**Non-Neoplastic Lesions of the Neck**

**CLASSIFICATION OF NON-NEOPLASTIC LESIONS OF THE NECK** (Box 12-1)

<table>
<thead>
<tr>
<th>Developmental Cystic Anomalies</th>
<th>Reactive, Inflammatory, and Tumor-like Lesions</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Branchial cleft anomalies</td>
<td>• Viral</td>
</tr>
<tr>
<td>• Thyroglossal duct cyst</td>
<td>• Protozoal</td>
</tr>
<tr>
<td>• Cervical thymic cyst</td>
<td>• Sarcoïdosis</td>
</tr>
<tr>
<td>• Bronchogenic cyst</td>
<td>• Others</td>
</tr>
<tr>
<td>• Dermoid cyst</td>
<td></td>
</tr>
<tr>
<td>• Others</td>
<td></td>
</tr>
</tbody>
</table>

**BENIGN CYSTIC LESIONS OF THE CERVICAL NECK**

- Cystic lesions of the neck represent a diverse group of lesions listed in Box 12-2.

**BRANCHIAL ANOMALIES (BA)**

**Definition:** Congenital malformations related to the branchial apparatus.

**Embryology**

- Branchial apparatus appears around the fourth week of gestation and consists of a paired series of six arches, five pouches, and five clefts or grooves.
- Embryologic development of the head and neck structures can be classified through the development of the branchial apparatus, including arches (ectoderm), clefts (ectoderm), and pharyngeal pouches (endoderm) (Table 12-1).

**Branchial Cysts, Sinuses, and Fistulas**

- Branchial cleft anomalies are divided according to p0570 the branchial apparatus involved and are further divided into cysts, sinuses, or fistulas:
  - Cysts are epithelial-lined structures that may p0530 occur as an isolated lesion or may occur in association with a sinus or fistula.

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<table>
<thead>
<tr>
<th>Arches (Mesoderm)</th>
<th>Pharyngeal Pouches (Endoderm)</th>
<th>Clefts (Ectoderm)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>First</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cartilage bar (Meckel cartilage):</td>
<td>Epithelial lining of the middle ear cavity, inner part of the tympanic membrane, eustachian tube, mastoid air cells</td>
<td>Epithelial lining of the external auditory canal, and outer part of the tympanic membrane</td>
</tr>
<tr>
<td>Ramus and body of mandible</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Maxilla</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Incus (body)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Malleus (head and neck)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Part of pinna of ear</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Muscles and ligaments:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Temporalis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Masseter</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pterygoids (medial and lateral)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Digastric (anterior belly)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tensor tympani</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tensor veli palatini</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sphenomandibular lig.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anterior two thirds of tongue</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Sphenomandibular lig.</strong></td>
<td>None</td>
<td></td>
</tr>
<tr>
<td><strong>Second</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cartilage bar (Reichert cartilage):</td>
<td>Epithelial lining of the tonsillar fossa and palatine tonsil</td>
<td>None</td>
</tr>
<tr>
<td>Incus (long process)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Malleus (manubrium)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stapes (long process)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Styloid process</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hyoid (lesser horn and upper body)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Part of pinna of ear</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Muscles and ligaments:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Facial (auriculotemporal, buccinator, frontalis, masseteric, occipitalis, orbicularis oculi, oris platysma)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Digastric (posterior belly)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stapedius</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stylohyoid</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stylohyoid lig.</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Innervation:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Third</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cartilage bar:</td>
<td>Inferior parathyroid glands, thymus, pyriform sinus</td>
<td>None</td>
</tr>
<tr>
<td>Hyoid (lower body and greater horn)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Muscles and ligaments:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stylopharyngeus</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Palatopharyngeus</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Posterior third (base or root) of tongue</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Innervation:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Glossopharyngeal</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Fourth</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cartilage bar:</td>
<td>Superior parathyroid glands, C-cells of ultimobranchial body</td>
<td>None</td>
</tr>
<tr>
<td>Thyroid</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Muscles and ligaments:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cricothyroid</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Levator palatini</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Posterior third (base) of tongue</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Innervation:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vagus (superior laryngeal branch)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Vasculature:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Arch of aorta</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Right subclavian artery</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Fifth and sixth</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cartilage bar:</td>
<td>C-cells of ultimobranchial body (5th pharyngeal pouch) 6th pharyngeal pouch: none</td>
<td>None</td>
</tr>
<tr>
<td>Cricoid</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Arytenoids</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Muscles and ligaments:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intrinsics muscles of larynx</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Upper esophageal muscles</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Innervation:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vagus (recurrent laryngeal)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Vasculature:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pulmonary arteries</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ductus arteriosus</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>


**Sinuses** are tracts with a single opening; the opening may be to skin, representing a branchial cleft or ectodermally derived sinus tract (cutaneous sinus tract), or to mucosa, representing a branchial pouch or endodermally derived sinus tract (mucosal sinus tract).

**Fistulas** are tracts with two openings, which can be cutaneous or mucosal.

**Clinical**
- Cysts present as nontender, fluctuant masses in appropriate locations; cysts may become inflamed and abscesses may develop, potentially associated with dysphagia, dyspnea, or stridor.
- Sinuses and fistulas are associated with discharge of mucoid and/or purulent secretions from the tract opening.
- Up to 10% of cases may be bilateral.
- Histogenesis of branchial cleft anomalies is controversial:
  - Among the structures proposed as the origins for these anomalies include the branchial apparatus (considered to represent the origin for these abnormalities), salivary gland inclusions, and thymic duct.

**First Branchial Anomalies** (Fig. 12-1)

**Clinical**
- In comparison to second branchial anomalies, first branchial anomalies are uncommon, representing from 1% to 8% of all branchial apparatus defects.
- Typically occur in the area of the external ear and may include cysts, sinuses, and fistulas.
- First branchial anomalies may be identified in a variety of locations, including pre-, post-, or infraauricular, at the angle of the jaw, associated with the earlobe, and in the external auditory canal or involving the parotid gland.
- Involvement of the external auditory canal may result in otalgia or otorrhea.
- Parotid involvement may result in an intra- or periparotid mass that may be mistaken for a parotid gland tumor.

**Pathology**

**Gross**
- Majority of first BA are cysts, representing more than two thirds (68%) of these anomalies:
  - Appear as solitary cystic lesions without an associated sinus tract
  - Sinuses and fistulas equally make up the remainder of these lesions:
  - Fistula tract in first branchial anomalies may extend from the skin over or through the parotid and open in the external auditory canal.

**Fig. 12-1. First branchial cleft cyst.**

A. Infra-auricular, freely movable, and fluctuant mass.
B. Left, First branchial cleft cyst (Work type I) is composed of keratinizing squamous epithelial lining devoid of adnexal structures; a dense lymphoid infiltrate is seen in the cyst wall; Right, first branchial cleft cyst (Work type II) is composed of keratinizing squamous epithelial lining with associated adnexal structures.

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Microscopic

First branchial lesions can be divided into two types as defined by Work, which are referred to as type I and type II lesions:

- Type I:
  - Contains only ectodermal elements, including keratinizing squamous epithelium without adnexal structures (i.e., hair follicles, sebaceous glands, sweat glands) or cartilage, thereby duplicating the membranous external auditory canal.
  - Represents a first cleft anomaly only.
  - Typically located medial, inferior, or posterior to the concha and pinna.
  - Sinuses parallel the external auditory canal and end in a blind sac at the level of the mesotympanum.
  - External auditory canal is intact and hearing is normal.

