# DEVELOPMENT OF SKIN AND ASSOCIATED STRUCTURES

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# OBJECTIVES

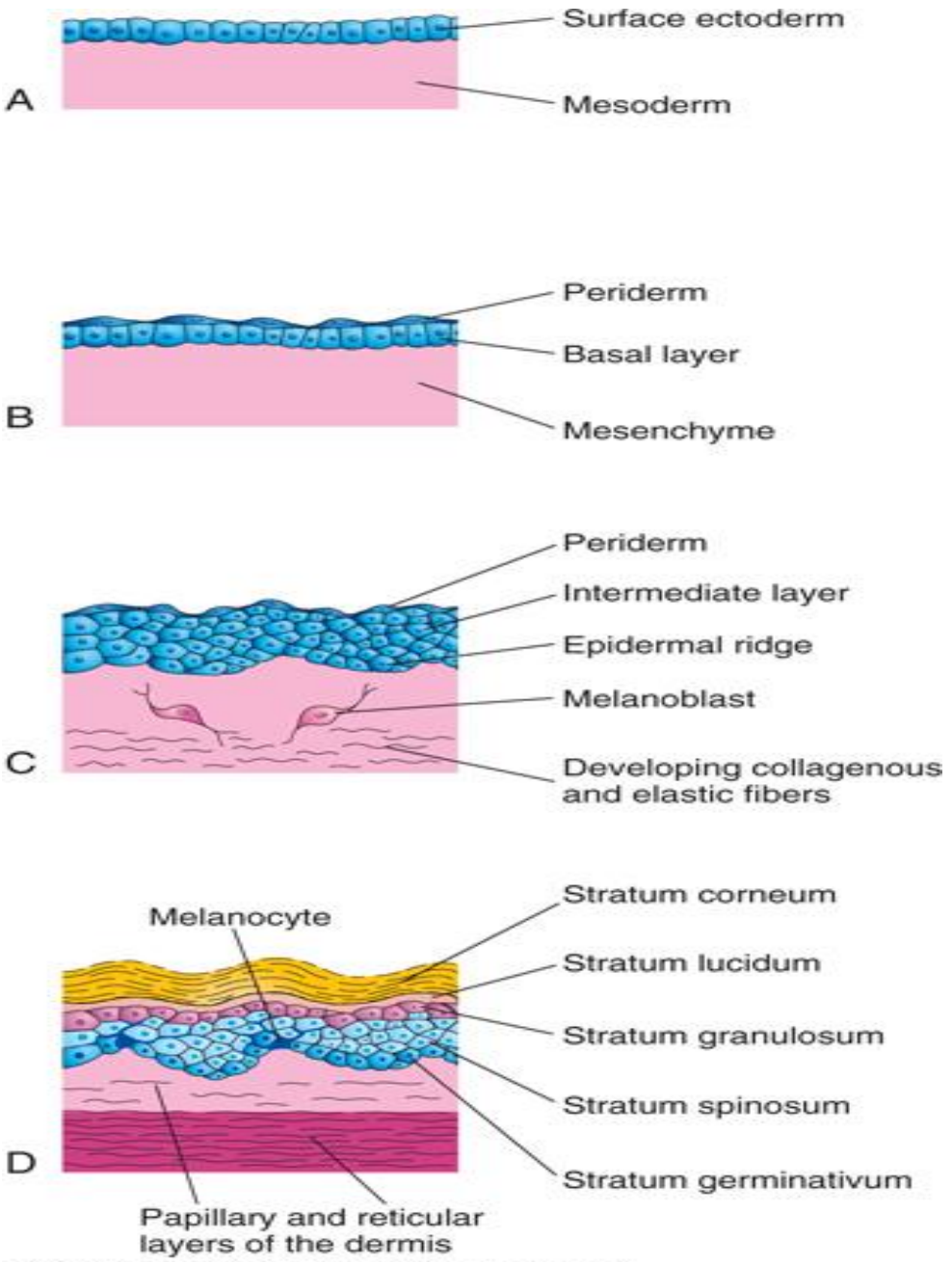
- Understand the development of different layers of the skin
- Understand development of skin associated/related structures
- Understand the embryological basis of congenital malformations of skin development

# INTRODUCTION

- The integumentary system consists of:
  - the skin
  - and its appendages:
    - sweat glands,
    - nails,
    - hairs,
    - sebaceous glands,
    - arrector muscles of hairs (arrector pili muscles),
    - mammary glands,
    - teeth

# DEVELOPMENT OF SKIN

- The skin, is a complex organ system
- It is the largest organ.
- Consists of two layers:
  - The **epidermis** derived from surface ectoderm
  - The **dermis** derived from **mesenchyme**
- There is Ectodermal (epidermal) - mesenchymal (dermal) reciprocal induction mechanisms mediated by signaling molecules including: the Wnt, FGF, TGFβ, and Hedgehog pathways.
- Skin structures vary from one part of the body to another e.g.
  - skin of the eyelids is thin and soft and has fine hairs,
  - skin of the eyebrows is thick and has coarse hairs.
- At 4 to 5 weeks, skin consists of a single layer of surface ectoderm overlying the mesoderm.

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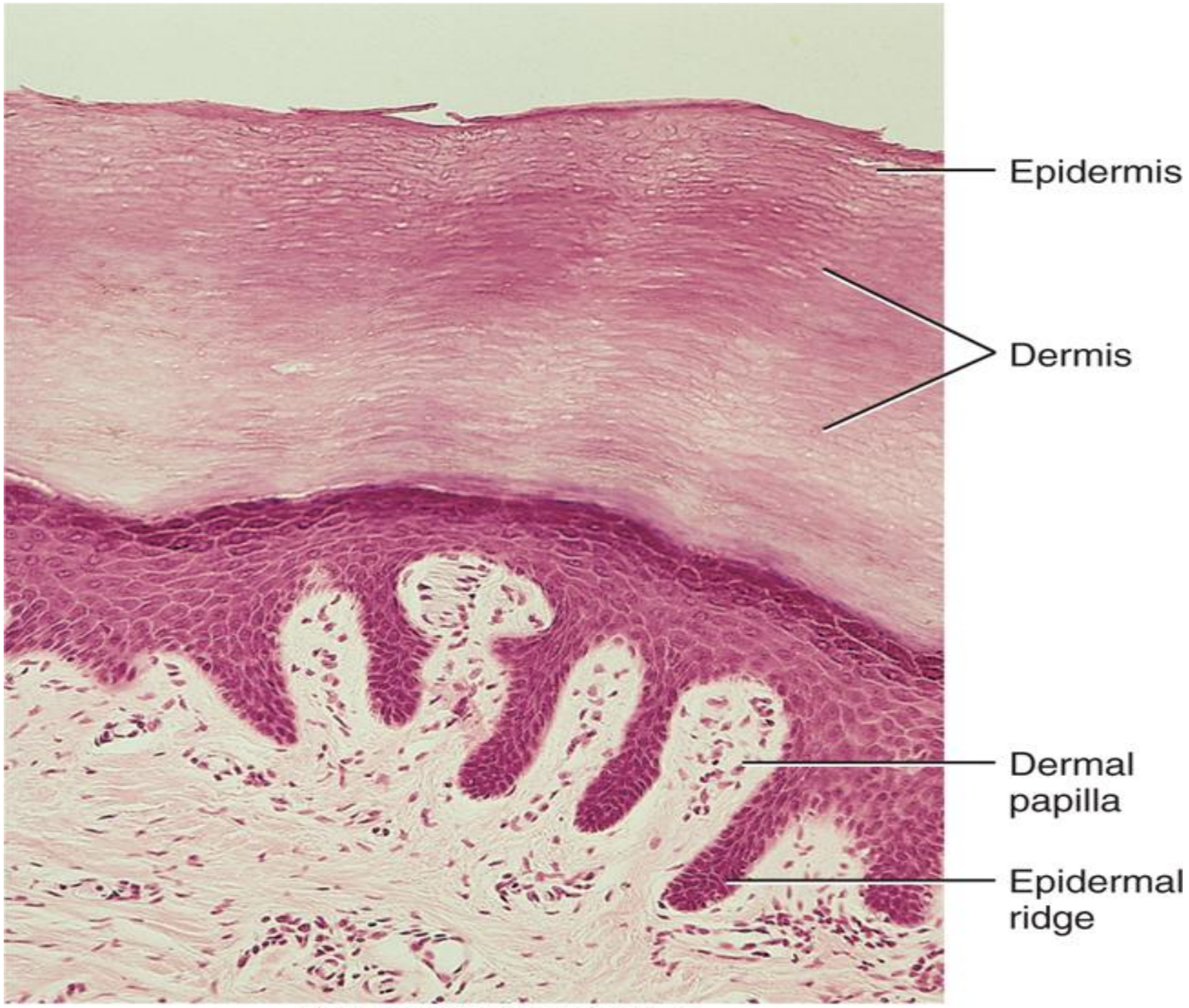


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Light micrograph of thick skin (x132). Observe the epidermis and dermis as well as the dermal papilla interdigitating with the epidermal ridges.

# Epidermis

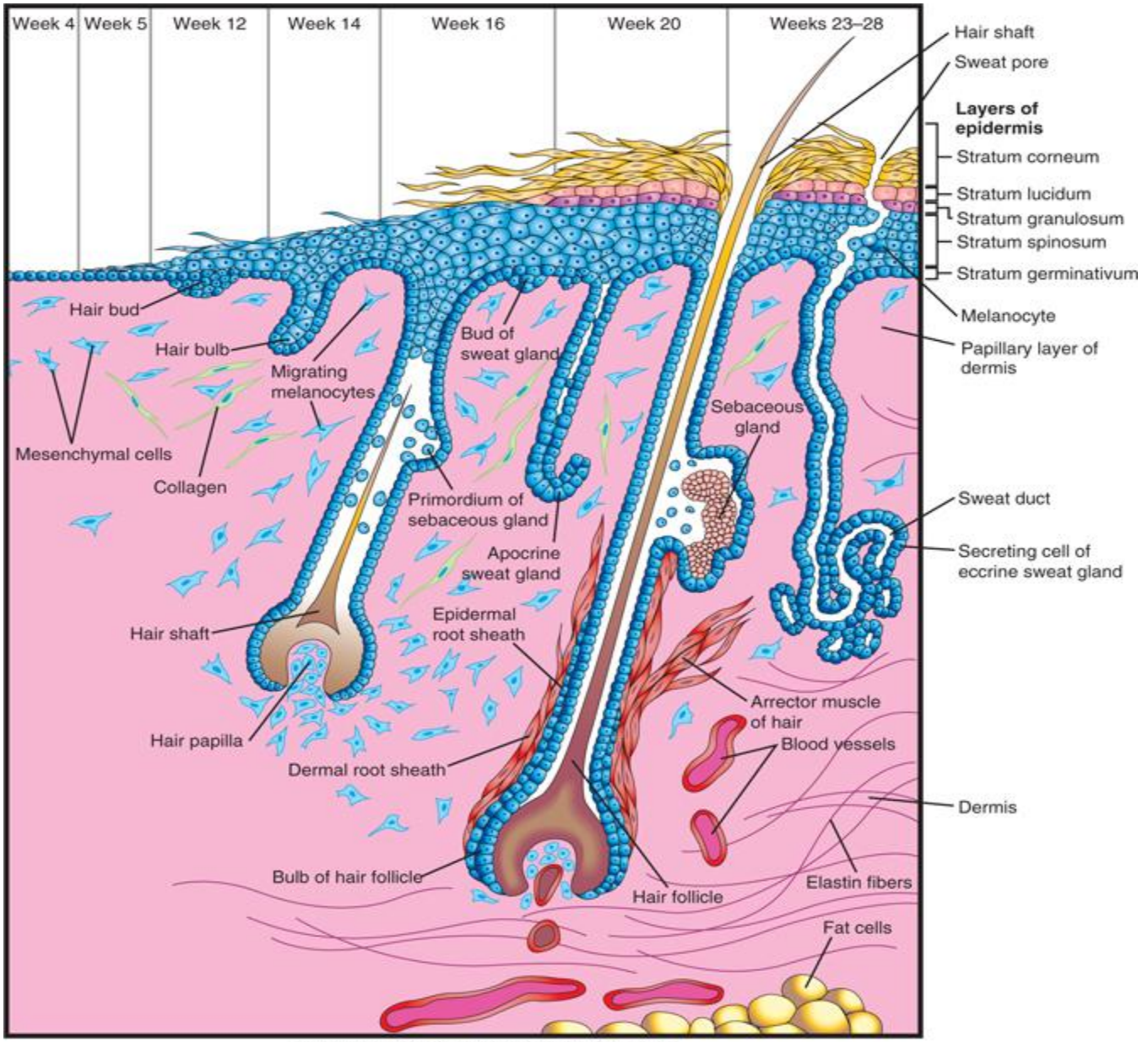
- Epidermal growth occurs in stages.
- The primordium is a single layer of surface ectodermal cells.
- These cells proliferate and form a layer of squamous epithelium, the **periderm**, and a **basal layer**.
- The cells of the periderm continually undergo **keratinization** and **desquamation**, and are replaced by cells from the basal layer.
- The exfoliated peridermal cells and **sebum** from **sebaceous glands**form a white greasy substance - **vernix caseosa** - that covers the fetal skin.
- The vernix:
  - protects the developing skin from constant exposure to amniotic fluid, with its high content of urine, bile salts, and sloughed cells, during the fetal period.
  - facilitates birth of the fetus.

- The basal layer of the epidermis becomes the **stratum germinativum** which produces other layers and epidermal ridges.
- The transformation of the surface ectoderm into the multilayered **definitive epidermis** is induced by the dermis.
- By 11 weeks, the **intermediate layer** is formed.
- Replacement of peridermal cells continues until approximately the 21st week; thereafter, the periderm disappears and the **stratum corneum** forms from the **stratum lucidum**.
- Epidermal ridges:
  - appear by 10$^{th}$ week
  - permanently established by 19 weeks
  - those of the hand appear approximately one week earlier than in the feet.

- The epidermal ridges produce grooves on the surface of the palms and soles, fingers and toes.
- The type of pattern genetically determined genetically and is specific for an individual - basis for fingerprints.
- **Abnormal chromosome complements** affect the development of ridge patterns; for instance, infants with Down syndrome have distinctive patterns on their hands and feet that are of diagnostic value.
- **Neural crest cells** migrate into the mesenchyme of the developing dermis and differentiate into **melanoblasts**.

- Melanoblasts migrate to the **dermoepidermal junction** and differentiate into **melanocytes** which contain **pigment granules**.
- Melanocytes appear in the developing skin at 40 to 50 days, immediately after the migration of neural crest cells.
- Only a few melanin - containing cells are normally present in the dermis.
- The melanocytes begin producing melanin before birth and distribute it to the epidermal cells.

Drawing of the successive stages in the development of hairs, sebaceous glands, and arrector muscles of hair. Note that the sebaceous gland develops as an outgrowth from the side of the hair follicle.

