Surgical Anatomy of the Thyroid and Parathyroid Glands

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EMBRYOLOGY OF THE THYROID GLAND

During the fourth week of development, the foramen cecum develops as an endodermal thickening in the floor of the primitive pharynx at the junction between the first and second pharyngeal pouches, immediately dorsal to the aortic sac. The medial thyroid primordium derives as a ventral diverticulum at the foramen cecum. During the fourth to seventh week of gestation, this primitive thyroid tissue penetrates the underlying mesenchymal tissue and descends anterior to the hyoid bone and the laryngeal cartilages to reach its final adult pretracheal position. During its descent, it is first spherical, and then enlarges and becomes bilobed as it grows caudally. The proximal portion of the diverticulum (connecting the gland and the foramen cecum) retracts and forms a solid fibrous stalk early in the fifth week. This thyroglossal duct ultimately atrophies, but any portion of it may persist to become the site of a thyroglossal duct cyst. The distal portion of this duct gives rise to the pyramidal lobe and levator superioris thyroideae in adults.1 The lateral thyroid primordia (from the fourth and fifth pharyngeal pouches) descend to join the central component during the fifth week of gestation.

Calcitonin-secreting parafollicular C cells arise within the ultimobranchial bodies (recognized within the lateral thyroid primordia) from neural crest cells of the fourth pharyngeal pouch. They fuse to the medial thyroid anlage during the fifth week of gestation. These cells are therefore restricted to a zone deep within the middle to upper third of the lateral lobes.

The thyroid primordium initially consists of a solid mass of endodermal cells, which later break up into a network of cords with the invasion of the surrounding mesenchyme.2 The epithelial cords organize into clusters of cells with a central lumen.
Follicles begin to appear at the beginning of the second month, and most follicles have been formed by the end of the fourth prenatal month.1 Thereafter, additional growth is by enlargement of existing follicles. By the end of the third month the gland begins to function, and is able to concentrate radioiodine and synthesize iodothyronines.3

**Thyroid Ectopia**

During the course of its development, the gland (or parts of it) may fail to reach its definitive adult position. Ectopic thyroid tissue can be found at any level along the pathway of its embryological descent. The entire gland may ascend with embryonic growth and lie close to its point of origin at the foramen cecum, giving rise to a lingual thyroid. Lingual thyroid masses have been found in as many as 10% of autopsies, although not all are clinically relevant.2 Alternatively, the tissue may be sublingual or prelaryngeal in location, and often may be mistaken for a thyroglossal duct cyst. It is essential to determine the presence or absence of functional thyroid tissue at this ectopic location before removal. About 70% of patients with lingual thyroid glands have no thyroid tissue in the neck.3,4 In many cases the lingual thyroid does not function normally.4

In some patients the thyroid gland may be in its normal anatomic location but accessory ectopic tissue may also be present. Although this tissue may be functional, it is often of insufficient size to maintain normal function if the main gland is removed. Nodules of thyroid tissue found within lymph nodes were initially believed to be ectopic foci, but now all such deposits are regarded as metastatic. Agenesis of the thyroid gland is a rare anomaly. When hemiagenesis occurs, the left lobe is more commonly absent.2

**EMBRYOLOGY OF THE RECURRENT LARYNGEAL NERVE**

The recurrent laryngeal nerve is originally associated with the sixth branchial arch. It supplies the region of the future larynx that lies caudal to the fifth pharyngeal pouch. The primordium of the vagus nerve is appreciated by the end of the fifth week, whereas the recurrent branch is apparent by the end of the sixth week. Initially, all of the aortic arches are cranial to the larynx, and so the recurrent nerve passes directly to the larynx.1 As the pharyngeal pouches disappear and the neck elongates, the aortic arch and associated system of vessels remain in the thorax, whereas the larynx moves cranially in the neck. As a result, the recurrent nerve located lateral to the arches must pass medially under the last arch to reach the larynx. This pathway creates a looplike configuration for which the nerve is named. On the left, the sixth arch persists until birth as the ductus arteriosus, and then regresses to form the ligamentum arteriosum. The recurrent laryngeal nerve must pass under it and reascend to reach the larynx.1 On the right, because the distal part of the sixth aortic arch degenerates, the right nerve is able to ascend as high as the right subclavian artery (part of the right fourth aortic arch). The recurrent nerves therefore become asymmetric.