- Type II:
  - Have ectodermal and mesodermal elements, including keratinized squamous epithelium, cutaneous adnexa, and cartilage, thereby duplicating the external auditory canal and pinna.
  - Typically localize to a point just below the angle of the mandible.
  - Sinus or fistula tracts extend upward over the angle of the mandible through the parotid gland toward the external auditory canal.

Type II anomalies are more intimately associated with the parotid gland than type I anomalies, although parotid tissue may be found in association with type I sinus or fistula tracts.

Tracts associated with type II defects may terminate short of the external auditory canal or may open up in the external auditory canal near the junction of the cartilaginous portion and osseous portion of the canal; communication with the middle ear is uncommon.

For either type I or type II defects, an associated prominent lymphoid component is not usually present, contrasting with second BA; only when inflamed or infected will there be an associated lymphoid component.

Some authorities recommend that, due to the overlapping histology between Work types I and II, all first branchial cleft anomalies be classified only as cysts, sinuses, or fistulas.

Unless inflamed, a prominent lymphoid component is not seen, contrasting to the findings that can be seen in second branchial cysts.

Differential Diagnosis

- Epidermoid cyst
- Dermoid cyst

Treatment and Prognosis

- Regardless of the histology, complete surgical excision is the preferred treatment:
  - Inadequate excision results in recurrence and increased risk of infection.
  - Incision and drainage are indicated in cases which abscesses have developed, and in this situation complete surgical excision must wait until resolution of the infection.
  - Type II anomalies are often intimately associated with the parotid gland, necessitating a superficial parotidectomy to ensure complete excision.
  - Although there is no consistent relationship between the tract and the facial nerve as it courses through the parotid gland, exposure and dissection of the nerve and its branches are required in Work type II anomalies.

Second Branchial Anomalies (Figs. 12-2 through 12-4)

Synonym: Second branchial cysts also referred to as parotid (cervical) lymphoepithelial cyst

Clinical

- Accounts for the majority of the branchial apparatus anomalies, representing from 92% to 99% of all cases.
- Equal gender predilection; typically occurs in the third through fifth decades of life:
  - Uncommon in patients older than 50 years of age:
    - Less than 3% of cysts present after the age of 50
    - Lateral neck cysts in patients 50 years of age and older should prompt diagnostic consideration for a metastatic cystic squamous cell carcinoma (see Chapter 13).
  - Occur along the anterior border of the sternocleidomastoid; mastoid muscle; most common at the level of the angle of the mandible
  - Present as a painless, fluctuant neck mass that may increase in size in the face of an upper respiratory tract infection, at which time they may become painful
  - Cysts are much more common than fistulas.
  - Sinuses and fistulas are most often identified at birth or in early childhood, presenting as a small opening above the clavicle through which mucoid secretions may be expressed; these are divided into three types:
    - Incomplete external, with an external (cutaneous) but no internal (pharyngeal) opening
    - Incomplete internal, with a pharyngeal but no cutaneous opening
Fig. 12-2. Second branchial cleft cyst.

A, Second branchial cleft cyst occurring along the anterior border of the sternocleidomastoid muscle as painless, fluctuant neck mass. B, Axial CT, enhanced: fluid-filled cyst (c) anterior to the left sternocleidomastoid muscle (s). The thin-walled cyst does not enhance after administration of intravenous contrast. Jugular veins (arrowheads). C, Axial contrast-enhanced CT shows a cyst in the right neck with a fairly thick, enhancing rim. The cyst is behind the submandibular gland, lateral to the carotid sheath structures, and along the anterior margin of the sternocleidomastoid muscle. This was an infected second branchial cleft cyst. (B, C, from Som PM, Curtin HD: Head and Neck Imaging, ed 5, Philadelphia, 2011, Elsevier, p 2244, Fig. 37-14, D.)

Complete, with pharyngeal and cutaneous openings:
- The cutaneous opening is seen anywhere along the anterior border of the sternocleidomastoid muscle from the hyoid bone to the sternum, with the epithelial tract coursing cephalad, between the internal and external carotid arteries, over cranial nerves IX and XII, deep to the posterior belly of the digastric muscle and terminating close to the middle constrictor muscle or with an internal opening in the pharyngeal wall and/or tonsillar region.
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Pathology

Gross

- Cysts are thin-walled cystic structures filled with cheesy material or serous, mucoid, or purulent fluid; nodular excrescences may be seen lining the cyst wall.

Histology

- Cyst lining epithelium is predominantly a stratified squamous epithelium seen in approximately 90% of cases; less frequently a purely columnar epithelial lining or a mixed lining may be seen.
- Cyst wall typically contains a nodular or diffuse lymphoid infiltrate often with germinal centers.
- Fibrosis and granulation tissue may be prominent and even replace the surface epithelium in cases associated with repeated infections.

Radiology

- Cysts appear as well-defined, low-density lesions surrounded by a thin, uniform wall.
- Noninflamed cysts have no or minimal CT mural enhancement.
- Infected cysts have increased CT density of the central fluid with rim enhancement and poorly defined cyst wall.
- Fistulas or sinus tracts may extend either toward the skin surface, supratonsillar fossa, as well as between the internal and external carotid arteries.

Histogenesis of second branchial cleft cysts is controversial:

- Among the structures proposed as the origins for these anomalies include the branchial apparatus (considered to represent the origin for these abnormalities), salivary gland inclusions, and thymic duct.

Fig. 12-3. Second branchial cleft cyst.

A, Resected, smooth-walled second branchial cleft cyst. Histologically, branchial cleft cyst wall lining epithelium is typically lined by (B) stratified squamous epithelium and (C) less frequently a purely ciliated columnar epithelium. Although not depicted here, the cyst wall typically contains a nodular or diffuse lymphoid infiltrate often with germinal centers.
SECTION 4 The Neck

Differential Diagnosis

- Thymic cyst
- Thyroglossal duct cyst
- Metastatic cystic squamous cell carcinoma, including HPV-associated and non-HPV-associated:
  - Absence of cytologic features of malignancy excludes the diagnosis of a metastatic cystic squamous cell carcinoma
  - Some examples of cystic metastatic squamous cell carcinoma may be composed of relatively bland cytomorphic features but even in such cases there are foci of cytologically atypical/malignant epithelial cells characterized by pleomorphic nuclei and increased mitotic activity:
    - Increased proliferation rate as determined by Ki67 (MIB1) staining would be present in metastatic carcinoma and absent in branchial cyst.
    - Diffuse and strong (nuclear and cytoplasmic) p16 immunoreactivity, representing a surrogate for p16 negativity.

Immunohistochemistry

- Cytokeratin(s) positive
- p16 negative:
  - Branchial cleft cysts can exhibit focal patchy weak to strong reactivity limited to the superficial squamous epithelium.
  - Absence of p16 may be helpful in distinguishing branchial cleft cyst from metastatic oropharyngeal nonkeratinizing squamous cell carcinoma but it is not as useful in cases of metastatic keratinizing squamous cell carcinoma as the latter are typically p16 negative.
- Thyroglobulin, TTF1, PAX8 negative
- Low proliferation rate (less than 5%) by Ki67 (MIB1) staining
CHAPTER 12 Non-Neoplastic Lesions of the Neck

marker for HPV-16, would confirm the diagnosis of metastatic cystic HPV-associated carcinoma of oropharyngeal origin, differentiating it from a branchial cleft cyst, which should be nonreactive for p16.