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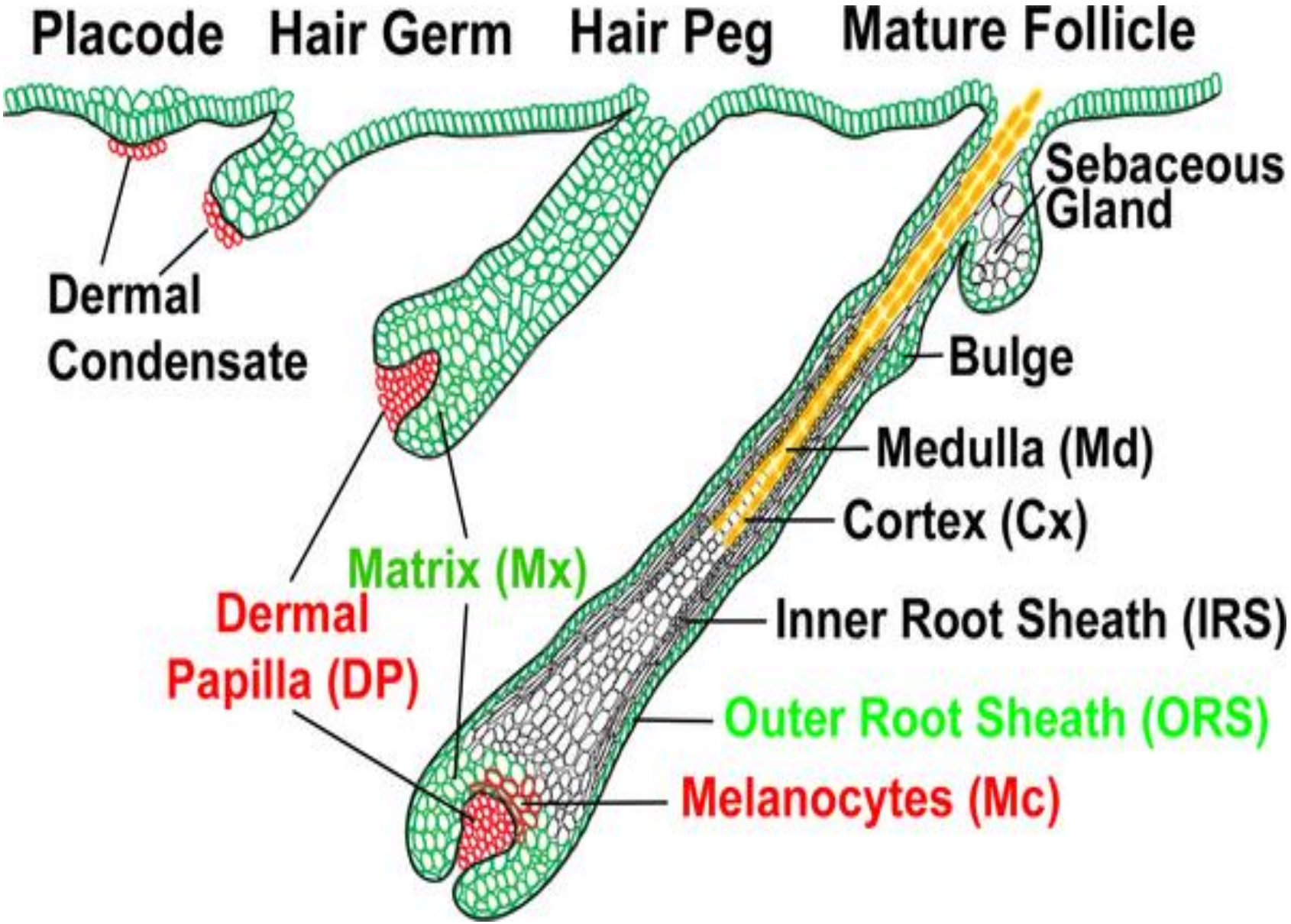
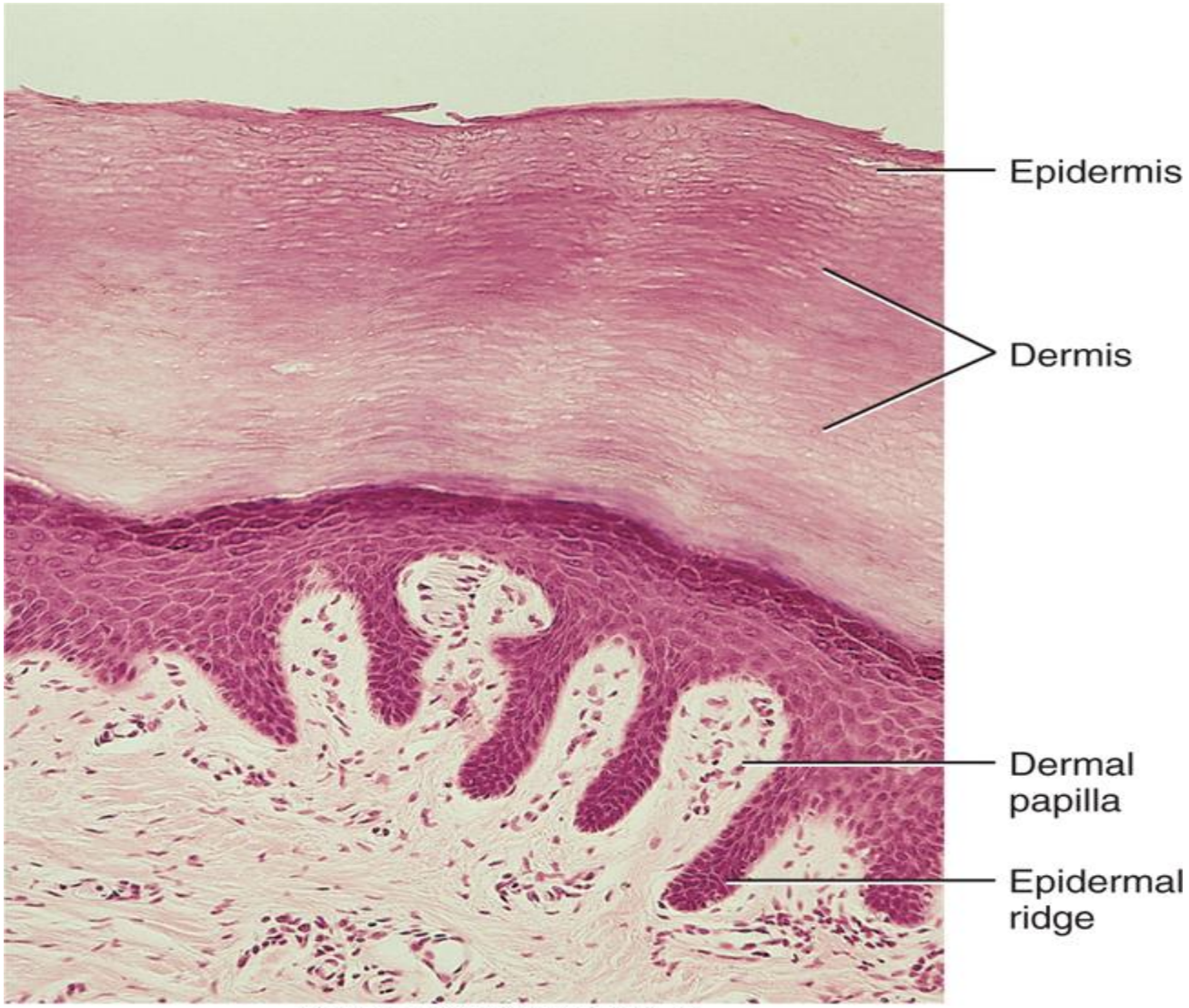

Placode
Hair Germ
Hair Peg
Mature Follicle
Sebaceous Gland
Dermal Condensate
Bulge
Medulla (Md)
Cortex (Cx)
Matrix (Mx)
Dermal Papilla (DP)
Inner Root Sheath (IRS)
Outer Root Sheath (ORS)
Melanocytes (Mc)

- The relative content of melanin inside the melanocytes accounts for the different colors of skin in different races and not the number of melanocytes.
- Skin is classified as thick or thin based on the thickness of the epidermis.
  - **Thick skin** covers the palms of the hands and the soles of the feet; it lacks hair follicles, arrector muscles of hairs, and sebaceous glands, but it has sweat glands.
  - **Thin skin** covers most of the rest of the body; it contains hair follicles, arrector muscles of hairs, sebaceous glands, and sweat glands.

# Dermis

- The dermis develops from mesenchyme derived from:
  - somatic layer of lateral mesoderm
  - dermatomes of the somites.
- By 11 weeks, the mesenchymal cells have begun to produce collagenous and elastic connective tissue fibers.
- The **epidermal ridges** form the dermis projects into the epidermis, forming **dermal papillae,** which interdigitate with the epidermal ridges.

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Light micrograph of thick skin (x132). Observe the epidermis and dermis as well as the dermal papilla interdigitating with the epidermal ridges. *(From Gartner LP, Hiatt JL: Color Textbook of Histology, 2nd ed. Philadelphia, WB Saunders, 2001.)*

- Some dermal papillae:
  - have c**apillary loops of blood vessels** to nourish the epidermis
  - others have sensory nerve endings.
- The developing afferent nerve fibers influence the spatial and temporal sequence of dermal ridge formation.
- By $5^{th}$ week, capillary - like vessels are present.
- These capillary - like structures differentiate to arterioles, arteries, venules and veins.
- By the end of the first trimester, the major vascular organization of the fetal dermis is established.

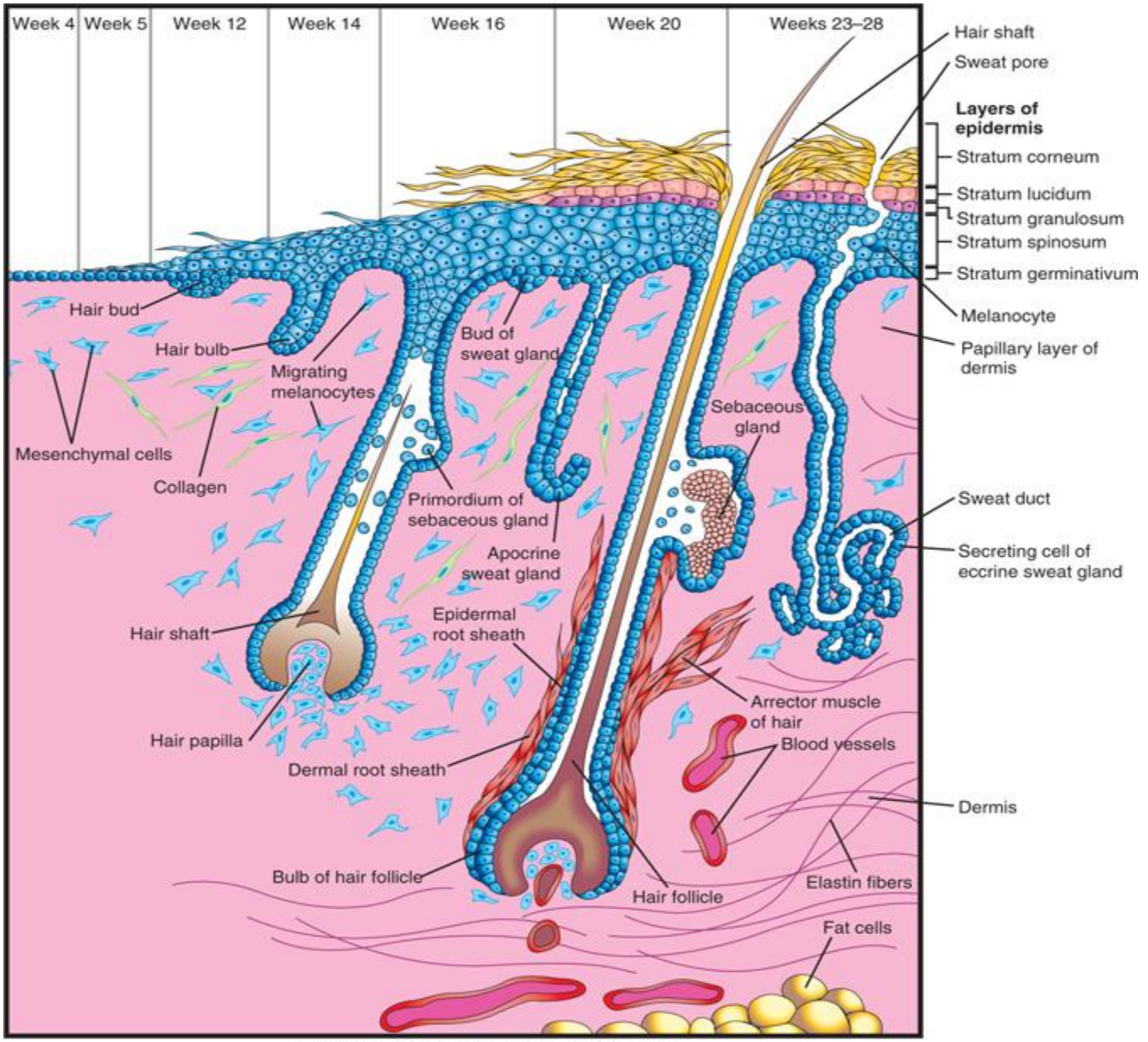
# Development of Glands

- The glands of the skin include:
  - eccrine sweat glands
  - apocrine sweat glands
  - sebaceous glands
  - mammary glands
- They are derived from the epidermis and grow into the dermis.

# Sebaceous Glands

- Cellular buds develop from the sides of the developing **epithelial root sheaths** of hair follicles.
- The buds invade the surrounding dermal connective tissue and branch to form several alveoli and their associated ducts.
- The central cells of the alveoli break down, forming an oily substance – **sebrum** - that protects the skin against friction and dehydration.
- Sebum is released into the hair follicle and passes to the surface of the skin to form **vernix caseosa.**
- Sebaceous glands in the glans of the penis and labia minora, develop as cellular buds from the epidermis that invade the dermis.

Drawing of the successive stages in the development of hairs, sebaceous glands, and arrector muscles of hair. Note that the sebaceous gland develops as an outgrowth from the side of the hair follicle.

