Epidermis & Dermis
Lectures Objectives

• Describe the layers of the epidermis and development of the integumentary system.
• Describe structure of the dermis, compare the structure and distribution of hair follicles, nails, sebaceous and sweat glands.
• Explain bases of skin color.
Introduction

• The organs of the **integumentary system** include the skin and its accessory structures including hair, nails, and glands, as well as blood vessels, muscles and nerves

• **Dermatology** is the medical specialty for the diagnosis and treatment of disorders of the integumentary system.
Structure of the Skin

- The skin (cutaneous membrane) covers the body and is the largest organ of the body by surface area and weight.
- Its area is about 2 square meters (22 square feet) and weighs 4.5-5kg (10-11 lb), about 16% of body weight.
- It is 0.5 – 4 mm thick, thinnest on the eyelids, thickest on the heels; the average thickness is 1 – 2 mm.
Divisions of skin

- Epidermis and derivatives – (ectoderm)
  - Epidermis proper
  - Hair follicles
  - Nails
  - Glands
    - Sebaceous
    - Sweat (eccrine & apocrine)
    - Mammary
- Dermis – Corium (mesoderm)
  - Papillary layer – loose CT
  - Reticular layer – dense Ct
- Subcutaneous (hypodermis) subcutis (mesoderm)
  - Areolar CT
  - Fatty components
Development of the Integumentary System
Functions of Skin

• Major functions of skin
  – Protection
  – Thermoregulation
  – Excretion
  – Secretion
  – Sensory reception – communication
  – Immuno protection – there are more lymphocytes in the skin than in circulation
Functions of Skin

• Problems of burn victims exemplify the importance of skin.
• Patients with severe burns has
  – Loss of sensation to temperature
  – Pain and pressure
  – Ionic balance drastically off
  – Fluid loss
  – Wildly fluctuating body temperature (5-8 degrees)
  – Bacterial and fungal infections increase
Epidermis

• Most superficial layer of skin

• Cornified stratified squamous epithelium
Epidermis

- Tow major types of skin based on thickness of epidermis
  - **Thick skin** on non hairy surfaces (epithelium up to 1.0 mm)
  - **Thin skin** on most hairy surfaces of the body (epithelium generally 0.1 mm)

- Thick vs thin does not reflect true thickness of skin including dermis
  - Skin on the back called thin but actually is thickest when dermal layer is included
Cells of Epidermis

- Four cell types in the epidermis
  - **Keratinocytes** (squames) – production of keratin and water barrier. More than 90% of cells in epidermis
  - **Melanocytes** – pigment production less than 5% of cells in epidermis
  - **Langerhans cells** – immune response, 1-3% cells in epidermis
  - **Merkel cells** – sensory reception and local endocrine control, 1-3% cells of epidermis
Epidermis

- Differentiation of keratinocytes (cytomorphosis)
  - Change shape (flatten)
  - Lose organelles
  - Form fibrous proteins
  - Become dehydrated
  - Produce products that thicken plasma membranes
Layers (Strata) of the Epidermis

- Stratum corneum
- Stratum lucidum
- Stratum granulosum
- Stratum spinosum
- Stratum basale
Stratum Basale (Germinativum)

- The **mitotically active** layer which generate the keratinocytes and their derivatives (i.e. Merkel cells)
- Cells anchored to basal lamina via anchoring fibrils and hemidesmosomes
- Highest metabolic requirement of all layers
- Active synthesis of **tonofilaments**, formation of extensive number of **desmosomes**
- Cells assume **cuboid** profiles
- Two major cell types:
  - Stem cells
  - Keratinocytes
- This layer contain the most undifferentiated cells of epidermis
Stratum Spinosum

- **Polyhedral** cells
- Cells are firmly bound by the filament-filled cytoplasmic spines and desmosomes
- Active synthesis of tonofilaments which provides cytoskeletal framework
  - Tonofilaments insert into the cytoplasmic part of the desmosomes
- Appearance of *membrane-coated granule (MCG)* in upper portion of this layer
  - These are laminated structures
  - Key to formation of effective water barrier
  - MCG contain lamellar disks that are formed by lipid bilayers
- **Mitotic figure** frequent (up to 3%)
  - All mitosis are confined to the *malpighian layer* (both stratum basale and stratum spinosum)
Stratum Granulosum

