avoid overresection in this area
  - Upper lateral cartilages may collapse inferomedially away from the nasal bones causing an inverted-V deformity.
  - Hump removal may disrupt attachments of upper lateral cartilages with septum, may require spreader grafts to prevent nasal valve collapse
  - Hump removal will create open roof deformity, so osteotomies are performed to medialize the nasal bones and upper lateral cartilages
- Osteotomies
  - To correct cosmetic deformities of bony upper third of nose (open roof, deviated/fractured nasal bones, narrow nasal vault, widened nasal vault)
  - Medial osteotomy—mobilizes the nasal bones to allow infracturing after the lateral osteotomies. Not always necessary to perform if removing the dorsal hump created a large open roof
  - Lateral osteotomy—reduces the width of the bony dorsum. When connected to medial osteotomies, the nasal bones along with a small portion of the maxilla are mobilized, allowing infracture of the bones. If the superomedial nasal bone is not completely mobilized, then the bones will not be adequately infractured
    - High-to-low-to-high lateral osteotomies: Leave a segment of the pyriform aperture undisrupted inferiorly to prevent medialization of the inferior turbinate
  - Intermediate osteotomy—an osteotomy performed between the medial and lateral osteotomies in conjunction with the other two
    - Provides additional medialization and infracturing of prominent nasal horns, rocker deformities, severely deviated bony vaults, or excessively convex nasal bones

- Complications of rhinoplasty
  - Asymmetric tip—caused by unequal reduction of tip or asymmetric dome-binding sutures. Treatment: revision rhinoplasty with tip techniques described above
  - Twisted nose—caused by inadequate straightening of septum, bony vault, or asymmetric tip. Treatment: revision rhinoplasty with tip techniques described above, septoplasty, osteotomies, camouflage grafts, straightening of entire nose
  - Bossing—knuckling of nasal tip caused by contractual scarring of weakened/overresected lower lateral cartilages. Patients with thin skin, bifid tips, strong cartilages, and those who have undergone vertical dome division may be at higher risk of bossing. Treatment: excise the weakened bossing area, cover with small cartilage graft
  - Saddle nose deformity—collapse of nasal dorsum caused by overresection of septum or failure to preserve a dorsocaudal L-strut. May also be caused by nasal trauma, granulomatous disease, cocaine abuse, or septal hematoma. Treatment: augmentation of nasal dorsum with cartilage or bone grafts
  - Pollybeak deformity—soft-tissue or cartilage fullness of the supratip
    - Cause/Treatment
      - inadequate tip support and decreased tip projection/use aforementioned techniques to increase tip projection
      - inadequate reduction of dorsal hump/resect additional dorsal hump
      - inadequate reduction of anterior septal angle/reduce additional anterior septal angle
      - excessive reduction of columella/columellar strut
      - supratip dead space scar formation/massage, skin taping, and kenalog injections; resect supratip scar and augment bony dorsum with cartilage graft to remove dead space and potential site of scar deposition
  - Inverted-V deformity—During dorsal hump removal, ensure preservation of the nasal mucoperichondrium, which supports the upper lateral cartilages. If nasal mucoperichondrium is violated, the upper lateral cartilages may collapse inferomedially away from the nasal bones. If the nasal bones are inadequately infractured with osteotomies, then the patient will have an inverted-V deformity in which the caudal edges of the nasal bones are overly visible. Treatment: new osteotomies with infracturing/narrowing of the bony nasal vault, placement of spreader grafts

FACIAL AGING

Non-surgical Cosmetic Interventions

Neurotoxin Derivatives

- OnabotulinumtoxinA—botulinum toxin A (BOTOX, Dysport, Xeomin)
- RimabotulinumtoxinB—botulinum toxin B (Myobloc)
  - *Clostridium botulinum* produces eight neurotoxins: A, B, C1, C2, D, E, F, and G
  - Inhibits the release of acetylcholine at the neuromuscular junction: flaccid paralysis
  - Inject perpendicular to the skin; inject directly into the muscle belly; in perioral and periocular regions (thin skin), inject subcutaneously
  - Rarely, neutralizing antibodies may lead to secondary non-responsiveness
- Glabellar Complex
  - Most common site of neurotoxin injection
  - Target Muscles
    - Corrugator Supercilii—draws eyebrow downward and medially (causes vertical rhytids of the glabella and nasion)
    - Procerus—pulls medial eyebrow downward (causes horizontal rhytids of the nasion)
    - Orbicularis Oculi—medial depressor supercilii pulls brow downward
  - 5–7 injection sites, avoid injecting too low over the orbit
  - Dose: 20–40 units, depending on severity and gender.
  - Upper lid ptosis—caused by lateral injections too close to the brow
    - Treatment: apraclonidine 0.5 % eye drops to stimulate Müller's muscle
  - Time until retreatment: ~3 to 4 months

- Forehead
  - More challenging site of Botox injection
    - More variable muscle anatomy
    - Find balance between iatrogenic brow ptosis vs. failure to efface rhytids
    - Overtreatment may create an expressionless appearance
    - Elderly patients sometimes use frontalis to improve visual field
    - Lateral injections increase risk of brow ptosis, but underinjecting laterally may create a quizzical look (Mr. Spock appearance)
  - Target Muscle
    - Frontalis—raises the eyebrow (causes horizontal rhytids of the forehead)
  - Approx 4–8 injection sites (up to 12)
  - Men: 20–30 units
  - Women: 10–20 units
  - Inject at least 1–2 cm above orbital rim to avoid brow ptosis (avoid first rhytid above brow)
  - Time until retreatment: ~4 to 6 months
- Crow's feet
  - Target Muscle
    - Lateral orbicularis oculi—assists in closing the eye and squinting (causes lateral orbital rhytids)
  - 2–5 injection sites per side
  - 16–30 units total
  - Superficial subcutaneous injections directed laterally (away from the orbit)
  - Snap test for lid laxity. If lower lid laxity is present, then risk of ectropion.
  - Upper lid ptosis—caused by medial injections too close to orbital rim. Inject at least 1 cm lateral to rim
    - Treatment: apraclonidine 0.5 % eyedrops to stimulate Müller's muscle
  - Time until retreatment: ~3 to 4 months
- Bunny Lines
  - Target Muscle
    - Transverse fibers of nasalis—compresses nasal cartilage and flares nostrils (causes rhytids that radiate inferiorly along the lateral nasal side walls)
  - 1–3 injection sites
  - 2–5 units total
  - Superficial subcutaneous injections
  - Do not inject the levator labii alequae nasi or levator labii superioris to avoid causing upper lip droop.
  - Time until retreatment: ~3 months
- Perioral Lines
  - Botox injections in this area are frequently used in combination with fillers to treat perioral rhytids
  - Target Muscle
    - Orbicularis oris—closes the mouth and puckers lips (causes perioral rhytids)
    - Buccinator, risorius, depressor anguli oris, depressor labii inferioris, levator anguli oris, levator labii superioris, zygomaticus major, zygomaticus minor, and mentalis all contribute to movements of the lips, but these muscles should be mostly avoided to prevent a paralyzed expression
  - 1–2 injections per lip quadrant
  - 4–10 units total
  - Inject within 5 mm of the vermillion border. Do not inject the Cupid's bow to prevent flattening the upper lip. Do not inject the modiolus to prevent oral incompetence
  - Avoid overtreatment to prevent oral incompetence, drooling, and speech impediments
  - Time until retreatment: ~2 to 3 months

- Peau D'Orange
  - Peau D'Orange refers to the dimpled appearance of the chin caused by a contraction of the mentalis muscle in patients with decreased collagen and subcutaneous fat
  - Target Muscle
    - Mentalis: raises and pushes up the lower lip
  - 1–2 injections
  - 2–8 units total
  - Time until retreatment: ~3 to 6 months
- Platysmal Bands
  - The goal of this injection is to decrease the prominence of the muscle itself, compared to previously mentioned injections, which are performed to improve the appearance of rhytids
  - Target Muscle
    - Platysma—depresses the mandible, lower lip, and corners of the mouth
  - 2–12 injections per band
  - 10–40 units per band. Treat two bands per session
  - Inject directly into the belly of the muscle. Avoid deep injections into the strap muscles that will cause dysphagia or dysphonia
  - Injections are most successful in either patients with good skin elasticity or in those who have undergone rhytidectomy
  - Time until retreatment: ~3 to 4 months

Fillers

- Ideal filler: biocompatible, nonallergenic, noncarcinogenic, inexpensive, nonmigratory agent that produces reliable, reproducible, long-lasting results and can be easily stored and transported
  - Autologous fat—no risk of allergic reaction or rejection; however, unpredictable results with high absorption rate
  - Paraffin, injectable liquid silicone, and Teflon paste—rarely used secondary to foreign body reaction, granuloma formation, inflammatory response (paraffinomas)
  - Bovine collagen (Zyderm, Zyplast)—good choice for fine wrinkles; skin-testing before injection because 3–3.5 % population has hypersensitivity, short duration, refrigeration requirement, fear of bovine spongiform encephalopathy
  - Calcium hydroxylapatite (Radiesse)—excellent results for deep folds, wrinkles (randomized clinical trials show superior effectiveness of Radiesse over hyaluronic acid fillers for the nasolabial fold), relatively long acting (6–18 months), hypoallergenic; should not be used for superficial lines
  - Hyaluronic acid (Restylane, Juvederm Ultra, Perlane, Hylaform, Hydrelle)—low risk of allergic reaction but use is contraindicated in patients with history of severe allergic reactions or anaphylaxis, effects last for ~6 to 8 months, easy to use and inject into subdermis; Tyndall effect may result in bluish tint if injected too superficially; overinjection may be reversed using hyaluronidase (Vitrase)

