

# Tongue Development

Embryology (/embryology/index.php/Main\_Page) - 17 Jan 2019



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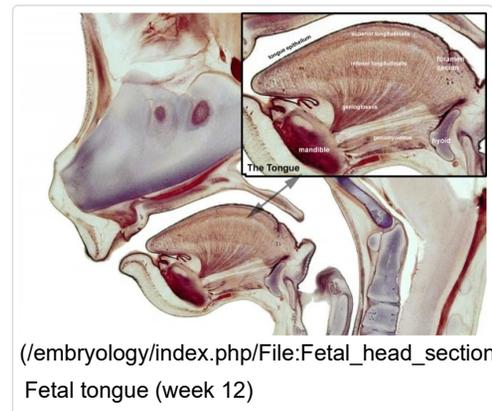
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## Introduction

The **tongue's** embryonic origin is derived from all pharyngeal arches contributing different components. As the tongue (Latin, *lingua*; Greek, *glossa*) develops "inside" the floor of the oral cavity, it is not readily visible in the external views of the embryonic (Carnegie) stages of development. Tongue muscle cells originate from somites (/embryology/index.php/Somitogenesis) mesoderm, while muscles of mastication derive from the unsegmented somitomeres. This current page gives a brief overview of early tongue development.

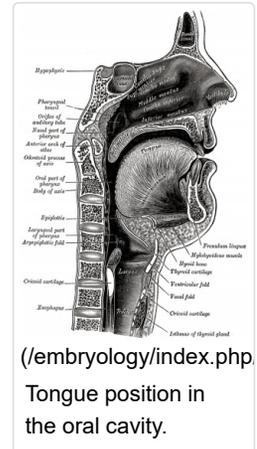
The dorsal tongue is covered by a stratified squamous epithelium, with numerous papillae and taste (/embryology/index.php/Sensory\_-\_Taste\_Development) buds. There are also 8 to 12 circumvallate papillae arranged in an inverted V-shape towards the base of the tongue. These notes cover development of the muscular tongue, not the sense of taste (/embryology/index.php/Sensory\_-\_Taste\_Development).

**Taste Links** (/embryology/index.php/Sensory\_-\_Taste\_Development): Introduction (/embryology/index.php/Sensory\_-\_Taste\_Development) | Student project (/embryology/index.php/2012\_Group\_Project\_3) | **Tongue Development** | Category:Taste (/embryology/index.php/Category:Taste) gastrointestinal tract (/embryology/index.php/Gastrointestinal\_Tract\_Development) | head (/embryology/index.php/Head\_Development) | Category:Tongue (/embryology/index.php/Category:Tongue)



(/embryology/index.php/File:Fetal\_head\_section)  
Fetal tongue (week 12)