• Presence of dense, refractile, basophilic granules of keratoxyalin which contain profilaggrin
• The basophilia is due to RNA within the granules (active sites of filaggrin synthesis)
• Tonofilaments have condensed into tonofibrils which are anchored in the matrix of the granules
• Many desmosomes present
• MCG are released into extracellular space
  – thicken external surface of membrane and seal adjacent membranes thus forming a water barrier (note no zonula occludens)
Stratum Lucidum

- Only in thickest skin
- Appears as transparent layer, no visible nuclei or organelles
- Sulfhydryl groups (-SH) replaced by disulfide bonds (S-S) thus forming cystine groups that cross linked and stabilize the keratin molecules
- Substance remaining in these cells called eleidin
  - Clear intracellular protein
  - Intermediary in formation of keratin from keratohyaline granules and tonofibrils
Stratum Corneum

- Plasma membranes thickened by previous emptying of MCG into intercellular space in the subjacent layer
- Desmosomes remain as membranous modifications
- All organelles lost
- Cells backed with keratin (tonofibrils embedded in matrix of keratohyalin)
- Cell structure not evident
• Stages of keratinocytes development
  – Proliferation
  – Differentiation
  – Exfoliation

Usually 28-45 days for complete cycle

• Thin skin lacks well developed:
  – Stratum corneum
  – Stratum lucidum
  – Stratum granulosum
Pigmentation system

- **Melanocytes**
  - Appear as clear (neuron-like) cells within st. basale.
    - Do not form desmosomes with keratinocytes
  - Extend dendritic-like processes throughout st. spinosum
  - Same number of melanocytes in all races
  - Produce melanin
  - Transfer melanin to keratinocytes
  - Originate from neural crest
- **Tyrosinase** catalyzes conversion of tyrosine to 3,4-dihydroxyphenyalanine (DOPA) and conversion of DOPA to dopaquinone which eventually forms melanin
Pigmentation system

Stages of melanocyte melanogenesis (melanization of the melanosome; a membrane-limited body derived from Golgi apparatus)

- **Premelanosome**
  - Circular vesicle
  - Tyrosinase activity
  - Fine peripheral granules

- **Immature melanosome**
  - Ovoid vesicle
  - Tyrosinase activity
  - Parallel filaments 10 nm periodicity

- **Mature melanosome**
  - Internal structure obscured by melanin
  - Tyrosinase activity still present

- **Melanin granule**
  - Solid melanin
  - No tyrosinase activity
Pigmentation system

• Transfer of melanin from melanocyte to keratinocytes is by a process termed “Cytocrine secretion”
  – Injection by melanocyte of melanin granules into a keratinocyte (exocytosis coupled with endocytosis)
• Because of rapid transfer more melanin found in keratinocyte than melanocyte
Pigmentation system

• Melanin accumulate on sunny side of nucleus
  – protection of nucleus from UV
• Dark skin absorbs and disperse UV better than light skin
• Racial differences due to:
  – Degree of melanin dispersion
  – Lysosomal action on melanosomes
    • Light races- melanin rapidly broken down
    • Dark races- melanin granules more resistant within st. spinosum
• Tanning increase melanin concentration not number of melanosomes
Other causes of skin color

• Carotene in dermis
  – Yellow-orange pigment (precursor of vitamin A)
  – Found in stratum corneum & dermis

• Hemoglobin
  – Red, oxygen-carrying pigment in blood cells
  – If other pigments are not present, epidermis is translucent so pinkness will be evident
Langerhans cells

• Appearance
  – Clear cells, generally has a dendritic appearance

• Location
  – St. basale and spinosum,
  – Process extend toward surface

• Act as antigen presenting cells with some phagocytic activity

• Absence of tonofibrils and desmosomes

• May contain melanin granules due to phagocytic activity of damaged keratinocytes

• Responsible for the initial allergic reaction due to contact hypersensitivity

• Bone marrow originated cell
Merkel’s cells

- Merkel cell is modified keratinocyte
  - Has tonofibrils
  - Forms desmosome
  - Slow adapting

- Mechanoreceptor
  - Associated with sensory nerve endings
  - Catecholamine containing granules on dark side of nucleus, mechanogated channels

- Local release of neuropeptides can modulate vascular smooth muscle contraction. Hence Merkel cell has potential to play a paracrine function in immediate response to stimulus
• Dermis – Corium
  – Papillary layer – loose CT
  – Reticular layer – dense Ct
Papillary Layer