- p16 may be overexpressed in almost 50% of benign branchial cleft cysts potentially limiting the diagnostic utility of p16 in this setting; in such an occurrence molecular testing (in situ hybridization, PCR) would be necessary to confirm presence of HPV and the malignant nature of the cyst.

Confusion and controversy exist between the diagnosis of metastatic cystic squamous cell carcinoma and that of a carcinoma arising in a branchial cleft cyst (so-called branchial cleft carcinoma or branchiogenic carcinoma); criteria for the diagnosis of a branchiogenic carcinoma include:

- The tumor occurs along the line extending from a point anterior to the tragus along the anterior border of the sternocleidomastoid muscle to the clavicle.
- Histology supports origin from a branchial cleft-derived structure (i.e., situated in the lateral aspect of the neck).
- Histology supports carcinoma arising in the wall of an epithelial-lined cyst.
- A minimum of 3-year follow-up demonstrates no evidence of a primary source for this neoplasm.
- Despite the fulfillment of these criteria, it is highly unlikely that carcinoma arises in a branchial cleft cyst; rather, these cystic squamous cell carcinomas take origin from a primary tumor in Waldeyer tonsillar ring:
  - Primary (Waldeyer ring) neoplasm may be so small as to defy clinical detection but nevertheless is capable of metastasizing.
  - Histology demonstrates partial or complete replacement of the lymph node by an epithelial-lined structure with central cystic change; the epithelium varies from areas that are bland, composed of uniform cells lacking pleomorphism, crowding, or loss of polarity, to overtly malignant-appearing epithelium composed of pleomorphic cells with increased cellularity, mitoses, and a loss of polarity.

Metastatic papillary thyroid carcinoma:

- Absence of architectural and cytologic features associated with papillary thyroid carcinoma would differentiate metastatic papillary thyroid carcinoma from second BA.
- Cystic metastatic papillary thyroid carcinoma to the neck may occur in the absence of a known history of a primary thyroid carcinoma and/or as an occult metastasis. Further, the primary thyroid-based carcinoma may be very small and clinically difficult to detect. Most often the metastasis originates from the ipsilateral thyroid lobe. Given the clinical scenario of unsuspected/unknown primary thyroid carcinoma, the histology of the neck mass may include a flattened/attenuated epithelial lining without papillary architecture histologically simulating the appearance of a branchial cleft cyst.
  - Attention to the nuclear features may alert the pathologist to the possible presence of metastatic papillary thyroid carcinoma.

In suspect cases, thyroglobulin, thyroid transcription factor 1 (TTF-1), and PAX8 reactivity would be present in metastatic papillary thyroid carcinoma and absent in BAs:

- Thyroglobulin reactivity is the single best marker for lesions of thyroid follicular epithelial cell origin and is generally absent in all other (nonfollicular epithelial cell origin) lesions.
- TTF-1 reactivity is not unique for follicular epithelial-derived lesions of the thyroid but can be present in other lesion types, including (but not limited to) medullary thyroid carcinoma and pulmonary adenocarcinoma; in contrast, thyroglobulin reactivity is a dedicated marker for lesions of thyroid follicular epithelial cell origin and represents the preferred immunomarkers in the evaluation for metastatic carcinomas of thyroid follicular epithelial cell origin.

Regardless of the histologic (nuclear) features, thyroid tissue located in lymph nodes situated lateral to the great neck vessels represents metastatic thyroid carcinoma; see Section 8, Thyroid Gland, for more complete discussion.

Treatment and Prognosis

- Complete surgical excision is the preferred treatment.

Depending on the extent of the fistula tract, a tonsillectomy may be needed.

Third Branchial Anomalies

- Third BAs are rare.
- May present as recurrent neck abscesses associated with stridor or as recurrent episodes of acute supplicative unilateral thyroiditis.
- A sinus or fistula open externally anterior to the lower third of the sternocleidomastoid muscle:
  - If complete, the internal opening of the sinus or fistula is in the piriform sinus following passage of the tract along the carotid sheath penetrating the thyrohyoid membrane cranial to the superior laryngeal nerve.

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Cysts occur anywhere along the sinus tract but are most commonly found in the region of the laryngeal ventricle or in the anteroinferior cervical triangle.

Pathology

Cysts are lined by a stratified squamous epithelium or ciliated epithelium; an associated marked lympho-cytic cell infiltrate may be present. Thymic tissue, derived from the third branchial cleft pouch, may or may not be present.

Treatment and Prognosis

Complete surgical resection of a third BA (cyst, sinus, fistula) is the preferred treatment and is necessary to prevent recurrence: Surgical procedure may require a subtotal thyroidec-tomy.

Fourth Branchial Anomalies

Fourth BAs are extremely rare. The majority of patients present before the age of 20 years. Clinical manifestations of fourth BAs are similar to those of third BAs, including recurrent neck abscesses or recurrent episodes of acute suppurative unilateral thyroditis.

Almost all fourth BAs are sinuses that may originate from the piform sinus:

The sinus tract usually has an internal opening at the apex of the piform sinus caudal to the superi-or laryngeal nerve, descends translaryngeally beneath the thyroid cartilage, exiting the larynx near the cricothyroid joint below the inferior constrictor muscle, and then continues superficial to the recurrent laryngeal nerve ending in the paratracheal region or in the thyroid gland.

Like third BAs, fourth BAs may or may not include thymic tissue.

Complete surgical resection of a fourth BA is the preferred treatment and is necessary to prevent recurrence: Surgical procedure may require a subtotal thyroidectomy.

THYROGLOSSAL DUCT CYST

Definition: Persistence and cystic dilatation of the thyroglossal duct in the midline of the neck.

Embryology

The thyroid gland is the first endocrine gland to appear during embryonic development.

Thyroid gland derives from three primordia, the median anlage, and lateral anilages:

Median anlage develops around the 24th day of gestation as a small, median endodermal thick-en ing on the primitive pharynx; this thickening forms a diverticulum, which is attached to the tongue by a narrow tube, the thyroglossal duct; its opening in the base of the tongue constitutes the foramen cecum.

Proximal opening persists as the foramen cecum of the tongue.

As a result of further cellular proliferations, the hollow thyroid diverticulum obliterates and divides into the right and left lobes, connected by the isthmus around the seventh week of gestation.

During development the thyroid descends and assumes a definitive position in the anterior neck; by this time the thyroglossal duct degenerates.

Clinical/Pathology

See Section 8, Thyroid Gland, for a more complete discussion including illustrations.

Majority of cases occurs in the midline of the neck above the thyroid isthmus but below the level of the hyoid bone:

Thyroglossal duct cysts are nearly always con-nected to the hyoid bone.

Uncommonly, thyroglossal duct cysts may occur lateral to midline but do not occur in the lateral portion of the neck (i.e., lateral to the jugular vein).

Clinical presentation of an uninfected thyroglossal duct cyst is usually that of an asymptomatic midline neck mass:

Mass typically moves upward on swallowing.

Inflamed or infected thyroglossal duct cysts may be associated with tenderness and pain.

Extrinsic airway compression in neonates with apnea, cyanosis, and respiratory compromise may uncommonly occur.

Thyroglossal duct cysts are smooth-walled, cystic structures that usually measure less than 2 cm.

In noninflamed cysts, the cyst lining is respiratory columnar epithelium but may also include squamous epithelium.

Presence of thyroid tissue in the cyst wall varies and may be dependent on the extent of specimen sampling; in generally, thyroid tissue can be found in more than 60% of the cases.