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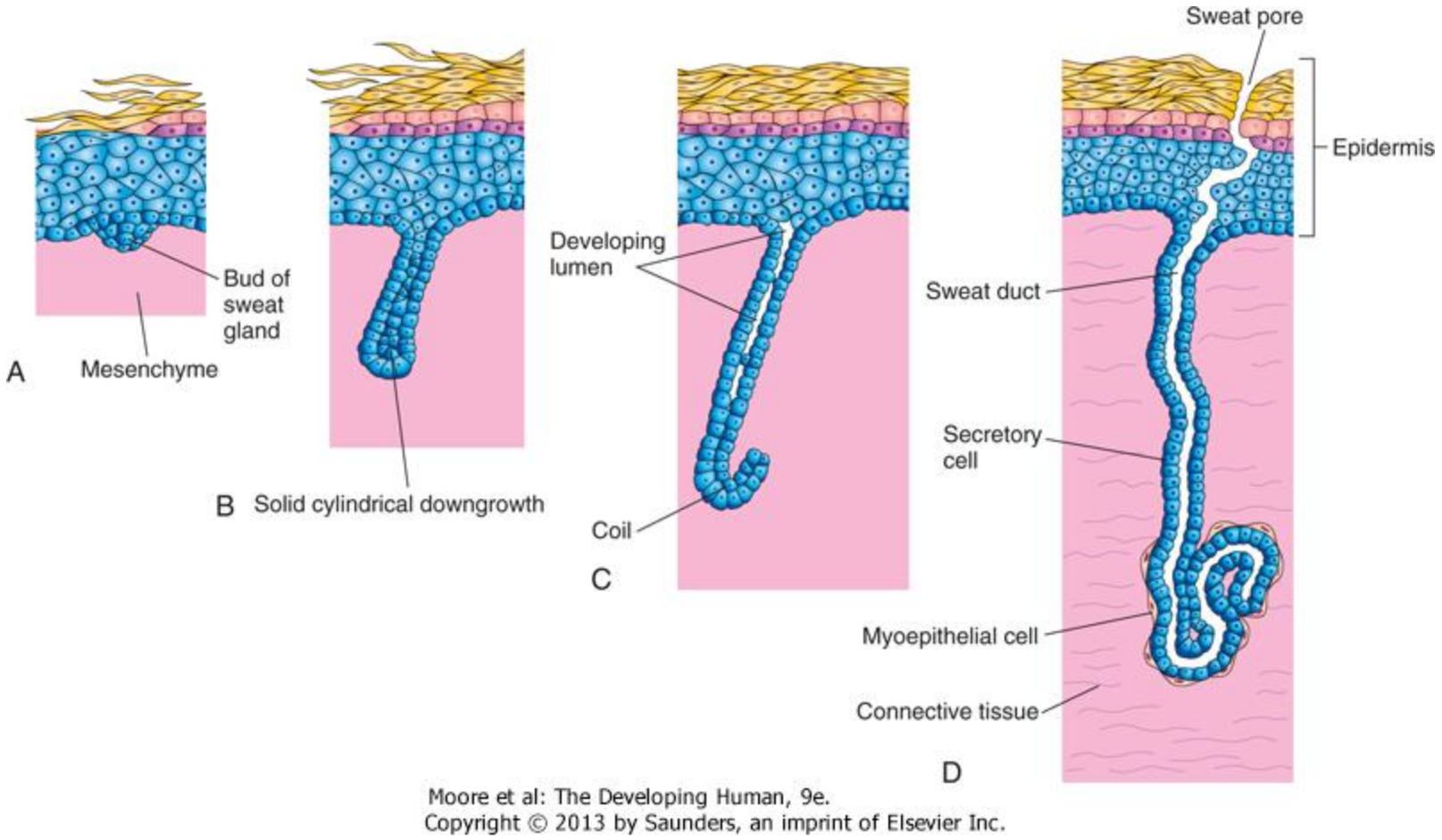
# Sweat Glands

- E**ccrine sweat glands** are located in the skin throughout most of the body.
- They develop as cellular buds from the epidermis that grow into the underlying mesenchyme.
- As the buds elongate, their ends coil to form the bodies of the secretory parts of the glands.
- The epithelial attachments of the developing glands to the epidermis forms the sweat ducts.
- The peripheral cells of the secretory parts of the glands differentiate into myoepithelial and secretory cells.

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Illustrations of the successive stages of the development of a sweat gland. **A** and **B,** The cellular buds of the glands develop at approximately 20 weeks as a solid growth of epidermal cells into the mesenchyme. **C,** Its terminal part coils and forms the body of the gland. The central cells degenerate to form the lumen of the gland. **D,** The peripheral cells differentiate into secretory cells and contractile myoepithelial cells.

- Myoepithelial cells are specialized smooth muscle cells that assist in expelling sweat from the glands.
- Eccrine sweat glands begin to function shortly after birth.
- Sudoriferous (producing sweat) **apocrine sweat glands** are mostly confined to the axillary, pubic and perineal regions, and the areolae of the breast.
- The glands develop from down growths of the stratum germinativum of the epidermis .
- The ducts of these glands open, not onto the skin surface, as do eccrine sweat glands, but into the canals of the hair follicles superficial to the entry of the sebaceous gland ducts.
- Secretion by apocrine sweat glands is influenced by hormones and does not begin until puberty.

# DISORDERS OF KERATINIZATION

- **Ichthyosis** is agroup of skin disorders resulting from excessive keratinization - formation of horny layers of skin.
  - The skin is characterized by dryness and scaling, which may involve the entire body surface.
- A **harlequin fetus** results from a rare keratinizing disorder that is inherited as an autosomal recessive trait.
  - The skin is markedly thickened, ridged, and cracked.
  - Most affected neonates die during the first week of life.
- A **collodion infant** is covered by a thick, taut membrane that resembles collodion or parchment.
  - The membranous skin cracks and begins to fall off in large sheets.
  - Deficiency of transglutaminase-1 is the most common cause.
  - Complete shedding may take several weeks, occasionally leaving normal-appearing skin.
- **Lamellar ichthyosis** is an autosomal recessive disorder. A neonate may appear to be a collodion baby; however, the scaling persists.
  - Growth of hair may be curtailed and development of sweat glands is often impeded.
  - Affected infants are unable to sweat.


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**A,** A child with congenital hypertrichosis and hyperpigmentation. Note the excessive hairiness on the shoulders and back. **B,** A child with severe keratinization of the skin (ichthyosis) from the time of birth.

# CONGENITAL ECTODERMAL DYSPLASIA

- A group of rare hereditary disorders involving tissues that are ectodermal in origin.
- The teeth are completely or partially absent and often the hairs and nails are affected.
- **Ectrodactyly - ectodermal dysplasia - clefting syndrome** is a congenital skin that involves both ectodermal and mesodermal tissues, consisting of:
  - **ectodermal dysplasia** associated with hypopigmentation of skin and hair,
  - scanty hair and eyebrows,
  - absence of eyelashes,
  - nail dystrophy,
  - hypodontia
  - microdontia,
  - **ectrodactyly**, and cleft lip and palate.

# ANGIOMAS OF SKIN

- Some transitory and/or surplus primitive blood or lymphatic vessels persist as either:
  - arteries,
  - venous,
  - **cavernous angiomas**,
  - often of a mixed type.
- Angiomas composed of lymphatics are called **cystic lymphangiomas** or **cystic hygromas**.
- True angiomas are benign tumors of endothelial cells.

- **Nevus flammeus** denotes a flat, pink or red, flame - like blotch that often appears on the posterior surface of the neck.
- A **port - wine stain hemangioma** which is sharply demarcated is a larger and darker angioma than a nevus flammeus and is nearly always anterior or lateral on the face and/or neck.
- **Common angioma** (pinkish-red blotch) may cross the median plane.
- A port-wine stain in the area of distribution of the trigeminal nerve is sometimes associated with a similar type of angioma of the meninges of the brain and seizures at birth (**Sturge-Weber syndrome**).

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Hemangioma (port-wine stain) in an infant.

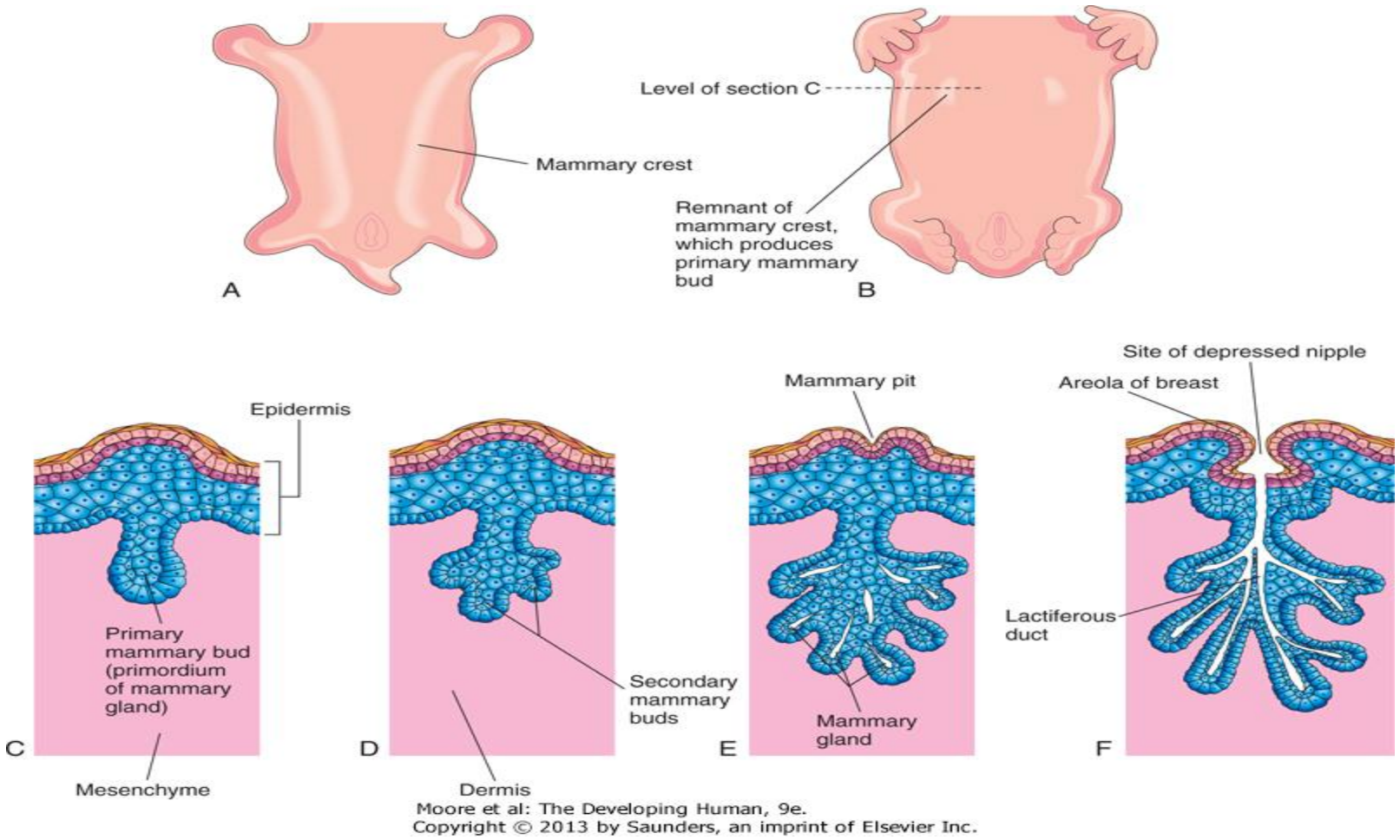
# ALBINISM

- G**eneralized albinism**, is an autosomal recessive trait where the skin, hairs, and retina lack pigment; however, the iris usually shows some pigmentation.
- Albinism occurs when the melanocytes fail to produce melanin because of the lack of the enzyme tyrosinase or other pigment enzymes.
- In *localized albinism* – **piebaldism** - an autosomal dominant trait, there is a lack of melanin in patches of skin and/or hair.

# Mammary Glands

- Mammary glands are modified and highly specialized types of sweat glands.
- Development of mammary glands also called mammogenesis is similar in male and female embryos.
- The first evidence of mammary development appears in the fourth week when mammary crests (ridges)/line develop along each side of the ventral surface of the embryo.
- These crests extend from the axillary region to the inguinal region.

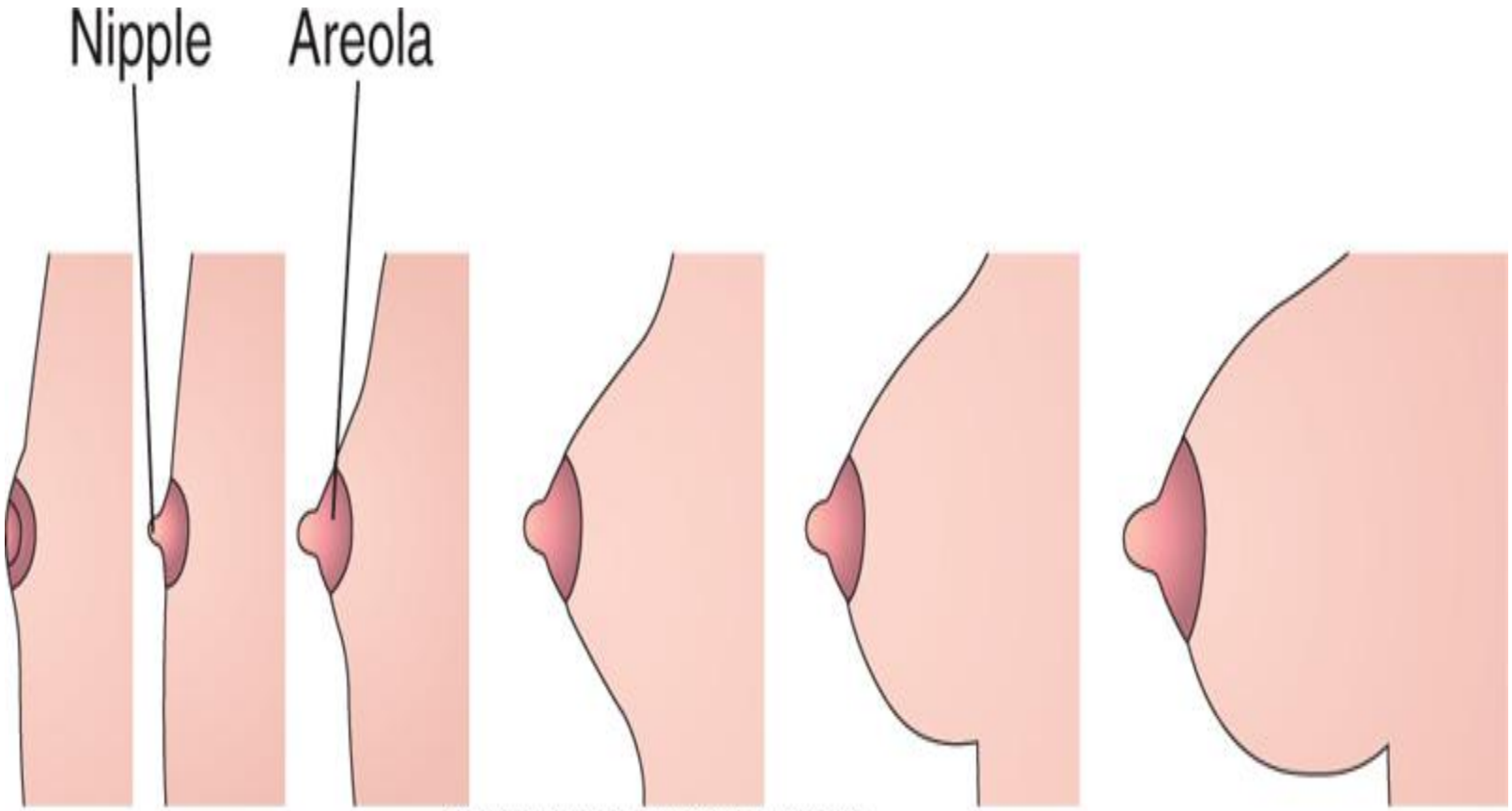
- The crests usually disappear except for the parts at the site of the future breasts.
- Involution of the remaining mammary crests in the $5^{th}$ week produces the primary mammary buds.
- These buds are down growths of the epidermis into the underlying mesenchyme.
- The changes occur in response to an inductive influence from the mesenchyme.




Development of mammary glands. **A,** Ventral view of an embryo of approximately 28 days showing the mammary crests. **B,** Similar view at 6 weeks showing the remains of these crests. **C,** Transverse section of a mammary crest at the site of a developing mammary gland. **D** to **F,** Similar sections showing successive stages of breast development between the 12th week and birth.

- Each primary mammary bud soon gives rise to several **secondary mammary buds**, which develop into **lactiferous ducts** and their branches.
- Canalization of secondary mammary buds is induced by placental sex hormones entering the fetal circulation.
- By term, 15 to 19 lactiferous ducts are formed.
- The fibrous connective tissue and fat of the mammary glands develop from the surrounding mesenchyme.
- During the late fetal period, the epidermis at the site of origin of the mammary gland becomes depressed, forming a shallow **mammary pit**.
- The nipples are poorly formed and depressed in neonates.
- Soon after birth, the **nipples** usually rise from the mammary pits because of proliferation of the surrounding connective tissue of the **areola**.

