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Oral Histopathology

口腔组织病理学

沈丽佳 主编

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沈丽佳 医学博士，教授。1958年11月出生，江苏人。1982年12月毕业于中山医学院口腔医学专业（光华口腔医学院），获口腔医学学士学位。 2006年6月毕业于第一军医大学病理学与病理生理学专业，获医学博士学位。1982年12月任广州市第一人民医院口腔科医师，1984年7月至今在暨南大学医学院口腔医学系历任助教、住院医师、讲师、副教授、教授。从事口腔医学临床、教学和科研工作31年。1997年至今任口腔组织病理学教研室主任、口腔医学硕士研究生导师，兼任广东省口腔医学会口腔病理学专业委员会副主任委员、《中国医学创新》特约编委、广州市科协科普志愿者协会广州科普讲师团成员。主编出版教材2部、多媒体电子音像教材1部。

主要研究方向是口腔癌及癌前病变发病机制。曾承担和参加学校、广东省卫生厅、广东省科技厅、国务院侨办、卫生部、国家自然科学基金等20多项科研项目。在国家级核心期刊、统计源期刊及国家级出版社出版的医学专著、医学教育专著中发表学术论文及教学研究论文80余篇。

从教30年来教学研究成果丰富：1989年获暨南大学教学成果优秀奖，2004年获暨南大学教学成果一等奖，2006年获暨南大学优秀多媒体教学软件一等奖，2006年获广东省高校多媒体教学课件二等奖，2008年获广东省高校教育技术151工程项目优秀项目二等奖，2009年“口腔病理学”网络课程多媒体课件获广东省计算机教育软件三等奖，2012年获广东省高校优秀教学资源一等奖，2012年获暨南大学教学成果一等奖。

近年在教学资源库建设、质量工程建设项目和教学改革研究方面取得显著成绩：2004年担任暨南大学校级精品课程“口腔组织病理学”课程负责人，2005年担任暨南大学教育技术创新工程项目“口腔病理学”网络课程项目负责人，2007年担任暨南大学网上优质示范课程“口腔组织学”课程负责人，2008年担任暨南大学校级精品课程“口腔组织胚胎学”课程负责人，2009年担任广东省高校省级精品课程“口腔组织病理学”课程负责人，2012年担任暨南大学教育技术创新工程项目“口腔专业英语”“口腔疾病防治”等网上优质示范课程项目负责人。

主讲“口腔组织胚胎学”“口腔病理学”“口腔生物学”“口腔疾病防治”“口腔专业英语”及研究生课程“口腔医学专业英语”“口腔组织病理学研究进展”等课程，具有丰富的教学实践经验，连续20年课堂授课教学评估成绩优秀。获得多项教学荣誉称号和奖励：2007年荣获广东省“南粤优秀教师”称号，2002年荣获暨南大学“十佳授课教师”称号，1987年、2006年、2009年和2013年四次荣获暨南大学“优秀教师”称号。

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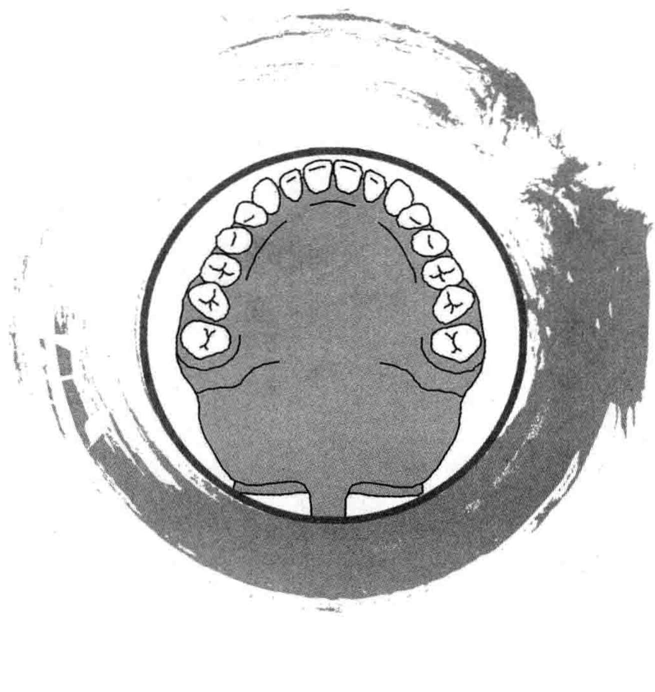

Chapter 1

Development of the Oral-Maxillofacial Region

Chapter Outline

Ⅰ Introduction

The term embryo or embryogenesis is properly used to refer to the first 8 weeks of development in humans. This period largely corresponds to the appearance of organs and organ systems. The term organogenesis thus is largely equatable with the embryonic period. Following the embryonic period is the fetal period. This is largely the time of growth and differentiation as opposed to the appearance of structures. Accordingly, one should not refer to an individual before the end of the eighth week as a fetus or after the ninth week as an embryo. It should be noted that these demarcations, terms, and time frames are based on humans.