Thyroid tissue may be normal, hyperplastic, and nodular or neoplastic (see below).

Surgery is the preferred treatment; en bloc surgical resection of the cyst, the middle third of the hyoid bone (Sistrunk procedure), and the suprahypophyseal tract up to the foramen cecum; this extended surgery prevents recurrence:

Adequate surgery results in cure with low, if any, recurrences.
Benign and malignant neoplasms may occur in the setting of a thyroglossal duct cyst.

C-cell–related lesions, including medullary carcinoma, do not occur in thyroglossal duct cysts due to the different embryologic derivation of the C-cells.

**CERVICAL THYMIC CYST** (Fig. 12-5)

**Definition:** Cervical thymic tissue sequestered from the main thymic gland during its embryologic descent:

- Sequestered thymic tissue may be solid (so-called accessory cervical thymic tissue) or cystic (cervical thymic cyst).

**Embryology and Anatomy**

- Thymus develops in the sixth week of gestation, arising primarily from the third branchial pouch (mesoderm); the fourth branchial pouch may provide minimal contribution to the development of the thymus.
- Thymic primordia descend in the neck along the course of the carotid sheath.
- Connection of the paired primordia to the pharynx is retained by the thymopharyngeal ducts.
- During the eighth week of gestation the thymic primordia fuse in the midline of the neck and then descend into the mediastinum.
- Failure of descent or failure to involute results in thymic abnormalities, including cervical thymic cyst.
- Cervical thymic cysts are considered to be congenital, although mediastinal thymic cysts are thought to be acquired.

**Clinical**

- Cervical thymic cysts are uncommon.
- Occur slightly more often in men; the majority of cervical thymic cysts (67%) occurs during the first decade of life with the rest occurring in the second to third decades:
  - Rarely, cervical thymic cysts occur in adults.

---

**Fig. 12-5. Cervical thymic cyst.**

- **A:** Multilocular smooth walled cystic proliferation with focal solid areas.
- **B and C:** Epithelial lined cyst with identification of lymphoid follicles and Hassall corpuscles within the cyst wall.
- **D:** A rather common finding in thymic cysts is the presence of cholesterol granulomas.
SECTION 4 The Neck

- Cervical thymic cysts and branchial cleft cysts tend to occur in the anterior cervical triangle.
- In contrast to cervical thymic cysts, which occur typically in the first decade of life, have a slight female predilection, generally are not associated with sinuses or fistulas, and have thymic tissue in their walls.
- Branchial cleft cysts tend to occur in the third decade of life, have equal gender predilection, commonly are associated with cysts and fistulas, and have lymphoid tissue in their wall.

### Treatment and Prognosis
- Treatment for cervical thymic cyst is simple surgical excision, which is curative.
- Cervical thymic cysts have no potential to undergo malignant transformation, which is not true of mediastinal thymic cysts.

### BRONCHOGENIC CYST (Fig. 12-6)

**Definition:** Bronchogenic cysts originate from buds or diverticula that separate from the foregut during the formation of the tracheobronchial tree:
- The majority of bronchogenic cysts are found in the mediastinum or in the lungs and are referred to as mediastinal bronchogenic cysts.
- Bronchogenic cysts may occur outside the mediastinum, with the skin or subcutaneous tissue representing the most common site of occurrence (referred to as cutaneous bronchogenic cysts), particularly near the suprasternal notch (manubrium sterni), and much less often in the lower neck or shoulder.

**Synonym:** Bronchial cyst

**Fig. 12-6. Bronchogenic cyst.**

Lower neck cystic lesion lined by ciliated respiratory epithelium; bronchial (sero-mucous) glands, as well as cartilage and smooth muscle are present.
CHAPTER 12 Non-Neoplastic Lesions of the Neck

Clinical

No gender predilection; occur over a wide age range from birth to the sixth decade of life:

- Average age of occurrence is in the third and fourth decades
- In the very young, mediastinal bronchogenic cysts may produce life-threatening respiratory distress with stridor and airway obstruction.
- In adults, mediastinal bronchogenic cysts are usually asymptomatic and identified by routine chest x-rays.

Radiology:

- Solitary, smooth, round-to-ovoid cyst in the mediastinum (middle, posterior, or superior) closely associated with the trachea or major bronchi
- An occasional example may be found within the wall of the bronchus, trachea, or esophagus, attached to the pericardium, or even within the outflow tract of the right ventricle or the interatrial septum.
- Rare examples have been reported in the pharyngeal region or lateral neck.
- Rare examples of congenital anomalies have been reported in association with mediastinal bronchogenic cyst, but typically these lesions are not associated with developmental anomalies.

Pathology

Gross

- Cysts are typically unilocular and thin-walled and may measure up to 15 cm in greatest dimension.
- Cysts have a smooth-appearing lining that on occasion may be trabeculated; the cyst content varies from serous fluid to serosanguineous to mucoid and, if infected, purulent material.

Microscopic

- Cyst lining usually is a ciliated respiratory epithelium and bronchial (mucous) glands, as well as cartilage and smooth muscle are usually present.
- Squamous metaplasia of the surface epithelium may be identified.

Differential Diagnosis

- Branchial cleft cyst
- Thyroglossal duct cyst
- Teratoma

NOTE:

- Presence of (sero)mucous glands, cartilage, and smooth muscle in bronchogenic cyst allows differentiation from a branchial cleft cyst and thyroglossal duct cyst, in which these components are not found.

Treatment and Prognosis

- Excision of the cyst via an external approach generally is curative.
- Malignant transformation of cervical (and mediastinal) bronchogenic cysts has not been described to date.

DERMOID CYST (Fig. 12-7)

Definition: Benign developmental cystic anomaly originating from ectoderm and mesoderm but not endoderm.

Clinical

- Head and neck are fairly common sites of occurrence for dermoid cysts, accounting for approximately 34% of all dermoid cysts.
- No gender predilection; may occur over a wide age range but are most common in the first decade of life.
- In the head and neck, dermoid cysts are predominantly subcutaneous lesions but may occur in other (mucosal) sites:
  - Among the more common sites of occurrence in head and neck are the orbit, oral cavity, and nasal cavity.

Fig. 12-7. Dermoid cyst.

Cyst is lined by stratified squamous epithelium with cutaneous adnexal structures (e.g., sebaceous glands) in the fibroconnective tissue wall. The adnexal structures may also include eccrine glands or apocrine glands (not shown), which are features not found in epidermoid cysts.
Less common sites of occurrence include the mandible, maxilla, middle ear, neck (midline or near midline), upper neck, and near the thyroid cartilage or associated with the thyroid gland, suggesting a thyroid nodule.

Dermoid cysts are slow-growing and not associated with pain.

Pathology

Thin-walled cysts containing gray-white friable material and range in size from a few millimeters to 12 cm in greatest dimension; internal aspect of has a smooth lining.

Histology

Dermoid cysts are lined by stratified squamous epithelium with cutaneous adnexal structures (e.g., hair shafts, sebaceous glands, eccrine glands, or apocrine glands) in the fibroconnective tissue wall.

Cyst content may include keratin or sebaceous material.

Dermoid cysts may rupture, resulting in a (florid) foreign body giant cell reaction.

Differential Diagnosis

- Epidermal inclusion cyst:
  - Like dermoid cysts, epidermal inclusion cysts are lined by stratified squamous epithelium and are filled with keratin.
  - In contrast to dermoid cysts, the epidermal inclusion cysts lack adnexal structures in the cyst wall.
- Teratomas:
  - Represent true neoplasms composed of tissues from all three germ layers.