## Some Recent Findings



- **SOX2 regulation by hedgehog signaling controls adult lingual epithelium homeostasis**<sup>[1]</sup> "Adult tongue epithelium is continuously renewed from epithelial progenitor cells, a process that requires hedgehog (HH) signaling. In mice, pharmacological inhibition of the HH pathway causes taste bud loss within a few weeks. Previously, we demonstrated that sonic hedgehog (SHH ([/embryology/index.php/Developmental\\_Signals\\_-\\_Sonic\\_hedgehog](/embryology/index.php/Developmental_Signals_-_Sonic_hedgehog))) over-expression in lingual progenitors induces ectopic taste buds with locally increased SOX2 expression, suggesting that taste bud differentiation depends on SOX2 downstream of HH. To test this, we inhibited HH signaling in mice and observed a rapid decline in Sox2 and SOX2-GFP expression in taste epithelium. Upon conditional deletion of Sox2, differentiation of both taste and non-taste epithelial cells was blocked, and progenitor cell number increased. In contrast to basally restricted proliferation in controls, dividing cells were overabundant and spread to supra-basal epithelial layers in mutants. SOX2 loss in progenitors also led non-cell-autonomously to taste cell apoptosis, dramatically shortening taste cell lifespans. Finally, in tongues with conditional Sox2 deletion and SHH over-expression, ectopic and endogenous taste buds were not detectable; instead, progenitor hyperproliferation expanded throughout the lingual epithelium. In summary, we show that SOX2 functions downstream of HH signaling to regulate lingual epithelium homeostasis." SOX ([/embryology/index.php/Developmental\\_Signals\\_-\\_Sox](/embryology/index.php/Developmental_Signals_-_Sox))
- **Review - How to make a tongue: Cellular and molecular regulation of muscle and connective tissue formation during mammalian tongue development**<sup>[2]</sup> The vertebrate tongue is a complex muscular organ situated in the oral cavity and involved in multiple functions including mastication, taste sensation, articulation and the maintenance of oral health. Although the gross embryological contributions to tongue formation have been known for many years, it is only relatively recently that the molecular pathways regulating these processes have begun to be discovered. In particular, there is now evidence that the Hedgehog, TGF-beta ([/embryology/index.php/Developmental\\_Signals\\_-\\_TGF-beta](/embryology/index.php/Developmental_Signals_-_TGF-beta)), WNT ([/embryology/index.php/Developmental\\_Signals\\_-\\_Wnt](/embryology/index.php/Developmental_Signals_-_Wnt)) and Notch ([/embryology/index.php/Developmental\\_Signals\\_-\\_Notch](/embryology/index.php/Developmental_Signals_-_Notch)) signaling pathways all play an important role in mediating appropriate signaling interactions between the epithelial, cranial neural crest and mesodermal cell populations that are required to form the tongue. In humans, a number of congenital abnormalities that affect gross morphology of the tongue have also been described, occurring in isolation or as part of a developmental syndrome, which can greatly impact on the health and well-being of affected individuals. These anomalies can range from an absence of tongue formation (aglossia) through to diminutive (microglossia), enlarged (macroglossia) or bifid tongue."
- **A Wnt ([/embryology/index.php/Developmental\\_Signals\\_-\\_Wnt](/embryology/index.php/Developmental_Signals_-_Wnt))/Notch ([/embryology/index.php/Developmental\\_Signals\\_-\\_Notch](/embryology/index.php/Developmental_Signals_-_Notch))/PAX ([/embryology/index.php/Developmental\\_Signals\\_-\\_Pax](/embryology/index.php/Developmental_Signals_-_Pax)) signaling network supports tissue integrity in tongue development**<sup>[3]</sup> "The tongue is one of the major structures involved in human food intake and speech. Tongue malformations such as aglossia, microglossia, and ankyloglossia are congenital birth defects, greatly affecting individuals' quality of life. However, the molecular basis of the tissue-tissue interactions that ensure tissue morphogenesis to form a functional tongue remains largely unknown. Here we show that ShhCre -mediated epithelial deletion of Wntless (Wls), the key regulator for intracellular Wnt trafficking, leads to lingual hypoplasia in mice. Disruption of epithelial Wnt production by Wls deletion in epithelial cells led to a failure in lingual epidermal stratification and loss of the lamina propria and the underlying superior longitudinal muscle in developing mouse tongues. These defective phenotypes resulted from a reduction in epithelial basal cells positive for the basal epidermal marker protein p63 and from impaired proliferation and differentiation in connective tissue and paired box 3 (Pax3)- and Pax7-positive muscle progenitor cells. We also found that epithelial WNT ([/embryology/index.php/Developmental\\_Signals\\_-\\_Wnt](/embryology/index.php/Developmental_Signals_-_Wnt)) production is required for activation of the Notch signaling pathway, which promotes proliferation of myogenic progenitor cells. Notch signaling in turn negatively regulated Wnt signaling during tongue morphogenesis. We further show that Pax7 is a direct Notch target gene in the embryonic tongue."
- **Noncanonical transforming growth factor  $\beta$  (TGF-beta) ([/embryology/index.php/Developmental\\_Signals\\_-\\_TGF-beta](/embryology/index.php/Developmental_Signals_-_TGF-beta)) signaling in cranial neural crest ([/embryology/index.php/Neural\\_Crest\\_Development](/embryology/index.php/Neural_Crest_Development)) cells causes tongue muscle developmental defects**<sup>[4]</sup> "Microglossia is a congenital birth defect in humans and adversely impacts quality of life. In vertebrates, tongue muscle derives from the cranial mesoderm, whereas tendons and connective tissues in the craniofacial region originate from cranial neural crest (CNC) cells....Thus, our data indicate that CNC-derived fibroblasts regulate the fate of mesoderm-derived myoblasts through TGF $\beta$ -mediated regulation of FGF and BMP signaling during tongue development."



(/embryology/index.php/File:Mark\_Hill.jpg)

This table allows an automated computer search of the external PubMed (http://www.ncbi.nlm.nih.gov/pubmed) database using the listed "Search term" text link.



- This search now requires a manual link as the original PubMed extension has been disabled.
- The displayed list of references **do not reflect any editorial selection of material based on content or relevance.**
- References also appear on this list based upon the date of the actual page viewing.

References listed on the rest of the content page and the associated discussion page (listed under the publication year sub-headings) do include some editorial selection based upon both relevance and availability. {More? References | Discussion Page (/embryology/index.php/Talk:Tongue\_Development) | Journal Searches (/embryology/index.php/Template:Journal\_Searches)}

Search term: *Tongue Embryology* (http://www.ncbi.nlm.nih.gov/pubmed/?term=Tongue+Embryology)