Skin Resurfacing

- Lasers
  - LASER (Light Amplification by the Stimulated Emission of Radiation)—a device that generates a collimated, coherent, monochromatic light
    - Collimated—all waves are parallel without divergence or convergence
    - Coherent—all waves are in phase with each other
    - Monochromatic—all waves are of a single wavelength
  - Indications—Vary with patients' goals and type of laser used
  - Actinic keratosis
  - Photoaging

- Pigment changes
- Lentigines
- Fine rhytids
- Acne management and scarring
- Ablative vs. Non-ablative
  - Ablative
    - Thermal injury to epidermis and dermis: re-epithelialization and stimulation of collagen growth
    - CO_2 (10,600 nm) and Er:YAG (2940 nm)
    - Both absorbed by water as method of thermal injury
    - Complications:
      - Hyperpigmentation/Hypopigmentation
      - Persistent erythema
      - Infection (most commonly candidiasis)
      - Scarring
  - Non-ablative
    - Stimulate collagen remodeling without significant damage to epidermis
    - Nd:YAG (1,320 nm) Intense Pulsed Light (IPL)
    - Multiple treatments typically required over 3–6 months
    - Complications:
      - Hypopigmentation/hyperpigmentation
      - Scarring

- Chemical Peels
- Indications for chemical peels
  - Actinic keratosis
  - Photoaging
  - Pigment changes
  - Lentigines
  - Fine rhytids
  - Acne management and scarring
- Depth of penetration: peels classified by layer of penetration
  - Superficial—epidermis to superficial papillary dermis
  - Medium—epidermis to the papillary/upper reticular dermis;
  - Deep—epidermis to midreticular dermis
- Considerations and patient variables
  - Agent and concentration used
  - Application method, number of layers
  - Pre-peel keratolytics (retinoids, α-hydroxy acids)
    - Tretinoin (retinoic acid) thickens epidermis, thins stratum corneum, reverses keratinocyte atypia
  - Degreasing agents
  - Occlusion/semiocclusion
  - Skin thickness
  - Pilosebaceous gland activity and density
- Types of chemical peel agents
  - Glycolic acid: sugarcane derived α-hydroxy acid, 20–70 % concentrations, superficial peeling agent; penetration dependent upon skin contact
  - TCA: coagulates protein in skin, neutralized by serum, less hypopigmentation, no cardiotoxic effects
    - 10–20 % superficial
    - 30–40 % medium
    - 45–50 % deep
  - Jessner: resorcinol, salicylic acid, lactic acid in ethanol
  - Phenol peels: deep peel, causes pigmentation changes

- Contraindications to chemical peels
  - Absolute
    - Hepatorenal disease
    - Cardiac disease
    - Unstable psychiatric disease
    - Allergy
    - Active herpes simplex
  - Relative
    - Physical restriction
    - Radiotherapy to face
    - Keloid former
    - Fitzpatrick types IV to VI
    - Latent herpes simplex
    - Telangiectasias
    - Medication use (estrogen, warfarins)
    - HIV (low CD4)
- Complications
  - Hypopigmentation/Hyperpigmentation
  - Hypertrophic scar
  - HSV reactivation or dissemination
  - Persistent erythema
  - Full thickness skin loss

FACIAL IMPLANTS AND SURGICAL AUGMENTATION

- Excellent adjuncts to rhinoplasty and aging face surgery
- Ideal facial implant: Non-carcinogenic/mutagenic, low rate of rejection/extrusion, stable position, feels natural after placement, easily sized and carved for customization, flexible, resists distortion
- Cheek/Midface Implants
  - Midfacial contour analysis
    - I: Malar hypoplasia
    - II: Submalar deficiency
    - III: Malar/zygomatic prominence w/ submalar recess
    - IV: Malar hypoplasia + submalar deficiency
    - Tear-trough deformity
  - Implant design and placement based on type of midfacial contour deficiency
  - Midfacial implants typically placed via intra-oral approach
  - Silicone polymers most common material
  - Complications:
    - Infections
    - Extrusion
    - V2 Hypoesthesia
    - Prolonged edema
- Chin/Mandible Implants
  - Mandible contour analysis
    - Zone 1: central mentum: area between mental foramen
    - Zone 2: midlateral: mental foramen to midpoint of mandibular body
    - Zone 3: posterolateral: posterior half of body including angle
  - Multiple materials available: silicone polymers, polyethylene (Medpore), expanded polytetrafluoroethylene (ePTFE, Gore-Tex)
  - Silicone polymers most widely used: Flowers, Mittelman, chin-jowl and pre-jowl
  - Extra and intra-oral approaches both widely used and accepted

- Complications:
  - Infection
  - Extrusion
  - Mental nerve hypoesthesia
  - Bone resorption (common but not clinically relevant)

SURGICAL TREATMENT OF THE AGING FACE

Facial Anatomy

- Subcutaneous fat compartments
  - Forehead fat pad (central surrounded by middle and lateral temporal on each side)
  - Orbital fat pads (superior, inferior, and lateral)
  - Cheek (medial, middle, and lateral temporal)
  - Nasolabial
  - Jowl and pre-platysmal fat
- SMAS (superficial musculoaponeurotic system)
  - A continuous, organized fibrous network of collagen and connective tissue fibers that connects the facial muscles with the dermis
  - Continuous with the platysma inferiorly and the superficial temporal fascia and galea aponeurotica superiorly
  - Relationship to facial nerve:
    - Upper face above zygomatic arch: SMAS is continuous with the temporoparietal fascia (superficial temporal fascia). Frontal branch of facial nerve crosses over the zygomatic arch and lies on the undersurface of the temporoparietal fascia. Dissection should be performed deep to the temporoparietal fascia to prevent injury to the facial nerve.
    - Lower face below zygomatic arch: SMAS covers facial nerve branches. Facial nerve innervates the deep surface of the muscles of facial expression except for the buccinator, mentalis, and levator anguli oris, which are innervated on the superficial surface.
- Layers of temporal region above the zygomatic arch
  - Skin
  - Temporoparietal fascia (superficial temporal fascia)
    - Frontal branch of facial nerve is on undersurface of TPFF
  - Loose areolar tissue
  - Deep temporal fascia
    - Above the superior orbital rim: the superficial and deep layers of the deep temporal fascia are fused together into a single sheet
    - Below the superior orbital rim: the superficial and deep layers of the deep temporal fascia are separated by the superficial temporal fat pad. This fat pad extends down to the zygomatic arch
    - Superficial layer of the deep temporal fascia attaches to the superficial edge of the zygomatic arch and is continuous with the periosteum of the arch and with the parotidomasseteric fascia inferiorly
    - Deep layer of the deep temporal fascia attaches to the deep edge of the zygomatic arch and is continuous with the posterior masseteric fascia
  - Deep temporal fat pad (buccal fat pad)
    - Buccal fat pad extends under the zygomatic arch into the temporal region, where it is called the deep temporal fat pad
    - Deep temporal fat pad is deep to the deep layer of the deep temporal fascia and superficial to the temporalis muscle
    - Extends 2–4 cm above level of zygomatic arch
  - Temporalis muscle
    - Covered by deep temporal fat pad until fat pad terminates
    - Above deep temporal fat pad, is covered by deep temporal fascia

- Periosteum
- Temporal bone

- Retaining ligaments
  - True retaining ligaments—fibrous bands that connect the periosteum to the dermis
    - Zygomatic ligament (McGregor's patch)—connects the zygomatic arch to the dermis
    - Lateral orbicularis retaining ligament—connects the superolateral orbital rim to the dermis
    - Mandibular retaining ligament—connects the periosteum of the mandible medial to the depressor anguli oris to the dermis
  - False retaining ligaments—fibrous bands that connect fascial layers to the dermis
    - Masseteric ligament—connects the anterior border of the masseter to the SMAS and dermis. Weakening of this ligament leads to jowls.
    - Platysma-auricular ligament—connects periauricular platysma to the dermis
- Mimetic Muscles
  - Innervated by facial nerve (temporal, zygomatic, buccal, mandibular, cervical)
  - Periorbital: frontalis, orbicularis oculi, corrugator supercilii, and procerus
  - Nasal: nasalis (compressor and dilator), depressor septi nasi
  - Cheek/Perioral: zygomaticus major, zygomaticus minor, levator anguli oris, levator labii superioris, levator labii superioris alequae nasi, risorius, buccinator, orbicularis oris, depressor anguli oris, depressor labii inferioris, mentalis, platysma
  - Ear: anterior, superior, and posterior auricular muscles
- Deep fat compartments
  - Forehead: galeal and retroorbicularis oculi fat (ROOF) pads
  - Cheek: sub-orbicularis oculi fat pad (SOOF) is deep to the orbicularis oculi and superficial to the inferior arcus marginalis, malar fat pad, buccal fat pad

CHARACTERISTICS OF THE AGING FACE

- Changes in the aging face are secondary to changes in the:
  - Soft tissue quality—skin texture, color, elasticity, and pigmentation
  - Soft tissue quantity—skin, muscle, connective tissue, and adipose volume
  - Soft tissue dynamics—muscular contraction
  - Underlying structure—bone, dentition, and cartilage support
- Aging skin characteristics
- Sunlight and photoaging
- Photodamage secondary to sun exposure
- UVB 290–320 nm, UVA 320–400 nm
- Sun damage
  - UVB: sunburn and skin cancer
  - UVA: deeper penetration into dermis, photoaging
  - Flattening of the dermal/epidermal junction
  - Loss of melanocytes
  - Loss of collagen, especially type III collagen
  - Loss of elastin and fragmentation/disorganization of remaining elastin
  - Loss of Langerhan's cells (mediators of immunologic response)
  - Decreased epidermal turnover
- Rhytids and soft tissue dynamics
  - Horizontal forehead lines
  - Glabellar frown lines (horizontal and vertical)
  - Crow's feet
  - Eyelid lines
  - Bunny lines
  - Preauricular lines