Treatment and Prognosis

Simple surgical excision is the preferred treatment and is curative.

INFECTION DISEASES OF THE NECK

Infections of the oral cavity, nasopharynx, oropharynx, and cervical neck include fungal, viral, bacterial, mycobacterial, protozoal, and other infectious agents.

The breadth of infectious diseases of these sites is extensive, and this section focuses on select infectious diseases of these anatomic sites.

MYCOBACTERIAL AND OTHER GRANULOMATOUS DISEASES

Definition: Infectious disease caused by Mycobacterium, a microorganism classified in the order Actinomycetales and the family Mycobacteriaceae.

Mycobacteria include:
- Mycobacterium tuberculosis:
- Mycobacterium caprae, Mycobacterium pinnipedii, Mycobacterium africanum, Mycobacterium microti, Mycobacterium canetti.

Nontuberculous (“atypical”) mycobacteria are also referred to as mycobacterium other than tuberculosis (MOTT):
- Some of the nontuberculous mycobacteria include M. avium-intracellulare, M. scrofulaceum, M. kansasii, and M. ulcerans.

Clinical

Mycobacterial infection of the head and neck is relatively uncommon.

Overall the incidence of Mycobacterium tuberculosis has decreased over the past five decades:
- Of reported cases of extrapulmonary mycobacterial infections, 12% affect head and neck sites.
- With the advent of the acquired immunodeficiency syndrome (AIDS) associated with immunocompromised conditions, there has been an increased incidence of infection by mycobacteria, especially caused by the nontuberculous (“atypical”) mycobacteria.
CHAPTER 12 Non-Neoplastic Lesions of the Neck

Nontuberculous (“atypical”) mycobacteria (MOTT):
- Only some are human pathogens.
- In the immune-competent patient, the nontuberculous mycobacteria do not cause pulmonary disease but often cause localized disease such as lymphadenitis (e.g., scrofula, see below) or a subcutaneous infection.
- In the immune-compromised patient these microorganisms cause pneumonia and potentially disseminated (systemic) disease.
- In the head and neck, all sites may be involved but infection usually involves the lymph nodes; less often involvement may include the tonsils, pharynx, oral cavity, sinonasal region, larynx, salivary glands, middle ear, and temporal bone.
- Head and neck involvement may result as a complication of pulmonary involvement (direct infection via expectoration of infected sputum), via hematogenous or lymphatic spread, or as an isolated occurrence as a primary upper aerodigestive tract infection.
- May occur in patients with coexisting carcinoma (e.g., squamous cell carcinoma).
- Symptoms vary according to the site(s) infected and include a neck mass (cervical adenopathy), sore throat, nasal obstruction, hoarseness, dysphagia.
- Clinical work-up in suspected cases includes chest x-ray, tuberculin skin test, microbiologic cultures, and molecular diagnostics:
  - Reference (“gold”) standard is microbiologic cultures and identification on specific media:
    - Allows for testing of drug susceptibility
    - Depending on the media used, incubation (i.e., growth) takes from 2 to as long as 6 to 10 weeks (or longer), potentially resulting in delay in diagnosis and treatment.
  - Media used in testing for tuberculosis includes:
    - Solid media includes Löwenstein-Jensen
    - Liquid media include the nonradiometric BACTEC Mycobacteria Growth Indicator Tube 960 (MGIT) system, which has replaced radiometric BACTEC 460 system susceptibility testing.
  - Liquid media–based culture is more sensitive and growth is more rapid as compared with solid media:
    - In liquid media growth may occur from 1 to 3 weeks as compared with 3 to 8 weeks for solid media.
  - Most rapid method for diagnosis of tuberculosis is the nucleic acid amplification test for direct detection of MTBC in clinical specimens (e.g., sputum, fluids, and tissue [formalin-fixed paraffin embedded]):
    - Sensitive as cultures but requires significantly less time to perform and result (4 to 5 hours)

- Allows for more rapid diagnosis but these tests do not differentiate species in MTBC
- Can detect as few as 10 organisms in clinical specimens as compared with more than 10,000 organisms required for positive identification on smears
- Available tests include Amplified Mycobacterium Tuberculosis Direct Test (Gen-Probe Inc.) and AMPLICOR Mycobacterium Tuberculosis Test (Roche Diagnostics).
- Sensitivity of nucleic acid amplification tests generally slightly lower for nonrespiratory specimens but useful in the diagnosis of extrapulmonary tuberculosis
- Susceptibility testing:
  - Once an isolate is available, drug susceptibility testing is performed.
  - New diagnostics using liquid media–based cultures are more sensitive and growth is more rapid as compared with solid media.
  - For MTBC, the initial isolate from every patient should be tested to all primary drugs:
    - Agar proportion is the standard method of testing susceptibility of MTBC to antituberculosis agents:
      - Isolates showing greater than 1% resistance to a single concentration of drug considered resistant to that drug
    - Liquid-based system allowing for quicker turnaround time for results as compared to agar is recommended:
      - Results available 5 to 7 days after bottles inoculated with MTBC
    - Molecular methods, including polymerase chain reaction, developed for rapid detection of mutations known to be associated with drug resistance including multidrug-resistant organisms (MDR-TB) and extensively drug-resistant tuberculosis (XDR-TB).

- Lupus vulgaris:
  - Represents mucocutaneous lesions of secondary tuberculosis
  - Results from hematogenous or lymphatic spread of disease
  - Nose and cheeks are the most common sites of occurrence.
  - May be ulcerative and destructive:
    - Destructive nature thought to be due to hyperensitivity to the microorganisms in patients with strong immune responses
    - Association in approximately 40% of cases with upper aerodigestive tract lesions and cervical lymphadenitis
  - Healing may result in scarring and deformity of involved region.

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**Fig. 12-8. Mycobacterium tuberculosis.**

A. The histologic hallmark of mycobacterial disease in the presence of normal immune status includes the presence of caseating (necrotizing) granulomatous inflammation characterized by well-formed granulomas including central areas of necrosis surrounded by histiocytes and multinucleated giant cells. B. By acid-fast bacilli (AFB) stain the microorganisms appear beaded with a red color. The microorganisms may be difficult to identify and may be located in necrotic foci and/or within multinucleated giant cells.

**Pathology** (Fig. 12-8)

- In the presence of normal immune status, changes include caseating (necrotizing) granulomatous inflammation in which the granulomas are:
  - Well formed
  - Surrounded by histiocytes and multinucleated giant cells
  - Composed of central areas of necrosis
  - May also include noncaseating type of granuloma formation

**Histology**

**NOTE:** Microorganisms are often extremely difficult to identify and may defy detection despite an extensive and diligent effort:

- Identification of microorganisms requires special stains and is based on the capability of forming stable mycolate complexes with certain aryl methane dyes referred to as acid-fastness
- Depending on the stain (acid-fast bacilli [AFB], Ziehl-Neelsen), the microorganisms when identified appear beaded with a red or purple color
- May be located in necrotic foci and/or within giant cells

**Differential Diagnosis**

- Sarcoidosis
- Other infectious necrotizing granulomatous diseases

**Treatment and Prognosis**

- The cornerstone for treatment is multidrug (antituberculous) therapy:
  - First line:
    - Isoniazid, rifampicin, ethambutol, and pyrazinamide
    - Duration of 6 months:
      - 2-month intensive therapy with the four drugs
      - 4-month continued therapy with isoniazid, rifampin
  - Second line:
    - Streptomycin, ethionamide, kanamycin, capreomycin, ofloxacin, rifabutin

- Among new cases of tuberculosis, approximately 5% worldwide are due to multidrug-resistant organisms (MDR-TB) defined as tubercle bacilli resistant to isoniazid and rifampin.