Craniofacial development is an extraordinarily complex process that requires the orchestrated integration of multiple specialized tissues, such as the surface ectoderm, neural crest, mesoderm, and pharyngeal endoderm, in order to generate the central and peripheral nervous systems, axial skeleton, musculature, and connective tissues of the head and face. Understanding the development of the structures of the face also requires knowledge of the pharyngeal or branchial arches. These arches form on either side of the foregut and correspond to the primitive branchial arches. The pharyngeal arch consists of a core of mesenchyme covered externally by ectoderm and covered internally by endoderm. The ectoderm is well around the stomodeum by the fourth week of embryonic development and contributes to the formation of the face and the nasal and oral cavities. The mesenchyme that fills the pharyngeal arches is derived from the following 3 origins: the paraxial mesoderm, the lateral plate mesoderm, and the neural crest cells. Although paraxial mesoderm and lateral plate mesoderm contribute to the musculature that develops in each particular arch, neural crest cells contribute to the skeletal portion of each arch.

Ⅱ Neural Crest

At the early stages of embryonic development, the vertebrate face has a common plan. A series of small buds of tissue called the facial primordia forms around the stomodeum, which forms the primitive mouth. The facial primordia are made up mainly of neural crest cells that have migrated from the cranial crest and settled.

These neural crest cells arise from the midbrain and the first two rhombomeres as two streams. The first stream migrates forward and intermingles and reinforces the mesenchyme situated beneath the expanding forebrain. This stream provides much of the connective tissue associated with the face. The second stream is directed toward the first branchial arch.

As the neural tube forms, a group of cells separate from the neuroectoderm. These cells have the capacity to migrate and differentiate extensively within the developing embryo, and they are the basis for structures such as the spinal sensory ganglia, sympathetic neurons, Schwann cells, pigment cells, and meninges. These cells are called neural crest cells. In the mammalian embryo these cells separate from the lateral aspect of the neural plate rather than from its crest. During their induction, neural crest cells undergo an epithelial mesenchymal transformation, a process whereby their cell adhesive properties and cytoskeletal organization change, allowing them to delaminate and migrate away from the neural tube.

Neural crest cells in the head region have an important role. In addition to assisting in the formation of the cranial sensory ganglia, they also differentiate to form most of the connective tissue of the head. Embryonic connective tissue elsewhere is derived from mesoderm and is known as mesenchyme, whereas in the head it is known as ectomesenchyme. In a dental context the proper migration of neural crest cells is essential for the development of the face and the teeth. All the tissues of the tooth(except enamel and perhaps some cementum) and its supporting apparatus are derived directly from neural crest cells, and their depletion prevents proper dental development.

Ⅲ Branchial Arches and Pharyngeal Pouch

During the fourth week of development, the pharyngeal arches form as a series of mesodermal proliferation on the left and right sides of the developing pharynx. The pharyngeal or branchial pouches form on the endodermal side between the branchial arches, and pharyngeal grooves form the lateral ectodermal surface of the neck region to separate the arches.

There are six pairs of branchial arches in fish, but only four are well developed in humans. The fifth and sixth branchial arched are transient structures.

A summary of the derivatives of the pharyngeal(i. e. , branchial)arches is as follows:

Pharyngeal arch	Nerve	Muscle	Skeleton
1st	Ⅴ	Muscles of mastication, anterior belly of the digastric, mylohyoid, tensor tympani, tensor veli palatini	Maxillary cartilage, mandibular or meckel cartilage
2nd	Ⅶ	Muscles of facial expression, stapedius muscle, posterior belly of digastric, and stylohyoid muscle	Stapes, styloid process, stylohyoid ligament, lesser cornu of hyoid, and the upper part of the body of the hyoid bone
3rd	Ⅸ	Stylopharyngeus	Hyoid (greater horn and lower part of body), thymus, inferior parathyroids

