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Head and Neck Embryology: An Overview of Development, Growth and Defect in the Human Fetus

Allison Baylis
University of Connecticut - Storrs, allinoel77@sbcglobal.net

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Abstract

The purpose of this research is to explore the growth and formation of the head and neck from embryological development through puberty in order to understand how this knowledge is necessary for the development of dental and medical treatments and procedures. This is a necessary aspect of the medical and dental school curriculum at the University of Connecticut Health Center Schools of Medicine and Dental Medicine that needs to be incorporated into the current study of embryology for first-year students. Working with Dr. Christine Niekrash, D.M.D, this paper will cover the embryology and growth of the head, face and oral cavity. The goal of this project will be to organize the information and recognize the resources needed to successfully introduce this part of human physiology to the UConn dental and medical students. One area in which this information is particularly relevant is the facial and oral deformities that can occur throughout fetal development.
Introduction

Embryological formation of the head and neck is a complex process that begins very early in human development. An understanding of this process is an important part of the curriculum for first-year medical and dental students because in order to understand and diagnose abnormalities, one must understand how and where in development they can occur.

This paper will outline the complex developmental processes of the head and neck region in the fetus. Beginning with neurulation and the formation of the head, the paper will discuss how the ectoderm, mesoderm and endoderm differentiate to become the numerous cell types that make up the head and neck region.

An overview will be provided of the development and growth of this region until puberty is reached. It is at this time that most of the bone formation and development is complete and the permanent dentition has erupted.

There will be an emphasis on the clinical manifestations of defects in normal growth and development. This will provide the link between embryological development and the potentiality for abnormalities to occur.

Much of the growth and development that is discussed in this paper occurs early in the pregnancy, even before a woman is aware that she has become pregnant. This could lead to environmental and toxic damages to the developing fetus. Women who smoke, consume alcohol and have poor nutrition during pregnancy are at greater risk for the birth defects of the head and neck outlined in this paper, as well as many others.
The Formation of the Head

At the time when the head region begins to form, the embryo is composed of three layers of tissue, the ectoderm, mesoderm and endoderm. These three germ layers become distinct during gastrulation in the third week of development. The neural folds fuse and form the neural tube, a process known as neurulation. The process of neurulation is completed in distinct steps that include the forming, shaping and bending of the neural plate and then the closing of the neural groove. If this process does not occur correctly, major Central Nervous System abnormalities can result.

In humans, the process of neurulation can be divided into the primary neurulation and secondary neurulation. In the first part of this two-stage process, the neural tube forms, which ultimately will become the brain and a large part of the spinal cord. The neuroepithelium is folded and shaped so that there can be fusion at the midline and a tube can be formed. In an extremely different process, secondary neurulation “involves condensation of a population of mesenchymal cells in the tail bud, to form an epithelial rod”. The formation of the secondary neural tube results in a canal whose lumen “is continuous with that of the primary neural tube” (Greene & Copp, 2009).

(From http://www.daviddarling.info/encyclopedia/N/neural_tube.html)
Formation of the head is defined by the migration of neural crest cells that arise from the rhombomeres, segments of the forming hindbrain which will give rise to differentiated neurons (Sanes, Reh & Harris, 2006). The two streams of neural crest cells come from the first two rhombomeres and aid in the development of the face and branchial arch system. Migrating as the first stream, the crest cells “intermingle and reinforce the mesenchyme situated beneath the expanding forebrain”. This first stream of cells becomes the connective tissue that is important for the development of the face, while the second is incorporated in the first branchial arch. The Hox family of Homeobox genes expressed in the rhombomeres are important in this stage for determining the pattern of development (Nanci, 2003).

Skull Development

The developing fetal skull can be divided into three sections that will eventually become fused, the cranial vault, cranial base and the face. When the brain is developing it
requires protection even though bone has not yet formed so it is surrounded by a membranous cranium that will eventually become the site of bone formation. At week nine of development, the mesenchymal cells will differentiate into osteoblasts that will form an osteoid matrix and begin to mineralize. The ossification process in the cranial vault, as well as the face and vomer, does not have a cartilage model to follow and is, therefore, of intramembranous origin. At birth, mineralization has not been completely finished which is why a newborn’s head must be treated very delicately. The six fontanels are attached by connective tissue because fusion between developing bones has not yet occurred. The sutures and fontanels are much more noticeable in the newborn head, but will disappear during the first few years of life. The neurocranium is much larger in proportion to the face because of the growth pattern after birth. “The neurocranium reflects the growth of the brain and follows the neural curve, whereas the facial area follows the somatic growth curve” (Castriota-Scanderbeg & Dallapiccola, 2005).