- Mismanagement of drugs used to treat MDR-TB can result in extensively drug-resistant tuberculosis (XDR-TB) defined as MDR-TB plus resistance to any fluoroquinolone and any second-line injectable anti-tuberculosis agent.

- In association with AIDS, therapy is lifelong.

**Scrofula** (Fig. 12-9)

**Definition:** Cervical lymph node involvement by mycobacteria is referred to as scrofula.

**Synonym:** Scrofulous gumma

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Fig. 12-9. Mycobacterial involvement of cervical lymph nodes (scrofula).

A, Unilateral, firm, red neck mass with focal ulceration of the skin. B, Extensive cutaneous ulceration. C, Histologic appearance includes replacement of the nodal architecture by caseating granulomas characterized by central necrosis surrounded by histiocytes and giant cells. D, Mycobacteria are extremely difficult to identify and require the aid of special histochemical stains (acid-fast bacilli [AFB] stain) with the microorganism appearing as a slender, beaded, red/purple rod seen here in a multinucleated giant cell.
Clinical

More common in women than men; may occur over a wide age range but primarily affects children.

Most commonly involves high cervical lymph nodes in the region of the submandibular gland

Periparotid, periauricular, and submental lymph nodes may be involved but are much less often affected.

Usually presents as a unilateral neck mass when caused by nontuberculous mycobacteria; bilateral involvement generally is related to systemic involvement caused by dissemination of \textit{M. tuberculosis}.

Patients are afebrile.

Causative microorganism may include \textit{M. tuberculosis} but most commonly caused by nontuberculous mycobacteria (\textit{M. scrofulaceum}, \textit{M. avium-intracellulare}, \textit{M. kansasii}).

Although scrofula may be an isolated infection, it may also be the initial presentation in patients with pulmonary disease.

May occur in patients with immune reconstitution inflammatory syndrome (IRIS):

IRIS represents a cohort of HIV-infected patients receiving combined antiretroviral therapy (cART).

Pathology

Involved lymph nodes are enlarged and firm.

Mucosal involvement appears as a granular exudate with or without associated ulceration; cutaneous ulceration may occur.

Histology

Irrespective of the causative microorganism, the histologic picture of mycobacterial infection is the same.

In the immune-competent host, the histologic hallmark of mycobacterial infection regardless of the causative microorganism is caseating (necrotizing) granulomatous inflammation characterized by:

Central necrosis surrounded by histiocytes and giant cells

In up to 25\% of cases of nontuberculous mycobacterial infections, a caseating granulomatous inflammatory response is not present.

In the immune-compromised patient the typical caseating granulomatous inflammatory response may not be present; rather, diffuse sheets of foamy histiocytes are present within which are AFB-positive microorganisms.

Histochemistry:

NOTE: Microorganisms are often extremely difficult to identify and may defy detection despite an extensive and diligent effort:

Identification of microorganisms requires special stains and is based on the capability of forming stable mycolate complexes with certain aryl methane dyes referred to as acid-fastness.

Depending on the stain (acid-fast bacilli [AFB], \textit{M. tuberculosis}, \textit{Ziehl-Neelsen}), the microorganisms, when identified, appear beaded, showing a red or purple color.

Cytogenetic and molecular genetics:

In situ hybridization and polymerase chain reaction have improved the diagnostic identification of mycobacterial organisms and, along with cultures, allow for differentiating \textit{M. tuberculosis} from nontuberculous mycobacteria.

Differential Diagnosis

- Sarcoidosis
- Cat scratch disease

Treatment and Prognosis

Treatment for scrofula caused by nontuberculous mycobacteria is surgical excision, which is considered curative:

Nontuberculous mycobacteria are nonresponsive to anti-mycobacterial tuberculosis medications.

For infection caused by \textit{M. tuberculosis}, treatment consists of antituberculous chemotheraphy, including:

- Isoniazid, streptomycin, or rifampin

Mycobacterial Spindle Cell Pseudotumor (Fig. 12-10)

Definition: Pseudoneoplastic spindle cell proliferation almost exclusively occurring in HIV-infected patients.

Synonyms: Mycobacterial pseudotumor; \textit{M. avium} intracellulare pseudotumor; spindled nontuberculous mycobacteriosis; histoid mycobacteriosis

Clinical

Uncommon lesion

No gender predilection; occurs over wide age range

Almost always found in immune-compromised individuals due to:

- AIDS/HIV-positive patients
- Patients receiving immunosuppressive therapy including steroids

Causative microorganism is \textit{M. avium} intracellulare

Sites of involvement includes lymph nodes, as well as extranodal sites such as skin, spleen, brain, and bone marrow:

- Rarely may occur in mucosal sites of the upper aerodigestive tract
- Presentation includes subcutaneous firm nodule or ulceration
CHAPTER 12 Non-Neoplastic Lesions of the Neck

Based on the CD68 reactivity the spindle cells represent macrophages. S100 protein, desmin, and muscle-specific actin may be positive. CD31 and CD34 negative

Cytogenetics and molecular genetics: Polymerase chain reaction assists in identifying mycobacteria.

Pathology

Histology

Cellular proliferation composed of bland-appearing, spindle-shaped cells in a storiform pattern. Multinucleated giant cells and foamy histiocytes are not present. Partial or complete effacement of nodal architecture

Histochemistry:

Special stains for mycobacteria, including AFB and Ziehl-Neelsen, show the presence of numerous AFB-positive organisms within the cytoplasm of the spindle cells.

Immunohistochemistry:

Spindle cells are CD68, lysozyme, α-antichymotrypsin, and vimentin positive.

Based on the CD68 reactivity the spindle cells represent macrophages. S100 protein, desmin, and muscle-specific actin may be positive. CD31 and CD34 negative

Cytogenetics and molecular genetics: Polymerase chain reaction assists in identifying mycobacteria.

Differential Diagnosis

Kaposi sarcoma: May occur concomitantly (in same lymph node) as mycobacterial spindle cell tumor

Morphologic features that favor Kaposi sarcoma over mycobacterial spindle cell tumor include:

– Prominent fascicular arrangement of spindle cells and slit-like spaces

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- Absence of granular, acidophilic cytoplasm
- Presence of increased mitotic activity
- Presence of hyaline globules and extravasated red cells

Immunohistochemical features seen in the spindle cells of Kaposi sarcoma that assist in differentiating it from mycobacterial spine cell tumor include:
- Reactivity for human herpesvirus-8 (HHV-8), also referred to as Kaposi sarcoma–associated herpesvirus (KSHV)
- Reactivity for CD31 and CD34
- Absence of CD68 and S100 protein, as well as muscle-specific actin and desmin

- Fibrohistiocytic tumor(s)
- Hodgkin disease, nodular sclerosing

Treatment and Prognosis

Treatment guidelines are based on the species of mycobacteria and susceptibility testing of the isolate that, in some cases, would be modified because of the immune status of the patient or other concurrent therapy.

If no isolate is obtained, recommendation would be to treat for tuberculosis:

Specific drugs chosen would depend on the likelihood of drug resistance based on demographic/epidemiologic factors.

Cervicofacial Actinomycosis (Fig. 12-11)

Definition: Chronic granulomatous and supplicative disease caused by gram-positive, microaerophilic, and anaerobic bacteria, the most common isolate in humans causing disease being Actinomyces israelii.