<pubmed limit=5>Tongue Embryology</pubmed>

#### Older papers

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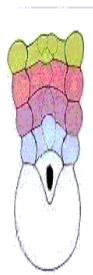
- **Mice with TGFβ activated kinase 1 (Tak1) deficiency in neural crest lineage exhibit cleft palate associated with abnormal tongue development**<sup>[5]</sup> "The repressive effect of the Tak1-mediated noncanonical TGFβ signaling on Fgf10 expression was further confirmed by inhibition of p38, a downstream kinase of Tak1, in the primary cell culture of developing tongue. Tak1 thus functions to regulate tongue development by controlling Fgf10 expression and could represent a candidate gene for mutation in human PRS clefting." FGF (/embryology/index.php/Developmental\_Signals\_-\_Fibroblast\_Growth\_Factor)
- **Bone morphogenetic protein-2 (BMP (/embryology/index.php/Developmental\_Signals\_-\_Bone\_Morphogenetic\_Protein)2) functions as a negative regulator in the differentiation of myoblasts, but not as an inducer for the formations of cartilage and bone in mouse embryonic tongue**<sup>[6]</sup> "In vitro studies using the myogenic cell line C2C12 demonstrate that bone morphogenetic protein-2 (BMP-2) converts the developmental pathway of C2C12 from a myogenic cell lineage to an osteoblastic cell lineage. Further, in vivo studies using null mutation mice demonstrate that BMPs inhibit the specification of the developmental fate of myogenic progenitor cells. ...BMP-2 functions as a negative regulator for the final differentiation of tongue myoblasts, but not as an inducer for the formation of cartilage and bone in cultured tongue, probably because the genes related to myogenesis are in an activation mode, while the genes related to chondrogenesis and osteogenesis are in a silencing mode."
- **Shh and ROCK1 modulate the dynamic epithelial morphogenesis in circumvallate papilla development**<sup>[7]</sup> "In rodents, a circumvallate papilla (CVP) develops with dynamic changes in epithelial morphogenesis during early tongue development. Molecular and cellular studies of CVP development revealed that there would be two different mechanisms in the apex and the trench wall forming regions with specific expression patterns of Wnt11 and Shh. ...Wnt, a well known key molecule to initiate taste papillae, would govern Rho activation and cytoskeleton formation in the apex epithelium of CVP. In contrast, Shh regulates the cell proliferation to differentiate taste buds and to invaginate the epithelium for development of von Ebner's gland (VEG)."

## Pharyngeal Arch Contributions

The tongue has contributions from all pharyngeal arches which changes with time. The tongue initially begins as swelling rostral to foramen cecum, the median tongue bud.

Animation shows the sequence of development of the tongue. The different colours represents the relative contribution from each pharyngeal arch.

- Arch 1 - oral part of tongue (anterior 3/2)
- Arch 2 - initial contribution to surface is lost
- Arch 3 - pharyngeal part of tongue (posterior 1/3)
- Arch 4 - epiglottis and adjacent regions



UNSW Embryology

(/embryology/index.php/Tongue\_Development\_Movie)

**Tongue**

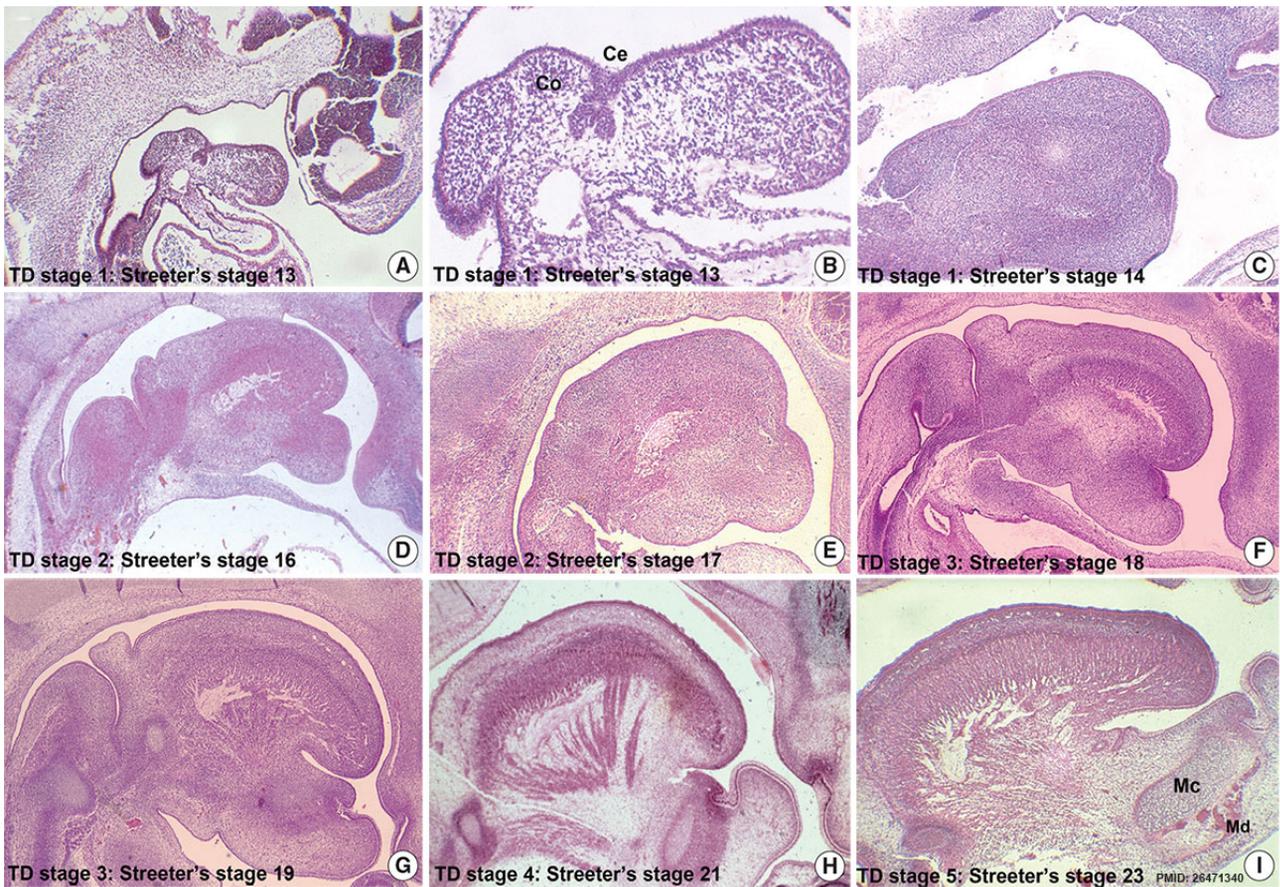
Page

(/embryology/index.php/Tongue\_Development\_Movie)