- Nasolabial lines
- Periorbital lines
- Marionette lines (bilateral, vertical lines at the corners of the mouth that descend around the chin)
- Peau d'orange
- Horizontal neck lines
- Platysmal bands—prominent medial platysmal fibers caused by either thickening or attenuation of the platysma. A potential complication of overagressive submental liposuction
- Nasal tip ptosis—partially caused by overactive depressor septi

- Volume Loss
  - Temporal depression—loss of temporal fat and muscle volume revealing the skeletal contour of the zygomatic carch, lateral orbital rim, and temporal/parietal lines
  - Tear trough deformity (nasojugal fold)—loss of fat in the medial and central orbital fat pads combined with descent of the suborbicularis oculi fat pad results in exposure of the medial portion of the inferior orbital rim. The tear trough depression results in an appearance of dark circles under the eyes
  - Bulbous tip skin secondary to nasal skin atrophy over upper 2/3 of nose without atrophy of sebaceous gland containing skin of the tip
- Soft tissue ptosis and laxity
  - Brow ptosis
    - Many patients will have tonic contraction of the frontalis muscle to compensate for brow ptosis that obscures vision
    - Look for a horizontal shadow between the orbital rim and upper palpebral fold
    - Connell's sign—upper eyelid skin extends laterally off the eyelid to the lateral periorbital region
    - Flower's maneuver—using a finger to hold up the eyebrow in the proper position
  - Upper eyelid hooding
    - Loss of orbicularis oculi volume and weakening of orbital septum allows for orbital fat pad pseudoherniation
    - Upper lid laxity and brow ptosis cause hooding of upper eyelid
    - Laterally, hooding is secondary to excess skin and tissue laxity
    - Medially, hooding is secondary to fat pad pseudoherniation
    - Dermatochalasis—excess skin of the upper or lower eyelid
  - Lateral canthal tendon laxity
    - Laxity of the lateral canthal tendon associated with aging has multiple sequelae:
    - Lateral canthal bowing—horizontal plane of lateral canthus should be slightly superior to horizontal plane of medial canthus. Laxity of lateral canthal tendon results in inferior rotation of the lateral canthus
    - Scleral show—the lower lid should be in line with the inferior limbus. Laxity of the lateral canthal tendon results in a visible strip of sclera between the inferior limbus and the lower lid
  - Festoons—Malar bags are located below the inferior orbital rim as a result of weakening of the orbicularis oculi muscle and descent of the suborbicularis oculi fat pad.
  - Jowls—Attenuation of the masseteric ligaments leads to descent of the masseter and the formation of jowls.
  - Witch's chin deformity—descent of the chin fat pad with development/deepening of prejowl sulci and submental crease
  - Submandibular gland ptosis
  - Nasal changes
    - Decrease in nasolabial angle secondary to nasal tip ptosis
    - Deepening of subnasale secondary to columellar ptosis

FACELIFT

- Evaluation
  - History
    - Smoking, CAD, DM—all increase risk of poor/delayed wound healing
    - Comorbid conditions—autoimmune disease, collagen vascular disease, granulomatous disease, history of keloid formation, bleeding disorders, skin disorders (Ehlers Danlos, progeria)
    - Sun exposure, alcohol, NSAIDS
    - Allergies, anesthetic risks, history of radiation, isotretinoin use, weight fluctuations
  - Physical Exam
    - Ideal surgical candidates have:
      - Loss of skin elasticity
      - Minimal photoaging
      - Thin-normal skin
      - Strong/prominent/anterior chin
      - High-Posterior hyoid position with sharp cervicomental angle
      - Superiorly positioned submandibular glands
      - Strong/prominent cheek bones and facial bones
      - Shallow nasolabial groove
  - Surgical Plan
    - As with all cosmetic surgery, vitally important to ensure that the patient's expectations and goals are realistic and in line with what can be realistically achieved surgically.
    - Mark patient while upright prior to surgery
    - Pre-op pictures posted in operating room during surgery
- Surgical Approaches
  - SMAS Techniques
    - SMAS imbrication/plication, Lateral Rhytidectomy
    - Traditional incision or "Short-scar Rhytidectomy"
    - Traditional face-lift incision through temporal hair, preauricular line, wrapping under ear lobe, to post auricular and posterior hair
    - Incision can be modified to end just posterior to earlobe for a "short scar" technique
    - Elevate a subcutaneous flap over midface and extending down onto the neck
    - Plication—Pull SMAS/platysma superior-posterior in vector perpendicular to nasolabial fold and secure with sutures
    - Lateral Rhytidectomy/Imbrication—Excise 2–4 cm preauricular strip of SMAS parallel to nasolabial fold and platysma. Same vector as plication. Secure with sutures
    - Advantages: less dissection, lower risk of facial nerve injury, less edema/bleeding, shorter healing time. If short scar used: no post-auricular incision
    - Disadvantages: not as effective for patients with severe cervical skin laxity or very deep nasolabial folds, patients may require second "tuck-up" procedures or scar revision
  - Deep Plane Face-lift
    - Traditional face-lift incision through temporal hair, preauricular line, wrapping under ear lobe, to post auricular and posterior hair. Create a myocutaneous flap (SMAS-platysma-fat pad-skin flap) and dissect in the sub-SMAS plane (deep plane). Sub-SMAS dissection is extended medially beyond the nasolabial folds and subgaleal in temporal region. This creates a thick myocutaneous flap with minimal subcutaneous dissection. The flap can be pulled superior-posterior in multiple vectors. Secure at level of SMAS and skin
    - Advantages: thick flap has low risk of sloughing/necrosis, addresses nasolabial folds, excellent neck/mandibular line results, minimal subcutaneous dissection decreases skin irregularities and risk of bleeding
    - Disadvantages: extensive dissection, prolonged edema, risk of injury to facial nerve with medial dissection

- Composite Face-lift
  - Modification of deep plane face-lift that includes dissection of the orbicularis oculi and zygomatic muscles to improve midface lifting.
  - Traditional face-lift incision the same as the deep plane incision with the addition of a blepharoplasty incision. Elevate orbicularis off malar eminence and reposition the orbital fat over the orbital rim. Reposition the skin/muscle in a superior-medial vector and excise excess. Creation of three mesenteries to reposition the zygomaticus, orbicularis, SMAS, and platysma
    - Meso-temporalis—elevation of a subgaleal plane contains the frontal branch of the facial nerve, above the level of the mesentery
    - Meso-zygomaticus—elevation in a deep-plane below the SMAS and platysma from the zygomaticus to just below the jaw line.
    - Medso-mandibularis—elevation in a pre-platysmal plane below the mesentary
  - Advantages: multiple vectors of pull address significant aging at the jowls/jawline, nasolabial fold/midface, and the orbicularis oculi
  - Disadvantages: malar edema, tension over temple region, more invasive technique with blind dissection over anterior maxilla
- Subperiosteal Face-lift
  - Addresses the midface and upper face. Via a tempora approach, the soft tissues of the orbit, upper maxilla, and malar region to the pyriform aperture are elevated from the bone and pulled superior-posteriorly
  - Advantages: excellent rejuvenation of midface and nasolabial fold, no tension over the temple region
  - Disadvantages: facial edema, pulling all muscles and soft tissues up causes widening of the face, does not address jowl region, distant temporal approach is technically challenging

- Complications
  - Hematoma (1–15 %), typically occur within 24 h of surgery
  - Most commonly injured nerve: great auricular nerve (7 %)
  - Facial nerve injury (0.4–2.6 %)
  - Skin flap necrosis/sloughing (1.1–3.0 %), most commonly occurs in the post-auricular and preauricular regions (skin flap is the thinnest, tension is the greatest, and furthest from the flap's blood supply)
  - Changes in hairline—avoid visible scarring and changes in the hairline by planning incisions carefully
  - Alopecia (temporary—8.4 %, permanent—1–3 %)—prevent alopecia by beveling incisions parallel to the growth pattern of the hair
  - Pixie ear deformity—caused by excessive inferiorly directed tension on the ear lobe. Prevent by placing a stay suture in the ear lobe and by closing incisions under minimal tension
  - Keloids or hypertrophic scars—perform multilayered closure under minimal tension to help prevent keloid formation
  - Infection (0.18 %)—low risk because of the rich vascular supply to the face and neck. Most common organisms include *Staphylococcus* (including MRSA) and *Streptococcus*

BROW-LIFT

- Anatomy
  - Female brow—located above the superior orbital rim; arched; highest point is located above a point between the lateral limbus and the lateral canthus; lateral brow extends to a line drawn tangential through the nasal ala and lateral canthus; medial and lateral brows lie in same horizontal plane
  - Male brow—located at the superior orbital rim; less arched
  - See muscular anatomy and rhytids in *Neurotoxin* section of this chapter
  - See layers of scalp and upper face in *Anatomic Considerations* section of this chapter.
  - Sentinel bridging vein—there are bridging veins running between the temporoparietal fascia and the deep temporal fascia that indicate the location of the frontal branch of facial nerve