Actinomycoses are endogenous saprophytic organisms in the oral cavity and tonsil.

Actinomycoses are often seen within tonsillar crypts, which represent a saprophyte and are unaccompanied by an inflammatory response.

Disease is classified according to the anatomic site involved and includes cervicofacial, abdominal, and pulmonary.

Clinical

Cervicofacial actinomycosis is the most common form of disease and is thought to arise secondary to dental manipulation and/or trauma.

No gender predilection; occurs in all age groups

Neck and area around the angle of the mandible are the most common sites of occurrence; however, clinical infection can occur anywhere in the head and neck.

- Most common symptom is that of a painless, slowly enlarging, indurated mass with or without suppuration; skin overlying the lesion has a characteristic purple color from which a draining sinus may be seen; fistulization is not uncommon.
- A definitive diagnosis is made bacteriologically; however, the organisms are difficult to culture.

Pathology

- Granulomatous reaction with central accumulation of polymorphonuclear leukocytes (abscess formation) and necrosis is identified.
- Within the abscess and enveloped by the neutrophils, microorganism colonies are seen:
  - Microorganisms form a characteristic appearance referred to as sulfur granules.
  - Granules are lobular, deep purple, and composed of a central meshwork of filaments that typically have eosinophilic club-shaped ends.
  - Sulfur granules can be identified in pus.
- Diagnosis can be made by fine-needle aspiration biopsy:
  - Smears and cell blocks of the aspirate may show characteristic colonies (sulfur granules) of actinomycoses.
  - Histochemistry:
    - Microorganisms stain best with gram and Gomori methenamine silver (GMS) stains.

Differential Diagnosis

- Nocardia infection

Treatment and Prognosis

- Intravenous penicillin G followed by oral penicillin is the preferred treatment.
- Patients allergic to penicillin can be given tetracycline.
- Prognosis is good if treated early.
- Osteomyelitis of the jaw is the most common complication; once infection reaches bone, tissue destruction may be extensive and involvement of the cranium, meninges, and brain may occur with lethal implications.

Sarcoidosis (Fig. 12-12)

Definition: Multisystem chronic granulomatous disease of unknown cause.

Clinical

No gender predilection; occurs in all age groups but seen most commonly in young adults.
CHAPTER 12 Non-Neoplastic Lesions of the Neck

Otolaryngologic symptoms vary according to site and include:

- Cervical adenopathy, pharyngotonsillitis with tonsillar enlargement, airway obstruction, nasal discharge, epistaxis
- Salivary gland involvement may clinically simulate Sjögren syndrome with salivary gland enlargement, xerostomia, and xerophthalmia
- Involvement of the parotid gland and uveal tract referred to as uveo- or parotid fever or Heerfordt syndrome may present with facial nerve paralysis

Any organ system may be involved; the most common include the lungs, skin, and lymph nodes.

Most common clinical presentation is with fever, weight loss, and hilar adenopathy.

Isolated extranodal head and neck involvement occurs only in a small percentage of cases and includes:

- Pharynx and tonsils
- Ear and temporal bones
- Sinonasal region, salivary glands, and larynx
- Site-specific involvement may occur as an isolated phenomenon or may coexist with systemic disease

Fig. 12-11. Cervicofacial actinomycosis.

A, Indurated, suppurative neck mass around the angle of the mandible; the skin overlying the lesion has a characteristic purple color. B, Cervical lymph node with central accumulation of polymorphonuclear leukocytes (abscess formation) and necrosis. C, Within the abscess and enveloped by the neutrophils, actinomycotic colonies are seen with a characteristic appearance referred to as “sulfur granules”; the granules are lobular, deep purple, and composed of a central meshwork of filaments, which typically have eosinophilic club-shaped ends. D, Microorganisms stain best with Gram (left) and Gomori methenamine silver (GMS) stains (right).
The Neck

Epithelioid histiocytes surrounded by a mixed inflammatory infiltrate:

- Typically there is no associated caseation
- Occasionally caseating granulomas may occur in sarcoidosis:
  - Necrosis is absent but some examples, especially extranodal lesions, may have small foci of centrally located necrosis.

- Langhans-type giant cells may be present.
- Intracytoplasmic inclusions including star-shaped and/or calcific laminated bodies called asteroid and Schaumann bodies, respectively, can be seen.
- Calcium oxalate crystals may be present in the cytoplasm of giant cells.
- Histochemistry:
  - All special stains for microorganisms are negative.
- Diagnosis of sarcoidosis is generally one of exclusion and is made by correlation of clinical, radiologic, and pathologic findings; although the pathologic

No laboratory findings specific for or diagnostic of sarcoidosis:

- Cutaneous anergy to skin test antigens (Kveim test) is positive in 60% to 85% of patients.
- Elevated angiotensin converting enzyme (ACE):
  - Used as a marker for sarcoid disease activity
  - Not unique to sarcoidosis but can be elevated in other diseases including diabetes, hyperthyroidism, multiple sclerosis, asthma, nephrotic syndrome, others
- ACE inhibitors used with varying success in the treatment of patients with sarcoidosis
- Cause remains unknown, but there is increasing evidence of finding mycobacterial DNA by polymerase chain reaction in sarcoid granulomas.

Pathology

Histology

Presence of multiple noncaseating granulomas consisting of well-formed nodular foci composed of epithelioid histiocytes surrounded by a mixed inflammatory infiltrate:

- Typically there is no associated caseation
- Occasionally caseating granulomas may occur in sarcoidosis:
  - Necrosis is absent but some examples, especially extranodal lesions, may have small foci of centrally located necrosis.

- Langhans-type giant cells may be present.
- Intracytoplasmic inclusions including star-shaped and/or calcific laminated bodies called asteroid and Schaumann bodies, respectively, can be seen.
- Calcium oxalate crystals may be present in the cytoplasm of giant cells.
- Histochemistry:
  - All special stains for microorganisms are negative.
- Diagnosis of sarcoidosis is generally one of exclusion and is made by correlation of clinical, radiologic, and pathologic findings; although the pathologic

Fig. 12-12. Cat scratch disease.

A, Woman presenting with enlarged (and tender) lymph nodes. B, Characteristic but not pathognomonic appearance of the abscess composed of a central area of necrosis with a stellate pattern admixed with polymorphonuclear leukocytes surrounded by palisading of histiocytes. C, Causative bacterium (Bartonella henselae) identified by Warthin-Starry stain appear as extracellular pleomorphic coccobacilli.
features are characteristic, they are not specific for sarcoidosis and the diagnosis of sarcoidosis can be rendered only in the absence of identifying an infectious agent.

**Differential Diagnosis**

- Noncaseating granulomatous inflammation can be seen in:
  - Tuberculosis (typical and atypical), fungal diseases, leprosy, cat scratch disease, and many other infectious diseases

**Treatment and Prognosis**

- Treatment for symptomatic sarcoidosis is with corticosteroid therapy.
- Prognosis is generally good, with up to 70% of patients improving or remaining stable following therapy.
- Advanced multisystem disease leading to extensive pulmonary involvement and respiratory failure may occur but is seen in only a small percentage of cases.

**BACTERIAL DISEASES**

**Cat Scratch Disease** (Fig. 12-13)

**Definition:** Infectious disease is caused by a pleomorphic, gram-negative bacterium, *Bartonella henselae*, resulting in lymphadenopathy.