The course of the recurrent nerves is determined largely by the pattern of the developing arteries. The most frequent variation occurs when the right subclavian artery arises from the distal aortic arch and passes to the right, posterior to the esophagus.1 The right recurrent nerve now arises from the vagus nerve at the level of the superior pole of the thyroid gland, and enters the larynx directly without forming a recurrent loop. This nonrecurrent nerve is present in about 0.5% to 1% of the population.1,5 The main danger to the nonrecurrent nerve is in mistaking it for the inferior thyroid artery during thyroidectomy, or in including it in ligation of the superior pole.

Another variation involves a reversal of the asymmetry between the two recurrent laryngeal nerves. This reversal occurs when a right-sided aortic arch is present, with
a right ligamentum arteriosum, causing the right recurrent nerve to loop around the right-sided arch, whereas the left nerveloops around the left subclavian artery. Rarely, a nonrecurrent left nerve may be present in these patients, if the left subclavian artery is retroesophageal.

ANATOMY OF THE THYROID GLAND

The thyroid gland derives its name from its resemblance to a shield (Greek: thyreos, shield; eidos, form). The thyroid gland weighs between 15 and 25 g in adults, and comprises 2 lateral lobes connected by a central isthmus. Each lobe is approximately 4 cm in length, 2 cm in width, and 2 to 3 cm in thickness. The isthmus measures about 2 cm in width, 2 cm in height, and 2 to 6 mm in thickness. The gland lies on the anterolateral aspect of the cervical trachea, with the isthmus related to the second, third, and fourth tracheal rings posteriorly. The superior pole lies lateral to the inferior constrictor muscle, and posterior to the sternothyroid muscle. The inferior pole extends to the levels of the fifth or sixth tracheal ring. Posterolaterally the gland overlaps the carotid sheath and its contents. A pyramidal lobe may be present in about 50% of patients, arising from either lobe or the isthmus, and is directed upward, usually to the left. If present, the levator glandulae thyroideae extends from the isthmus or lateral lobe to the hyoid bone or thyroid cartilage. It may be innervated by a branch of the ansa cervicalis or the superior laryngeal nerve.

The thyroid is enveloped by the layers of the deep cervical fascia, and is covered by the strap muscles anteriorly and the sternocleidomastoid muscle more laterally. The true thyroid capsule is tightly adherent to the gland, and continues into the parenchyma to form fibrous septae separating the gland into lobules. Posteriorly, the middle layer of the deep cervical fascia condenses to form the posterior suspensory ligament of Berry, connecting the lobes of the thyroid to the cricoid cartilage and the first two tracheal rings.

The blood supply to the thyroid gland is derived from two pairs of arteries. The superior thyroid artery which is described as the first branch of the external carotid artery, travels along the inferior constrictor muscle with the superior thyroid vein to supply the upper pole of the gland. In this position, the artery lies superficial to the external branch of the superior laryngeal nerve as it courses to supply the cricothyroid muscle. In 16% of cases, the superior thyroid artery may be a branch of the common carotid artery. After passing deep to the infrahyoid strap muscles, the artery divides into anterior and posterior branches at the level of the superior pole to supply their respective surfaces of the lobe. Before branching at the superior pole, each artery gives off a superior laryngeal artery which travels across the thyrohyoid membrane with the superior laryngeal nerve to enter the larynx, and a cricothyroid artery which lies on the cricothyroid membrane near the lower border of the thyroid cartilage. The larger inferior thyroid artery is a branch of the thyrocervical trunk that arises from the subclavian artery. It courses along the anterior scalene muscle, turns medially behind the common carotid artery to descend on the posterior aspect of the lateral lobes before entering the inferior thyroid pole. In its course behind the common carotid artery, the artery exhibits a variable relationship to the sympathetic chain. This vessel may be absent in 6% of patients.

The thyroid ima artery is inconsistently present, and arises from the innominate artery, either subclavian artery, right common carotid artery, internal mammary, or aortic arch to supply the thyroid gland near the midline. It may occasionally replace the inferior thyroid artery as one of the principle vessels supplying the gland. It is more common on the right side. Because of its relation to the anterior aspect of the trachea, the thyroid ima artery is in danger of injury during a tracheotomy.
There is a dense network of connecting vessels within the thyroid capsule, with branches passing into the connective tissue between the lobules to form extensive capillary plexuses around individual follicles. The veins draining the capillary plexuses give rise to the inferior, middle, and superior thyroid veins. These join the internal jugular or innominate veins. The paired inferior thyroid veins lie on the anterior aspect of the trachea and anastomose freely with each other before draining into the innominate veins. They represent a potential source of bleeding during thyroidectomy or tracheotomy.4

The lymphatics of the gland generally drain with the veins. Those traveling with the superior and middle thyroid vessels drain into the upper and middle deep cervical chain nodes respectively. Lymphatics draining with the inferior thyroid vessels empty into the lower deep cervical chain nodes and the supraclavicular, pretracheal, and prelaryngeal nodes. In addition, lymphatics have been identified that drain directly into the subclavian vein without traveling through lymph nodes.3

The thyroid gland has a predominantly sympathetic innervation, from the superior, middle, and inferior cervical ganglia.