| Play (/embryology/images/5/57/Tongue\_001.mp4)

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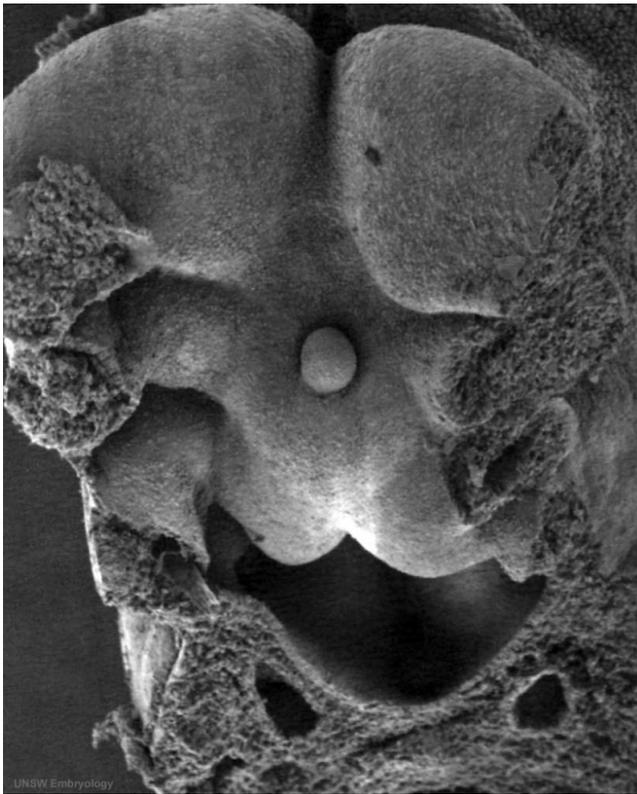
## Embryonic



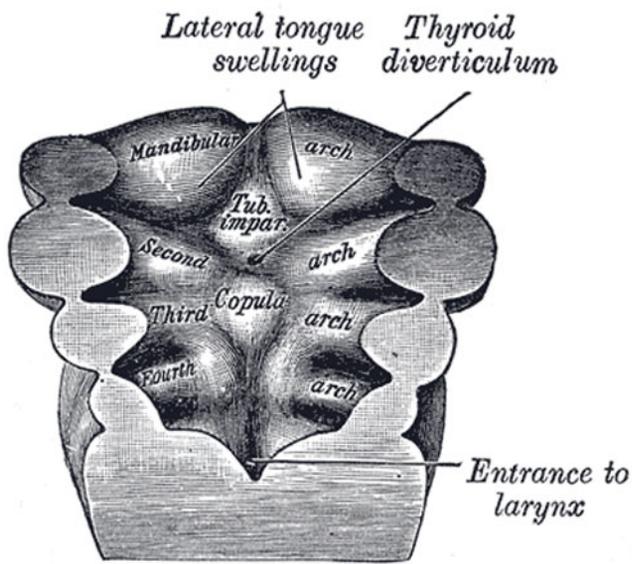
(/embryology/index.php/File:Human\_embryonic\_tongue\_01.jpg)

Human embryonic tongue development (mid-sagittal section)<sup>[8]</sup>

## Week 4



(/embryology/index.php/File:Stage13\_sem3.jpg)

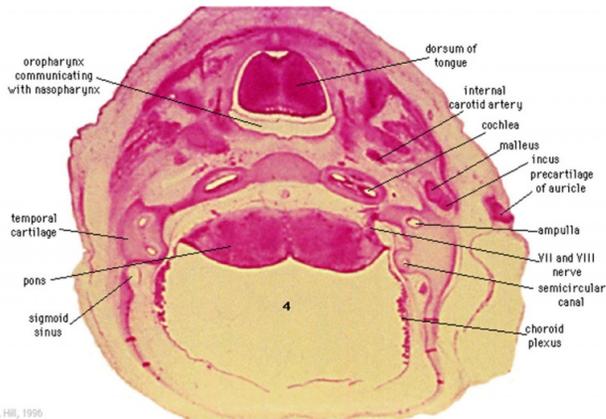


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Links: Carnegie stage 13 (/embryology/index.php/Carnegie\_stage\_13) | Week 4 (/embryology/index.php/Week\_4)

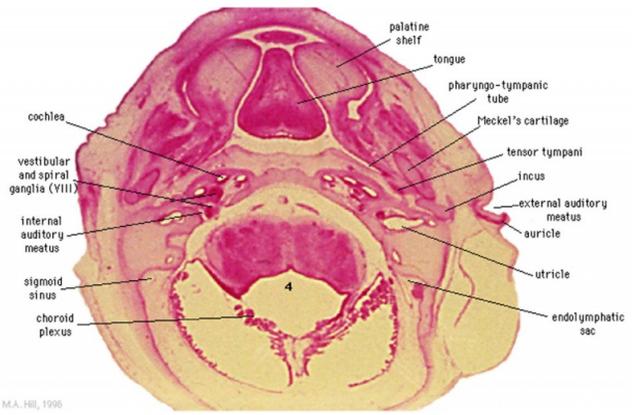
## Week 8

These histology images are from the Carnegie Stage 22 human embryo.