**Clinical**

- No gender predilection; occurs in all ages
- Mode of transmission is by direct contact from a cat scratch, bite, or lick through a skin break:
  - There is no evidence to support transmission from human to human.
  - The infected cat is not ill and appears to be infectious for only a limited time.
- In the majority of cases, a history of exposure to a cat can be obtained and the primary inoculation site identified typically seen from 7 to 12 days following contact.
- Primarily occurs in immunocompetent individuals:
  - May occur as localized disease in solid organ transplant recipients
- Symptoms include enlarged and often tender lymph nodes with potential involvement of the submental, submandibular, cervical, occipital, and supraclavicular lymph nodes as well as cervical lymph nodes in the anterior and posterior triangles of the neck:
  - Obstruction and inflammation may be seen in salivary glands with involved lymph nodes.
- Constitutional symptoms include low-grade fever, malaise, myalgias, headaches, and anorexia; less common manifestations/complications include granulomatous conjunctivitis (Parinaud ocuuloglandular syndrome), thrombocytopenic purpura, encephalitis, osteomyelitis, and hepatosplenomegaly. A positive skin test can confirm the diagnosis.
- Cutaneous lesions appear as a red papule, which may become crusted or pustular.

**Pathology**

- Changes in the affected lymph node vary with time:
  - Early lesions show:
    - Follicular hyperplasia and histiocytic proliferation
  - Intermediate stage lesions show:
    - Granulomatous inflammation
  - Late lesions show:
    - Abscess formation
    - Appearance of the abscess includes a central area of necrosis with a stellate pattern and admixture of polymorphonuclear leukocytes surrounded by palisading of histiocytes; this pattern is suggestive of the diagnosis
    - Nodal sinuses are packed with monocytes
  - Skin lesions show necrotic areas within the dermis surrounded by histiocytes.
- Histochemistry:
  - Cat scratch bacilli can be identified by Warthin-Starry stain and appear as extracellular pleomorphic coccocabacilli.
- Staining and culturing for acid-fast microorganisms is negative.

**Differential Diagnosis**

- Toxoplasmosis
- Lymphogranuloma venereum

**Treatment and Prognosis**

- Treatment is supportive and includes analgesics and warm compresses.
- Self-limiting disease that typically runs its course within a few months
- In cases with suppuration, needle aspiration may relieve pain; incision and drainage may produce sinus tract inflammation.
- Antibiotic therapy appears to be of little benefit.

**Bacillary Angiomaticosis (BA)** (Fig. 12-14)

**Definition:** Pseudoneoplastic capillary proliferative lesion that occurs as a complication of HIV infection and usually presents as a cutaneous vascular lesion and is caused by an opportunistic bacterial infection
The Neck

of multiple erythematous papules with or without crusting.

• May involve other organs sites including lymph nodes, spleen, and liver, as well as mucosal sites of the upper respiratory tract and conjunctiva
• Occurs most often in immunocompromised patients but may occur in patients with intact immune system
  ○ May occur in association with Kaposi sarcoma
  ○ May occur in solid organ transplant recipients (adults and pediatric patients)
• Laboratory diagnosis:
  ○ Serologic demonstration of antibodies by direct immunofluorescence and enzyme immunoassay

Fig. 12-13. Sarcoidosis.
A, Oral cavity (soft palate) sarcoidosis appearing as multiple, irregular nodules with a cobblestone appearance. B through D, Histologic picture of sarcoidosis irrespective of location includes multiple well-formed, noncaseating granulomas consisting of nodules of epithelioid histiocytes surrounded by a mixed inflammatory infiltrate; Langhans-type giant cells are seen in some of the nodules. A diagnosis of sarcoidosis is suggested/established following exclusion of a possible infectious cause, to this end, special stains for microorganisms are negative.

Synonyms: Epithelioid angiomatosis; epithelioid hemangiomata-like vascular proliferation

of multiple erythematous papules with or without crusting.

• May involve other organs sites including lymph nodes, spleen, and liver, as well as mucosal sites of the upper respiratory tract and conjunctiva
• Occurs most often in immunocompromised patients but may occur in patients with intact immune system
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CHAPTER 12 Non-Neoplastic Lesions of the Neck

Small capillaries are arranged around ectatic vessels, which are lined by prominent appearing endothelial cells; fibrotic stroma is seen separating the lobular proliferation. Scattered neutrophils and neutrophilic debris can be seen adjacent to the capillary proliferation. Cytologic atypia, mitotic figures, and necrosis are not usually present but occasionally may be seen. Solid areas may be present and may obscure the vascular proliferation.

A variable edematous, mucinous, or fibrotic stroma is seen separating the lobular proliferation.

An important histologic feature in BA is the presence of neutrophils and neutrophilic debris adjacent to the capillary proliferation, associated with the neutrophils are granular clumps.

BA typically lacks spindled cells, interconnecting vascular channels, or hyaline globules.

Overlying epithelium may be ulcerated, thinned, or show pseudoepitheliomatous hyperplasia.

Proteomic analysis with identification of immunoreactive antigens found to be useful for an improved Bartonella-specific serodiagnosis.

Pathology

Gross

Varies widely from cutaneous erythematous papules to mushroom-shaped papules and nodules to deep seated rounded lesions without change in skin color.

Exceptionally, may appear as a mucosal-based, erythematous nodular proliferation.

Histology

Regardless of its clinical presentation, the histologic features are the same and include a well-circumscribed lobular capillary proliferation with overall features similar to those seen in lobular capillary hemangioma.

Small capillaries are arranged around ectatic vessels, which are lined by prominent appearing endothelial cells.

Cytologic atypia, mitotic figures, and necrosis are not usually present but occasionally may be seen.

Solid areas may be present and may obscure the vascular proliferation.

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Fig. 12-14. Bacillary angiomatosis.

A, Lymph node replacement by well-circumscribed lobular proliferations. B, Small capillaries are arranged around ectatic vessels, which are lined by prominent appearing endothelial cells; fibrotic stroma is seen separating the lobular proliferation. Scattered neutrophils and neutrophilic debris can be seen adjacent to the capillary proliferation. C, Left, Vascular proliferation with prominent endothelial cells and scattered neutrophils associated with granular-appearing areas; right, Warthin-Starry staining shows the granular material to contain bacteria; bacteria are interstitially located.
Treatment and Prognosis

• Treatment for BA is directed at the causative microorganism: Full-dose erythromycin is effective, often resulting in the resolution of the lesions.
• If left untreated, BA is progressive and potentially life threatening.

Fungal, Viral, and Protozoal Diseases

• Fungal, viral, and protozoal diseases of the cervical neck are rare.
• HPV-associated and EBV-associated carcinomas originating from the oropharynx (tonsil, base of tongue) and nasopharynx, respectively, may metastasize to cervical neck lymph nodes (see Section 3, The Pharynx, and Chapter 13 for more complete discussion of these cancer types).

Further Reading

References may be accessed online at ExpertConsult.
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FURTHER READING

Branchial Cleft Anomalies


First Branchial Anomalies


Second Branchial Anomalies


Third Branchial Anomalies


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Fourth Branchial Anomalies


Thyroglossal Duct Cyst

p3390 See Section 8 for references.

Cervical Thythic Cyst


Bromchogenic Cysts


Dermond Cyst


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Mycobacterial Infections, Including Scrofula


Mycobacterial Spindle Cell Pseudotumor


Cervicofacial Actinomycosis


Sarcoidosis


Cat Scratch Disease and Bacillary Angiomatosis


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# Codes Change List

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