- Evaluation
  - Examine a completely relaxed face
    - Brow position
    - Upper brow fat pad
      - Should be located over the orbital rim
      - In aging face, brow fat pad is ptotic over the upper lid region. If this is unrecognized, and only an upper blepharoplasty is performed rather than brow-lift, then may have an unnatural appearance
    - Dermatochalasis
    - Forehead and glabellar rhytids
- Surgical Approaches
  - Direct brow
    - Incision made directly above the brow, perform skin excision and suspend the orbicularis oculi up to the pericranium. Best suited for men with bushy eyebrows
    - Advantages: good suspension of the orbicularis oculi, can use to correct brow asymmetry
    - Disadvantages: scar on the face, does not address the forehead, glabella, or rhytids
  - Mid-forehead
    - Incision is made within a deep forehead rhytid
    - Advantages: useful in bald men, good suspension of the brow, does not alter hairline
    - Disadvantages: visible scar, does not address rhytids
  - Coronal
    - Incision is made behind the hairline in a bicoronal fashion, flaps are raised in a subgaleal plane (just above the periosteum) down to the supraorbital rims and nasal dorsum, release the procerus attachments and cut the corugators
    - Advantages: scars hidden behind hairline, excellent exposure of entire forehead
    - Disadvantages: raises the hairline, hypoesthesia/paresthesia posterior to incision, extensive undermining required, cannot perform in men with male-pattern baldness or women with high hairlines
    - Perform pre-trichial incision in women with high hairlines
  - Endoscopic
    - Performed endoscopically through small incisions made in the scalp behind the hairline
    - Advantages: small, hidden incisions, Decreased risk of hematoma, alopecia, scarring, and hypoesthesia/paresthesia
    - Disadvantages: learning curve, possibly shorter-lasting results

BLEPHAROPLASTY

- Anatomy
  - Outer lamella—skin and orbicularis oculi
  - Inner lamella—tarsus and conjunctiva
  - Orbicularis oculi—circumferential muscle around the eyes composed of thicker orbital voluntary muscle and thinner involuntary palpebral muscle
  - Medial canthal tendon—pretarsal orbicularis oculi heads join to form a superficial tendon that inserts on the anterior lacrimal crest and a deep tendon that inserts on the posterior lacrimal crest
  - Lateral canthal tendon—lateral heads of the orbicularis oculi join to form the lateral canthal tendon that inserts on orbital tubercle of Whitnall
  - Orbital septum—a facial layer lying just deep to the orbicularis oculi muscle separating the preseptal and postseptal compartments. Originates at the arcus marginalis of the orbital rim and joins with either the capsulopalpebral fascia (lower lid) or the levator aponeurosis (upper lid) before inserting on the tarsal plate

- Superior palpebral sulcus—the sulcus that is formed on the upper eyelid at the location where the levator aponeurosis inserts onto the lid skin
  - Caucasians: 8–10 mm above the lid margin (higher eyelid crease)
  - Asians: 3 mm above the lid margin (low or nonexistent eyelid crease)
- Whitnall's ligament—a thickening of the levator aponeurosis approximately 15–20 mm superior to the tarsus that suspends the levator muscle between the trochlea and the lacrimal gland fossa
- Orbital fat compartments
  - Lower lid—three fat compartments (medial, central, and lateral); inferior oblique muscle separates medial and central fat compartments
  - Upper lid—two compartments (medial and central); trochlea separates the medial and central compartments; the lateral compartment contains the lacrimal gland with a small covering of fat

- Evaluation
  - See "Characteristics of the Aging Face" section of this chapter
  - Medical evaluation—dry eye syndromes, collagen vascular diseases, Graves' ophthalmopathy, hypothyroid myxedema, visual problems, bleeding disorders, keloid formation, glaucoma
  - Vertical eyelid retraction—excessive upper eyelid retraction with >10 mm (males) or >13 mm (females) distance between upper and lower lid margins
  - Lid lag—delay in complete closure of upper eye lid usually secondary to scarring
  - Blepharochalasis—rare disorder of upper eyelids with no known etiology characterized by recurrent attacks of painless lid edema that results in loss of skin elasticity and atrophic skin
  - Brow position—important to evaluate brow position for ptosis that should be corrected with brow-lift rather than blepharoplasty
  - Dermatochalasis—acquired condition of increased laxity of the eyelid skin and associated orbital fat prolapse
  - Steatoblepharon (psuedoherniation)—prolapse of orbital fat through the orbital septum behind the orbicularis oculi resulting in baggy, full lids
  - Festoons—malar bags are located below the inferior orbital rim as a result of weakening of the orbicularis oculi muscle and descent of the suborbicularis oculi fat pad
  - Lid distraction test (snap test)—gently grasp the midportion of the lower lid and pull it outwardly from the globe. Laxity of 10 mm or more indicates the need for lid-shortening procedures. The eyelid is then released and the pattern and rate of snap back is assessed. A slow return indicates poor lid tone and eyelid support
  - Schirmer's test—filter paper is placed under the lower lid margin and the length of paper-soaking is measured after 5 min. Normal—10–15 mm. Severe dry eye—5 mm or less
  - Ocular acuity examination
- Upper Lid
  - Address upper lid prior to lower lid to reduce risk of lagophthalmos
  - Inferior incision within the upper lid crease (superior palpebral sulcus), then use forceps to grasp redundant lid skin to find amount of redundant tissue that can be removed without causing lagophthalmos. Make the superior skin incision. More skin is taken laterally than medially to address lateral hooding and to prevent scarring of medial lid. Remove skin. Evaluate underlying muscle and remove strip of muscle. Fat removal performed as needed
  - Be more conservative in men, avoid lateral extension of incision because scar cannot be covered with makeup
- Lower Lid
  - Three basic approaches
    - Transconjunctival
      - Useful in patients with isolated fat herniation without excess skin. Approach does not disrupt the orbicularis oculi muscle. Can be performed via retroseptal or preseptal approaches

        - Advantages: lower risk of ectropion, no visible scar, no concern for causing hypopigmentation in dark-skinned patients
        - Disadvantages: does not address excess skin (requires separate external skin excision)
    - Transcutaneous (skin flap or skin-muscle flap)
        - Advantages: useful for patients with significantly excessive redundant and lax skin, skin-muscle flap is an easier dissection with little bleeding
        - Disadvantages: visible scar, higher risk of ectropion (skin-muscle flap violates the orbicularis oculi), skin flap technique causes ecchymosis
- Complications
    - Lagophthalmos—inability to completely close the eye; distance between the eyelid margins measured in millimeters when the eyes are gently closed; higher risk of lagophthalmos when brow-lift and upper lid blepharoplasty are performed simultaneously
    - Retrobulbar hematoma—devastating complication that could result in blindness (0.04 % incidence); immediate decompression is essential
    - Superficial hematoma—usually self-limiting, but can be treated with aspiration or incision and drainage to prevent fibrosis
    - Ectropion—etiology is excessive skin or skin-muscle excision, scar contracture, or failure to tighten a eyelid laxity
    - Milia—inclusion cysts along the incision line; treat with uncapping and removing the cyst
    - Dry eyes—preoperative dry eyes may worsen after upper lid blepharoplasty; damage to lacrimal gland may disrupt lacrimal flow

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Chapter 32

Head and Neck Reconstruction: Local, Pedicled and Free Flaps; Facial Nerve Reanimation

Joelle Glick and Joshua D. Rosenberg

PEARLS

- Flap vascularization can be random with the flap blood supply dependant on the subdermal plexus or axial with a specific named artery supplying the entire flap
- Transposition (linear configuration) is the most common type of local flap and is used for a variety of small to medium sized defects throughout the face and neck

APPROACH TO FACIAL RECONSTRUCTION

- Characterize defect
  - Skin color
  - Skin thickness
  - Tissue composition
    - Internal lining (mucosa, conjunctiva)
    - Structural layer (muscle, cartilage, bone)
    - Outer lining (skin, vermillion)
  - Location and subunits involved
- Design reconstructive ladder for defect
  - Healing by secondary intention
  - Primary closure
  - Delayed primary closure
  - Split-thickness skin graft
  - Full-thickness skin graft
  - Tissue expansion
  - Local flap
    - Random
    - Axial
  - Regional flap
  - Free flap
- Account for key facial landmarks and ideal areas for tissue recruitment
- Design flaps to align with resting skin tension lines (RSTLs)
- Account for patient history
  - Radiation, immunocompromised state, tobacco, risk of recurrence, overall medical condition.

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CLASSIFICATION OF FLAPS

- Vascular supply
  - Random cutaneous: no named vessels; rely on vascular supply of dermal and subdermal plexus
  - Arterial cutaneous/axial pattern: incorporates named artery supplying the entire flap
  - Myocutaneous/fasciocutaneous: incorporates a named segmental vessel that sends perforating vessels to the overlying muscle and skin
- Composition: composition of defect to be reconstructed should dictate composition of flap to be used
  - Cutaneous
  - Fasciocutaneous
  - Musculocutaneous
  - Osteomusculocutaneous
  - Combination of above
- Method of Transfer and Design: most common method of describing flaps
  - Local skin flaps are primarily used to reconstruct external facial defects that are too large for primary closure. They provide optimal color match, contour, texture, and are easily applied and readily available.
  - Local flaps can be classified by method of movement into pivotal, advancement, or hinged flaps. They may also be classified by blood supply: random vs. axial (i.e., paramedian forehead flaps)
  - Defects that are too extensive to repair with local or random flaps can be repaired with regional or free flaps
  - Microvascular free flaps involve autotransplantation of skin, soft tissue, muscle, or bone isolated on a supporting vascular supply

LOCAL FLAPS

Local Flaps Classified by Tissue Movement

Pivotal Flaps

- Four types: Rotation, Transposition, Interpolated, and Island Flaps
- Moved toward the defect by rotating the base of the flap around a pivotal point
- The greater the pivot, the shorter the flap
- Must be designed to account for reduction of effective length when flaps are pivoted through an arc of 180°
- Rotation (curvilinear configuration) (Fig. 32.1)
  - Ideal for triangular defects
  - Designed immediately adjacent to defect
  - Less dependent on tissue elasticity: good for scalp defects
  - Disadvantages: defect must be modified to create triangular defect, and resulting cutaneous deformity at the base of the flap may need to be repaired in second stage removal