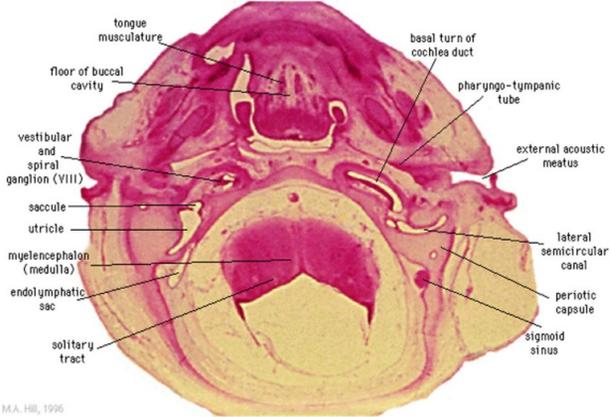
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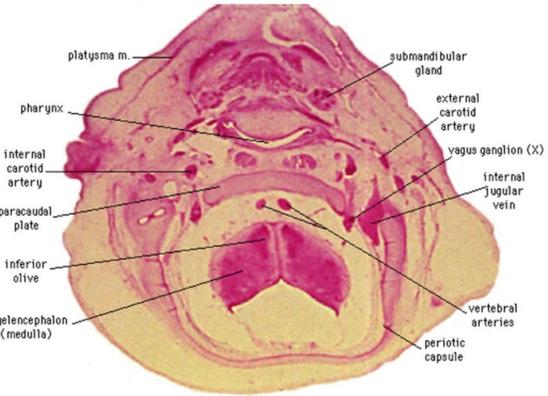
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(/embryology/index.php/File:Stage\_22\_image\_061.jpg)



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(/embryology/index.php/File:Stage\_22\_image\_062.jpg)  
Carnegie Stage 23 oral cavity floor



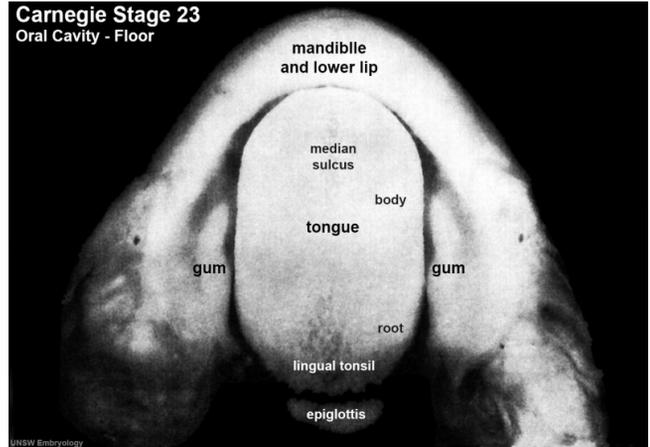
© M.A. Hill, 1996

(/embryology/index.php/File:Stage\_22\_image\_063.jpg)

**Carnegie Stage 23 oral cavity floor**



(/embryology/index.php/File:Stage23\_embryo\_oral\_cavity\_01.jpg)

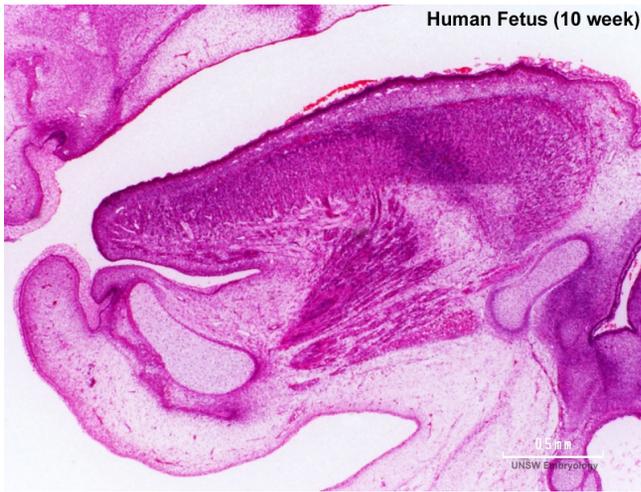


(/embryology/index.php/File:Stage23\_embryo\_oral\_cavity\_02.jpg)

**Links:** Carnegie stage 22 (/embryology/index.php/Carnegie\_stage\_22) | Carnegie stage 23 (/embryology/index.php/Carnegie\_stage\_23) | Week 8 (/embryology/index.php/Week\_8)

**Fetal**

**Week 10**



Section shows detail of the tongue muscular structure, formed from occipital somites.  
The genioglossus (fan-shaped muscle) lies between the tongue and mandible and is innervated by the hypoglossal nerve (CN12). Poking out your tongue is a test of this nerve. Note the tongue connective tissue and vasculature are derived from neural crest.