Continued

Pharyngeal arch	Nerve	Muscle	Skeleton
4th	X	Cricothyroid muscle, constrictor pharynges	Thyroid cartilage
6th	XI	Sternocleidomastoid, trapezius muscle	Cricoid cartilage

Fate of Pharyngeal Pouch and Branchial Groove:

- The first pouch elongates into tubotympanic recess and forms the auditory tube and tympanic cavity.
- The second pouch forms the epithelial lining of Crypts(spaces) of the Palatine tonsils.
- The third pouch forms the inferior parathyroid gland and thymus gland.
- The fourth pouch expands into two parts. The dorsal component forms the superior parathyroid gland, and the ventral portion gives rise to the thyroid gland.
- Four branchial grooves separate the branchial arches externally on each side, only one pair of branchial grooves forms a structure in the adult. The first branchial groove is involved in the formation of the external auditory meatus, and the first branchial membrane forms the tympanic membrane. The other branchial grooves develop to lie in a larger depression called the cervical sinus; this sinus is normally obliterated during development.

Ⅳ Formation of the Face

Early development of the face is dominated by the proliferation and migration of ectomesenchyme involved in the formation of the primitive nasal cavities. At about 28 days, localized thickenings develop within the ectoderm of the frontal prominence, just rostral to the opening of the stomatodeum. These thickenings are the olfactory placodes. Rapid proliferation of the underlying mesenchyme around the placodes bulges the frontal eminence forward and also produces a horseshoe-shaped ridge that converts the olfactory placode into the nasal pit. The lateral arm of the horseshoe is called the lateral nasal process, and the medial arm the medial nasal process. The region of the frontal prominence where these changes take place and the nose will develop also is referred to as the frontonasal process. The medial nasal processes of both sides, together with the frontonasal process, give rise to the middle portion of the nose, middle portion of the upper lip, anterior portion of the maxilla, and the primary palate.

The maxillary process grows medially and approaches the lateral and medial nasal processes but remains separated from them by the naso-optic groove and the bucconasal groove. The medial growth of the maxillary process pushes the medial nasal process toward the midline, where it merges with its anatomic counterpart from the opposite side. In this way the upper lip is formed from the maxillary processes of each side and the medial nasal process, with fusion occurring between the forward extent of the maxillary process and the lateral face of the medial nasal process. The lower lip is formed, of course, by merging of the two streams of ectomesenchyme of the mandibular processes. The merging of the two medial nasal processes results in the formation of that part of the maxilla carrying the incisor teeth and the primary palate and part of the lip.

An unusual type of fusion occurs between the maxillary process and the lateral nasal process. As with most other processes associated with facial development, the maxillary and lateral nasal processes initially are separated by a deep furrow. The epithelium in the floor of the groove between them forms a solid core that separates from the surface and eventually canalizes to form the nasolacrimal duct. Once the duct has separated, the two processes merge by infilling of the mesenchyme.

The face develops between the twenty-fourth and thirty-eighth days of gestation. By this time some of the epithelium covering the facial processes already can be distinguished as odontogenic, or tooth forming. On the inferior border of the maxillary process and the superior border of the mandibular arch, the epithelium begins to proliferate and thicken. This thickened area is the odontogenic epithelium. Odontogenic epithelium also develops on the lateral aspect of the medial nasal process, but not until the thirty-seventh day of development, when the processes fuse, the primary epithelial band can be observed. Thus the primary epithelial band is an arch-shaped continuous plate of odontogenic epithelium that forms in the upper jaw from four separate zones of epithelial proliferation.

Ⅴ Formation of the Palate

Initially, a common oronasal cavity is bounded anteriorly by the primary palate and is occupied mainly by the developing tongue. Only after the development of the secondary palate is distinction between the oral and nasal cavities possible. The palate proper develops from primary and secondary components.

The development of palate begins at the end of the 5th week, and is completed by the end of the 12th week.

1. The Primary Palate

Early in the 6th week, the primary palate begins to develop from the deep part of the intermaxillary segment, as median palatine process. It lies behind the premaxillary part of the maxilla, and fuses with the developing secondary palate.

The primary palate represents only a small part lying anterior to the incisive fossa of the adult hard palate.

2. The Secondary Palate

The secondary palate is the primordia of hard and soft palate posterior to the incisive fossa. It begins to develop early in the 6th week from the internal aspect of the maxillary processes, as lateral palatine process.