- **Loose CT**
  - Delicate collagenous fibers,
  - Fewer reticular and elastic fibers
  - Fibers attach to basement membrane hence perpendicular to surface
- **Passage for vessels**
  - direct nutritive responsibility for epithelium
- **Reticular lamina produced by cells in this layer**
  - has an inductive effect on overlying epidermis
- **Route for ducts of sweat glands**
Papillary Layer

- Dermal papillae
  - More papillae in thicker epidermis
- Pegs (rete ridges)
  - Ridges alter topography of overlying epidermis to produce fingerprints
- Site of Meissner’s corpuscles
  - Important use in reading braille
Reticular Layer

- Major component (mass) of skin
- Dense fibrous CT highly interwoven
- Provide structural support for derivatives
  - Hair follicles
  - Associated glands
Hypodermis (Subcutaneous Layer)

- Loose CT
- Serves for:
  - Protection
  - Fat storage
  - Houses
    - Secretory portion of eccrine sweat glands
    - Deep portions of the hair follicles
  - Frequent Pacinian corpuscles (pressure receptors) are found in this layer
- Not truly component of skin
  - Corresponds to superficial fascia
Eccrine Sweat Gland

- Not associated with hair follicles
- Sweat is cell product
  - Regulation of body fluid
    - Sweat secretion may lead to total dehydration (1-2 liter per hour)
  - Some elimination of body wastes
  - Regulate body temperature
    - Major source of evaporative heat loss
- Distributed over entire body
  - Absent in: glands penis, clitoris, labia minora
  - High concentration in: palms and soles
- Morphology – simple coiled tube (tubular) with ductal (smaller lumen) and secretory (larger lumen) portions
Eccrine Sweat Gland

- Secretory component – only in **deepest** dermis or hypodermis.
  - Lined with a simple epithelium of (two types) pyramidal cells
    - **Clear serous cell**
      - Base away from lumen
      - Large nucleus, pale cytoplasm
      - Involved in salt absorption and fluid transport
      - Many mitochondria, glycogen, and intercellular canaliculi
    - **Dark mucous cells**
      - Inverted pyramid, base toward lumen
      - Small nucleus
      - Basophilic
      - Involved in production of glycoproteins
      - Golgi apparatus
  - Thus nuclei of secretory portion appear at two levels like pseudostratified epithelium
Eccrine Sweat Gland

- Ductal component
  - Two concentric layers of cuboidal cells
  - Luminal surface appears thickened because of densely packed tonofilaments
  - Ductal cells separated from basement membrane (basal lamina) by incomplete layer of myoepithelia cells
  - Distal component of duct reabsorbs Na and Cl
Eccrine Sweat Gland

Two types of eccrine glands in terms of stimulus sensitivity

• Palmar – plantar
  – Increase secretion response to mental (emotional) state
  – Only minimal response to heat stress
  – Adrenergic

• General eccrine
  – Response predominantly to heat stress
  – Cholinergic
Apocrine Sweat Glands

- Component of Pilosebaceous Unit (hormonal control)
- Develops from distal region of hair follicle in embryo
- Atrophies on most follicles except in specific regions: axilla, external auditory meatus, eyelids, ano-genital areas
Apocrine Sweat Glands

• Morphology – simple tubular glandular epithelium, secretory coil in deep dermis, duct opens into distal hair follicle
  – Lumen of tube varies with functional state, but much larger than lumen of an eccrine sweat gland
  
  – Simple epithelium
    • when contracted (empty) appears simple cuboidal to low columnar;
    • when distended appears almost like simple squamous
  
  – All cells attached to basal lamina; however attachment not clear because basal lamina partially covered by incomplete layer of myoepithelial cell
(a) Apocrine sweat gland

(b) Merocrine sweat gland
Apocrine Sweat Glands

- Secretion appears apocrine “pinching off” of apical cytoplasm. EM reveals exocytosis
  - Secretion: viscous milky to clear, contains proteins, carbohydrates, ferric iron, fatty acids
  - Initially odorless – characteristic body odor formed after bacterial decomposition
  - Function unknown possibly bactericidal, or pheromone—amorous inclinations
  - Primarily adrenergic (emotional) stimulus for secretion, some cholinergic stimulus
Sebaceous Gland