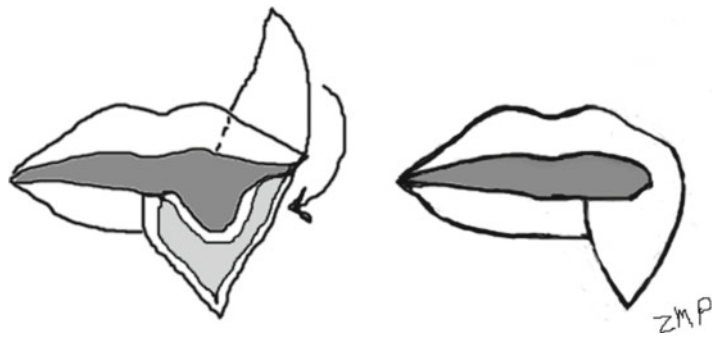

Fig. 32.1 Abbe–Estlander rotational flap, commonly used to reconstruct defects of the lip involving the commissure

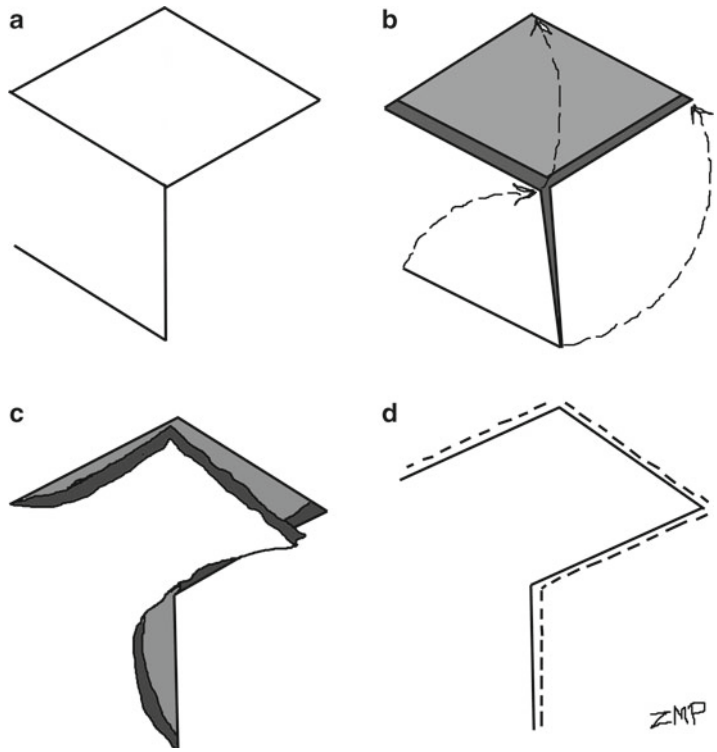

Fig. 32.2 Rhomboid flap

- Transposition (linear configuration)
  - Most common type of local flap
  - Used for small-to-medium-sized defects of almost any configuration or location
  - Disadvantage: incision lines often do not parallel RSTLs
  - Rhomboid (Fig. 32.2)
    - Some advancement, mostly pivotal
    - Skin mobility and extensibility are important
    - Advantage of minimizing the standing cutaneous deformities and dissipating wound closure tension more evenly along border of the flap
  - Bilobed (Fig. 32.3)
    - Double transposition flap
    - Ideal for 1 cm cutaneous defects of nasal tip, but used for cheek defects as well.
  - Z-Plasty (Fig. 32.4)
    - Double transposition flap
    - Consists of two triangles, each with independent pivot points; one in clockwise and one in counterclockwise direction
    - Ideal for scar revision to: lengthen scar, change direction, interrupt scar linearity
    - Z-plasty angles and scar lengthening:
      - Less than 30°: tip necrosis
      - 30°: 25 %
      - 45°: 50 %
      - 60°: 75 %

Fig. 32.3 Bilobed flap

Fig. 32.4 Z-plasty flap, ideal for scar revision

- Interpolated (linear configuration)
  - Pedicle must pass over or under intervening tissue
  - Base located some distance away from defect
  - Disadvantage: requires second stage procedure
  - Paramedian forehead flap
    - Used to repair large defects of the nose
    - Reliable axial blood supply based on supratrochlear artery and vein
  - Melolabial interpolated flap
    - Transfer of tissue from cheek to nose to reliably reconstruct alar defects
    - May be based on cutaneous or subcutaneous pedicle
    - Random vs. axial blood supply (angular branch of facial artery)

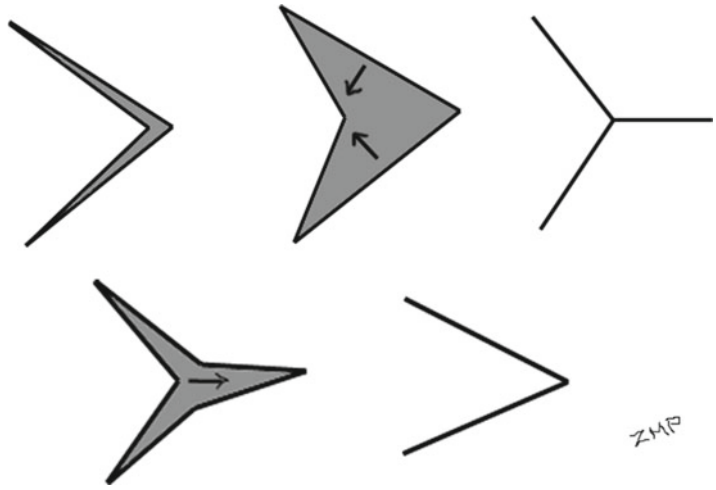

Fig. 32.5 V–Y and Y–V flaps

Advancement Flaps

- Monopedicled
  - Created by making parallel incisions that allow the tissue to "slide" in a single vector over defect
  - Primary movement: incised flap is pushed or pulled forward by stretching the skin
  - Secondary movement: occurs in direction opposite the movement of the advancing edge of the flap
  - Complete undermining is necessary
  - Excision of standing cutaneous deformities (Burrow's triangles) may also facilitate movement of the flap
- Bipedicle
  - Designed to allow advancement into the adjacent defect in a vector that is perpendicular to the flap axis
  - Used to close defect in area of high visibility by moving defect into area of low visibility (forehead→scalp)
- V–Y (Fig. 32.5)
  - Not stretched toward the recipient site, but advanced by recoil or by being pushed
  - Secondary triangular donor defect is then repaired by advancing the two edges of the remaining donor site wound toward each other
  - Wound suture line assumes a Y configuration
  - Common limb of Y represents suture line resulting from closure of secondary defect
  - Ideal for lengthening columella (in repair of cleft lip nasal deformities)
- Y–V (Fig. 32.5)
  - Y-shaped incision made initially
  - Rather than being pushed toward the area for supplementation, the flap is pulled or stretched toward the area for supplementation
  - Flap augments the area of the common limb of the Y while reducing the triangular area
  - Used to decrease redundancy of an area by moving tissue away from the site

Hinged Flaps

- Have a unique method of tissue movement
- Flap dissected in the subcutaneous tissue plane and turned over onto the defect like a page in a book

- Epithelial surface of flap is turned downward to provide internal lining for facial defect that requires internal and external lining surfaces
- Exposed subcutaneous surface of the hinge flap is covered by a second flap
- Always used with another flap or graft that provides the external coverage of the defect
- Vascular supply derived from the soft tissue border of the defect that it is designed to repair
- Often have limited and restricted vascularity
- Commonly used for repair of full-thickness nasal defects and salivary fistulas

REGIONAL FLAPS

Regional Skin Flaps with Their Blood Supply

- Deltopectoral: first–fourth intercostal perforators from the internal mammary artery
  - Donor site from shoulder and chest
  - Reach limited by pedicle
- Nape of neck: occipital artery
- Pectoralis major: thoracoacromial artery, lateral thoracic (supplies inferior one-fifth), IMA perforators
  - Donor site location easily accessible
  - Donor site and pedicle generally outside of radiation field
  - Ease of harvest
  - Pedicle not skeletonized
  - Large density of arterial perforators
  - Disadvantages: functional deficit at donor site, limited reach to lateral canthus, disfiguration in women, bulky flap
- Trapezius: occipital, suprascapular, transverse cervical arteries
  - Can provide thin tissue suitable for pharyngeal defects
  - Can be used as salvage flap for carotid coverage
  - Little donor morbidity
  - Disadvantages: vascular anatomy is variable, longer operating room time, special patient positioning needed
- Latissimus dorsi: thoracodorsal artery
  - Good for large defects
  - Donor site deficit less noticeable
  - Large arc of rotation
  - Disadvantages: longer operating time, prolonged wound drainage, unprotected pedicle
  - May also be harvested for free tissue transfer.
- Temporoparietal: superficial temporal artery and vein
  - Thin and pliable
  - Multiple applications in scalp, skull base, and midfacial reconstruction
  - May be harvested for free tissue transfer
  - Disadvantages: Harvest may result in alopecia at donor site.
- Sternocleidomastoid: occipital artery, superior thyroid artery, branch from the thyrocervical trunk
  - Used for closure of defects in mouth, oro-, pharyngo-, and tracheocutaneous fistulae and at parotid bed.
  - Restricted arc of rotation limits application of flap
  - Carotid coverage may be lost if SCM is used
- Platysma: occipital, postauricular, facial, superior thyroid, transverse cervical arteries
  - Limited role in head and neck reconstruction
- Postauricular: posterior auricular artery

FREE FLAPS

- Advantages over local or regional flaps
  - Two-team approach
  - Immediate single stage reconstruction

- Large number of donor sites available
- Unrestricted positioning and reach
- Large amount of composite tissue
- Potential for sensate, motor, and secretory function
- Improved vascularity and healing (especially in patients who will require radiation therapy)
- Can cover any defect (large tumor free margins)
- Permits primary placement of osseointegrated implants