**ANATOMY OF THE RECURRENT LARYNGEAL NERVE**

As described earlier, the recurrent laryngeal nerves are asymmetric. The nerve on the left arises from the vagus where it crosses the arch of aorta. The recurrent nerve then loops around the aorta to ascend in the tracheoesophageal groove posterior to the thyroid gland on that side to enter the larynx. The right recurrent laryngeal nerve arises from the vagus as this nerve crosses anterior to the right subclavian artery. The recurrent nerve then loops around the artery and ascends in the tracheoesophageal groove, posterior to the thyroid gland, to enter the larynx behind the cricothyroid articulation and the inferior cornu of the thyroid cartilage.8

As the nerve ascends, it is covered by a layer of fascia that also encloses the trachea and the inferior thyroid vein. The left recurrent nerve is generally more closely applied to the trachea in the lower part of its ascending course than is the right nerve. At the level of the lower pole of the thyroid gland, the right nerve is slightly more anterior than the left.8,9 The connective tissue surrounding the nerve is usually thicker on the right.8 The nerve runs at a slight angle across the tracheoesophageal groove and then becomes parallel and closely applied to the trachea. During the middle part of its course, the nerve is found within the tracheoesophageal groove in about half of the population.8 In the other half of patients it may be found anterior or posterior to the groove (within the suspensory ligament of Berry, anterolateral to the trachea in the substance of the thyroid gland, or lateral to the esophagus).

As the recurrent laryngeal nerves ascend toward the middle of the thyroid gland, they are intimately associated with the inferior thyroid artery. Multiple variations have been described in the relationship of the nerve to the inferior thyroid artery and its branches. The 3 basic configurations include nerve anterior to the artery, nerve between branches of the artery (found in about 50% of patients on the right), and nerve posterior to the artery (found in about 50% of patients on the left).4,8,9

The recurrent laryngeal nerve may divide before entering the larynx. It is believed that only one of these branches is motor, and the others are sensory. It innervates all the intrinsic muscles of the larynx except the cricothyroid, and provides sensory innervation to the subglottic area and proximal trachea. An ascending branch of the recurrent laryngeal anastomoses with a branch of the superior laryngeal to form the Galen anastomosis. Branches from this anastomosis pierce the transverse arytenoid muscle to reach the mucosa of the posterior laryngeal wall.10,11
Classically, the recurrent laryngeal nerve is found intraoperatively in the Simon triangle, formed by the common carotid artery laterally, the esophagus medially, and the inferior thyroid artery superiorly. The nerve can also be reliably found where it enters the larynx just behind the inferior cornu of the thyroid cartilage.

**ANATOMY OF THE SUPERIOR LARYNGEAL NERVE**

The superior laryngeal nerve originates at the inferior ganglion of the vagus nerve (nodose ganglion) near the jugular foramen. It courses posterior and medial to the internal carotid artery and descends anterior and inferior toward the larynx. At the level of the greater cornu of the hyoid it divides into a large internal branch and a smaller external branch. The internal branch courses between the thyrohyoid muscle and the thyrohyoid membrane, piercing the latter along with the superior laryngeal artery and vein. The internal branch supplies sensation to the supraglottis and pyriform sinus.\(^\text{12}\)

At the level of the superior horn of the thyroid cartilage, the external branch turns medially and runs posterior and parallel to the oblique line. It can penetrate the inferior constrictor and run along its deep surface at any point along this course, or remain on its surface.\(^\text{13}\)

The external branch is typically deep to the superior thyroid artery, but can cross anterior or between branches as the artery enters the gland 14% to 18% of the time.\(^\text{14}\) The nerve is variable in its relationship to the highest point of the superior pole of the thyroid gland. A classification of the external branch with respect to the superior pole, described by Cernea and colleagues,\(^\text{15}\) places 37% of external branches at risk of injury during thyroid surgery, passing below the level of the upper pole of the thyroid gland or within 1 cm above it.

