







Lactiferous ducts are formed by coalescing passageways formed within the developing mammary gland.

- Mammary gland development is similar across all sexes. However, at puberty, hormones influence further growth and development of the mammary glands of the female sex.
- Rarely, supernumerary mammary glands may arise (Correlation 4.3).

## 4.4 Nail Development

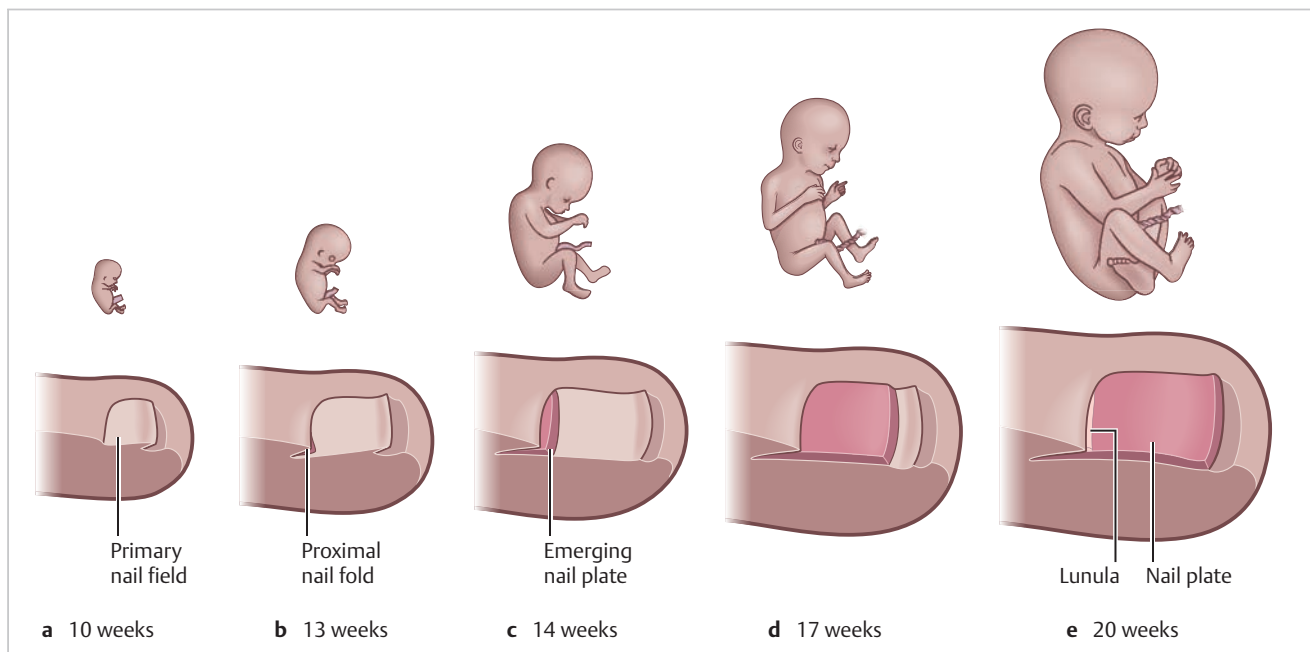
Fingernails and toenails are specialized keratinized structures located on the dorsal aspect of the digits. Components of nails include the keratinized nail plate, nail bed (tissues under the nail plate), nail matrix (produces nail plate), nail folds, and cuticle.

- The steps of nail development include the following (► Fig. 4.4):
  - The first sign of nail development is the appearance of epidermal thickenings called **primary nail fields** on the dorsal aspect of the digits.
  - The lateral and proximal borders of the nail field are demarcated by grooves called **nail folds**. The proximal nail fold overlies matrix cells that will produce the **nail plate**, a hardened structure composed of compressed keratinocytes. The crescent-shaped **lunula** near the nail base marks the location of the nail matrix.
  - The nail plate advances from the proximal nail fold and grows toward the distal tip of the digit.
- Fingernails develop ahead of toenails, consistent with the cranial-to-caudal development pattern of the fetus:
  - Fingernail epidermal thickenings appear around week 10 and reach the distal fingertips around week 32.
  - Toenail epidermal thickenings appear around week 14 and reach the distal tip of the toes around week 36.

