**Tissues**

- **Histogenesis** – Various cell types develop in concert to form a tissue
- **Cytodifferentiation** – Individual cells become increasingly specialized, finally reaching a terminal differentiated state

**Integument - Skin**

Ectoderm → Epidermis

Mesenchyme → Dermis

**Derivatives:**
- Hair
- Mammary Gland
- Teeth (Chapter 13, pp 298-303)

**Ectoderm → Epidermis**

- Ectoderm - Single layer - Simple Cuboidal Epithelium
- Layers – 4 weeks of gestation – Periderm
  - Flattened cells – involved in exchange between the basal layer and the amniotic fluid

**Periderm**

- Peridermal cells (slough off)
- Apoptosis
- Gone by 21st Week

**Basal Layer**

- Basal layer (stratum germinativum, stratum basale) - Stem Cells of epidermis
- Intermediate layer - Keratinocytes - keratin = intermediate filaments

**Keratinocytes**

- Stratum corneum
- Stratum granulosum
- Stratum spinosum
- Stratum basale
Epidermal Layers

Stratum Basale – Stem Cells
- Growth Stimulators - e.g. Epidermal Growth Factor (EGF), Fibroblast Growth Factor (FGF), Insulin-like Growth Factor (IGF), Transforming Growth Factor (TGF)
- Growth Inhibitors - e.g. Transforming Growth Factor (TGF), Tumor Necrosis Factor (TNF), Interferons.

Stratum Spinosum – Keratin produced in cytoplasm - Keratinocytes
- Stratum Granulosum – post-mitotic cells - Keratohylin granules – protein (histidine-rich and sulfur-rich) – Keratin aggregates
- Stratum Corneum – Dead cells – lose their nuclei – bags of keratin.
  - 15-20 layers thick. Shed 1300 cells/cm²/hr. – House Dust

Other Cell Types

Melanocytes – melanoblasts are migratory neural crest cells that invade the epidermis. Contain pigment granules called melanosomes. Number of melanocytes is constant – variation in the amount of melanin synthesized (from tyrosine via tyrosinase)
- Langerhans cells – from bone marrow – immune system macrophage-like cells - immune surveillance and contact sensitivity (skin allergies)
- Merkel cells - Pressure detecting mechanoreceptors – prominent in thick skin of palm and plantar (sole) regions. Neural crest derived.

Dermis

Derived from Somite - Mesenchyme cells

Cells produce collagen fibers and elastin fibers
- Dermal papillae form in conjunction with epidermal ridges
- Papillary layer = Superficial region just beneath the epidermis
- Reticular layer = thick, irregular layer beneath the papillary layer
- Hypodermis = between the reticular layer and the subcutaneous fatty connective tissue

Dermatoglyphics

Ridge/papillae pattern
- Volar Pads on ventral fingers and toes – transient, 6-11 weeks
- Epidermal ridges form between 11 and 17 weeks
- Pattern of Whorls, Loops, Arches

Fingerprints - once established - pattern is permanent - even after grafting
- It even regenerates
Induction – Dermis controls epidermis type, e.g. course hair, fine hair, no hair.

Integument Anomalies

Collodion Baby – Periderm persists forming a cocoon around the newborn that must be removed.

Melanoma – Cancer of melanocyte - deadly

Basal Cell Carcinoma – BCC – most common cancer – high cure rate – involves Sonic Hedgehog signaling pathway

Lamellar Ichthyosis – Skin that scales off in flakes
Integument - Skin

Ectoderm → Epidermis; Mesenchyme → Dermis

Derivatives:
**Hair**
- Mammary Gland
- Teeth (Chapter 13, pp 298-303)

Hair Development

(12th Week)

Hair germ - stratum germinativum proliferation
Hair peg - downward extension as a solid cylinder of epidermis
Hair Bulb - deepest epidermal part
Germinal Matrix - cells of the bulb that gives rise to the hair.

Hair Development

Hair Papillae - Mesenchyme papillae in the bulb
Hair Follicle – Bulb and Papillae
Lanugo - Fetal hair - fine and unpigmented, shed and replaced by coarser hair before birth

Two layers surrounding the hair shaft:
- inner epithelial root sheath
- outer dermal root sheath

Hair growth - germinal matrix pushes differentiated cells distally
Adult Hair

- Hair shaft
- Granules of trichohyalin – imparts hardness to hair
- Bulb
- Dermal root sheath
- Epithelial root sheath
- Sebaceous gland
- Sebum
- Vernix Caseosa (fetal sebum)
- Arrector pili muscle

Epidermal Glands

Holocrine Gland (Sebaceous Gland)

- Holocrine secretion - cells fill up and explode
- Sebaceous Gland:
  - Buds from the sides of developing hair follicles
  - Not all hair - some hairs lacks sebaceous glands
  - Branches to form several alveoli and ducts
  - Sebum - oily lubricant
  - Stem cells renew secretory cells

Epidermal Glands

Apocrine Gland

- Apocrine glands
- Apocrine secretion - small portions of cytoplasm pinches off and released into the lumen
- Unbranched, highly coiled
- Associated with hair follicle
- Function in sexual and social communication
- Restricted to certain areas (scrotum, labia minora)
- Secretion begins at puberty

