Teeth, orofacial development and cleft anomalies

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Variability of jaws in vertebrates. (A) cartilaginous fish – shark; (B) an example of a bone fish; (C) amphibian – frog; (D) reptile – turtle; (E) reptile – python; (F) reptile – crocodile; (G) bird – goose; (H) mammal - dolphin.

(From Seichert et al., 2006).



Variability of dentition in mammals. (A) opossum; (B) hedgehog; (C) coati; (D) porcupine; (E) baboon; (F) deer, note the atavistic canine (c); (G) armadillo; (H) mandible of elephant with horizontally replacing molars (molars are permanently shifting mesially, where they are finally shed, while a new molar emerges distally; (I) dolphin; (J) toothless ante-eater (tamanoir).

(From Seichert et al., 2006).



Human tooth pattern. (A) Deciduous dentition (green) in a child. (B) Permanent dentition (orange and blue) in an adult. (C) Relationship between the deciduous and permanent dentition.



The tooth formula of a permanent dentition in human. Two incisors (I1, I2); one canine (C); two premolars (P1, P2); three molars (M1, M2, M3). Two terminologies can be used to indicate anatomical directions (A, B).



Human adult dentition. Tooth formula is similar in both jaws:
two incisors, one canine, two premolars and three molars.
C – canine; P2 , P2 - the second upper and lower premolar,
respectively; M3 and M3 – the third upper and lower molar,
respectively.







The sequence of morphological stages which characterize tooth development. The shape of the dental epithelium on frontal sections is shown in orange, dental mesenchyme in green. The first morphological sign of tooth formation is a thickening of the oral epithelium, which later forms a dental lamina. The dental lamina gives rise to the epithelial tooth buds with the surrounding condensed mesenchyme. Then the main morphological change concerns the development of the cervical loop (asterisk), which characterizes the cap stage. The mesenchyme enclosed in the cap cavity is called tooth papilla (dark green). At the early bell stage, cusps formation is initiated, and the cervical loop progressively elongates and further delimitates the mesenchyme of the tooth papilla. At the late bell stage, the root formation initiates by further extension of the dental epithelium, which forms the Hertwig's epithelial root sheet (arrowhead). Functional differentiation of specific cells is initiated at the epithelium-mesenchyme interface (dashed line). The cells become postmitotic and then start to elongate and polarize. Firstly odontoblasts appear on the mesenchymal side and later ameloblasts become visible on the epithelial side (see in the rectangle).



Schematic illustration showing the distribution patterns of neural crest cells originated from the anterior midbrain (A), posterior midbrain (B), and anterior hindbrain (C). Colored dots show the crest cells emigrating by the end of the 5-somite stage (red), at the 6-somite stage (green), and at the 7-to 8-somite stage (blue). Deep color dots demonstrate a large number of cells, and light color ones a small number. In general, the early-emigrating crest cells migrate to the more distal region, while those emigrating at the later stage are distributed in the more proximal part.





Stages of tooth development shown in the cheek region of the prenatal mouse mandible. (A) 3D reconstructions document the spatial arrangement of the dental and adjacent oral epithelium. A frontal section has been drawn to present the shape of the dental epithelium in the central part of a 3D model (modified according to Peterkova et al, 2002). (B) Frontal histological sections. Bar = 50um.



Fig. 14-9. Development and cruption of the primary dentition. Notice that the ectodermal dental lamina gives rise to the enamel organ, which secretes the enamel of the tooth, whereas the neural crest cells that initially form the dental papilla differentiate into the odontoblasts, which secrete the dentin.







Classical interpretation of the early development of human dentition. Human teeth develop from a U-shaped dental lamina (DL), which exists in each upper and lower jaw. Externally, another U-shaped structure is located and called a vestibular lamina (VL). The latter structure is presented as the anlage of oral vestibule.



A developmental relationship between developing dentition and oral vestibule in human. A scheme of the dental (red) and vestibular (yellow and blue) epithelium in human embryos is based by computer aided 3D reconstructions. The prospective oral vestibule (yellow) has different origins in the lip and cheek regions of both: upper (**A**) and lower (**B**) jaws. The remaining vestibular epithelium is in blue.



The trigeminal (fifth cranial) nerve consists of large sensory branches and a small motor branch. There are three sensory branches: the ophthalmic to the orbit and forehead, the mandibular to teeth of the lower jaw and tongue, and the maxillary to the maxillary sinus and teeth of the upper jaw.



Malocclusion is the term used when the occlusion, or bite, is not ideal.

crossbite, too much of an over/under bite as pictured below, or other other discrepancies.



(*A*), Normal occlusion; (*B*), Class I malocclusion; (*C*), Class II malocclusion; (*D*), Class III malocclusion. Note the position of the mesial cusp of the maxillary molar relative to the mandibular molar in each type of occlusion.