### 4.4.1 Hair Development

**Hair follicles** are the epithelial structures that surround and produce hairs. The first sign of hair development is the appearance of hair germs at the end of month 2 in the region of eyebrows and scalp. Hair follicle development proceeds in a cranial-to-caudal manner. Steps of hair follicle development include the following (► Fig. 4.5):

- In the region where a hair follicle will develop, the stratum basale forms in a crowded region of epidermal cells known as a **hair germ**. Cells from these structures grow downward into the dermis, forming a solid epithelial cord (**hair bud**).
- The distal aspect of the hair bud enlarges to become a hair bulb. Adjacent mesenchyme from the dermis condenses and grows into the hair bulb, forming the **dermal papilla**.
- The hair bulb cells immediately adjacent to the dermal papilla are called the germinal matrix. These cells proliferate and give rise to keratinocytes that advance toward the skin surface and compose the hair shaft. The periphery of the hair follicle surrounding the hair shaft is composed of an inner **epidermal root sheath** and a surrounding **dermal root sheath**.
- Hair pigment (**melanin**) is provided to the hair shaft cells (**keratinocytes**) by **melanocytes** that arise from migratory neural crest–derived precursor cells that colonize the hair bulb.
- **Arrector pili** muscles are tiny smooth muscle bundles that are autonomously innervated and cause hair to stand “on end” when they contract. The smooth muscle arises from dermal mesenchyme adjacent to the developing hairs, attaching the dermal root sheath of the follicle to the papillary layer of the dermis.



**Fig. 4.4** Nails develop beginning in week 10 for fingers (week 14 for toes) with the appearance of primary nail fields (a). The nail plate emerges from the matrix located at the proximal nail fold (b) and advances toward the distal tip of the digit (c–e). The nail plate reaches the distal tip of the fingers at around week 32 (or around week 36 for toes).

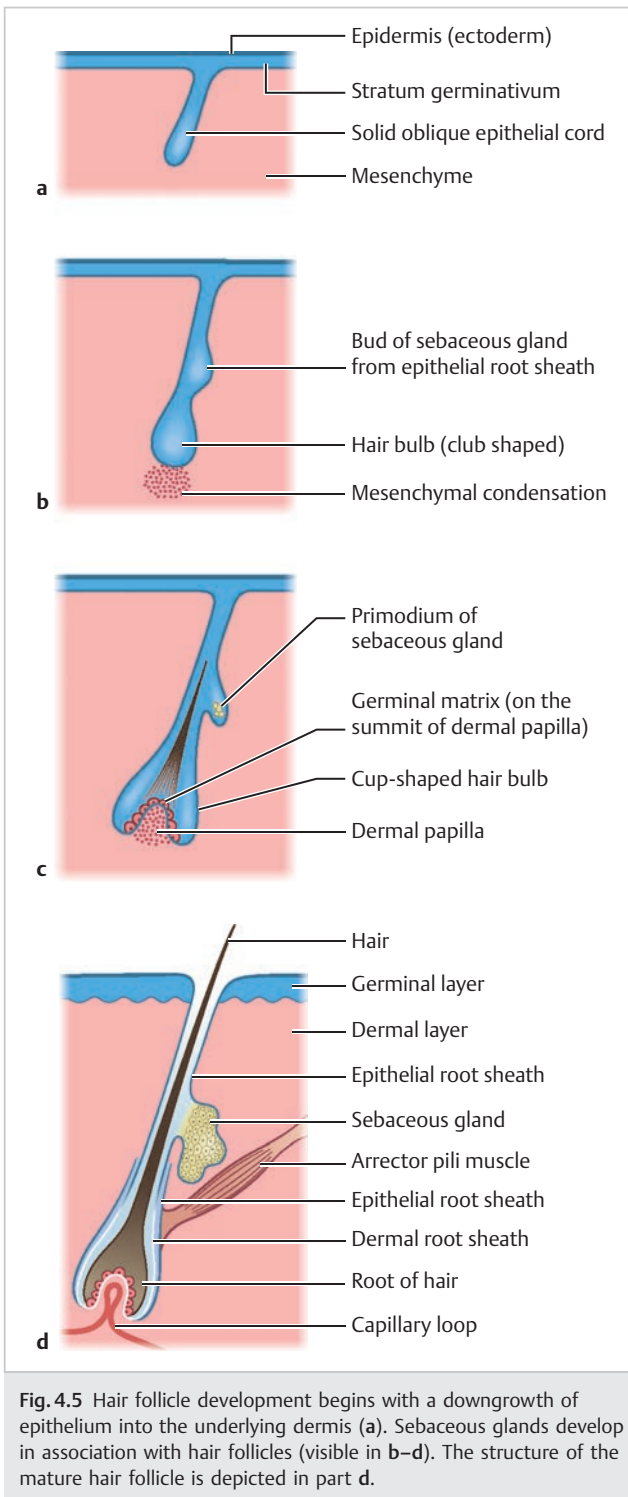


Fig. 4.5 Hair follicle development begins with a downgrowth of epithelium into the underlying dermis (a). Sebaceous glands develop in association with hair follicles (visible in b–d). The structure of the mature hair follicle is depicted in part d.