In the beginning, the lateral palatine processes project inferomedial on each side of the tongue. With the development of the jaws, the tongue moves inferiorly. During the 7th and 8th weeks, the lateral palatine processes elongate and ascend to a horizontal position above the tongue.

Gradually the lateral palatine processes grow medially and fuse in the median plane and also fuse with the posterior part of the primary palate and the nasal septum. The process of fusion with the nasal septum begins anteriorly during the 9th week, extends posteriorly and is completed by the 12th week.

Ⅵ Formation of the Tongue

The tongue begins to develop at about the 4th week. The pharyngeal arches meet in the midline beneath the primitive mouth. Local proliferation of the mesenchyme then gives rise to a number of swellings in the floor of the mouth.

First, a swelling(the tuberculum impar)arises in the midline in the mandibular process and is flanked by two other bulges, the lingual swelling. These lateral lingual swellings quickly enlarge and merge with each other and the tuberculum impar to form a large mass from which the mucous membrane of the anterior two thirds of the tongue is formed. The root of the tongue arises from a large midline swelling developed from the mesenchyme of the second, third, and fourth arches. This swelling consists of a copula(associated with the second arch)and a large hypobranchial eminence(associated with the third and fourth arches). As the tongue develops, the hypobranchial eminence overgrows the copula, which disappears afterwards. The posterior part of the fourth arch marks the development of the epiglottis.

The tongue separates from the floor of the mouth by a down-growth of ectoderm around its periphery, which subsequently degenerates to form the lingual sulcus and gives the tongue mobility. The muscles of the tongue have a different origin; they arise from the occipital somites, which have migrated forward into the tongue area, carrying with them their nerve supply, the twelfth cranial(hypoglossal)nerve.

Ⅶ Development of the Salivary Glands

Proliferation of oral epithelial cells results in the formation of a small bud in the connective tissue and which is connected to the oral epithelium by an epithelial cord. The process of branching of the epithelial cord required interaction between the epithelium and mesenchyme. Then the process of canalization and lumen formation within the branched cords occurs. Following development of the lumen in the buds, the epithelial cells differentiate into the secretory cells, mucous or serous, and myoepithelial cells of the mature gland.

The parotid glands begin to develop at the early 6th week from ectodermal buds near angles of stomodeum that grow towards the ears that canalize to form ducts and acini at the 10th week. Capsule develops from surrounding connective tissue. Secretion starts at the 18th week.

The submandibular glands begin to develop at the late 6th week from endodermal buds in floor of stomodeum on both sides of the tongue. Acini formation begins at the 12th week and secretion activity start at the 16th week. Growth continues after birth with formation of mucous acini.

The sublingual glands begin to develop at the 8th week from multiple endodermal epithelial buds in paralingual sulcus lateral to submandibular gland. Branching, rebranching and lumen formation of the buds give rise to 10 to 20 ducts that open independently into the floor of the mouth.

The minor salivary glands develop in the same way during the 3rd month. They remain as separate scattered acini and ducts in the lamina propria of the oral epithelium.

Ⅷ Development of Jaw Bones

1. Development of the Mandible

The cartilage of the first arch (Meckel's cartilage) forms the lower jaw in primitive vertebrates. In human beings, Meckel's cartilage makes little contribution to the adult mandible but provides a framework around which the bone of the mandible forms.

At 6 weeks of development this cartilage extends as a solid hyaline cartilaginous, surrounded by a fibrocellular capsule, from the developing ear region (otic capsule) to the midline of the fused mandibular processes. The two cartilages of each side do not meet at the midline but are separated by a thin band of mesenchyme. The mandibular branch of the trigeminal nerve (the nerve of the first arch) has a close relationship to Meckel's cartilage, beginning two thirds of the way along the length of the cartilage. At this point the mandibular nerve divides into lingual and inferior alveolar branches, which run along the medial and lateral aspects of the cartilage respectively. The inferior alveolar nerve further divides into incisor and mental branches more anteriorly.

The mandible first appears as a band of dense fibrocellular tissue that lies on the lateral side of the inferior dental and incisive nerves. Ossification takes place in the membrane covering the outer surface of Meckel's cartilage and each half of the bone is formed from a single center. Ossification proceeds medially below the incisive nerve and then spread upwards between this nerve and Meckel's cartilage and so the incisive nerve is contained in a trough or a groove of bone formed by the lateral and medial plates united beneath the nerve. A similar spread of ossification in the backward direction produces at first a trough of bone in which lies the inferior dental nerve and much later the mandibular canal is