(/embryology/index.php/File:Human\_week\_10\_fetus\_04.jpg)

**Links:** Week 10 (/embryology/index.php/Fetal\_Development\_-\_10\_Weeks) | week 10 - sagittal section

(/embryology/index.php/File:Human\_week\_10\_fetus\_01.jpg)

## Week 12 - 24

The following measurements of fetal tongue circumference show linear growth during the second trimester and are based upon multiple (2-10) separate ultrasound measurements.<sup>[9]</sup>

### Fetal Tongue Circumference

Fertilisation Age (weeks)	Gestational Age (weeks)	Mean Circumference (mm)
12	14	28
13	15	33
14	16	36
15	17	37
16	18	43
17	19	48
18	20	51
19	21	55
20	22	58
21	23	62
22	24	64
23	25	70
24	26	73

Table data<sup>[9]</sup> Tongue circumference measured by transvaginal ultrasonography between 14 and 17 **GA**

(/embryology/index.php/Gestational\_Age) weeks, and by abdominal ultrasound between 18 and 26 **GA**

(/embryology/index.php/Gestational\_Age) weeks of gestation.

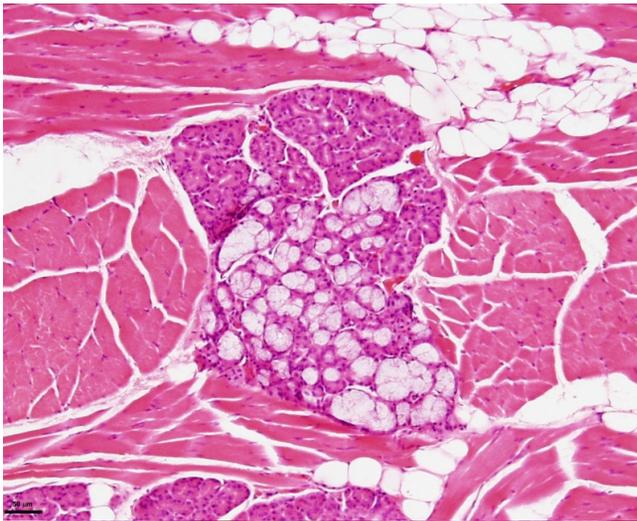
**Links:** tongue | fetal (/embryology/index.php/Fetal\_Development) | ultrasound (/embryology/index.php/Ultrasound)

## Tongue Muscles

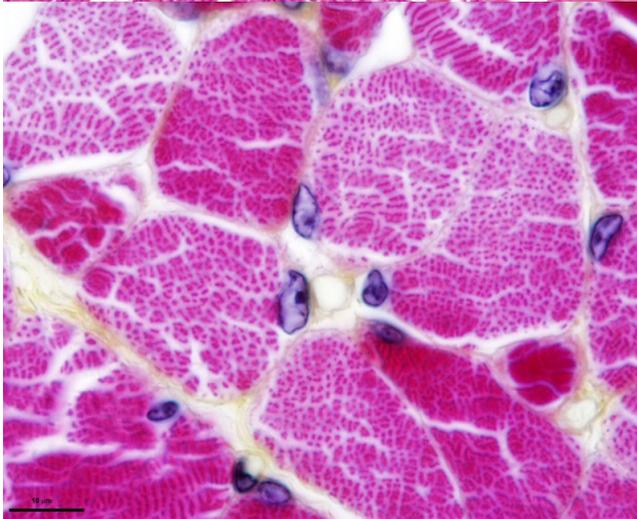
- Tongue muscles originate from the somites.
  - Masticatory muscles (MM) originate from the somitomeres. These muscles develop late and are not complete even at birth.
  - Tongue muscles develop before masticatory muscles and complete by birth.

Developing muscle fibers within the tongue. Note the multinucleated appearance of each muscle fiber and their overall organization. Muscle goes through the same developmental changes as other skeletal muscle.

See also: Embryonic and postnatal development of masticatory and tongue muscles.<sup>[10]</sup>



(/embryology/index.php/File:Skeletal\_muscle\_histology\_017.jpg)



(/embryology/index.php/File:Skeletal\_muscle\_histology\_018.jpg)

**Links:** Skeletal Muscle Histology ([/embryology/index.php/Skeletal\\_Muscle\\_Histology](/embryology/index.php/Skeletal_Muscle_Histology))

## Tongue Innervation

The tongue is innervated by a range of cranial nerve connections related to muscles, oral mucosa, taste buds, and minor salivary glands.

- trigeminal nerve (V) - lingual branch
- facial nerve (VII) - chorda tympani branch
- glossopharyngeal nerve (IX)
- hypoglossal nerve (XII) - motor components of innervated muscles.