Diagrammatic representation of the generation of biological replacement teeth. Suitable sources of epithelial and mesenchymal cells are expanded in culture to generate sufficient cells. The two cell populations are combined to bring the epithelial and mesenchymal cells into direct contact, mimicking the *in vivo* arrangement. Interaction between these cell types leads to formation of an early stage tooth primordium, equivalent to a tooth bud or cap, around which the mesenchyme cells condense (dark blue dots) (see also Box 1). The tooth primordium is surgically transplanted into the mouth and left to develop. (Volponi et al, 2010)

























Double second upper incisor











Normal development



yellow – thickened dental epithelium of the mn (medial nasal process); red – thickened dental epithelium of the mx (maxillary process); In – lateral nasal process md –mandibular process



The early development of the human upper jaw and dental arch in a scheme. The scheme shows frontal aspect of the embryonic human face and the oral aspect of the upper jaw arch before (A) and after the critical period of the fusion of the facial processes (B) and dental epithelium (C). In the 5th week old embryo (A), the medial nasal (mn) and the maxillary (mx) processes are not yet fused. (B) During normal development (I), the facial processes fuse giving rise to a continuous upper lip and jaw arch. Origin of the upper jaw cleft results from failing fusion of the mn and mx (III). During normal development (I), the fusion of the facial processes is followed by a fusion of their dental epithelia and formation of a continuous dental lamina in week 6-7 human embryo. At the site of the fusion of the dental epithelia, the germ of the lateral incisor (i2) emerges, containing material from both the mn and mx under (C/I). Developmental anomalies of i2 (duplication, hypoplasia, absence) are typically associated with a presence of the upper jaw cleft (C/III). However, incisor anomalies also frequently occur in normally formed upper jaw arch. This can be explained by a defect in fusion of the two incisor components (C/II). Red, yellow and green – dental epithelium of the respective mn, mx and mandibular process (md).

Normal development (epithelium from mesenchymal view)



computer-aided 3D reconstructions at ED 40-42



FIGURE 14-8. Development of the palate as seen from below.



A. Frontal section through the head of a $61/_2$ -week old embryo. The palatine shelves are located in the vertical position on each side of the tongue.

B. Ventral view of the palatine shelves after removal of the lower jaw and the tongue. Note the clefts between the primary triangular palate and the palatine shelves, which are still in a vertical position.



A. Frontal section through the head of a $7^{1/2}$ -week old embryo. The tongue has moved downward and the palatine shelves have reached a horizontal position.

B. Ventral view of the palatine shelves after removal of the lower jaw and the tongue. The shelves are in a horizontal position.



Pierre-Robin Syndrome







Mutation in IRF6 (Interferon Regulatory Factor 6)

causes

VAN der WOUDE Syndrome (Salivary fistula + BCLP)



Atypical clefts



INCIDENCE OF OROFACIAL CLEFT

EMBRYOTOXICITY

$2. \quad \bullet \bullet \bullet \bullet \bullet \bullet \bullet \phi \circ \circ$



Spontaneous abortions



- Czech Republic 1965 1999
- A official statistics no records of abortions during first month of pregnancy
- B situation after mathematical extrapolation of data using exponential curve

Newborns with an orofacial cleft in Czech Rep.









The mean incidence of all CL/P in 1983-1997.



White - lower than 1.76 clefts per 1000 newborns. Grey - from 1.76 to 1.96 clefts per 1000 newborns. Black - more than 1.96 clefts per 1000 newborns. Districts with the highest (black) and the lowest (white) incidence of orofacial clefts in the Czech Rep. (1964 - 1982 and 1983 - 1997)



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Primary prevention of malformations

Planning of pregnancy:

- avoiding of the exposition to embryotoxic factors by professional employment (chemicals, psychical stress)
- investigation of mother's health (internal, gynecological, stomatological)
- optimalization of alimentation and life style (smoking, abusus of alcohol)
- treatment of chronic diseases (e.g. diabetes, epilepsy, thyroid gland disturbances, asthma) and optimalization of medical treatment (drug doses and scheme of therapy)

Secondary prevention of malformations

Prenatal diagnostics:

- Ultra-sonography (detecting of external malformations, heart defects, sex of embryos)
- Amniocentesis during weeks 14-16 (chromosomal aberrations, metabolic diseases, sex chromatin patterns, alpha-fetoprotein assay)
- Chorionic villus sampling (biopsies several weeks earlier than amniocentesis)

-Unilateral incomplete cleft lip in fetus at 34 weeks' gestation.



Smith A S et al. AJR 2004;183:229-235

-Bilateral complete cleft lip in fetus at 18 weeks' gestation.



Smith A S et al. AJR 2004;183:229-235

Warfarin syndrome



Hypoplastic nose, flat face, low nasal bridge, altered calcification (Smith, 1982)