- Characteristics of ideal free flap
  - Minimal donor site morbidity
  - Two-team approach for resection and harvest of flap
  - Adequate length and caliber of vessels
  - Tissue composition similar to that of defect
  - Bulk and color matched to that of defect
  - Innervation with sensation/motor function feasible
  - Excellent cosmetic potential
  - Donor site previously unviolated
  - Potential for osseointegration
- Signs for monitoring cutaneous free flap
  - Color
  - Temperature
  - Capillary refill
  - Swelling
  - Palpable pulse
  - Needle stick
  - Doppler probe

Free Flaps with Their Neurovascular Supply

- Fasciocutaneous free flaps
  - Radial forearm
    - Artery: radial artery; perforators travel in lateral intermuscular septum (brachioradialis-flexor carpi radialis)
    - Venous: venae comitantes and/or cephalic vein
    - Nerve: lateral antebrachial cutaneous
  - Lateral arm
    - Artery: terminal branch of profunda brachii and posterior radial collateral artery, travels in spiral groove, septocutaneous perforators travel in lateral intermuscular septum
    - Venous: venae comitantes of above vessels
    - Nerve: posterior cutaneous nerve of forearm
  - Anterolateral thigh
    - Artery: Cutaneous perforator from descending branch of lateral circumflex femoral artery (from profunda femoris)
    - Nerve: lateral femoral cutaneous nerve of the thigh
- Muscle and myocutaneous free flaps
  - Rectus abdominis
    - Vascular: deep (superior and) inferior epigastric arteries and veins; inferior pedicle larger and provides musculocutaneous perforators supplying the skin
    - Nerve: any of the intercostal nerves
  - Latissimus dorsi
    - Vascular: thoracodorsal vessels, off of subscapular vessels
    - Nerve: thoracodorsal nerve
    - Can be elevated as free or regional pedicled flap

- Gracilis
  - Artery: terminal branch of adductor artery (from profunda femoris)
  - Vein: venae comitantes, join or drain separately into profunda femoris vein
  - Nerve: anterior branch of obturator nerve (motor supply)
  - Functional muscle transfer, primary use for facial reanimation
- Visceral free flaps
  - Jejunum
    - Vascular: single vascular arcade from the superior mesenteric artery (usually second arcade)
    - Peristalsis maintained by action of autonomic plexuses
  - Gastro-omental
    - Vascular: based on right gastroepiploic artery
- Bone composite free flaps
  - Fibula
    - Vascular: peroneal artery and vein; perforators run in posterior intermuscular septum
    - Nerve: peroneal communicating branch
    - Bone: up to 25 cm of bone available, contourable due to segmental blood supply
  - Iliac crest
    - Artery: deep circumflex iliac artery off of external iliac artery; internal oblique supplied by ascending branch of DCIA
    - Venous: deep circumflex iliac vein usually composed of two venae comitantes
    - Natural shape conforms to that of native mandible
  - Scapula
    - Artery: circumflex scapular artery off of subscapular artery, divides into transverse and descending branches to supply two separate skin paddles (scapular and parascapular)
    - Bone: separate thoracodorsal blood supply to bony component, 10–12 cm length from inferior lateral aspect of bone
  - Radial Forearm
    - Up to 10 cm and 40 % of radial circumference can be taken
    - Not suitable for osseointegration
  - Lateral arm flap
    - Up to 10 cm and one-sixth of humeral circumference can be taken
  - Dorsalis pedis
    - Artery: dorsalis pedis artery
    - Nerve: superficial peroneal nerve
    - Thin sensate cutaneous flap from dorsal foot
    - second metatarsal included for osseocutaneous flap
  - Rib
    - Intercostal vascular pedicle
    - Marginal blood supply to skin

FACIAL NERVE RE-ANIMATION

- See Otology section

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Chapter 33
Head and Neck Trauma

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PEARLS

- Occlusion classification is defined as follows: Class I: mesiobuccal cusp of maxillary first molar fitting into the buccal groove of the mandibular first molar; Class II: mesiobuccal cusp of maxillary first molar mesial to the buccal groove of the mandibular first molar → "OVERBITE"; and Class III: mesiobuccal cusp of maxillary first molar distal to the buccal grove of the mandibular first molar → "UNDERBITE"
- In cases of possible esophageal trauma, endoscopy is more reliable than imaging

INITIAL ASSESSMENT OF THE HEAD AND NECK TRAUMA PATIENT

- Initial survey—ABCDEs
  - Airway—must establish severity of any obstruction or impending airway compromise
    - Methods for maintaining airway patency
      - Nasopharyngeal/oral airway
      - Nasotracheal intubation
      - Oral intubation
      - Fiber-optic intubation
      - Needle cricothyrotomy
      - Cricothyrotomy
      - Tracheostomy
  - Breathing
    - Determine respiratory drive and other factors influencing (drugs, EtOH, medications), mask bag or machine ventilation when necessary
  - Circulation
    - Establish two large bore IVs (at least 18 gauge) and resuscitate with IV fluids
    - Blood products on standby for large blood loss—type O needed if untyped
    - Control all sites of hemorrhage with direct pressure or packing
  - Disability
    - Initial survey should determine the severity of any traumatic brain injury with Glasgow Coma Scale
    - Assessment determined by scoring eye opening, verbal and motor responses

Severity	GCS score
Mild	13–15
Moderate	9–12
Severe	<8

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- Exposure
  - Obtain full history: mechanism, time, events surrounding injury, previous medical history, medications
  - Secondary survey performing a full physical exam
- Physical examination
  - A regimented approach in every evaluation "top-down approach"
  - Upper third facial exam
- Frontal sinus
- Lacerations
- Motor/sensory function
  - Middle third facial exam
    - Ocular exam
      - Use an "external-to-internal" approach
      - Proptosis
      - Ptosis
      - Enophthalmos
      - Telecanthus
      - Pupillary response
      - Additional input from a dedicated ophthalmologic evaluation should always be considered
    - Midface assessment
      - Zygoma: displacement, lacerations, swelling, erythema, motor function of zygomatic and buccal branch of facial nerve, sensation of cranial nerve V2
      - Nasal: fractures/step off/crepitus, epistaxis, septal hematoma, septal dislocations, mucosal tears, edema, obstruction
      - Naso-orbital-ethmoid: telescoping of nasal, ethmoid, and lacrimal bones; loss of dorsal height; canthal ligament displacement; lacrimal duct tears; CSF leak
    - Maxilla assessment
      - Mobility of palate in AP and lateral direction, loss or injury to teeth, lacerations
  - Lower third
    - Mandibular occlusion
    - Bite changes
  - Otologic
    - Tuning fork assessment
    - Hemotympanum
    - Facial nerve function
    - Mastoid ecchymosis: an indication of fracture of middle cranial fossa, and may suggest underlying brain trauma

UPPER FACIAL TRAUMA

- Frontal sinus fractures
  - Anatomy
    - Pneumatization of sinus begins at 5 years to adolescence
    - Paired pneumatized cavities in frontal bone—anterior and posterior frontal sinus walls divided by midline septum
    - Drainage of sinus via the nasofrontal duct
    - Frontal sinus completely lined by respiratory mucosa-predisposition to mucocele formation with occlusion of sinus drainage
    - Arterial supply via supraorbital, supratrochlear, and anterior ethmoidal arteries
    - Considerations: anterior wall most resistant of facial bones to fracture—typically high velocity

- Diagnosis
  - Frontal forehead and superior orbital rim depression, sensory deficit of cranial nerve V1, periorbital ecchymosis and edema, CSF rhinorrhea
  - High-resolution thin-cut CT scans are gold standard for imaging modality for visualizing frontal sinus fractures and duct flow tract
- Classification
  - Anterior wall fracture
  - Posterior wall fracture
  - Floor fracture
  - Through-and-through fracture
  - Nasofrontal recess injuries
- Management
  - Goals: (1) eliminate factors predisposing to infection or mucocele formation, (2) restoration of normal sinus function or obliteration, repair of cosmetic defects
  - Timing of treatment: early surgical exploration and repair
  - Exposure: use of existing overlying lacerations, "gull-wing" and trephine incisions, bicoronal incisions
  - Anterior wall fractures
    - Linear fractures with minimal displacement: conservative measures only, can typically observe patients as low risk for mucosal disruption
    - Displaced fractures: open fracture site, assess mucosa for tears or disruption, reduce and fixate fracture, observe patients for long-term complications (i.e., mucoceles)
    - Comminuted fractures: open fracture site, remove loose bone, inspect mucosa and posterior wall for any injury, reduce fracture and fixate segments with plates or mesh
  - Posterior wall fractures
    - Non-displaced fractures without evidence of CSF leak, frontal outflow involvement, or dural exposure: observation
    - Displaced fractures: (displacement greater than the width of posterior table) sinus must be explored via osteoplastic flap or subcranial approach, mucosa and dura inspected, obliteration versus cranialization
    - Comminuted, displaced fractures: neurosurgical emergencies, typically addressed with cranialization
  - Nasofrontal outflow fractures
    - Disruption leads to highest risk mucocele formation
    - Addressed with recess reconstruction, sinus septectomy, lynch operation, sinus obliteration, or endoscopic frontal sinusotomy
- Complications
  - Possibility of late complications—imperative for long-term follow-up and imaging

Early	Late
Forehead numbness	Chronic sinusitis
CSF leak	Forehead contour deformity
Intracranial infections	Osteomyelitis
	Subdural empyema
	Mucocele formation

- Naso-orbito-ethmoid fractures
- Definition: fracture involving nasal bones, nasal process of frontal bone, and frontal process of maxilla
- Anatomy
  - Bones: nasal, perpendicular plate of septum, nasal process of frontal, cribriform plate, lamina papyracea, medial orbit, lesser wing of sphenoid
  - Neurovasculature: Anterior ethmoidal artery and nerve, olfactory nerve