Epidermal Glands

Eccrine Gland (Sweat Gland)

- Eccrine secretion - directly across plasma membrane
- Solid unbranched epithelial downgrowth
- Bud coils at tip to form secretory portion
- Duct forms at attachment with epidermis
- Central cells degenerate to from lumen
- Secretory cells differentiate from cells lining duct
- Myoepithelium from ectoderm, smooth muscle-like

Integument - Skin

- Ectoderm → Epidermis; Mesenchyme → Dermis

Derivatives:
- Hair
- Mammary Gland
- Teeth (Chapter 13, pp 298-303)
**Mammary Glands**

- Modified appocrine glands
- Milk Lines – two bands of ectodermal thickenings
- Cranial to caudal - ventrolateral body wall
- Species-specific
- Supernumerary breast polymastia
- Supernumerary nipple polythelia

**Mammary Gland Development**

- Week 5 - Primary bud = Thickening of epidermal cells – from ridge
- Down growth into the dermis
- Two Mesodermal components
  - Fibroblastic cells – controls branching pattern
  - Fatty cells – controls shape of duct system
- Week 10-12 - Branching to form many secondary buds
  - Secondary buds lengthen and branch
  - Ducts canalize to form lactiferous ducts

**Boys vs. Girls**

- Testicular Feminization Syndrome
- Testosterone receptor mutations
- Mesenchyme mediated signaling

**Physiology – Post-Natal Breast Development and Breast Feeding**

- Estrogen stimulate duct growth
- Progesterone stimulate formation of lobes of secretory alveoli
- Hypothalamus
  - Block of prolactin - lactating hormone
  - Milk protein synthesis
  - Prolactin
  - Lactating breast
Integument - Skin

Ectoderm → Epidermis; Mesenchyme → Dermis

Derivatives:
- Hair
- Mammary Gland
- **Teeth** (Chapter 13, pp 298-303)

Tooth Development

Ectoderm - enamel
Mesoderm - everything else

Teeth - 2 sets form
- primary dentition (deciduous or milk teeth)
- secondary dentition (permanent teeth)

General anatomy - Enamel, dentin, dental pulp, boney socket, periodontal ligament, cementoblast, cementum.

32 permanent teeth
- 16 top; 16 bottom

20 with deciduous teeth
- 10 top; 10 bottom
- medial, lateral incisors; canine, 1st and 2nd premolar

12 w/out deciduous teeth
- 6 top; 6 bottom
- 1st, 2nd, 3rd molars, (3rd molar, wisdom, often fails to develop or erupt)

Tooth Development

6th Week - U-shaped thickening of oral epithelium called dental laminae - follows curve of the jaw.

Mesenchyme is derived from neural crest migration

Reciprocal Epithelial-Mesenchymal interactions

Stages:
- **Bud** – Ectoderm grows into the mesenchyme
- **Cap** - Tooth bud forms a cup around the mesenchyme (dental papilla)
- **Bell** - Tooth is bell shaped – around dental papilla

Bud Stage

Bud Stage, ectodermal swellings (10 per jaw) that grow into the mesenchyme

Lef1 (lymphoid enhancer factor 1) – defines ectoderm

Msx1 – defines mesenchyme

BMP4, FGF8 and SHH – induce the mesenchyme to participate in tooth formation

Cap Stage

Dental papilla signals (BMP4, FGF3, Activin) ectoderm

Formation of the Enamel knot – signaling center

Dental mesenchyme controls the specific form of the tooth
Dental papilla → Dental pulp

Epithelium → Enamel organ – produces enamel, connected to the oral epithelium via dental lamina (stalk) which degenerates.

Bell Stage

Enamel organ - 2 layers – Outer epithelium & Ameloblast (enamel producing cells). Stellate reticulum is between the 2 layers. Dental pulp cells form Odontoblast layer (secrete dentin).

Odontoblast - produce predentin - deposited next to enamel epithelium. Predentin calcifies to become dentin. Odontoblast regresses, cytoplasmic extensions remain in dentin. Pulp cavity is reduced to form the root canal - vessels and nerves pass.

Ameloblast – Induced by Odontoblasts - produce amelogenins and enamels (organic components of enamel). Enamel – 95% inorganic (hydroxyapatite crystals); 5% organic.
Mesenchyme surrounding the tooth forms the dental sac. Dental sac gives rise to cementoblasts and the peridontal ligament.

Root Development

Epithelial root sheath - contiguous with ameloblast layer in crown

Mesenchymal cells next to this cell layer differentiate into odontoblasts and secrete predentin – contiguous with crown dentin

Cementoblasts (produce cementum) form from inner cells of the dental sac - cementum covers the surface of the dentin - cements the root to the jaw

Outer cells of dental sac - bone formation - forms the alveolus (bony socket) and the periodontal ligament

Enamel
Dentin
Gingiva
Dental pulp
Periodontal ligament
Cementum
Cementoblasts
Bony socket
18 months postnatal

Crown
Root