The hypoglossal nerve (CN XII) provides the motor innervation of the intrinsic and extrinsic tongue muscles allowing protrusion, retraction, and changes in the shape of the tongue. Motor units within the hypoglossal motor system can be categorized as predominantly fast fatigue resistant.<sup>[11]</sup>

The human tongue innervation has been recently analysed histologically and described as extremely dense and complex.<sup>[12]</sup> The structure of the motor endplate junctions (neuromuscular junctions) was found to be of the multiple en grappe (grapelike cluster) form. The transverse muscle group that comprises the core of the tongue was found to have the most complex innervation. The pattern of innervation of the human tongue also has specializations not found in other mammalian tongues, this allows for fine motor control of tongue shape.

The pathway of the hypoglossal nerve can be imaged using magnetic imaging (MRI) while computer tomography (CT) can show the bony anatomy of the neurovascular foramina of the skull base. Clinically, the nerve pathway can be divided into three regions: intra-axial, cisternal, skull base and extracranial segments.<sup>[13]</sup>

**Links:** Cranial Nerve Development ([/embryology/index.php/Neural\\_-\\_Cranial\\_Nerve\\_Development](/embryology/index.php/Neural_-_Cranial_Nerve_Development))



Macroglossia associated with Beckwith-Wiedemann syndrome.

**Links:** Trisomy 21 ([/embryology/index.php/Trisomy\\_21](http://embryology/index.php/Trisomy_21)) | Medlineplus - Macroglossia (<http://www.nlm.nih.gov/medlineplus/ency/article/002250.htm>)

## Microglossia

Term means an abnormally small tongue. A recent study has identified cranial neural crest fibroblasts non-canonical transforming growth factor  $\beta$  (TGF $\beta$ ) regulation of FGF and BMP signalling can cause similar tongue muscle developmental defects.<sup>[4]</sup>

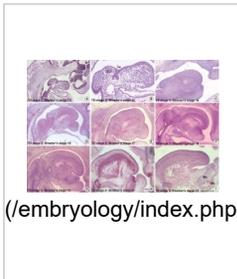
## Ankyloglossia

Ankyloglossia (tongue-tie) is the general clinical term for the short lingual frenulum (less than 2 cm), that limits the range of movement of the tongue, prevalence ranges between 4.2% and 10.7%. This is associated with speech development disorders and has been suggested as also associated with feeding disorders. There is still no accurate classification for this condition.<sup>[16]</sup> Frenotomy, frenectomy, and frenuloplasty are the main surgical treatment options to release or remove an ankyloglossia, though there is still discussion about surgical intervention.

A short lingual frenulum is also associated with a number of genetic syndromes such as: ROR2-Related Robinow Syndrome, Dystrophic Epidermolysis Bullosa, Oral-Facial-Digital Syndrome Type I, Opitz Syndrome (X-Linked Opitz G/BBB Syndrome) and Van der Woude syndrome.

**Links:** Medline Plus - Tongue tie (<http://www.nlm.nih.gov/medlineplus/ency/article/001640.htm>) | ROR2-Related Robinow Syndrome (<http://www.ncbi.nlm.nih.gov/bookshelf/br.fcgi?book=gene&part=rob>) | Dystrophic Epidermolysis Bullosa (<http://www.ncbi.nlm.nih.gov/bookshelf/br.fcgi?book=gene&part=ebd>) | Oral-Facial-Digital Syndrome Type I (<http://www.ncbi.nlm.nih.gov/bookshelf/br.fcgi?book=gene&part=ofd1>) | X-Linked Opitz G/BBB Syndrome (<http://www.ncbi.nlm.nih.gov/bookshelf/br.fcgi?book=gene&part=opitz>)

## Additional Images



embryonic

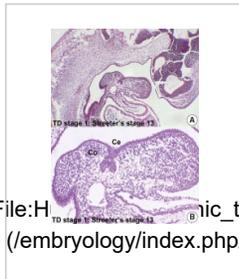


image - stage 13 (low and high)



image - stage 13 (low)

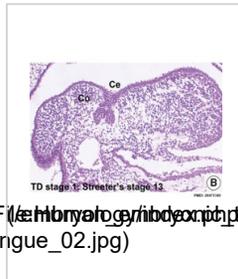


image - stage 13 (high)

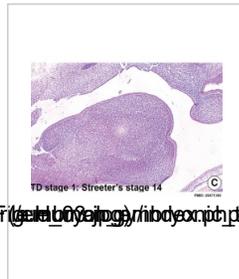


image - stage 14

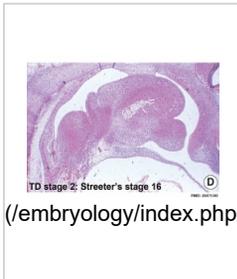


image - stage 16



image - stage 17

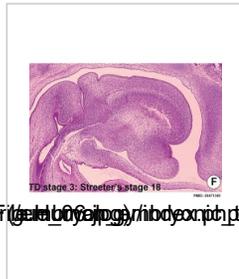


image - stage 18

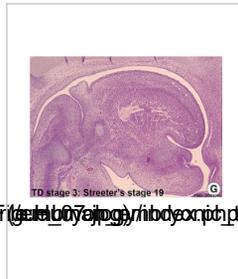


image - stage 19



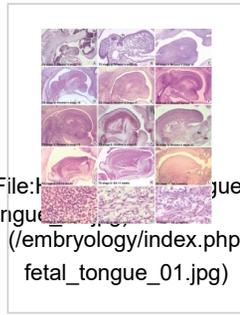
image - stage 21



image - stage 23



fetal



embryo and fetal

(/embryology/index.php/File:Human\_embryonic\_tongue\_01.jpg)

(/embryology/index.php/File:Human\_embryonic\_tongue\_01.jpg)

(/embryology/index.php/File:Human\_embryonic-fetal\_tongue\_01.jpg)

## Historic

### Historic Disclaimer - information about historic embryology pages [Expand]

Human Embryology and Morphology (/embryology/index.php/Book\_-\_Human\_Embryology\_and\_Morphology). Keith, A. (1902) London: Edward Arnold.