The skull base is actually the first part of the skull that begins to take shape as the mesenchymal tissue migrates to the areas that will become the ethmoid, auditory, nasal and optic centers as well as the floor that will support the developing brain in the seventh week. The chondrocranium is formed from cartilage which will give rise to ossification centers and ultimately become bone. At this time the middle and external ear develop, but the inner ear will develop separately. Defects of the middle ear and pinna are linked and will not necessarily affect the inner ear. Many of the bones that make up the skull base will undergo significant changes from their state during fetal development to maturity (Castriota-Scanderbeg & Dallapiccola, 2005).
The facial area is developed from both the frontal prominence and the pharyngeal arches but will eventually become one cohesive structure. The nasal placodes and mandibular arches begin their formation in the fifth week from the frontal prominence. The nasal placodes are “paired ectodermal thickenings” that arise in the fourth week of development. Specialized cells from the placodes will become olfactory neuroepithelium that line the nasal fossae. After the nasal placodes have formed they become involved in the formation of the nasal pits, and eventually the nasal sacs, along with the frontonasal prominence and the first branchial arch. When the nasal sacs invaginate a separation between the oral and nasal cavities occurs. The frontonasal prominence and the maxillary prominence continue to emerge (Van de Water & Staecker, 2005). This will give rise to the nasal and frontal bones, the primary palate, the nasal capsule and part of the upper lip. The cheeks and corners of the mouth will take shape in the eighth week and when the orbits over the nose form the face will begin to finally take a recognizable shape. Facial development nears completion when the nose reaches its mature form and the sinuses begin to emerge, but the development will not be completed until well into puberty (Castriota-Scanderbeg & Dallapiccola, 2005).

The Fate of the Pharyngeal Arches

The pharyngeal, or branchial arches, begin to form during the fourth week of development because neural crest cells begin to move to the areas that will become the head and neck. In the human there are six arches and they are separated by pharyngeal grooves externally and the pharyngeal pouches internally. The arches are composed of mesenchyme covered by both ectoderm externally and endoderm internally. When the neural cells migrate to the arches and surround them, they begin to increase in size. The
pharyngeal arches give rise to much of the skeletal muscle and connective tissue in the head and neck region (Moore & Persaud, 1993).

The center of each arch is composed of cartilage that has formed as a result of condensation of the mesenchyme. The cartilage in the first arch has been named Meckel’s cartilage and that of the second is Reichert’s cartilage, though none of the other arch cartilages have specific names. Each arch also has two nerves, one sensory and one motor, that will eventually innervate the muscle that is derived from that arch (Nanci, 2003).

The first pharyngeal arch, or mandibular arch will eventually become the mandibular and maxillary processes that will take part in jaw and nasal cavity formation. It will also give rise to two bones in the ear, the malleus and incus, and the ligaments associated with them. An abnormality in the first arch will cause congenital defects in the eyes, ears, palate and jaw (Moore & Persaud, 1993).

The second pharyngeal arch, or hyoid arch, “overgrows the third and fourth” arches and forms the cervical sinus. The neck begins to take shape in the sixth and seventh week of fetal development when “the second and fourth branchial grooves and
cervical sinus are obliterated”. The bones that arise from the second arch are the stapes in the ear, the styloid process of the temporal bone, the lesser cornu and the hyoid bone, as well as the stylohyoid ligament (Moore & Persaud, 1993).

The third pharyngeal arch is also involved in the formation of the hyoid bone and also becomes the greater cornu. The fourth and sixth arches will fuse to form the laryngeal cartilages. The fifth cartilage does not appear to have any contribution to the adult anatomy.