The external branch of the superior laryngeal nerve supplies motor input to the inferior constrictor and the cricothyroid muscles.\(^\text{12}\) Iatrogenic injury is possible during thyroid, parathyroid, carotid, or cervical spine surgery.\(^\text{16}\) The reported incidence of superior laryngeal nerve injury after thyroidectomy ranges from 0% to 58%, and is most likely underdiagnosed.\(^\text{17}\) Injury typically presents with symptoms of hoarseness, huskiness, decreased pitch or volume, and early voice fatigue. The consequences are significantly worse in the setting of bilateral injury.\(^\text{18}\) Video stroboscopy of unilateral injury reveals posterior glottic rotation to the affected side, vocal cord bowing, and decreased mucosal wave with inferior displacement of the ipsilateral vocal cord.\(^\text{19}\) Laryngeal electromyography is the gold standard evaluation of injury to the external branch of the superior laryngeal nerve, as shown by an absence of interference patterns with high-pitched vocalization and electrical silence.\(^\text{17}\)

Prevention of injury to the external branch of the superior laryngeal nerve has historically been underemphasized in thyroid and parathyroid surgery. Steps to maximize identification and preservation of the nerve are division of the sternothyroid muscle, careful dissection in the cricothyroid space that lies between the medial surface of the thyroid lobe and the cricothyroid muscle, and meticulous isolation and division of superior thyroid vessels.\(^\text{16}\)

**EMBRYOLOGY AND ANATOMY OF THE PARATHYROID GLANDS**

The parathyroid glands derive from the endoderm of the third and fourth pharyngeal pouches, starting in the fifth week of development.\(^\text{20}\) Their function is the production of parathyroid hormone, which regulates the distribution of calcium in the bloodstream and bone. Typically, paired superior and inferior glands develop for a total of four, although up to 13% incidence of supernumerary glands has been described, up to
11 glands in large autopsy series. Each gland typically weighs 35 to 40 mg, measures 3 to 8 mm in all 3 dimensions, and can vary in color from light yellow to reddish brown.

The inferior parathyroid glands arise from the third pharyngeal pouch endoderm and have a common origin and migration with the thymus. Starting at the region of the pharyngeal wall, they migrate inferior and medially in the neck, eventually separating from thymus tissue before it enters the anterior mediastinum. This long course of descent can lead to a large area of possible ectopic inferior parathyroid glands that can be found anywhere from the level of the mandibular angle to the pericardium. The most common ectopic location for an inferior gland is in the anterior mediastinum; this is found in 5% of ectopic cases.

The inferior parathyroid gland can be found within 1 cm inferior, lateral, or posterior to the inferior pole of the thyroid in 50% of cases, and is typically anterior to a plane drawn along the course of the recurrent laryngeal nerve. In an autopsy series of 503 cases, 17% could be found on or within the capsule of the thyroid gland, whereas 26% could be found within the cervical part of the thymus. Rarely (2.8%), the inferior gland was found superior to the intersection of the recurrent nerve and the inferior thyroid artery. Two-thirds of supernumerary cases in this series revealed the fifth gland inferior to the lower pole of the thyroid associated with the thyrothymic ligament or the thymus, whereas one third had the supernumerary gland in the vicinity of the thyroid between the orthotopic superior and inferior parathyroids.

The fourth pharyngeal pouch gives rise to the superior parathyroid glands, which have a much shorter embryologic descent than their inferior counterparts. After losing contact with the pharynx in the sixth week of development, it attaches to the caudally migrating thyroid, and remains in contact with the posterior midportion of the thyroid lobe. This limited course leads to a smaller variability in location compared with the inferior gland, and in 85% of cases the superior parathyroid can be found at the posterior aspect of the thyroid lobe in a 2-cm diameter area centered 1 cm above the crossing of the inferior thyroid artery and the recurrent nerve. In the large autopsy series mentioned earlier, 2% of ectopic superior thyroid glands were found at the level of the superior pole of the thyroid, and less than 1% were superior to it.

Because the embryologic descent of the inferior parathyroid crosses that of the superior gland, they can rarely be found at the same level, above or below the crossing of the inferior thyroid artery and recurrent laryngeal nerve. In this instance, it may not be possible to differentiate the superior and inferior glands. Symmetry in the approximate location of the glands when comparing right with left has been reported at 80% for the superior and 70% for the inferior glands. Thus, when unable to locate a missing parathyroid, contralateral dissection for comparison may be useful. Given their variable topography in the neck, keeping the embryology of the parathyroid glands in mind is critical when planning parathyroid surgery.

REFERENCES