- Medial canthal ligament (MCL): attaches tarsal plate to medial orbital wall, made up of superior suspensory ligament (Whitnall) and inferior suspensory ligament (Lockwood)
- Lacrimal system: composed of gland, superior and inferior canaliculi, lacrimal sac, nasolacrimal duct
  - Rests between anterior and posterior lacrimal crests of medial orbital wall
  - Important pupillary and canthal measurements
  - Avg. interpupillary distance ~60 mm
  - Avg. intercanthal distance ~30 mm (approx. width of eye)

- Diagnosis
  - Symptoms: diplopia, anosmia, nasal obstruction, epistaxis, periorbital edema, epiphora
  - Telecanthus: widening of intercanthal distance, rounding of medial canthal ligament or flattened nasal bones
  - MCL involvement tested with "eyelid traction test"
  - Jones dye test: utilized to assess the nasolacrimal duct patency and level of obstruction
  - Imaging modality is CT fine cuts of orbits
- Classification
  - Type 1: MCL attached to single large displaced NOE bone fragment, typically unilateral
  - Type 2: comminuted central bone segment with fractures remaining external to MCL insertion
  - Type 3: comminuted single fragment with fractures extending into bone with detachment of MCL
- Management
  - Not surgical emergency, may wait for swelling to resolve or medical clearance to be obtained
  - Goals: (1) identify, reduce, and fixate fractured segments, (2)repair telecanthus, (3) assess and repair nasolacrimal drainage, (4) restore cosmesis
  - Repair
    - Type 1 fractures: displaced fractured segment reduced and low-profile miniplate fixation at two points
    - Type 2 fractures: typically require transnasal wiring to opposite stable side
    - Type 3 fractures: extensive exposure required, i.e., coronal incisions, often primary bone grafting is needed to reestablish a stable point of fixation, transnasal wires often used for re-establishing intercanthal distance
  - Approaches:
    - Use of lacerations
    - Transconjunctival
    - Transcaruncular
    - Extended medial canthal
    - Coronal incision
- Complications
  - Persistent telecanthus
  - Diplopia
  - Epiphora
  - Frontal sinusitis
  - Scleral show/lower lid abnormalities
  - Osteomyelitis
  - CSF leak
- Orbital fractures
  - Anatomy
    - Orbit made up of 7 bones
      - Maxilla, zygoma, lacrimal, ethmoid, palatine, sphenoid, and frontal bones
    - Three main apertures at apex
      - Optic canal: Optic nerve, ophthalmic artery
      - Superior orbital fissure: CN III, IV, V_1, VI, ophthalmic vein
      - Inferior orbital fissure: CN V_2

- Considerations: orbital floor ascends 30° from anterior to posterior and has a "Lazy S" configuration

- Diagnosis
  - Examination
    - Subconjunctival and periorbital ecchymosis
    - Periorbital edema
    - Epistaxis
    - V_2 Hypesthesia
    - Enophthalmos/hypophthalmos/exophthalmos
    - Proptosis
    - Entrapment
    - Diplopia
    - Visual acuity
  - CT imaging key in diagnosis of injuries
    - Coronal cuts best to assess internal orbit
    - Sagittal cuts to assess the status of orbital floor
    - Axial cuts to assess medial walls
  - Superior orbital fissure syndrome: injury to CN III, IV, V_1, and VI resulting in upper lid ptosis, proptosis, fixed and dilated pupil, and V_1 hypesthesia
    - Orbital apex syndrome if all the above symptoms + blindness
- Classification
  - "Pure" fractures: solely the orbital floor or wall without rim involvement
  - "Impure" fractures: combination of orbital floor/wall and rim involvement
- Management
  - Indications for repair
    - Enophthalmos >2 mm
    - Hypoglobus
    - Muscle entrapment
    - Diplopia
  - Contraindications:
    - Hyphema
    - Retinal tear
    - Globe perforation
    - Sinusitis
    - Only seeing eye
  - Timing of repair
    - Immediate: non-resolving oculocardiac reflex with entrapment, early enophthalmos or hypoglobus, entrapment
    - Delayed w/in 2 weeks: symptomatic diplopia, large floor fractures with possibility of latent enophthalmos, significant hypoglobus, progressive infraorbital hypesthesia
    - Observation: minimal diplopia, good ocular motility
  - Surgical approaches:
    - Transconjunctival incision: pre versus post septal incision
    - Subciliary incision
    - Brow incision
    - Lower eyelid incision
  - Reconstructive options
    - Titanium mesh
    - Bone graft
    - Porous polyethylene sheets
    - Composite porous polyethylene and titanium mesh
    - Resorbable materials
    - Preformed orbital implants

- Complications
  - Enophthalmos
  - Diplopia
  - Ectropion/entropion
  - Blindness
  - Infection of hardware or extrusion of graft
  - Cheek hypesthesia
  - Orbital hematoma

MIDFACE TRAUMA

- Zygomaticomaxillary complex fractures
- Anatomy
  - Zygoma articulates with greater wing of sphenoid, frontal bone, temporal bone, and maxilla
  - Four sutures:
    - Zygomaticofrontal suture
    - Zygomaticomaxillary suture
    - Zygomaticotemporal suture
    - Zygomaticosphenoid suture
  - Diagnosis
    - Subconjunctival and periorbital ecchymosis/edema, epistaxis, V2 hypesthesia, diplopia, hypophthalmos, enophthalmos, trismus, loss of malar prominence
  - Management
    - Goals: (1) stabilization of zygomatic arch, (2) restoration of normal contour and projection
    - Techniques:
      - Closed reduction for non-comminuted simple fractures
      - Open reduction for trismus, orbital complications, facial asymmetry
    - Approaches
      - Sublababial: zygomaticomaxillary fracture/midface buttresses
      - Extended Upper Blepharoplasty: zygomaticofrontal/lateral orbital rim fracture
      - Orbital floor involvement: transconjunctival, subciliary
      - Isolated arch fracture: Gillies approach or sublabial
  - Complications
    - Cosmetic deformity/continued loss of malar prominence
    - Trismus
    - Inadequate reduction
    - V2 hypoesthesia
- Nasal fractures
  - Anatomy
    - Upper vault: paired nasal bones, frontal process of maxilla
    - Middle vault: upper lateral cartilages, majority of septum, nasal process of maxilla
    - Lower vault: lower lateral cartilages, inferior edge of septum
    - Blood supply:
      - Internal carotid artery via ophthalmic artery
      - External carotid artery via facial and internal maxillary artery
    - Sensation: via sensory branches V1 and V2 of trigeminal nerve
      - External nose: infraorbital, anterior ethmoidal, infratrochlear
      - Internal nose: anterior and posterior ethmoidal and sphenopalatine
  - Diagnosis
    - Presentation: swelling, ecchymosis, deviation, laceration, pain, epistaxis, septal hematoma, nasal deformity, nasal obstruction, epiphora, crepitus on palpation, rule out possible CSF leak (beta2-transferrin)
    - Diagnosis typically on physical exam—CT rarely indicated for isolated fractures

- Management
  - Closed reduction: if evaluated early enough, can be performed within the first 2 h of trauma and up to 2 weeks of injury
  - Open reduction/Rhinoplasty: repair of late fracture
  - Septal hematoma: contained beneath mucoperichondrium and must be drained immediately due to risk of
    - Cartilage resorption, loss of nasal support, saddle deformity
- Complications
  - Nasal obstruction
  - Septal perforation
  - Continued nasal deformity
  - Secondary revision
  - Epistaxis
  - V2 sensory deficit
  - Unfavorable scars

- Maxillary fractures (Le Fort fractures)
  - Anatomy
    - Facial structure composed of nine bones: maxilla, zygoma, lacrimal, nasal, ethmoid, sphenoid, palate, vomer, inferior turbinate
    - Facial buttresses
      - Vertical:
        - Nasomaxillary
        - Zygomaticomaxillary—strongest load bearer
        - Pterygomaxillary
      - Horizontal
        - Frontal bar
        - Infraorbital rim
        - Zygomatic arch
        - Maxillary arch
      - Blood supply: anterior and posterior ethmoid arteries, facial artery, internal maxillary artery
      - Innervation: second division of CN V
  - Diagnosis
    - Facial distortion
    - Elongated face
    - Mobile maxilla
    - Bilateral periorbital and subconjunctival ecchymosis
    - Malocclusion
  - Classification
    - Le Fort classification
      - I: horizontal fracture across the lower maxilla
        - Typically due to an anteriorly based force
      - II: pyramidal fracture separating the maxilla and nasal bones from the remaining superior structures
        - Force delivered at the level of nose
      - III: craniofacial separation of maxilla, naso-orbital-ethmoid complex, zygoma from skull base
        - High-velocity impact at the level of orbits
  - Management
    - Goal to restore normal facial height, width, projection, and function
    - Typically approached with either "top-down" or "bottom-up" → depending on stable points of fixation
    - Incisions: intraoral, coronal, periorbital

- Le Fort I: mobilized maxilla placed in MMF and plates used to secure ZM buttress and piriform apertures
- Le Fort II: mobilized fragment placed in MMF and then fixate ZM buttress
- Le Fort III: coronal flap to address the frontozygomatic and nasofrontal sutures

- Complications
  - Malunion, plate exposure
  - Forehead/cheek hypesthesia
  - Osteomyelitis
  - Dental injury