<table>
<thead>
<tr>
<th>Arch</th>
<th>Nerve</th>
<th>Muscles</th>
<th>Skeletal Structures</th>
<th>Ligaments</th>
</tr>
</thead>
<tbody>
<tr>
<td>First (mandibular)</td>
<td>Trigeminal (V)</td>
<td>Mastication</td>
<td>Malleus</td>
<td>Anterior ligament of malleus</td>
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<td></td>
<td></td>
<td>Mylohyoid and anterior belly of digastric</td>
<td>Incus</td>
<td>Sphenomandibular ligament</td>
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<td></td>
<td></td>
<td>Tensor tympani</td>
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<td></td>
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<td>Tensor veli palatine</td>
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<tr>
<td>Second (hyoid)</td>
<td>Facial (VII)</td>
<td>Muscles of facial expression</td>
<td>Stapes</td>
<td>Stylohyoid ligament</td>
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<td></td>
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<td>Stapedius</td>
<td>Styloid process</td>
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<td>Stylohyoid</td>
<td>Lesser cornu of hyoid</td>
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<td></td>
<td></td>
<td>Posterior belly of digastric</td>
<td>Upper part of body of</td>
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<td></td>
<td>hyoid bone</td>
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<td>Third</td>
<td>Glossopharyngeal (IX)</td>
<td>Stylopharyngeus</td>
<td>Greater cornu of hyoid</td>
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<td>Lower part of body of</td>
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<td></td>
<td>hyoid bone</td>
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<tr>
<td>Fourth and Sixth</td>
<td>Superior laryngeal</td>
<td>Cricothyroid</td>
<td>Thyroid cartilage</td>
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<tr>
<td></td>
<td>branch of vagus (X)</td>
<td>Levator veli palatine</td>
<td>Cricoid cartilage</td>
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<td></td>
<td>Recurrent laryngeal</td>
<td>Constrictors of pharynx</td>
<td>Arytenoid cartilage</td>
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<tr>
<td></td>
<td>branch of vagus (X)</td>
<td>Intrinsic muscles of larynx</td>
<td>Corniculate cartilage</td>
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<tr>
<td></td>
<td></td>
<td>Striated muscles of the esophagus</td>
<td>Cuneiform cartilage</td>
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</tbody>
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**The Pharyngeal Pouches**

The pharyngeal pouches form as outgrowths of the pharyngeal arches when they become lined by the pharynx. There are four pairs of pouches, and similarly to the pharyngeal arches, the fifth pair of pouches does not have any known developmental purpose. The
first pharyngeal pouch forms the tympanic cavity, mastoid antrum and Eustachian tube. The second pouch becomes segmented and one of the segments forms the tonsils and lymphatic nodules. The third pouch forms bulbous portions that will have several different fates. One will become the inferior parathyroid gland and another section the thymus. The fourth pouch also differentiates into several different structures, including the superior parathyroid gland which will fuse with the inferior portion. It will also become the parafollicular, or C cells, associated with the thyroid gland that produce calcitonin, a hormone that regulates calcium levels in the body (Moore & Persaud, 1993).

**PHARYNGEAL POUCH DERIVATIVES**

<table>
<thead>
<tr>
<th>Pouch</th>
<th>Derivatives</th>
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<tbody>
<tr>
<td>1</td>
<td>middle ear cavity, endodermal aspect of tympanic membrane, pharyngotympanic tube</td>
</tr>
<tr>
<td>2</td>
<td>palatine tonsil</td>
</tr>
<tr>
<td>3</td>
<td>inferior parathyroid gland, thymus</td>
</tr>
<tr>
<td>4 &amp; 5</td>
<td>superior parathyroid gland, parafollicular cells of thyroid gland</td>
</tr>
</tbody>
</table>

(From "Pharynx." Bionalogy Home Page. 20 Apr. 2009 <http://www.bionalogy.com/pharynx.htm>.)
Fetal Facial Formation

The stomodeum is the rudimentary mouth that forms between the first pharyngeal arches around the fourth week of development in the center of the area that will become the face. The neural crest cells of the arches contribute to the development of the skeleton, while the mesoderm will provide the musculature for the face and neck. Around the fifth week of fetal development the face begins to take shape starting with the nasal placodes that will become the nasal pits after evagination. The frontal nasal prominences form above the stomodeum like a primordial lip. When the mandibular prominences merge they will form the beginnings of lower lip, chin and mandible. The nose is actually the result of a fusion of five separate prominences: “the frontal prominence forms the bridge of the nose; the two medial nasal prominences form the crest, tip and central portion of the lip, or intermaxillary segment; and the lateral nasal prominences form the sides. Complete fusion of the medial nasal prominences is important because this is where cleft lip and palate can occur (Nybery, et al, 2003). Next, the nasolacrimal groove and duct develop in the seventh week. The nasolacrimal duct is important in the “drainage of excess tears from the conjunctiva of the eye into the nasal cavity” (Larsen, 1997).