- There are three different types of hairs:
  - **Lanugo hair** is formed in month 3 of development. It is soft, fine hair that covers most of the body surface. The function of lanugo hair is to bind **vernix**, a waxy protective covering of fetal skin composed of fetal skin cells and sebum. Lanugo hair is shed about 4 weeks prior to birth and is replaced with the other two types of hairs: vellus and terminal.
  - **Vellus hair** is short, thin, contains little pigment, and covers much of the body surface. Vellus hair plays a role in thermoregulation, wicking sweat away from the body to increase efficiency of evaporative cooling.
  - **Terminal hair** is longer, thicker, and more pigmented than vellus hair. At birth it is found in the scalp, eyebrows, and eyelashes. At puberty, sex hormones stimulate terminal hair to replace vellus hair in some locations of the body, such as the face, armpits, and pubic areas.

## 4.5 Teeth Development

Two sets of teeth, deciduous and permanent teeth, develop and erupt in a predictable sequence in childhood.

- Teeth are primarily composed of tissues derived from two embryonic sources: ectoderm and mesenchyme.
  - The enamel covering of teeth is derived from ectoderm.
  - All other tissues are derived from mesenchyme (cranial neural crest cell origin).
- The process of teeth development depends on reciprocal epithelial–mesenchymal interactions between oral epithelium and mesenchyme. The stages of tooth development include the following (► Fig. 4.6):
  - **Bud stage:** Early in week 6, ectodermal proliferation results in the formation of tooth buds (tooth precursors).
  - **Cap stage:** Early in the fetal period, there is an ingrowth of mesenchyme into the tooth bud. The mesenchymal ingrowth will give rise to cells and tissues in the center of teeth including **odontoblasts** (dentin-producing cells) and **dental pulp**. The overlying **ectodermal cap** contains **ameloblasts** that will produce the **enamel** covering of the tooth. Mesenchyme adjacent to the tooth will form the **dental sac**, a structure that will become **cementum** (bone-like substance that covers the root) and the **periodontal ligament** (attaches tooth to bony socket).
  - **Bell stage:** Teeth increase in size and become bell-shaped. Tissue differentiation continues, and dentin and enamel are produced. The roots of teeth develop at this stage.
  - **Tooth eruption:** The process of tooth eruption is the emergence of teeth through the bone and overlying mucosa into the mouth.
    - Between 6 and 24 months after birth, 20 **deciduous teeth** erupt gradually and are shed at various times throughout childhood.
    - At about 6 years of age through adulthood, 32 **permanent teeth** replace deciduous teeth. Permanent teeth develop later in a similar manner to deciduous teeth.