- The smooth muscle fibers of the nipple and areola differentiate from surrounding mesenchymal cells.
- The **rudimentary mammary glands** of newborn males and females are identical and are often enlarged.
- Some secretion, often called "witch's milk" (galactorrhea), may be produced caused by maternal hormones.
- The breasts of neonates contain lactiferous ducts but no alveoli (secretory parts of glands).
- In females, the breasts enlarge rapidly during puberty, mainly because of development of the mammary glands and the accumulation of the fibrous stroma and fat associated with them.
- Full development occurs at approximately 19 years.
- Normally, the lactiferous ducts of males remain rudimentary throughout life.

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Sketches of progressive stages in the postnatal development of the female breasts. **A,** Neonate. **B,** Child. **C,** Early puberty. **D,** Late puberty. **E,** Young adult. **F,** Pregnant female. Note that the nipple is inverted at birth (**A**). At puberty (12-15 years), the breasts of females enlarge because of development of the mammary glands and the increased deposition of fat.

# GYNECOMASTIA

- **Gynecomastia** refers to the development of the rudimentary lactiferous ducts in the male mammary tissue.
- During midpuberty, approximately two thirds of boys develop varying degrees of hyperplasia of the breasts.
- This subareolar hyperplasia may persist for a few months to 2 years.
- A decreased ratio of testosterone to estradiol is found in boys with gynecomastia.
- Approximately 80% of males with **Klinefelter syndrome** have gynecomastia, which is associated with an XXY chromosome complement.

# ABSENCE OF NIPPLES (ATHELIA) OR BREASTS (AMASTIA)

- These rare birth defects may occur bilaterally or unilaterally.
- They result from failure of development or disappearance of the mammary crests.
- These conditions may also result from failure of mammary buds to form.
- More common is **hypoplasia of the breast**, often found in association with gonadal agenesis and Turner syndrome.
- Poland syndrome is associated with hypoplasia or absence of the breast or nipple.

# APLASIA OF BREAST

- The breasts of postpubertal females often differ somewhat in size.
- Marked differences are regarded as anomalies because both glands are exposed to the same hormones at puberty.
- In these cases, there is often associated rudimentary development of muscles of the thoracic wall, usually the pectoralis major.

# SUPERNUMERARY BREASTS AND NIPPLES

- An extra breast (**polymastia**) or nipple (**polythelia**) occurs in approximately 1% of the female population - inherited.
- An extra breast or nipple usually develops just inferior to the normal breast.
- **Supernumerary nipples** are also relatively common in males; often they are mistaken for moles.
- Less commonly, **supernumerary breasts** or nipples appear in the axillary or abdominal regions of females.

- In these positions, the nipples or breasts develop from extra mammary buds that develop from remnants of the mammary crests.
- They usually become more obvious in women when they are pregnant.
- Approximately one third of affected persons have two extra nipples or breasts.
- **Supernumerary mammary tissue** very rarely occurs in a location other than along the course of the mammary crests.
- It probably develops from tissue that was displaced from these crests.

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Female infant with an extra nipple (polythelia) on the left side.

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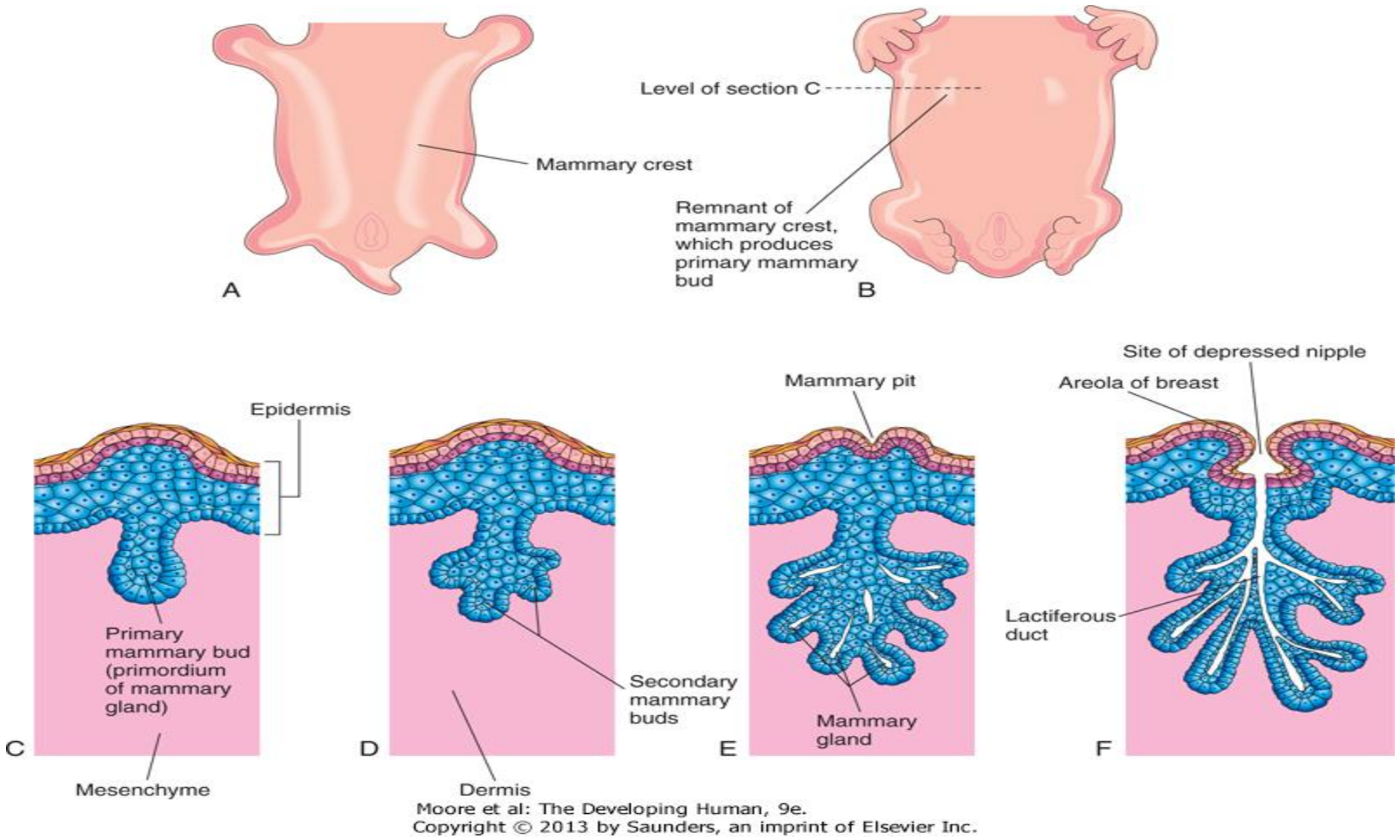
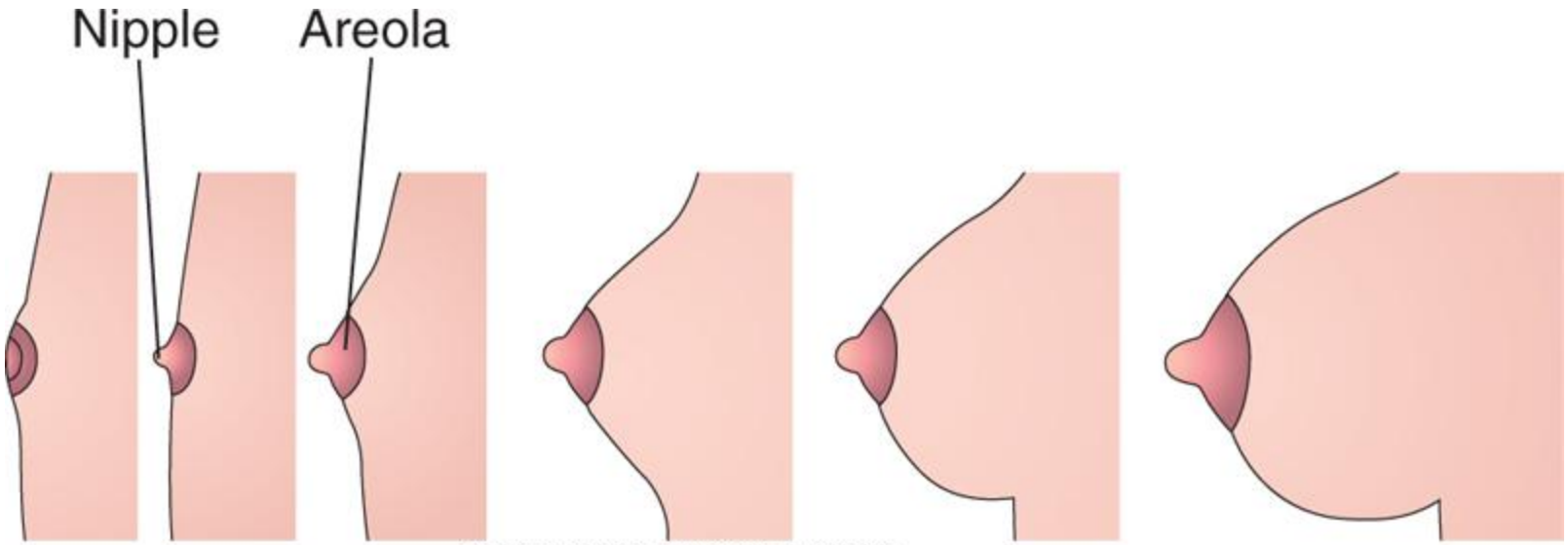
A man with polythelia (extra nipples) in the axillary and thigh regions. *Insets* are enlargements of the nipples (*arrowheads*). The *broken line* indicates the original position of the left mammary crests.

# INVERTED NIPPLES

- Sometimes the nipples fail to elevate above the skin surface after birth or during puberty, that is, they remain in their prenatal location.
- Inverted nipples may make breast-feeding of an infant difficult; however, a number of breast-feeding techniques can be used to reduce this difficulty.




Development of mammary glands. **A,** Ventral view of an embryo of approximately 28 days showing the mammary crests. **B,** Similar view at 6 weeks showing the remains of these crests. **C,** Transverse section of a mammary crest at the site of a developing mammary gland. **D** to **F,** Similar sections showing successive stages of breast development between the 12th week and birth.



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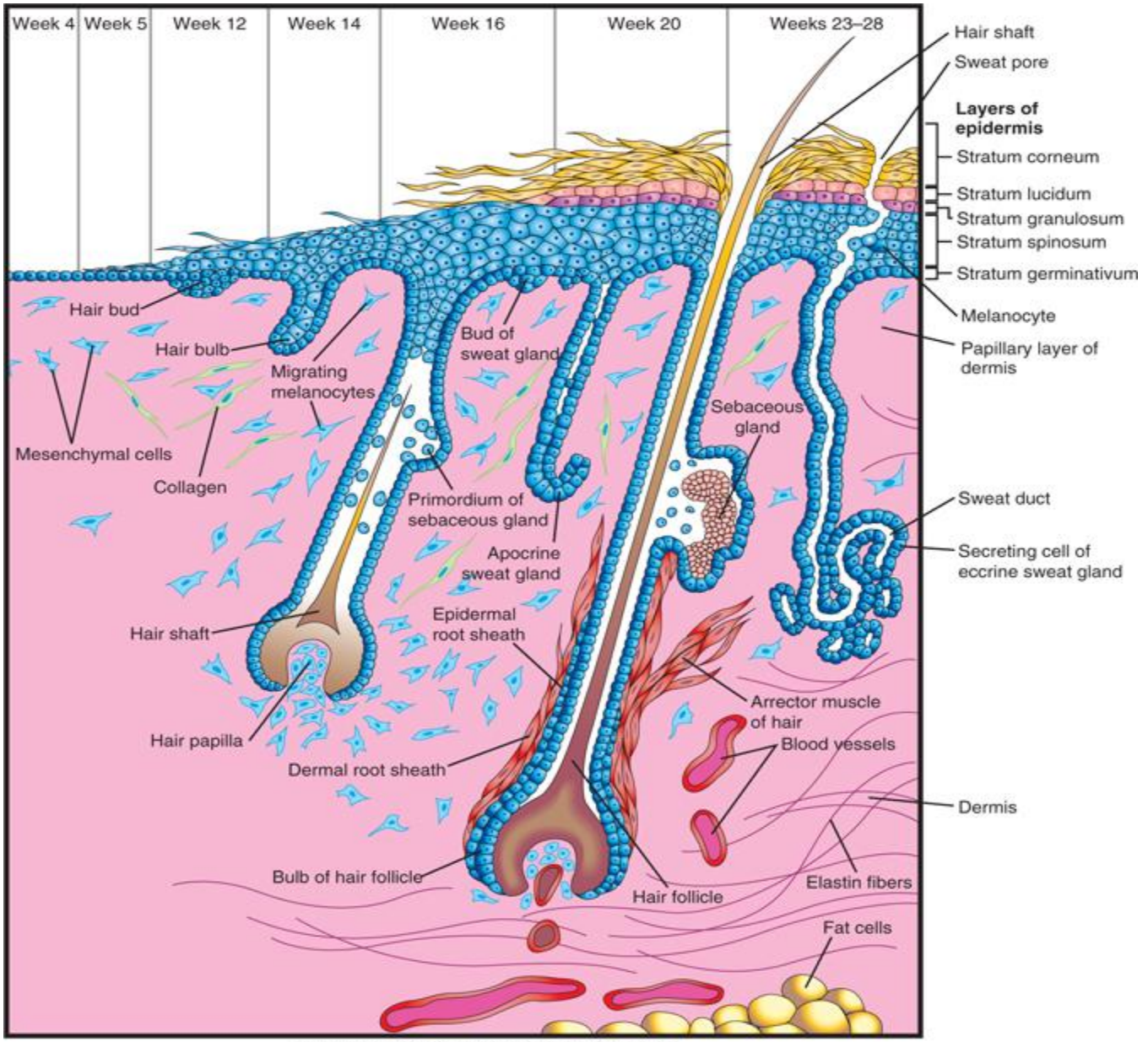
# Development of Hairs

- Hairs begin to develop early in the fetal period, but they do not become easily recognizable until approximately the 20$^{th}$ week.
- Hairs are first recognizable on the eyebrows, upper lip, and chin.
- The **hair follicles** begin as proliferations of the stratum germinativum of the epidermis, and extend into the underlying dermis.
- The **hair buds** soon become club shaped, forming **hair bulbs**.

- The epithelial cells of the hair bulbs constitute the **germinal matrix**, which later produces the hair shafts.
- The hair bulbs (primordia of hair roots) are soon invaginated by small mesenchymal **hair papillae**.
- The peripheral cells of the developing hair follicles form the **epithelial root sheaths**, and the surrounding mesenchymal cells differentiate into the **dermal root sheaths.**
- As cells in the germinal matrix proliferate, they are pushed toward the surface, where they become keratinized to form **hair shafts**.
- The hairs grow through the epidermis on the eyebrows and upper lip by the end of the $12^{th}$ week.

Drawing of the successive stages in the development of hairs, sebaceous glands, and arrector muscles of hair. Note that the sebaceous gland develops as an outgrowth from the side of the hair follicle.

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- The first hairs to appear - **lanugo** - are fine, soft, and lightly pigmented.
- Lanugo hairs help to hold the vernix caseosa on the skin.
- Lanugo is replaced by coarser hairs during the perinatal period.
- This hair persists over most of the body, except in the axillary and pubic regions, where it is replaced at puberty by even coarser terminal hairs.
- In males, similar coarse hairs also appear on the face and often on the chest - anterior wall of thorax.