During the sixth and seventh week the nasal and maxillary processes begin to expand and fuse to form the upper lip. The lower lip begins to form earlier when the mandibular swellings become continuous and the mandibular depression is filled in “by proliferation of mesenchyme”. The buccopharyngeal membrane “ruptures to form a broad, slitlike embryonic mouth” and will not take its mature shape until well into the second month of development when the “maxillary and mandibular swellings creates the cheeks” (Larsen, 1997).

Robinow Syndrome, or fetal face syndrome, is a rare genetic disorder that results in children with facial abnormalities that makes them appear like they have not completely gone through full fetal development. The head is enlarged and the forehead appears to be abnormally shaped and bulging. The nose is small and malformed with flared nostrils and a sunken bridge. The eyes are very widespread. There are other abnormalities that occur that are associated with other parts of the body (CIGNA, 2007).

**Formation of the Primary and Secondary Palates**

The palate as a whole forms from two primordia which can be classified as the primary and secondary palate. At around the sixth week of development the primary palate begins to take shape, arising from the medial nasal process. Composed of mesoderm, this “wedge-shaped mass” will eventually extend to form the floor of the nasal cavity (Moore & Persaud, 1993).

Around the eighth or ninth week of development the secondary palate begins to develop from two lateral palatine processes, but this is not completed until the third month of gestation. The two processes grow vertically on either side of the tongue, but as
the oral cavity develops “the tongue moves inferiorly” and the processes move up and
toward each other so that they can fuse (Moore & Persaud, 1993). As this shifting occurs
the oral cavity begins to develop along with the formation of the mandible.

In order for the fusion of the two palatine processes to occur a significant amount
of force is necessary, but the nature of this force is unknown. Multiple physiological
changes that are occurring at this time in fetal development have been attributed to this
phenomena. One possible explanation is that the force is “generated by the progressive
accumulation and hydration of hyaluronic acid” (Ferguson, 1993). During this stage of
development there is also a significant increase in the concentration of
glycosaminoglycans, “which attract water and make the shelves turgid”. It has also been
proposed that “the presence of contractile fibroblasts in the palatine shelves” may play a
role in creating the intrinsic force necessary to push the two processes together so that
their fusion may occur (Nanci, 2003). The specific steps in the formation of the tongue
and head attribute to this growth pattern.

When fusion of the palate occurs, the two layers of epithelia must align and
become adjoined with only a midline seam. Before the fusion begins DNA synthesis
stops for at least a day and the epithelial cells undergo a physiological cell death so that
the basal epithelial cells become exposed. Junctions are formed due to the carbohydrate-
rich surface coat because this allows for a simpler adhesion process. The seam that forms
at the junction is then composed of two epithelial cell layers that must eventually become
one when “the growth of the seam fails to keep pace with palatal growth so that the seam
first thins to a single layer” (Nanci, 2003).
Fusion is completed around the twelfth week when the midline edge seam (MES) disappears completely. The epithelial cells then begin to differentiate to form the other structures associated with the palate. On the nasal side the cells become pseudostratified ciliated columnar epithelium. On the oral side the cells become stratified squamous, non-keratinizing epithelium. The hard palate forms when “ossification occurs in the anterior two-thirds of the palate” and the soft palate is formed because ossification does not occur in this area. When these cells do not differentiate correctly then problems such as a cleft palate may occur (Meng, Bian, Torensma, Von den Hoff, 2009).

The maxilla is not derived from a primary cartilage, but rather ossification begins where the anterosuperior dental nerve and inferior orbital nerve divide and is linked to the cartilage that makes up the nasal capsule. It does however have a secondary cartilage, the zygomatic cartilage, that contributes to the maxilla growth. Bone growth continues both posteriorly and anterorly and troughs form to house the nerves and tooth germs just as in the mandible so that the teeth are held in place. It is at this time that ossification of the hard palate occurs. The maxilla increases in size after birth due to the development of the maxillary sinuses (Nanci, 2003).
Cleft palates occur once in 2500 births and are more common in females (Moore & Persaud, 1993). There are multiple forms of this congenital defect as it can be unilateral or bilateral and involve the uvula and hard and soft palates. On an embryological level, a cleft palate occurs because there has been insufficient fusion of the palatine processes or formation of the nasal septum. Other factors that may cause a cleft palate include “lack of growth”, inability of the palatine shelf to elevate, failure of the septum to fuse, inability of the epithelium to breakdown or “defective merging of the mesenchyme of the shelves”. There are also specific environmental factors that may contribute, including “infectious agents, x-ray radiation, drugs, hormones, and nutritional deficiencies” (Nanci, 2003).