LOWER FACE TRAUMA

- Mandibular trauma
  - Anatomy
    - Distribution of mandibular fractures
      - Coronoid process 1 %
      - Condyle 26–29 %
      - Ramus 2–4 %
      - Body 16–30 %
      - Angle 25 %
      - Symphysis/parasymphysis 17–22 %
    - Muscle
      - Open jaw: lateral pterygoids
      - Close jaw: medial pterygoids, masseter, temporalis muscle
    - Blood supply:
      - Inferior alveolar artery
    - Nerve supply
      - Inferior alveolar nerve
    - Terminology:
      - Intercuspation: interdigitation of maxillary and mandibular teeth
      - Crossbite: malocclusion of maxillary and mandibular teeth → off in the lateral and anterior plane
      - Occlusion classification
        - I: mesiobuccal cusp of maxillary first molar fitting into the buccal groove of the mandibular first molar
        - II: mesiobuccal cusp of maxillary first molar mesial to the buccal groove of the mandibular first molar → "OVERBITE"
        - III: mesiobuccal cusp of maxillary first molar distal to the buccal groove of the mandibular first molar → "UNDERBITE"
      - Favorable fractures—reduced with masticatory muscle contraction
      - Unfavorable fractures—distracted with muscle contraction
  - Diagnosis
    - Tenderness on palpation, malocclusion, trismus, swelling, paresthesia, step offs, protrusion, or deviation upon opening
    - Imaging: panorex films typically standard, CT typically ordered if suspecting additional fractures or need further detail
  - Management
    - Goals: (1) achieve reduction and stabilization of fracture, (2) restore pretrauma occlusion, (3) restore facial contour
    - Conservative treatment:
      - Soft/liquid diet, jaw exercise, oral hygiene
      - Indicated for minimal or no displacement and normal occlusion
    - Closed reduction:
      - Arch bars placed + treatment listed above

- Indicated for non-displaced, minimally displaced, pediatric fractures, comminuted fractures, coronoid fractures
- Contraindications: severe asthma, COPD, seizures

■ Open reduction:
- Indications: displaced fractures with malocclusion or severe mobility, unfavorable fractures, atrophic edentulous mandibles

○ Complications
■ Hypoesthesia of inferior alveolar nerve
■ Malunion/nonunion
■ Plate exposure
■ Nerve injury to marginal mandibular nerve
■ Condylar head necrosis
■ TMJ ankylosis

TEMPORAL BONE TRAUMA

See Otology Section

Neck trauma

- Anatomy
  - ○ Four components
    - ■ Airway
    - ■ Vascular
    - ■ Nervous
    - ■ Gastrointestinal
  - ○ Muscular landmarks
    - ■ Platysma—defines deep vs. superficial injury
    - ■ Sternocleidomastoid
- Diagnosis
  - ○ Symptoms
    - ■ Airway injury: hoarseness, stridor, respiratory distress, subcutaneous emphysema
    - ■ Esophageal injury: salivary leakage, subcutaneous emphysema, neck or mediastinal abscess
    - ■ Vascular injury: expanding hematoma, bruits, active hemorrhage
    - ■ Nerve injury: cranial nerve deficits
  - ○ Imaging
    - ■ CT angiography
      - Initial diagnostic imaging of choice to evaluate vasculature
      - Signs of injury include contrast extravasation, air adjacent to carotid sheath, hematoma
      - Sensitivity ranging between 90 and 100 % and specificity between 93 and 100 %
    - ■ Esophagram
      - Can be done to evaluate for pharyngeal or esophageal penetration
      - Higher incidence in Zone 1 and 2
- Classification
  - ○ Neck zones
    - ■ Zone 1
      - Most inferior zone defined by sternal notch inferiorly and cricoid cartilage superiorly
      - Carotid arteries
      - Vertebral and subclavian arteries
      - Trachea
      - Subclavian, innominate, and jugular vein
      - Esophagus
      - Thoracic duct

        - Zone 2
            - Defined by cricoid inferiorly and angle of the mandible superiorly
            - Carotid artery
            - Jugular and vertebral veins
            - Pharynx and larynx
            - Trachea
            - Recurrent laryngeal and vagal nerves
        - Zone 3
            - Most superior zone from angle of mandible to the skull base
            - Carotid and vertebral artery
            - Jugular vein
            - Sympathetic trunk
    - Vascular injuries
        - Incidence of vascular injury higher in Zone 1 and 3
            - Vessels are fixed to bony structures, larger vessels, muscles at the thoracic inlet, and skull base
            - Zone 2 vessels displaced from concussive force following impact
- Management
    - Selective neck exploration
        - Indication for surgical exploration based on symptoms upon presentation
        - Symptomatic patients (see above for symptoms)
            - Exploration in operating room
            - If stable can be CT angiography prior to intervention, especially in Zone 1 and 3 injuries
        - Asymptomatic patients
            - Diagnostic studies
            - If there are positive findings then are taken to operating room for neck exploration
    - Mandatory neck exploration: if appropriate personnel and diagnostic capabilities are available then patient should undergo exploration or if stable can be transferred
    - CT angiography
    - Aerodigestive tract injury
        - Needs to be repaired within 24 h after injury to avoid morbidity and mortality
        - Endoscopy
            - More reliable than imaging
            - Rigid and flexible esophagoscopy, bronchoscopy
            - Rigid technique allows for better view of the proximal esophagus
            - Flexible esophagoscopy provides better resolution with magnification and the ability to insufflate
        - Swallow studies
            - Gastrografin or barium
            - Less accurate than endoscopy

LARYNGEAL TRAUMA (ALSO FIND IN LARYNGOLOGY)

- Anatomy
    - Thyroid cartilage, cricoid cartilage, epiglottis, arytenoid cartilage, corniculate cartilage
        - Thyroid cartilage ossifies at 20–23 years of age from inferior to superior
    - Hyoid bone: suspended above by suprahyoid musculature and tongue muscles
    - Thyrohyoid membrane, hyoepiglottic ligament, vocal ligament, cricothyroid ligament, thyroepiglottic ligament
    - Extrinsic and intrinsic muscles of larynx
    - Superior laryngeal artery, superior thyroid artery
    - Superior laryngeal nerve, recurrent laryngeal nerve

- Diagnosis
  - Symptoms
    - Pain/tenderness over larynx, odynophagia, dysphagia, hoarseness
    - Dyspnea, stridor, hemoptysis, ecchymosis, subcutaneous emphysema, loss of laryngeal landmarks, larynx deviation
    - Stridor
      - Inspiratory: supraglottic obstruction due to hematoma or edema
      - Expiratory: subglottic source
      - Biphasic: injury at the level of glottis
  - Evaluation
    - Endoscopy: flexible fiber-optic laryngoscopy and tracheoscopy
    - Imaging
      - Cervical spine imaging, chest X-ray to rule out tracheal deviation and pneumothorax
      - CT scan with fine cuts through larynx
- Classification
  - Schaefer classification system
    - Group 1: minor endolaryngeal hematoma or laceration with fracture
    - Group 2: more severe edema, hematoma, minor mucosal disruption with exposed cartilage, or non-displaced fractures
    - Group 3: massive edema, large mucosal lacerations, exposed cartilage, displaced fractures, or vocal cord immobility
    - Group 4: same as above but add disruption of anterior larynx, unstable fractures, two or more fracture lines, severe mucosal injuries
    - Group 5: complete laryngotracheal separation
- Management
  - Group 1: supportive therapy with steroids, antibiotics, reflux medications, humidification, and voice rest
  - Group 2: serial examination, edema can worsen with time, tracheostomy if patient worsens
  - Group 3
    - Tracheotomy
    - Surgical exploration and repair if vocal fold tear, disruption of anterior commissure, endolaryngeal laceration, immobile vocal fold, cartilage exposure, displaced cartilage fractures, arytenoid subluxation, or dislocation
  - Group 4: tracheotomy and repair of injuries and possible stent placement
  - Group 5: because of airway separation at cricothyroid membrane or cricotracheal junction should secure airway via intubation and then perform tracheotomy
  - Inhalation injury
    - Close observation for 24 h following injury
    - Serial exam with flexible laryngoscopy
  - Endolaryngeal tears
    - Tracheotomy
    - Surgical repair through open approach
  - Endolaryngeal hematoma
    - Close observation with serial examinations with supportive treatment
    - Expanding hematomas may need tracheotomy
  - Laryngeal fractures
    - Non-displaced fractures may be observed
    - Displaced thyroid and cricoid fractures need reduction and fixation with miniplate fixation, wire or suture fixation
- Caustic ingestion
  - Categories of materials
    - Acids: toilet bowl cleaner, battery fluid sulfuric acid
      - Coagulation necrosis with eschar formation, less likely for deep penetration
      - More likely to have gastric injury because of slightly alkaline pH of esophagus

        - Alkali: lime, detergent, hair-relaxing agents
            - Liquefaction necrosis leads to deeper penetration into tissues
        - Bleach: irritant but causes minimal damage
- Diagnosis
    - History: age, amount, agent, and timing of ingestion
    - Symptoms: odynophagia, dysphagia, shortness of breath, dysphonia, chest pain, tachycardia, abdominal pain
- Airway stability is most important consideration, evaluation best done with fiber-optic laryngoscopy
- Management
    - Limit fluid intake, gastric lavage, and induced vomiting are contraindicated
    - No neutralizing agents
    - Place nasogastric feeding tube during endoscopy, blind placement risks perforation
    - Imaging plays minimal role acutely
    - Technetium-labeled sucralfate can determine the presence of esophageal injury in pediatric population
    - Endoscopy
        - Should be performed between the first 24 and 48 h following ingestion
        - Full extent of injury not visible until after the first 24 h
        - Necrotic tissue sloughs off esophagus after several days and weakens esophageal wall giving patient a higher risk for perforation
    - Medical
        - Proton pump inhibitors, histamine H2 blockers, sucralfate
- Classification
    - First degree: mucosal erythema
    - Second degree: erythema with noncircumferential exudate, can form stricture
    - Third degree: circumferential exudate, high rate of stricture formation
    - Fourth degree: circumferential exudate and esophageal wall perforation, high risk of sepsis and mediastinitis
- Complications:
    - Esophageal perforation
    - Esophageal strictures
    - Esophageal carcinoma: one in seven patients develop malignancy

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