- **Melanoblasts** migrate into the hair bulbs and differentiate into **melanocytes**.
- The relative content of **melanin** accounts for different hair colors.
- **Arrector muscles of hairs**, small bundles of smooth muscle fibers, differentiate from the mesenchyme surrounding the hair follicles and attach to the **dermal root sheaths** of the hair follicles and the **papillary layer of the dermis**, which interdigitates with the epidermis.
- Contractions of the arrector muscles depress the skin over their attachment and elevate the skin around the hair shafts, causing the hairs to stand up ("goose bumps").
- The arrector muscles are poorly developed in the hairs of the axillary region and in certain parts of the face.
- The hairs forming the eyebrows and the cilia forming the eyelashes have no arrector muscles.

Light micrograph of a longitudinal section of a hair follicle with its hair root *(R)* and papilla *(P)* (x132).


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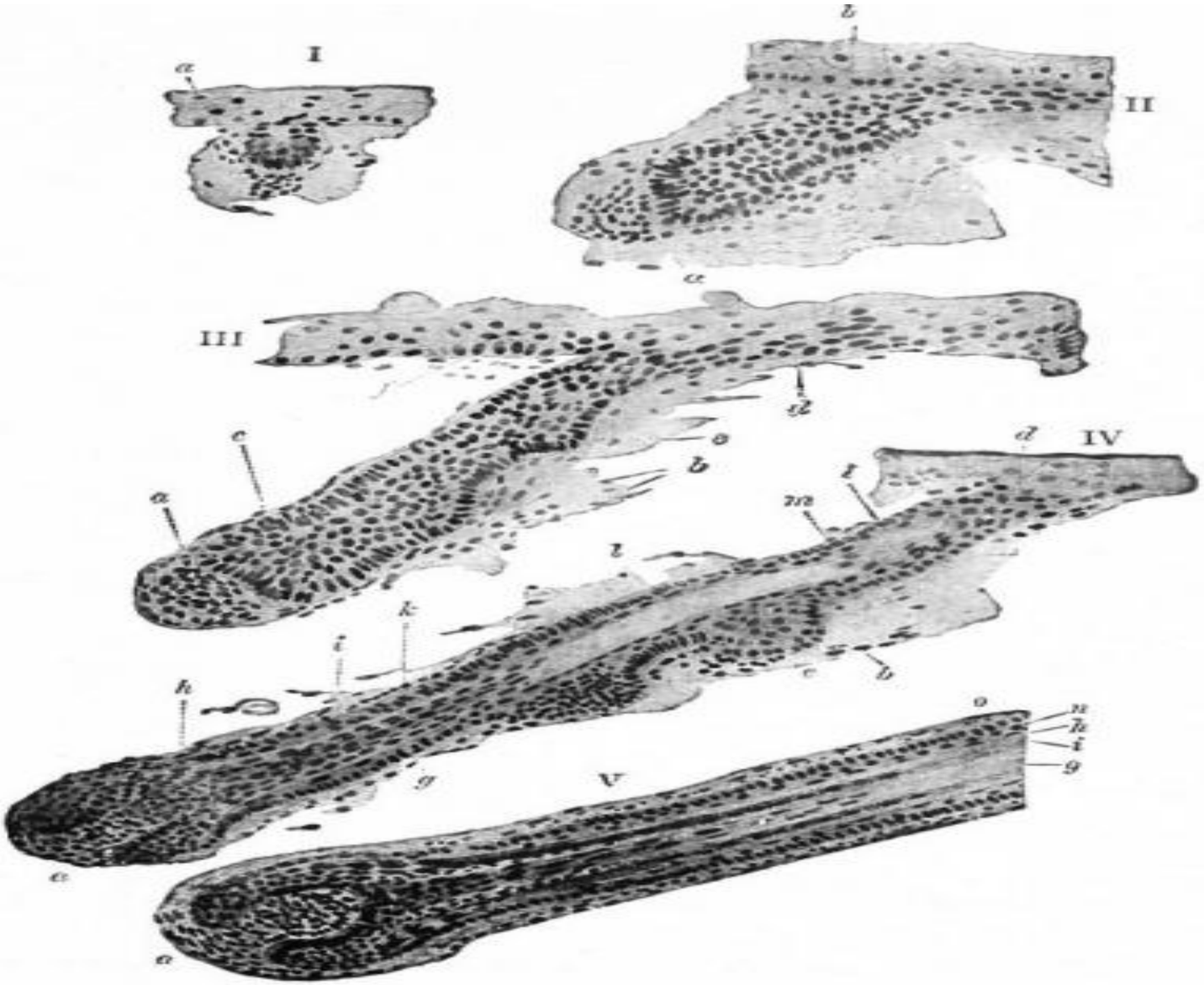



FIG. 355.—Five stages in the development of a human hair. *Stöhr.*

- **I-II** - about three months, local thickenings of the epidermis appear (beginning in the region of the forehead and eye-brows) and grow obliquely into the underlying dermis in the form of solid buds the hair germs. As the buds continue to elongate they become club-shaped and the epithelium at the end of each molds itself over a little portion of the dermis in which the cells have become more numerous and which is known as the hair papilla.
- **III - IV** - As the epidermal bud grows deeper, its central cells become spindle-shaped and undergo keratinization to form the beginning of the hair shaft; the peripheral layers constitute the anlage of the root sheath. The hair shaft grows from its basal end, new keratinized cells being added from the epithelium nearest the papilla as the older cells are pushed toward the surface of the skin.
- **V** - The surface cells of the hair shaft become flattened to form the cuticle of the hair. The hairs appear above the surface about the fifth month. Of the cells of the root sheath, those nearest the hair become scale-like to form the cuticle of the root sheath; the next few layers become modified (keratinized) to form Huxley's and Henle's layers. Outside of these is the stratum germinativum, the basal layer of which is composed of columnar cells resting upon a distinct basement membrane. The stratum germinativum is continued over the tip of the papilla, where its cells give rise to new cells for the hair shaft.

# ALOPECIA

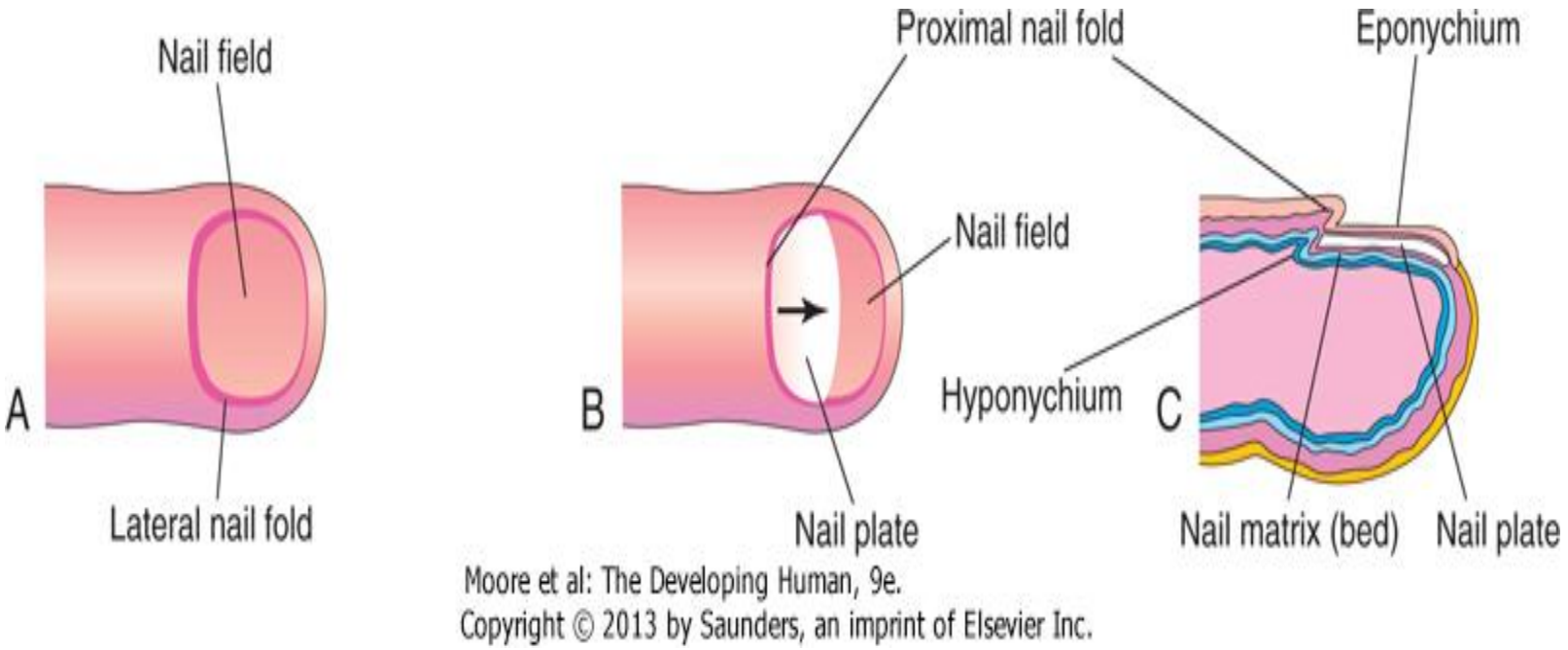
- Absence or loss of scalp hairs may occur alone or with other defects of the skin and its derivatives.
- **Congenital alopecia** (**hair loss**) may be caused by failure of hair follicles to develop, or it may result from follicles producing poor - quality hairs.

- **HYPERTRICHOSIS**
  - **Excessive hairiness** results from the development of supernumerary hair follicles, or from the persistence of lanugo hairs that normally disappear during the perinatal period.
  - It may be localized (e.g., on the shoulders and back) or diffuse.
  - **Localized hypertrichosis** is often associated with spina bifida occulta.
- **PILI TORTI**
  - In this familial disorder, the hairs are twisted and bent (Latin *tortus*, twisted).
  - Other ectodermal defects (e.g., distorted nails) may be associated with this condition.
  - Pili torti is usually first recognized at 2 to 3 years of age.

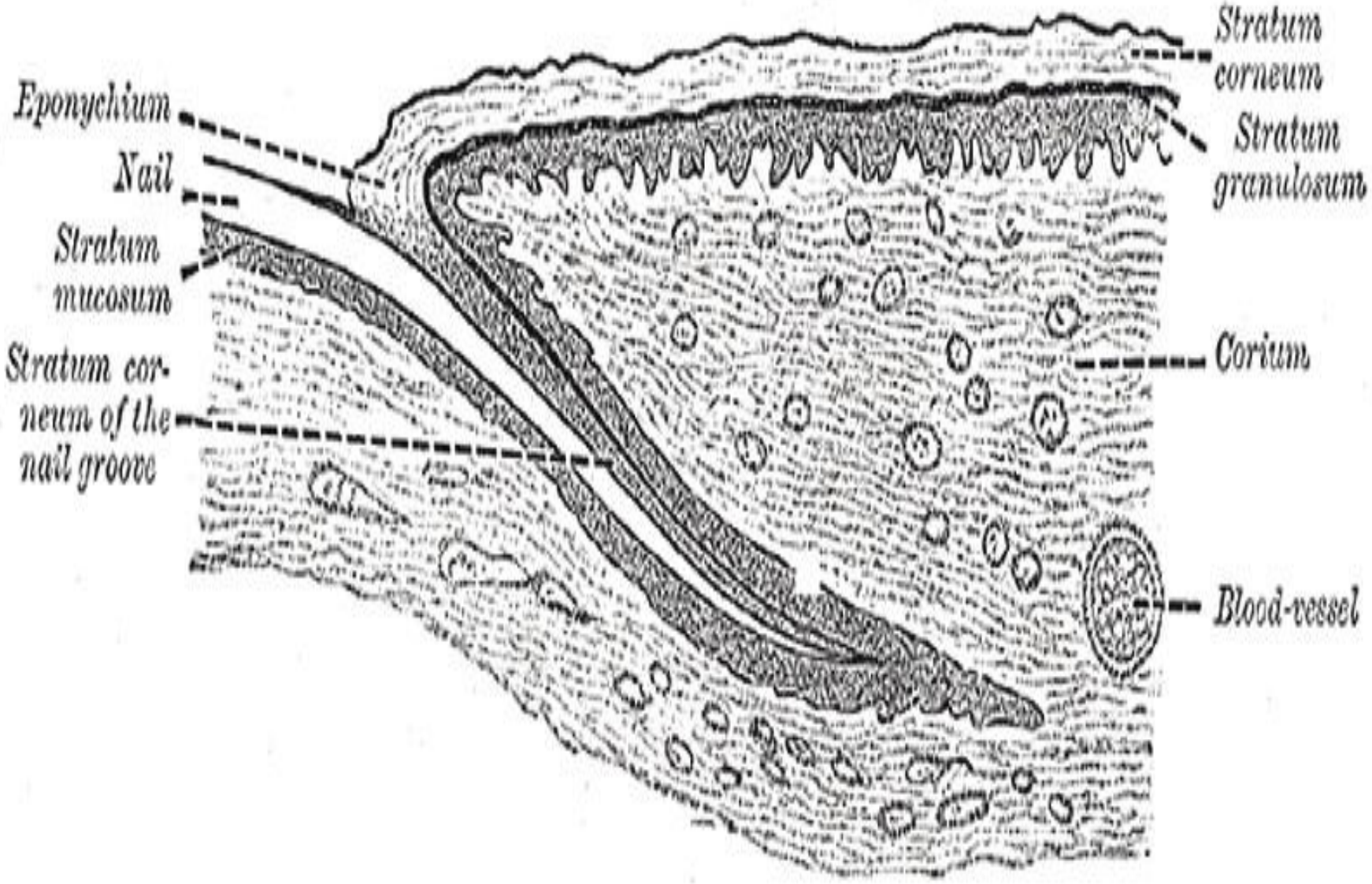
# Development of Nails

- Toe nails and fingernails begin to develop at the tips of the digits at approximately 10 weeks.
- Development of **fingernails** precedes that of **toenails** by approximately 4 weeks.
- The primordia of nails appear as thickened areas or **nail fields** of the epidermis at the tip of each digit .
- Later these **fields** migrate onto the dorsal surfaces of the nails, carrying their innervation from the ventral surface.
- The nail fields are surrounded laterally and proximally by folds of epidermis, the **nail folds**.

- Cells from the proximal nail fold grow over the nail field and become keratinized to form the **nail plate** .
- At first, the developing nail is covered by a narrow band of epidermis, the **eponychium**.
- Eponychium degenerates, exposing the nail, except at its base, where it persists as the **cuticle**.
- The skin under the free margin of the nail is the **hyponychium** .
- The fingernails reach the fingertips by approximately 32 weeks; the toenails reach the toe tips by approximately 36 weeks.
- Nails that have not reached the tips of the digits at birth indicate prematurity.




Successive stages in the development of a fingernail. **A,** The first indication of a nail is a thickening of the epidermis, the nail field, at the tip of the finger. **B,** As the nail plate develops, it slowly grows toward the tip of the finger. **C,** The fingernail reaches the end of the finger by 32 weeks.