Generally restorative surgery for cleft palates is done around one to two years of age. There are “several types of operative procedures” that can be used for the repair based on the type and severity of the case. As cosmetic surgery techniques begin to improve, the success of these surgeries to reconstruct normal and functioning palates increases. Children with a cleft palate are generally candidates for speech therapy from an early age to improve the quality and ease their speech (Crowley, 1974). Unfortunately, after surgery children may experience scarring of the palate and other growth abnormalities of the oral cavity (Meng, et al, 2009).

(From Behr, Amy. Johns Hopkins Medicine, based in Baltimore, Maryland. 20 Apr. 2009.)
**Mandible Formation**

At the sixth week of development a cartilaginous rod forms, also known as Merkel’s cartilage for the anatomist that first defined it, from the region around the ear to the midline mandibular processes and are separated by mesenchyme. The mandibular nerve splits at this time into the lingual and inferior alveolar branches and will line the cartilage. During week 7 the first ossification center forms and from this point bone develops out from the midline. A trough forms on each side below the incisor nerve that has branched from the anterior alveolar nerve. This trough will eventually become a canal and after birth the two pieces of the forming mandible will fuse at the midline.

A canal also forms backward to contain the alveolar nerve. Medial and lateral alveolar plates form so that tooth germs can form in a trough between them. Therefore, as the teeth develop they will each have their own space to occupy. The bone of the mandible will to continue to form after the teeth have developed to support them.

Around ten weeks the mandible is recognizable and much of the bone has formed. After this point there will be a strong dependence for formation on three cartilaginous growths: the condylar cartilage, the coronoid cartilage and the symphyseal cartilage. The condylar cartilage will be converted almost entirely to bone, but the small portion of cartilage that remains at the articular end is necessary for the continuous growth of the mandible. The coronoid and midline symphyseal cartilages are also important for growth and development, but disappear before birth and in the year after respectively.

The growth of the jaw continues throughout the years before puberty and misalignment of teeth and bones is common and can be attributed to problems with the muscles or joints or genetics. Later in life it is possible that this can contribute to
temporomandibular joint disorder (TMD) in which patients may experience joint pain, a locking or popping of the jaw and other symptoms (Stay, 2005). Children and teens with jaw or teeth misalignment, which can result in an overbite, under-bite or cross bite, are often treated with orthodontics to correct the bite.

**Development of the Nasal Cavities and Sinuses**

The nasal prominences form around the nasal placodes and will “form the floors of depressions called nasal pits” which fuse during the sixth week to become one single sac. At first the oronasal membrane separates the oral and nasal cavities, but when this ruptures the two spaces will become connected. The primordial choanae are “the openings between the nasal cavity and nasopharynx” (Moore & Persaud, 1993).

At the same time that the secondary palate is forming, the nasal septum begins to take shape, arising from the frontonasal process and the medial nasal processes. The septum grows downwards toward the primary and secondary palates so that the nasal cavity is divided into two passages, “which open into the pharynx behind the secondary palate through an opening called the definitive choana” (Larsen, 1997). In order for the olfactory epithelium to form, epithelial cells on the roof of the nasal cavities must specialize. “Some epithelial cells differentiate into olfactory receptor cells (neurons). The axons of these cells constitute the olfactory nerves (Cranial Nerve I), which grow into the olfactory nerves of the brain” (Moore & Persaud, 1993).

There are four distinct types of sinuses that will form, though only two will develop before birth. In the third fetal month the maxillary sinuses, those that are present in the maxillary bones, form “as invaginations of the nasal sac that slowly expand in the maxillary bones”. They will be very small at birth but will continue to grow during
the first few years of life. Two months later the ethmoid sinuses, those that sit between the eyes, will form in the ethmoid bone. They will continue to grow until approximately the time that the child reaches puberty. At birth the sinuses are so small they cannot even be detected by radiographs and this can make diagnosing infection more difficult (Rosin, 1998). In the first few years after birth, the sphenoid and frontal sinuses will form within the bones of the same name (Larsen, 1997). Surprisingly, the development of the sinus passageways plays one of the greatest roles in determining the size and shape of the face. Their growth during fetal development and through puberty will alter appearance and result in the changing of the voice later in life.