- No nerve supply, only hormonal regulation
- Develops as portion of Pilosebaceous unit as a bud from the wall of a hair follicle below the apocrine gland within the dermis
- Prominent distribution over face, neck, upper chest and back.
- On upper back they are highly developed while the hair follicle remains rudimentary hence referred to as Sebaceous follicles
Sebaceous Gland

- Sebum – whole cell product (holocrine), almost entirely lipid
  - Secreted continually, not diurnally
  - Acts as a permeability barrier, bacteriostatic, fungistatic, pheromone
  - Acne – androgen increase which decreases estrogen activity
- Germinal epithelium layer adjacent to basal lamina
  - As cells form sebum they take on foamy appearance, lose nuclei and most visible organelles; center of gland most highly differentiated
Hair Follicles

- Pilosebaceous apparatus includes: hair follicle, sebaceous gland, apocrine sweat gland and smooth muscle
- Reduced importance of hair in human
  - Conserve body temperature
  - Protect against physical trauma
  - Provide sense of environment
  - Personal adornment
  - Functional reserve of epithelial cells after injury
- Variation with sexes. Same number hair follicles males and females (estimated 2 million) 100,000 on scalp. Difference in distribution between sexes
Hair types

Three types of hairs (1 preterm, 2 mature)

- Lanugo – lost shortly after birth
- Vellus – covers most of the body before puberty
  - Very fine non pigmented equivalent to lanugo
  - Follicle extend to mid dermis
  - Converted to terminal follicles after puberty in axillary and anogenital regions in both sexes
    - In males also have conversion on face extremities and trunk
- Terminal –
  - Coarse, pigmented, on scalp, eyelids, eyebrow
  - Follicle extends through dermis into hypodermis
  - Structure of terminal hair more complex (medulla and cortex)

- Keratinocytes do not undergo desquamation, they form hard keratin
Structure of Hair

• Shaft -- visible
  – Medulla, large, vacuolated and moderatel keratinized cells
  – Cortex, heavily keratinized, compactly grouped fusiform cells
  – Cuticle,
    • Cuboidal midway up the bulb, then columnar.
    • Higher up, form flattened, heavily keratinized, shinglelike cells

• Root -- below the surface
• Follicle surrounds root
Structure of Hair

• Follicle surrounds root
  – Internal root sheath
    • Transient structure whose cells degenerate and disappear above the level of sebaceous gland
  – External root sheath
  – Continuous with the epidermal cells
  – Glassy membrane
  – Thickening of the basal lamina
  – Connective tissue sheath

  • Denser part of dermis surround the follicle
Structure of Hair

- Base of follicle is **bulb**
  - Dermal papilla
  - Blood vessels
  - Germinal cell layer
Hair Related Structures

- **Arrector pili**
  - Smooth muscle in dermis contracts with cold or fear.
  - Forms goosebumps as hair is pulled vertically

- **Hair root plexus**
  - Detect hair movement
Hair Growth

• The hair growth cycle consists of a growing stage and a resting stage.
  – Growth cycle = growth stage & resting stage
    • Growth stage (anagen)
      – lasts for 2 to 6 years
      – matrix cells at base of hair root producing length
    • Resting stage (catagen and telogen)
      – lasts for 3 months
      – matrix cells inactive & follicle atrophies
  – Old hair falls out as growth stage begins again
    • normal hair loss is 70 to 100 hairs per day
Hair Growth

- Male sex hormone (androgen) influence terminal hair follicles. In contrast, estrogen influences melanocytes.
- Both rate of growth and the replacement cycle can be altered by illness, diet, high fever, surgery, blood loss, severe emotional stress, and gender.
- Chemotherapeutic agents affect the rapidly dividing matrix hair cells resulting in hair loss.
Hair Color

• Hair color is due primarily to the amount and type of melanin.

• Graying of hair occurs because of a progressive decline in tyrosinase.
  – Dark hair contains true melanin
  – Blond and red hair contain melanin with iron and sulfur added
  – Graying hair is result of decline in melanin production
  – White hair has air bubbles in the medullary shaft
Structure of Nails

- Tightly packed keratinized cells
- Nail body
  - visible portion pink due to underlying capillaries
  - free edge appears white
- Nail root
  - buried under skin layers
  - lunula is white due to thickened stratum basale
- Eponychium (cuticle)
  - stratum corneum layer
Nail Growth

- Nail matrix is below nail root -- produces growth
- Cells transformed into tightly packed keratinized cells
- 1 mm per week
- Certain nail conditions may indicate disease