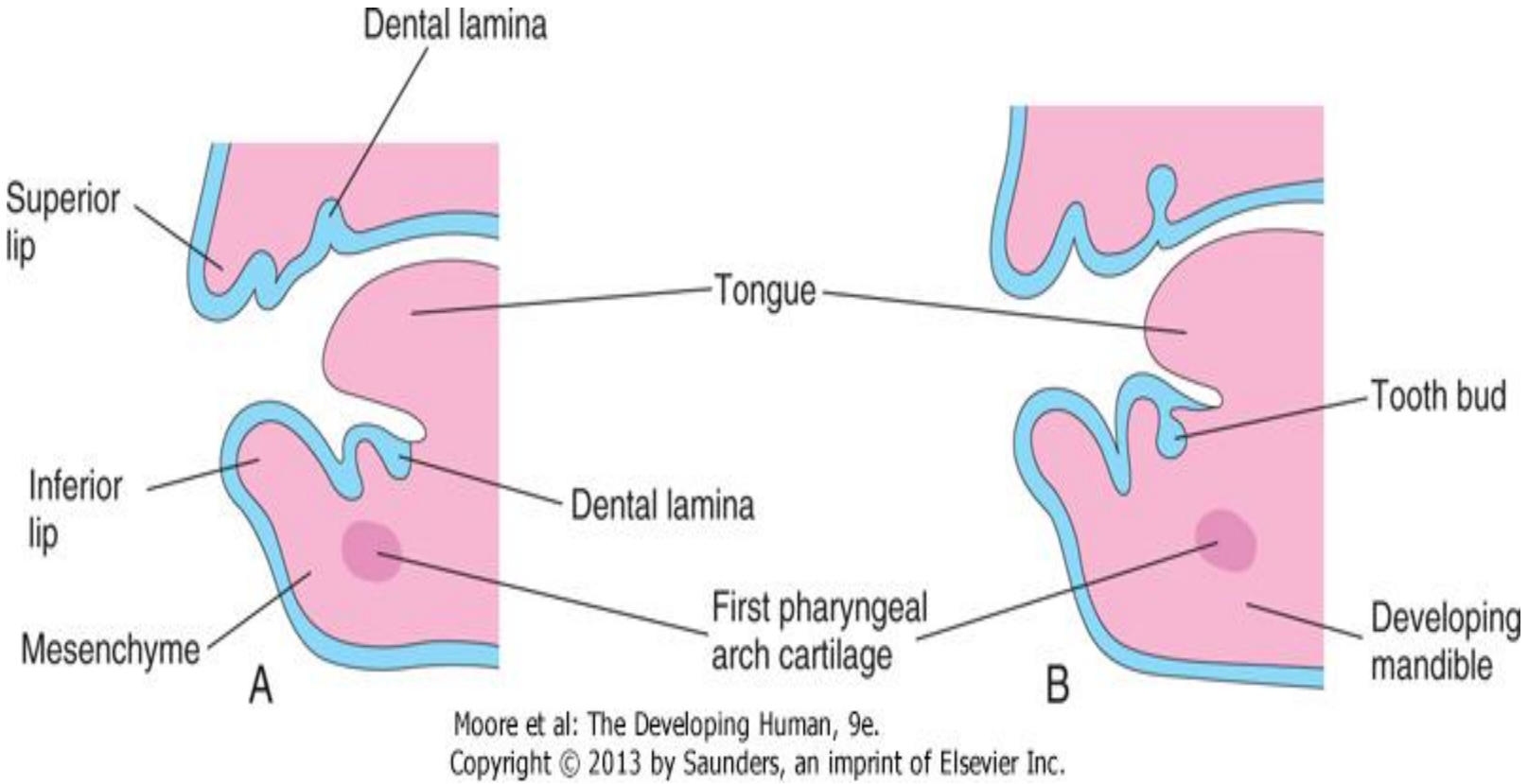

Eponychium
Nail
Stratum mucosum
Stratum corneum of the nail groove
Stratum corneum
Stratum granulosum
Corium
Blood-vessel

# APLASTIC ANONYCHIA

- Anonychia is c**ongenital absence of nails**.
- Anonychia results from failure of nail fields to form or from failure of the proximal nail folds to form nail plates.
- The abnormality is permanent.
- Aplastic anonychia (defective development or absence of nails) may be associated with extremely poor development of hairs and with defects of the teeth.
- Anonychia may be restricted to one or more nails of the digits of the hands and/or feet.

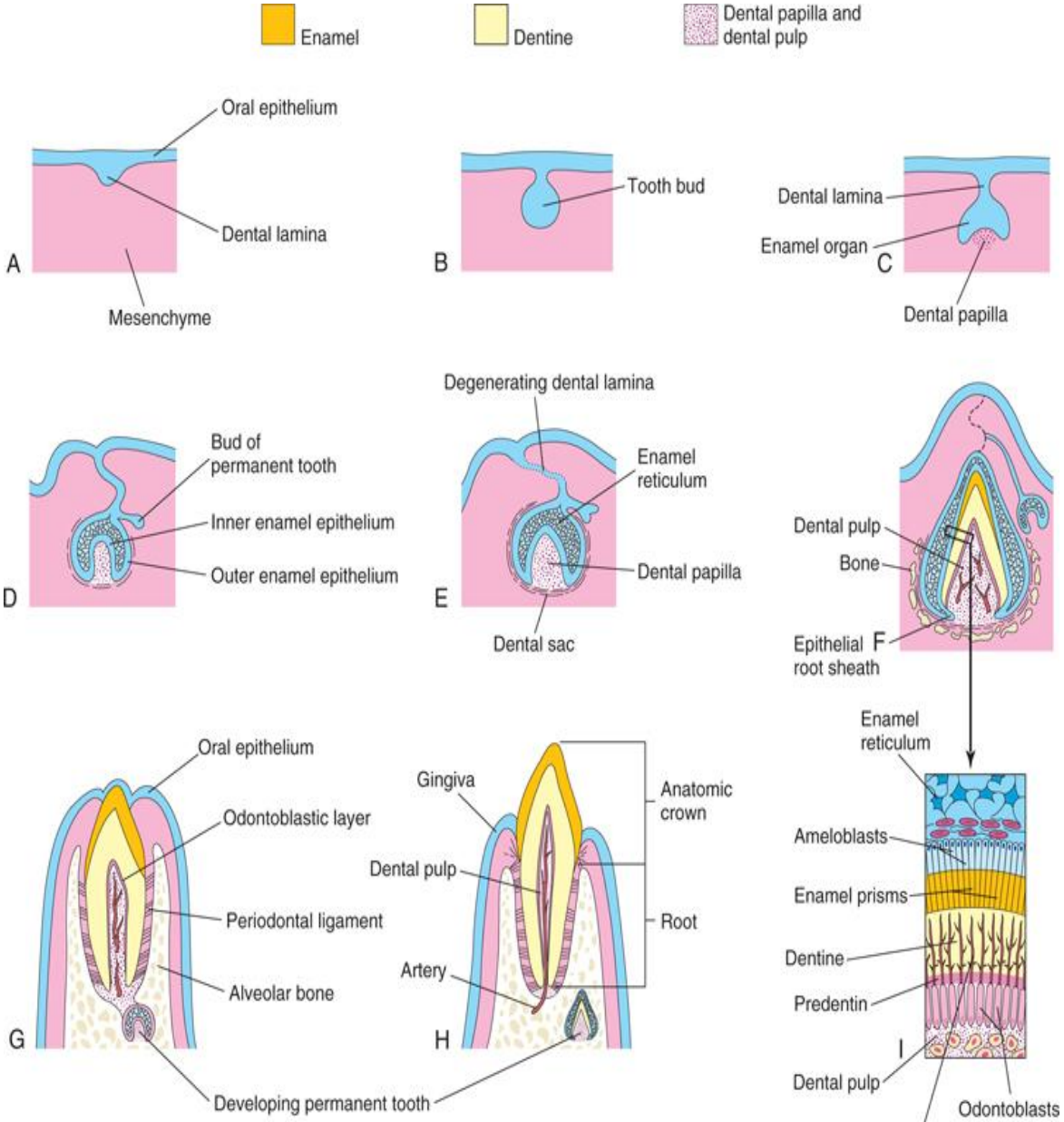
# Development of Teeth

- Two sets of teeth normally develop:
  - primary dentition or **deciduous teeth**
  - secondary dentition or **permanent teeth**.
- Teeth develop from:
  - oral ectoderm,
  - mesenchyme,
  - neural crest cells.
- The **enamel** is derived from ectoderm of the oral cavity
- All other tissues differentiate from the surrounding mesenchyme and neural crest cells.
- As the mandible and maxilla grow to accommodate the developing teeth, the shape of the face changes.




Sketches of sagittal sections through the developing jaws illustrating early development of the teeth. **A,** Early in the sixth week, showing the dental laminae. **B,** Later in the sixth week, showing tooth buds arising from the laminae.

Schematic drawings of sagittal sections illustrating successive stages in the development and eruption of an incisor tooth. **A,** At 6 weeks, showing the dental lamina. **B,** At 7 weeks, showing the tooth bud developing from the dental lamina. **C,** At 8 weeks, showing the cap stage of tooth development. **D,** At 10 weeks, showing the early bell stage of a deciduous tooth and the bud stage of a permanent tooth. **E,** At 14 weeks, showing the advanced bell stage of tooth development. Note that the connection (dental lamina) of the tooth to the oral epithelium is degenerating. **F,** At 28 weeks, showing the enamel and dentine layers. **G,** At 6 months postnatally, showing early stage of tooth eruption. **H,** At 18 months postnatally, showing a fully erupted deciduous incisor tooth. The permanent incisor tooth now has a well-developed crown. **I,** Section through a developing tooth showing ameloblasts (enamel producers) and odontoblasts (dentine producers).

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- **Odontogenesis** (tooth development) is a property of the oral epithelium.
- Odontogenesis is a continuous process involving reciprocal induction between neural crest mesenchyme and the overlying oral epithelium.
- Odontogenesis is divided into stages for descriptive purposes based on the appearance of the developing tooth.
- The first tooth buds appear in the anterior mandibular region; later, in the anterior maxillary region and then progresses posteriorly in both jaws.
- Tooth development continues for years after birth.
- The first indication of tooth development occurs early in the $6^{th}$ week as a thickening of the oral epithelium.
- These U - shaped bands - **dental laminae** - follow the curves of the primitive jaws.

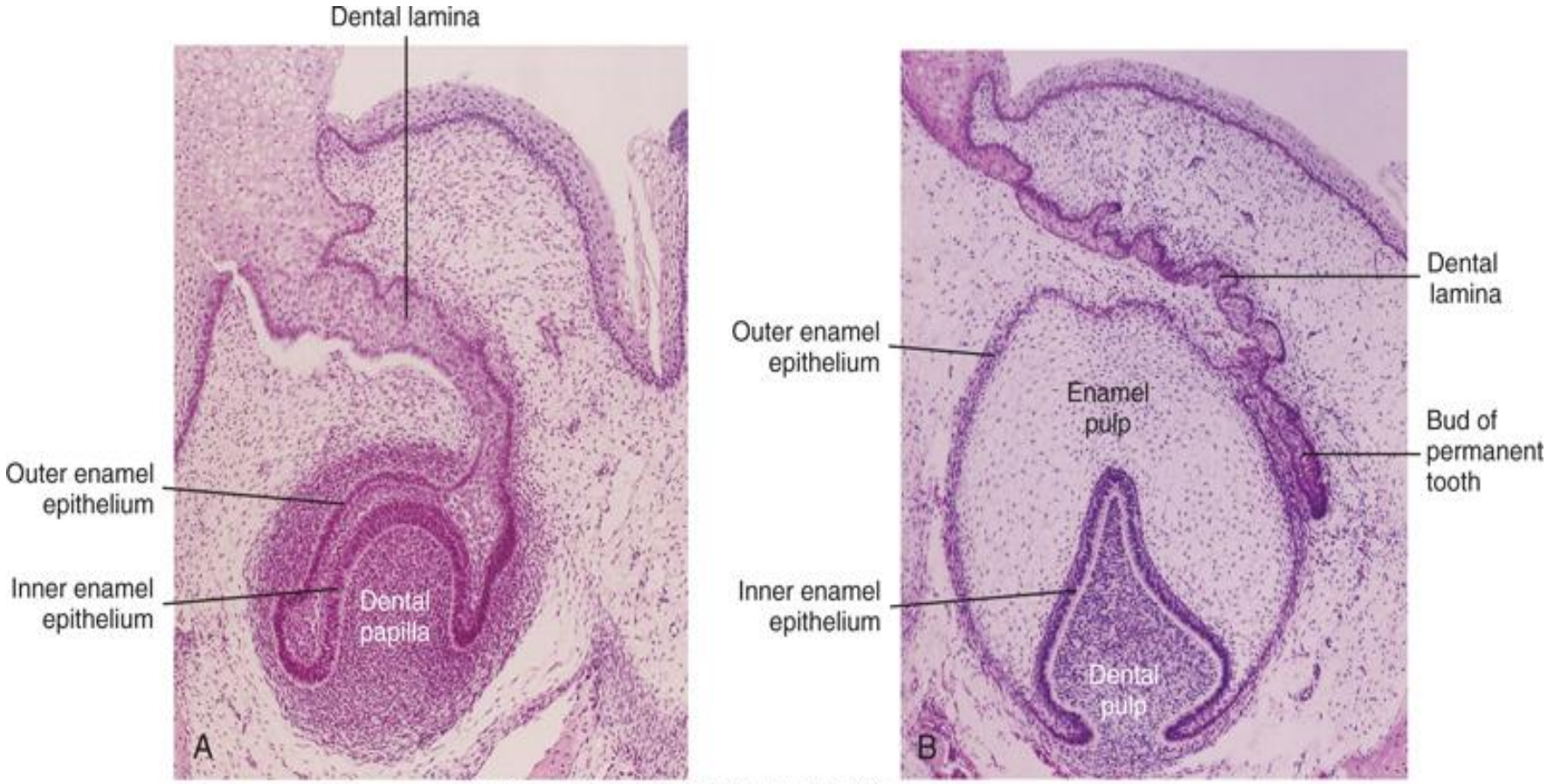
| TOOTH | USUAL ERUPTION TIME | SHEDDING TIME |
|---|---|---|
| **Deciduous** | | |
| Medial incisor | 6-8 mo | 6-7 yr |
| Lateral incisor | 8-10 mo | 7-8 yr |
| Canine | 16-20 mo | 10-12 yr |
| First molar | 12-16 mo | 9-11 yr |
| Second molar | 20-24 mo | 10-12 yr |
| **Permanent*** | | |
| Medial incisor | 7-8 yr | |
| Lateral incisor | 8-9 yr | |
| Canine | 10-12 yr | |
| First premolar | 10-11 yr | |
| Second premolar | 11-12 yr | |
| First molar | 6-7 yr | |
| Second molar | 12 yr | |
| Third molar | 13-25 yr | |

# Bud Stage of Tooth Development

- Each dental lamina develops 10 centers of proliferation from which swellings - **tooth buds** - grow into the underlying mesenchyme.
- These buds develop into the **deciduous teeth**.
- The tooth buds for **permanent teeth** that have deciduous predecessors begin to appear at approximately 10 weeks from deep continuations of the dental lamina.
- They develop lingual (toward the tongue) to the **deciduous tooth buds.**
- The permanent molars have no deciduous predecessors and develop as buds from posterior extensions of the **dental laminae** (horizontal bands).
- The tooth buds for the permanent teeth appear at different times, mostly during the fetal period.
- The buds for the second and third permanent molars develop after birth.
- The deciduous teeth have well-developed crowns at birth, whereas the permanent teeth remain as tooth buds.