(From "AAAAI - Patients & Consumers Center: December 2005: Diagnosis, treatment and prevention of sinusitis." AAAAI - American Academy of Allergy Asthma and Immunology - www.aaaai.org. 21 Apr. 2009.)

**Formation of the Lips**

The mandibular arches give rise to the lower lip and the upper lip forms from the maxillary processes, the lateral nasal prominences and the intermaxillary segment, as defined earlier. Between the fifth and sixth weeks of development the components that will become the lower lip begin to form, but it is not until the seventh week that the lip is distinguishable amongst the other swellings and processes in the facial region. By week
nine the formation of the upper lip has almost been completed and by the time the fetal period is completed it will have taken the adult form and will change very little during the rest of development (Yoon, Chung, Seol, Park & Park, 2000).

A cleft lip can occur on either the top or bottom lip, though a cleft of the bottom lip is extremely rare. A cleft lip occurs “about once in 1000 births” and are more common in males. There are a variety of abnormalities that can occur “from a small notch in the lip to complete division of the lip and alveolar part of the maxilla”. A unilateral cleft lip is diagnosed when only one side of the maxillary process fails to merge with the nasal prominence, while a bilateral cleft occurs on both sides. With a bilateral cleft, because the deformation of the upper lip prevents the connection of the lip and alveolar part of the maxilla, it appears that the bottom portion of the nose and a portion of the upper lip are hanging freely (Moore & Persaud, 1993).

(From "Cleft Lip and/or Palate." Children's Hospital of Wisconsin in Milwaukee, WI, is a member of Children's Hospital and Health System - Home Page. 2009. 20 Apr. 2009.)
Cleft lip correction surgery is often done very shortly after birth to avoid anatomical abnormalities that may occur during the growth of the lips, jaws and nose. Generally, the surgeon must create a more normally shaped nose and nostrils and correct for the deformation of the upper lip and sometimes the lower lip as well. Often a cleft lip is associated with a cleft palate and this can be dealt with surgically at the same time as the lip reformation. Children with cleft lips often experience dental abnormalities when the teeth form and erupt in the mouth and are frequently candidates for orthodontic treatment (Crowley, 1974).

Development of the Tongue

Around the fourth week of embryonic development the structure that will become the tongue begins to form from the first, second, third and fourth pharyngeal arches. Part of the tongue is also derived from the floor of the pharynx. Three swellings (the median tongue bud and two distal tongue buds), form and grow rapidly during the fifth week. The tongue itself will continue to expand throughout fetal development.

(From "THE CORRESPONDENCES." Higher Meanings. 1985. 20 Apr. 2009 <http://www.highermeaning.org/Authors/LSO/HumanForm/HumanForm1.shtml>.)
The lateral tongue buds grow at a more rapid pace than the median tongue bud, and therefore overgrow it beginning in the fifth week. The place where these two swellings fuse is indicated in the anatomy by the median sulcus, which can be seen in the adult tongue. The copula, the name given to the midline swelling that begins late in the fourth week, is eventually overgrown in the fifth and sixth week by the hypopharyngeal eminence (Larsen, 1997). When the anterior and posterior portions of the tongue fuse the groove that forms in a V-shape at their intersection is called the terminal sulcus (Moore and Persaud, 1993).

The thyroid gland has its origin in the tongue as a small mass that eventually undergoes invagination. The anatomy of the tongue reflects the origination of the gland through the remnant named the foramen cecum. When the thyroid gland is in the stage of development it is attached by means of the thyroglossal duct that in normal growth and development atrophies and leaves only a “circular depression in the tongue”, the foramen cecum (Crowley, 1974). Abnormalities in the atrophy of the duct may result in thyroglossal cysts which usually are benign. If the cyst continues to enlarge it may cause difficulty in swallowing after birth and then it must be removed. If no symptoms occur but the cyst is detected during infancy then the removal may be postponed until it becomes a problem (DeMattei and Aubertin, 1996).

Multiple cranial nerves are involved with the innervation of the tongue. All of the tongue muscles are innervated by the hypoglossal nerve (cranial nerve XII) except for the palatoglossus which is innervated by the pharyngeal plexus of the vagus (nerve X). This muscle is involved in swallowing and elevating the posterior portion of the tongue (Larsen, 1997). The lingual nerve, which is a branch of the mandibular division of the
trigeminal nerve (Cranial Nerve V3), is responsible for providing general sensory information from the anterior two-thirds of the tongue. The posterior one-third of the tongue is innervated by the superior laryngeal branch of the vagus nerve (Cranial Nerve X) which relays sensory information. The third pharyngeal arch is involved with the glosopharyngeal nerve (Cranial Nerve IX) which “carries both general sensation and taste from the mucosa to the tongue root” as well as vallate papillae, the large taste buds on the terminal sulcus (Tamatsu and Gasser, 2004). The taste buds are innervated on the anterior two-third of the tongue by a branch of the facial nerve (nerve VII) known as the chorda tympani.