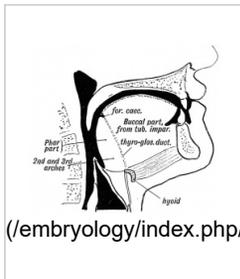


Fig. 30. Showing the Buccal and Pharyngeal parts of the Tongue

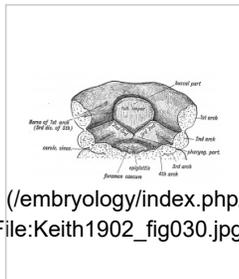


Fig. 31. Showing the origin of the tongue in the floor of the primitive pharynx.

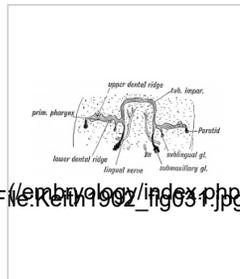


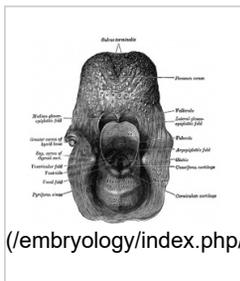
Fig. 32. Showing the origin of the Submaxillary and Sublingual Glands

(/embryology/index.php/File:Keith1902\_fig030.jpg)

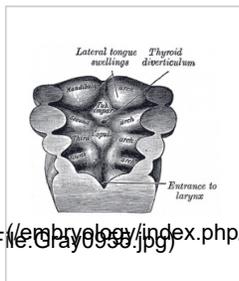
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(/embryology/index.php/File:Keith1902\_fig032.jpg)

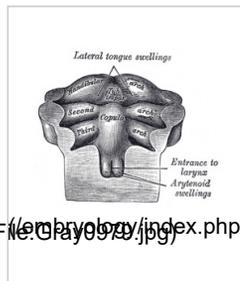
Anatomy of the Human (/embryology/index.php/Anatomy\_of\_the\_Human\_Body\_by\_Henry\_Gray) Gray, H. (1918) Philadelphia: Lea & Febiger.



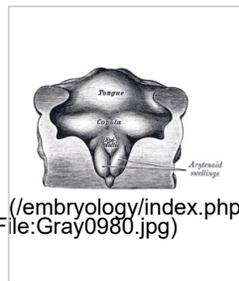
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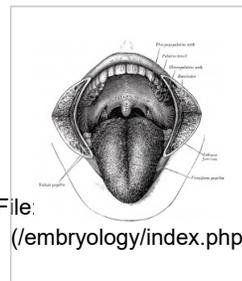
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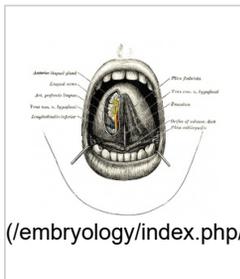
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Text-Book of Embryology (/embryology/index.php/Book\_-\_Text-Book\_of\_Embryology\_(1921)) Bailey, F.R. and Miller, A.M. (1921). New York: William Wood and Co. - Tongue Development (/embryology/index.php/Book\_-\_Text-Book\_of\_Embryology\_12#The\_Tongue)

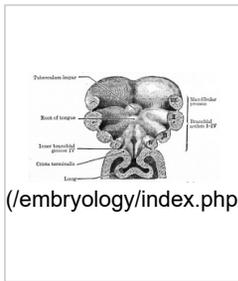


Fig. 249. Floor of the pharyngeal region of a human embryo of about 3 weeks

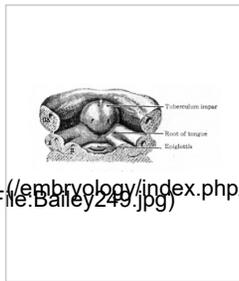


Fig. 250. Floor of pharyngeal region of a human embryo of 12.5 mm

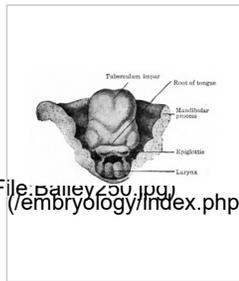


Fig. 251. Dorsal view of the tongue of a human embryo of 20 mm

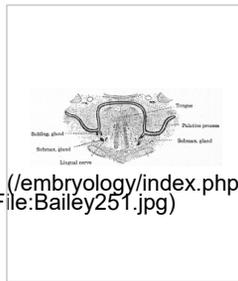


Fig. 255. From a transverse section through the tongue and oral cavity of a mouse embryo

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