# Cap Stage of Tooth Development

- Invagination of the tooth bud by mesenchyme that forms the **primordium of the dental papilla and dental follicle** converts the tooth bud into a cap.
- The ectodermal part of the developing tooth, the **enamel organ** produces enamel.
- The internal part of each cap - shaped tooth, the **dental papilla**, is the primordium of dentin and dental pulp.
- The *outer cell layer* of the enamel organ is the **outer enamel epithelium**, and the *inner cell layer* lining the papilla is the **inner enamel epithelium**.

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Photomicrograph of the primordium of a lower incisor tooth. **A,** A 12-week-old fetus (early bell stage). A cap-like enamel organ is formed and the dental papilla is developing beneath it. **B,** Primordium of a lower incisor tooth in a 15-week-old fetus (late bell stage). Observe the inner and outer enamel layers, the dental papilla, and bud of the permanent tooth.

- The central core of loosely arranged cells between the layers of enamel epithelium is the **enamel reticulum** (stellate reticulum).
- As the enamel organ and dental papilla develop, the mesenchyme surrounding the developing tooth condenses to form the **dental sac** (dental follicle), a vascularized capsular structure.
- The dental sac is the primordium of the *cement* and *periodontal ligament.*
- The **cement** is the bone-like, mineralized connective tissue covering the root of the tooth.
- The **periodontal ligament**, derived from neural crest cells, is a specialized vascular connective tissue that surrounds the root of the tooth, attaching it to the alveolar bone.

# Bell Stage of Tooth Development

- As the enamel organ differentiates, the developing tooth assumes the shape of a bell.
- The mesenchymal cells in the dental papilla adjacent to the internal enamel epithelium differentiate into **odontoblasts**, which produce predentine and deposit it adjacent to the epithelium.
- Later, the **predentine** calcifies and becomes dentine, the second hardest tissue in the body.
- As the dentine thickens, the odontoblasts regress toward the center of the dental papilla; however, their finger - like cytoplasmic processes - **odontoblastic processes** - remain embedded in the dentine.
- Cells of the ***inner enamel epithelium*** differentiate into **ameloblasts** under the influence of the odontoblasts, which produce enamel in the form of prisms (rods) over the dentine.

Photomicrograph of a section of the crown and neck of a tooth (x17). Observe the enamel *(E),* dentine *(D),* dental pulp *(P),* and odontoblasts *(O).*


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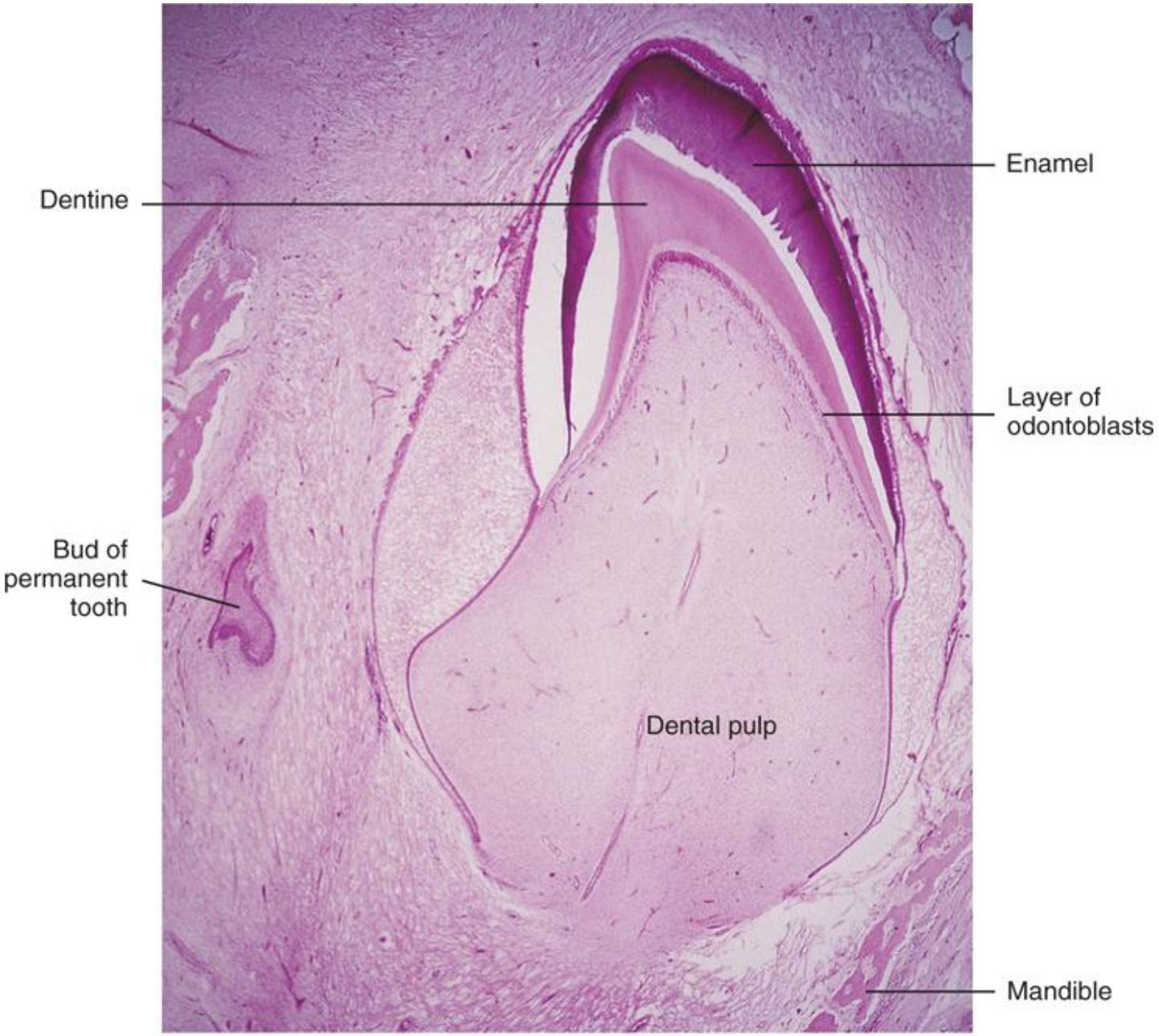
- As the enamel increases, the ameloblasts migrate toward the ***outer enamel epithelium***.
- Enamel is the hardest tissue in the body.
- It overlies and protects the dentine from being fractured.
- Enamel and dentine formation begins at the cusp (tip) of the tooth and progresses toward the future root.
- The **root of the tooth** begins to develop after dentine and enamel formation are well advanced.
- The inner and outer enamel epithelia come together at the **neck of the tooth** (cementoenamel junction), where they form a fold, the **epithelial root sheath**.
- This sheath grows into the mesenchyme and initiates root formation.

Photomicrograph of a section of a lower incisor tooth in a term fetus. The enamel and dentine layers and the pulp are clearly demarcated.

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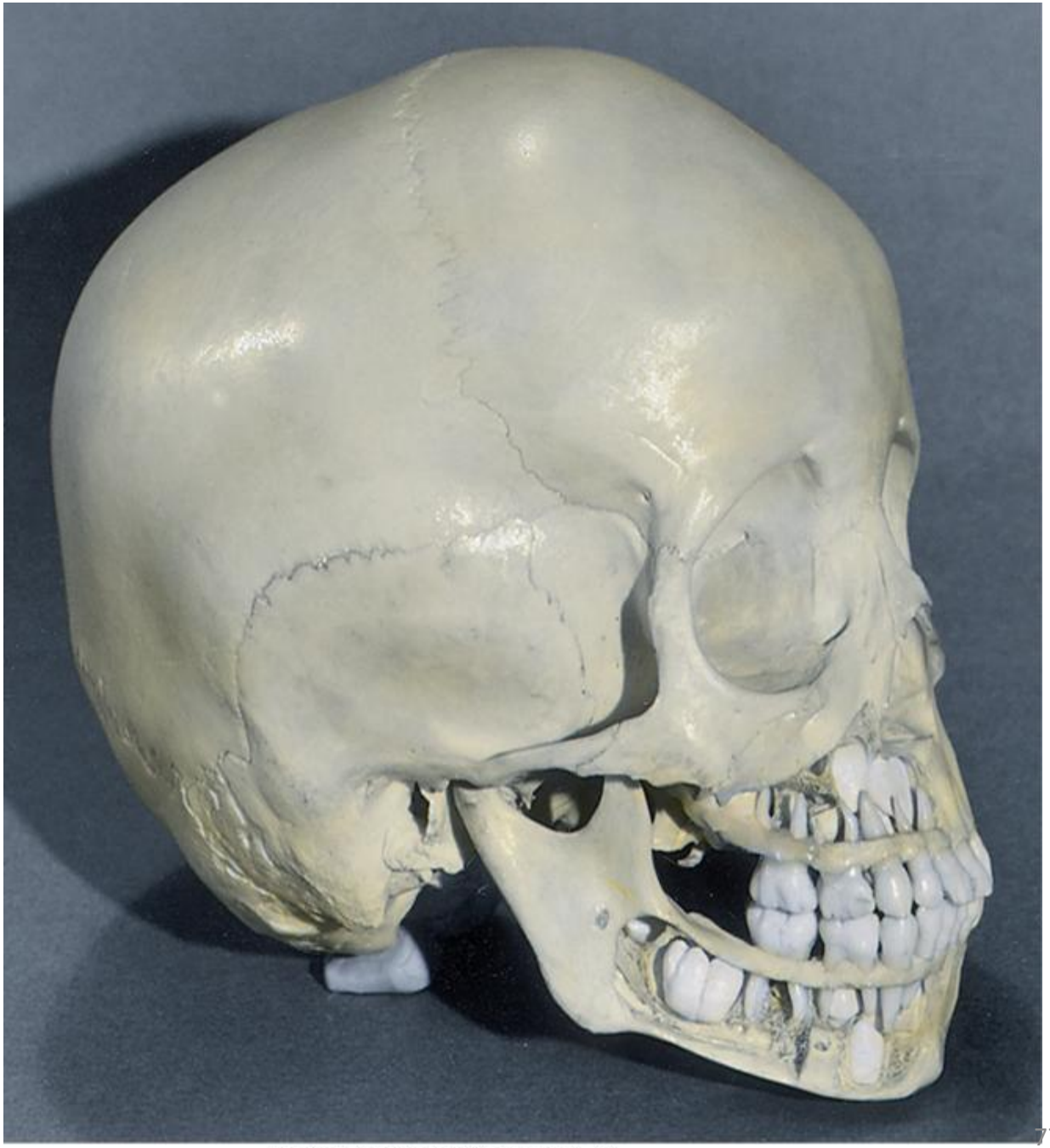
- The *odontoblasts* adjacent to the epithelial root sheath form dentine that is continuous with that of the crown.
- As the dentine increases, it reduces the **pulp cavity** to a narrow **root canal** through which the vessels and nerves pass.
- The inner cells of the dental sac differentiate into **cementoblasts**, which produce cement that is restricted to the root.
- Cement is deposited over the dentine of the root and meets the enamel at the neck of the tooth.
- As the teeth develop and the jaws ossify, the outer cells of the dental sac also become active in bone formation.
- Each tooth soon becomes surrounded by bone, except over its crown.
- The tooth is held in its **alveolus** (bony socket) by the strong **periodontal ligament**, a derivative of the dental sac.
- Some fibers of this ligament are embedded in the cement of the root; other fibers are embedded in the bony wall of the alveolus.

# Tooth Eruption

- As the **deciduous teeth** develop, they begin a continuous slow movement toward the oral cavity.
- This process (**eruption**) results in the emergence of the tooth from the dental follicle in the jaw to its functional position in the mouth.
- The **mandibular teeth** usually erupt before the **maxillary teeth**, and girls' teeth usually erupt sooner than boys' teeth.
- The child's dentition contains **20 deciduous teeth**.
- As the root of the tooth grows, its crown gradually erupts through the oral epithelium.
- The part of the oral mucosa around the erupted crown becomes the **gingiva** (gum).

A 4-year-old child's cranium. Bone has been removed from the mandible and maxilla to expose the relationship of the developing permanent teeth to the erupted deciduous teeth.



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- Usually eruption of the deciduous teeth occurs between the 6th and 24th months after birth.
- The mandibular medial or **central incisor teeth** typically erupt 6 to 8 months after birth, but this process may not begin until 12 or 13 months in some children.
- Despite this, all 20 deciduous teeth are usually present by the end of the second year in healthy children.
- Delayed eruption of all teeth may indicate a systemic or nutritional disturbance such as hypopituitarism or hypothyroidism.
- The complete permanent dentition consists of 32 teeth.
- The **permanent teeth** develop in a manner similar to that described for deciduous teeth.

- As a permanent tooth grows, the root of the corresponding deciduous tooth is gradually resorbed by **osteoclasts** (odontoclasts).
- Consequently, when the deciduous tooth is shed, it consists only of the crown and the uppermost part of the root.
- The permanent teeth usually begin to erupt during the sixth year and continue to appear until early adulthood.
- The shape of the face is affected by the development of the paranasal sinuses and the growth of the maxilla and mandible to accommodate the teeth.
- It is the lengthening of the **alveolar processes** (bony sockets supporting the teeth) that results in the increase in the depth of the face during childhood.

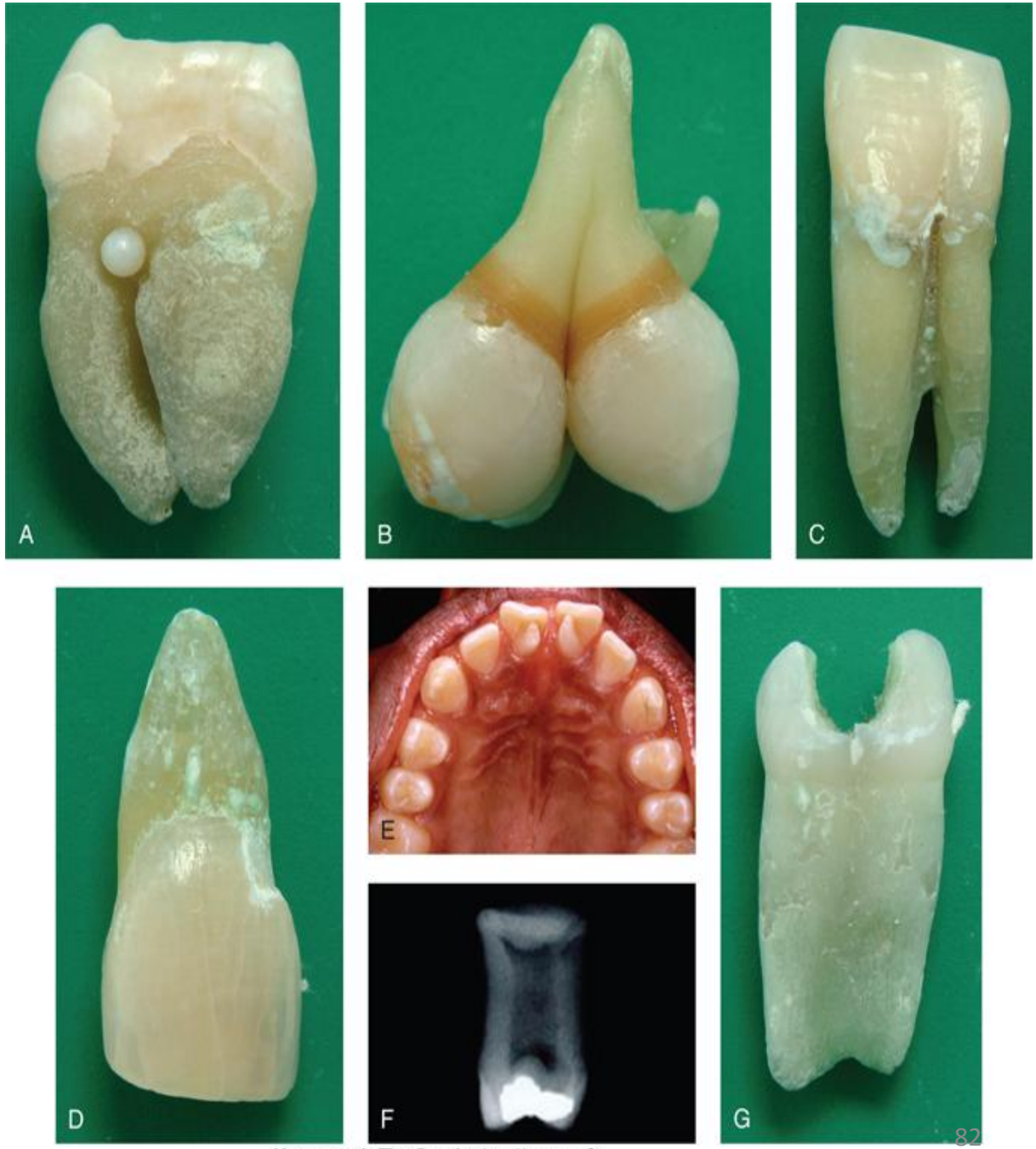
# NATAL TEETH

- Natal teeth are erupted at birth.
- There are usually two in the position of the mandibular incisors.
- Natal teeth are observed in approximately one in 2000 newborn infants.
- Natal teeth may produce maternal discomfort during breast-feeding.
- In addition, the infant's tongue may be lacerated or the teeth may detach and be aspirated; for these reasons, natal teeth are sometimes extracted.
- Because these are prematurely erupting decidual teeth, spacers may be required to prevent overcrowding of the other teeth.