Abnormalities in the development of the tongue are rare, but can often be seen in infants that have been diagnosed with Downs Syndrome. Ankyloglossia, more commonly known as tongue-tie, occurs when the frenulum is extended to the tip of the tongue and therefore inhibits normal movement and protrusion. Often the frenulum will stretch and correct itself, but the difficulty that occurs during breast feeding often leads to
the necessity of surgical correction (Chu and Bloom, 2009). Macroglossia, an unusually large tongue, is very uncommon. In some cases normal sized tongues appear large because there is underdevelopment of the mandible. Even more rare is microglossia, an extremely small tongue, which can also be the result of abnormal jaw formation. Both of these abnormalities may lead to difficulty with speech and swallowing (Ruscello, Douglas, Tyson & Durkee, 2005).

The Salivary Glands
The saliva produced by the salivary glands has multiple functions that include aiding in lubrication during mastication and vocalization, digestion, taste and pH buffering (Tucker, 2007). The salivary glands are formed from epithelial cells that form buds and undergo branching morphogenesis to produce “successive generations of buds and a hierarchical ramification of the gland” (Nanci, 2003). The buds grow into the mesenchyme as invaginations and the connective tissue associated with these glands arises from neural crest cells.

Around the sixth week of development the parotid glands begin to form from the oral ectodermal lining. At ten weeks, as these buds grow outward toward the ears that they will become canals. Salivary secretion will not start until week 18. Also in the sixth week the submandibular glands begin to take shape from buds, but these will grow lateral to the tongue. The acini, or the area of the gland where the secretion occurs, starts to develop at week 12 and they begin to produce secretions around week 16. These glands continue to grow and produce more acini even after birth. The sublingual glands begin formation in the eighth week of development and will grow into the paralingual sulcus.
After the branching of these glands occurs, they will become 10 to 12 separate canalized glands which open on the floor of the mouth (Moore & Persaud, 1993).


**Tooth Formation**

By the fifth week of development a horseshoe-shaped band of thickened epithelium forms on the maxillary and mandibular bones. These are essentially the primordial dental arches. The dental lamina forms and development of the teeth occurs in three distinct phases based on the characteristics of the developing teeth, the bud, bell and cap stages. Ectoderm and mesoderm give rise to the teeth. Enamel is derived from the ectoderm. The mesoderm forms the dentin and the pulp. All of the teeth do not develop at the same time and formation of the dentition continues long after birth (Moore & Persaud, 1993).

Around week six of development, tooth formation begins when the thickened epithelium invaginates into the mesoderm and produces tooth buds that look like small swellings. Each tooth develops from its own individual bud (Crowley, 1974). The
deciduous teeth, or those that will be lost before adulthood, grow into the mesenchyme (Nanci, 2003). This ectoderm also gives rise to tooth buds that will form the permanent dentition.

During the cap stage, the dental papilla form as invaginations that “gives the developing tooth a caplike appearance” (Moore & Persaud, 1993). The cells begin to condense so that a thick grouping of cells forms and provides density. The dental papilla, formed from the mesoderm, becomes the dentin and dental pulp and the enamel organ, derived from the ectoderm, forms on the outer layer so that enamel can be produced. The enamel organ rests upon the top of the dental papilla like a cap. It is at this time that histodifferentiation occurs and the different elements of the tooth and surrounding tissue become distinct. Glycosaminoglycans play an important role in this stage because they are “hydrophilic and so pull water off the enamel” (Nanci, 2003). They also give rigidity to the developing tooth structure. Both ectoderm and endoderm are needed for tooth formation to occur.

In the bell stage, invagination continues and this allows the tooth to begin to take its mature shape. Odontoblasts begin to produce predentin which will calcify and become dentin. The enamel will eventually form from ameloblasts over this layer starting at the cusp of the tooth and moving down to the root (Slootweg, 2007). The crown of the tooth will begin to take shape and the teeth will differentiate into their specific types.