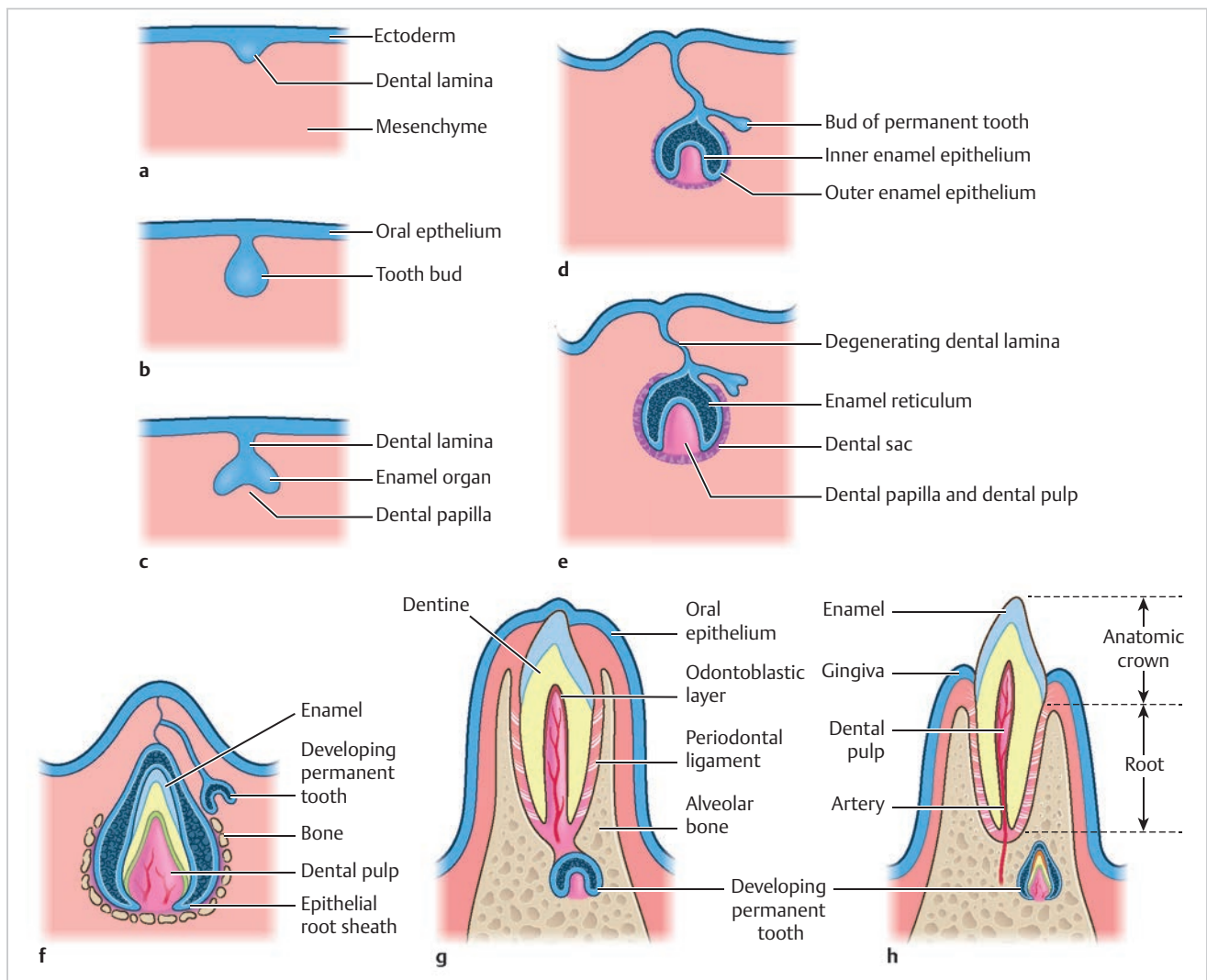


Fig. 4.6 (a–h) Tooth development depends on reciprocal interactions between the oral epithelium and underlying mesenchyme. Developmental tooth stages include the bud stage (b), cap stage (c), and bell stage (d–e). The mature tooth (h) consists of an enamel covering derived from ectoderm. Other structures composing the tooth are derived from mesenchyme (cranial neural crest cell origin).

## Clinical Correlations

### Correlation 4.1: Clinical—Ichthyosis

Ichthyosis is a skin condition characterized by atypical keratinization.<sup>3</sup> Ichthyosis can be present at birth since the process of keratinization begins prior to birth. Characteristics of ichthyosis include scaly or dry skin, and the clinical manifestations range from mild to severe. The most severe form is called harlequin ichthyosis. At birth, the skin of infants with harlequin ichthyosis is “armor-plated” and is marked by deep fissures. Infants with harlequin ichthyosis typically do not survive for long periods after birth due to restricted respiration, poor feeding, and dehydration.

### Correlation 4.2: Clinical—Developmental Pigment Variations

Neural crest cell–derived melanocytes produce and secrete melanin, the pigment that is responsible for coloration of skin, hair, and eye structures. There are congenital skin pigment variations that arise from atypical melanocyte development or altered melanin production. Some examples of pigment variations include:

- **Albinism**, which is characterized by absence of pigment in hair, eyes, and skin. A lack of melanin in eye structures may lead to visual deficits. Individuals are more susceptible to harmful

effects of ultraviolet radiation from sun exposure. Albinism can result from a variety of underlying genetic variants that impact melanin production.

- **Piebaldism** is a rare congenital skin variation characterized by unpigmented patches of skin. Affected regions of skin have an absence of melanocytes. Piebaldism also has a genetic basis (*KIT* gene mutation).
- **Congenital dermal melanocytosis (Mongolian blue spots)** is a type of skin pigment variation that appears as a slate-blue discolored region, often located over the sacral region. This is thought to arise from incomplete transdermal migration of neural crest cell melanocyte precursors. Incomplete migration results in the presence of melanocytes in the deep reticular layer of dermis instead of the normal epidermal location.

### Correlation 4.3: Clinical—Supernumerary Mammary Glands

Accessory mammary tissue can develop along the mammary ridges that normally regress.<sup>4</sup> **Polythelia** is the presence of an additional nipple, and **polymastia** is the presence of additional mammary glands. These congenital variations are classified based on the type of mammary tissue present (nipple, areola, glandular tissue).

## References

- [1] Hu MS, Borrelli MR, Hong WX, et al. Embryonic skin development and repair. *Organogenesis*. 2018;14(1):46–63
- [2] Slominski A, Tobin DJ, Shibahara S, Wortsman J. Melanin pigmentation in mammalian skin and its hormonal regulation. *Physiol Rev*. 2004;84(4):1155–1228
- [3] Akiyama M. ABCA12 mutations and autosomal recessive congenital ichthyosis: a review of genotype/phenotype correlations and of pathogenetic concepts. *Hum Mutat*. 2010;31(10):1090–1096
- [4] Caouette-Laberge L, Borsuk D. Congenital anomalies of the breast. *Semin Plast Surg*. 2013;27(1):36–41