# ENAMEL HYPOPLASIA

- Defective enamel formation causes pits and/or fissures in the enamel of teeth.
- These defects result from temporary disturbances of enamel formation.
- Various factors may injure ameloblasts, the enamel builders (e.g., nutritional deficiency, tetracycline therapy, and infectious diseases such as measles).
- **Rickets** occurring during the critical in utero period of tooth development (6-12 weeks) is a common cause of enamel hypoplasia.
- Rickets, a disease in children who are deficient in vitamin D, is characterized by disturbance of ossification of the epiphysial cartilages and disorientation of cells at the metaphysis.

Some common birth defects of teeth. **A,** Enamel pearl (furcation of a permanent maxillary third molar). **B,** Gemination and tetracyline staining (maxillary third molar). **C,** Fusion (permanent mandibular central and lateral incisors). **D,** Abnormally short root (microdont permanent maxillary central incisor). **E,** Dens invaginatus (talon cusps on the lingual surface of the permanent maxillary central incisor). **F,** Taurodont tooth (radiograph of the mesial surface of the permanent maxillary second molar). **G,** Fusion (primary mandibular central and lateral incisors).

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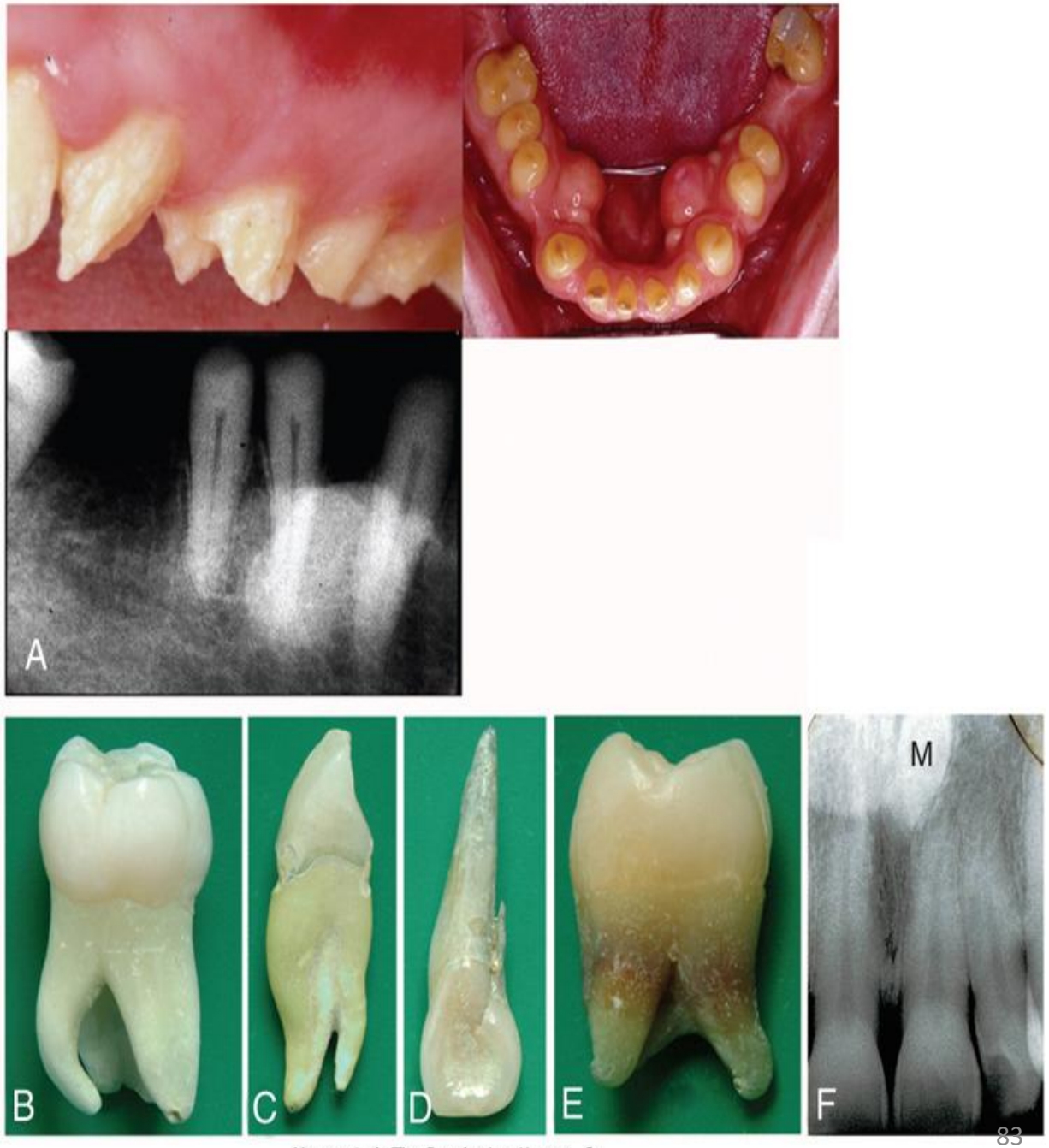
More common birth defects of teeth. **A,** Amelogenesis imperfecta. **B,** Extra root (mandibular molar). **C,** Extra root (mandibular canine). **D,** Accessory root (maxillary lateral incisor). Extra roots present challenges for root canal therapy and extraction. **E,** Tetracycline staining (root of maxillary third molar). **F,** A midline supernumerary tooth (M, mesiodens) located near the apex of the central incisor. The prevalence of supernumerary teeth is 1% to 3% in the general population

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# Variations of Tooth Shape

- Abnormally shaped teeth are relatively common.
- Occasionally there is a spherical mass of enamel- **enamel pearl** - on the root of a tooth that is separate from the enamel of the crown.
- The pearl is formed by **aberrant groups of ameloblasts**.
- In other cases, the maxillary lateral incisor teeth may have a slender, tapering shape (peg-shaped incisors).
- **Congenital syphilis** affects the differentiation of the permanent teeth, resulting in incisors with central notches in their incisive edges.
- The molars are also affected and are called **mulberry molars** because of their characteristic features.

# NUMERICAL ABNORMALITIES

- One or more **supernumerary teeth** (mesiodens) may develop, or the normal number of teeth may fail to form.
- Many studies report a higher prevalence in females.
- Supernumerary teeth usually develop in the area of the maxillary incisors and can disrupt the position and eruption of normal teeth.
- The extra teeth commonly erupt posterior to the normal ones (or remain unerupted) and are asymptomatic in most cases.
- In **partial anodontia**, one or more teeth are absent; this is often a familial trait.
- In **total anodontia**, no teeth develop; this is an extremely rare condition.
- It is usually associated with congenital ectodermal dysplasia.

- Occasionally a tooth bud either partially or completely divides into two separate teeth.
- A partially divided tooth germ is called **gemination**.
- The result is a **macrodontia** (large teeth) with a common root canal system.
- Small teeth (microdontia) also occur.
- If the tooth germ completely divides into two separate teeth, the result is twinning with one additional tooth in the dentition.
- Fusion of two teeth results in one fewer tooth in the dentition.
- This condition can be differentiated radiographically from gemination by two separate root canal systems found with fusion.

# DENTIGEROUS CYST

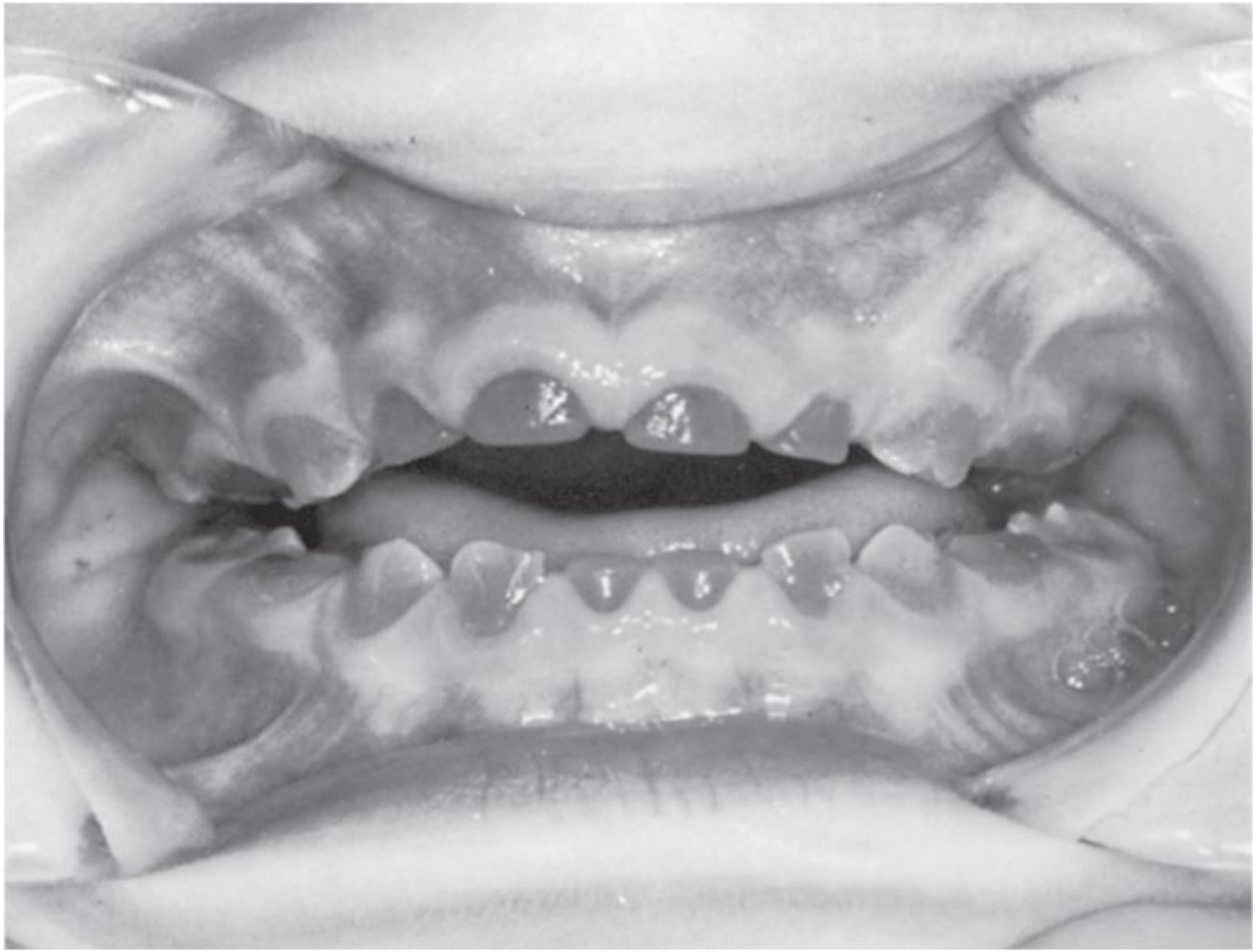
- A cyst may develop in a mandible, maxilla, or maxillary sinus that contains an unerupted tooth.
- The dentigerous (tooth-bearing) cyst develops because of cystic degeneration of the enamel reticulum of the enamel organ of an unerupted tooth.
- Most cysts are deeply situated in the jaw and are associated with misplaced or malformed secondary teeth that have failed to erupt.

# AMELOGENESIS IMPERFECTA

- Amelogenesis imperfecta is a complex group of at least 14 different clinical entities that involve developmental **aberrations in enamel formation** in the absence of any systemic disorder.
- This is a **inherited ectodermal birth defect** that primarily affects the enamel only.
- The enamel may be hypoplastic, hypocalcified, or hypomature.
- Depending on the type of amelogenesis imperfecta, the enamel may be hard or soft, pitted or smooth, and thin or normal in thickness.
- The incidence of amelogenesis imperfecta ranges from 1 in 700 to 1 in 8000, depending on the population studied.
- Multiple modes of inheritance patterns are involved.
- Classification of this condition is based on clinical and radiographic findings, as well as mode of inheritance.

# DENTINOGENESIS IMPERFECTA

- The teeth are brown to gray-blue with an opalescent sheen because the odontoblasts fail to differentiate normally and poorly calcified dentine results.
- Both deciduous and permanent teeth are usually involved.
- The enamel tends to wear down rapidly, exposing the dentine.
- This anomaly is inherited as an autosomal dominant trait with the genetic defect in most cases localized on chromosome 4q and this condition is relatively common in Caucasian children.



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The teeth of a child with dentinogenesis imperfecta.

# DISCOLORED TEETH

- Foreign substances incorporated into the developing enamel and dentine discolor the teeth.
- The hemolysis associated with erythroblastosis fetalis or hemolytic disease of the newborn may produce blue to black discoloration of the teeth.
- All **tetracyclines** are extensively incorporated into the teeth.
- The critical period at risk is from approximately 14 weeks of fetal life to the $10^{th}$ postnatal month for deciduous teeth, and from approximately 14 weeks of fetal life to the eighth postnatal year for permanent teeth.

- **Tetracycline staining** affects both enamel and dentine because it binds to hydroxyapatite.
- The brownish-yellow discoloration (mottling) of the teeth, produced by tetracycline, is due to the conversion of tetracycline to a colored by-product under the action of light.
- The dentine is probably affected more than the enamel because it is more permeable than enamel after tooth mineralization is complete.
- The enamel is completely formed on all but the third molars by approximately 8 years of age.
- For this reason, tetracyclines should not be administered to pregnant women or children younger than 8 years of age.