After the dentin and enamel have become well formed the root of the tooth will begin to develop. The epithelial root sheath is where the inner and outer dental epithelial layers come together at the apex of the tooth and this area initiates root formation.
Odontoblasts continue to form dentin which is a continuation of the crown and grows down to form the root canal where the blood vessels and nerves can enter the tooth. Cementum, produced by cementoblasts, covers the dentin of the root and bone forms around each of the teeth to hold them in place in the jaw.

It is at this time that tooth abnormalities may occur in the shape or number of the teeth. If an individual does not grow a sufficient number of tooth buds this will result in a missing tooth and if an extra bud forms then they will have more than the normal number of teeth (Crowley, 2004). Enamel hypoplasia is caused by a defect in the enamel that results in pits and grooves in the crowns of the teeth. This occurs when there is a disruption of the ameloblasts during enamel formation that can be caused by such factors as an infectious disease or a nutritional deficiency. Other deformations of the crown
include pearls, or small circular masses of enamel, irregular and unsmooth crown surfaces and double crowns. The roots can also become divided, distorted or fused. Rickets, a vitamin D deficiency generally related to bone health, can cause the “disturbance of ossification” and greatly affect permanent tooth development. Individuals may also develop Dentinogenesis Imperfecta, or the genetic discoloration of the teeth from a brown to a gray-blue. This enamel is much more susceptible to wear, exposing the underlying dentin, making the teeth less strong. (Moore & Persaud, 1993).

Even though teeth do not begin to erupt until six to eight months after birth, they begin to move toward the exterior as soon as development begins. Generally the mandibular teeth erupt before the maxillary teeth and this occurs earlier in girls than in boys. Teething is often painful for small children because in order for eruption to occur the tooth must break through the epithelial lining of the mucosa of the oral cavity. The primary dentition usually consists of twenty teeth that will be exfoliated starting around age six when the permanent teeth begin to erupt. It is extremely important that these newly erupted teeth are well-cared for because they should last the entire adult lifetime (Moore & Persaud, 1993).

**Tooth Eruption Chart for Primary Teeth**

<table>
<thead>
<tr>
<th>Tooth</th>
<th>Dental Name</th>
<th>Eruption Age</th>
<th>Root Fully Formed</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Central Incisor</td>
<td>7-9 Months</td>
<td>20-22 Months</td>
</tr>
<tr>
<td>B</td>
<td>Lateral Incisor</td>
<td>7-9 Months</td>
<td>20-22 Months</td>
</tr>
<tr>
<td>C</td>
<td>Canine</td>
<td>17-22 Months</td>
<td>30-35 Months</td>
</tr>
<tr>
<td>D</td>
<td>First Molar</td>
<td>12-17 Months</td>
<td>27-32 Months</td>
</tr>
<tr>
<td>E</td>
<td>Second Molar</td>
<td>24-33 Months</td>
<td>38-48 Months</td>
</tr>
</tbody>
</table>
Lower Teeth

<table>
<thead>
<tr>
<th>Tooth</th>
<th>Dental Name</th>
<th>Eruption Age</th>
<th>Root Fully Formed</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Central Incisor</td>
<td>6-8 Months</td>
<td>18-20 Months</td>
</tr>
<tr>
<td>B</td>
<td>Lateral Incisor</td>
<td>7-9 Months</td>
<td>20-22 Months</td>
</tr>
<tr>
<td>C</td>
<td>Canine</td>
<td>17-22 Months</td>
<td>30-35 Months</td>
</tr>
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<td>E</td>
<td>Second Molar</td>
<td>24-36 Months</td>
<td>38-48 Months</td>
</tr>
</tbody>
</table>

(From "Teething and Eruption." Teeth Dental Information Adults Children. Dental Care Guide. Dentistry. 2004. 20 Apr. 2009.)

The formation of the tissues surrounding the teeth is also very important for the development of the root. The tissue arises from the dental follicle and will differentiate when the “root sheet fragments and ectomesenchymal cells of the dental follicle penetrate between the epithelial fenestrations and become apposed to the newly formed dentin of the root”. Some cells become cementum-forming cells on the tooth root surface and some will take part in the mineralized organic matrix of supporting bone. Periodontal ligament fibers insert into both cementum and supporting bone to anchor the teeth into the arches (Nanci, 2003).

(From Muratsu, Kazumasa. "Section 4-1. Teeth hold the micro cosmos. Its kinds and structure." TEETH ARE OUR ORGANS. 20 Apr. 2009.)
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