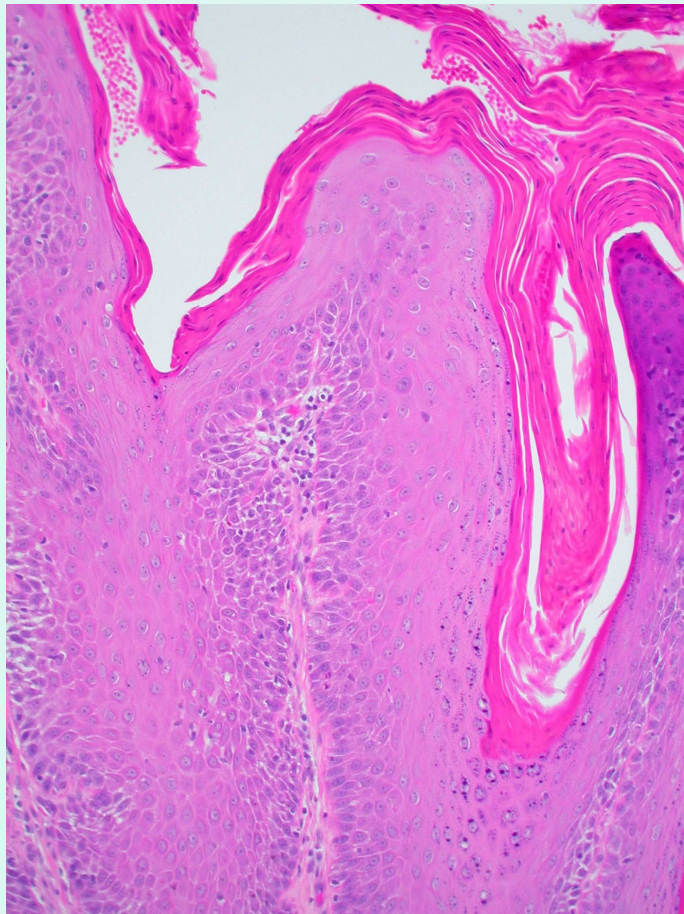


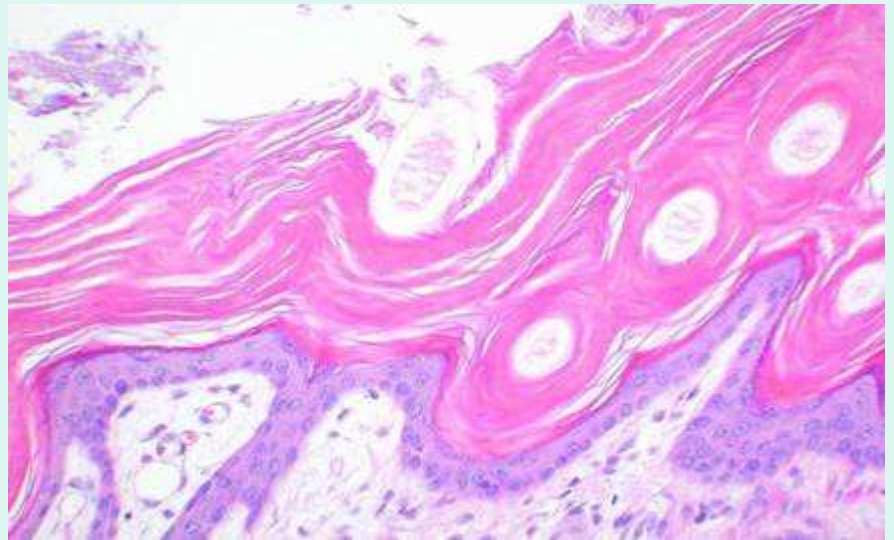
Pathologic changes associated with the stratum corneum

EA Mauldin
Laboratory of Pathology and Toxicology
School of Veterinary Medicine
University of Pennsylvania

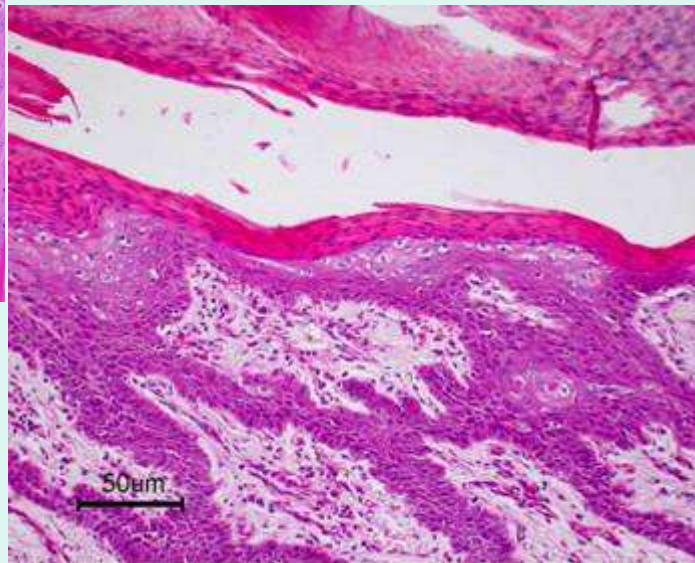




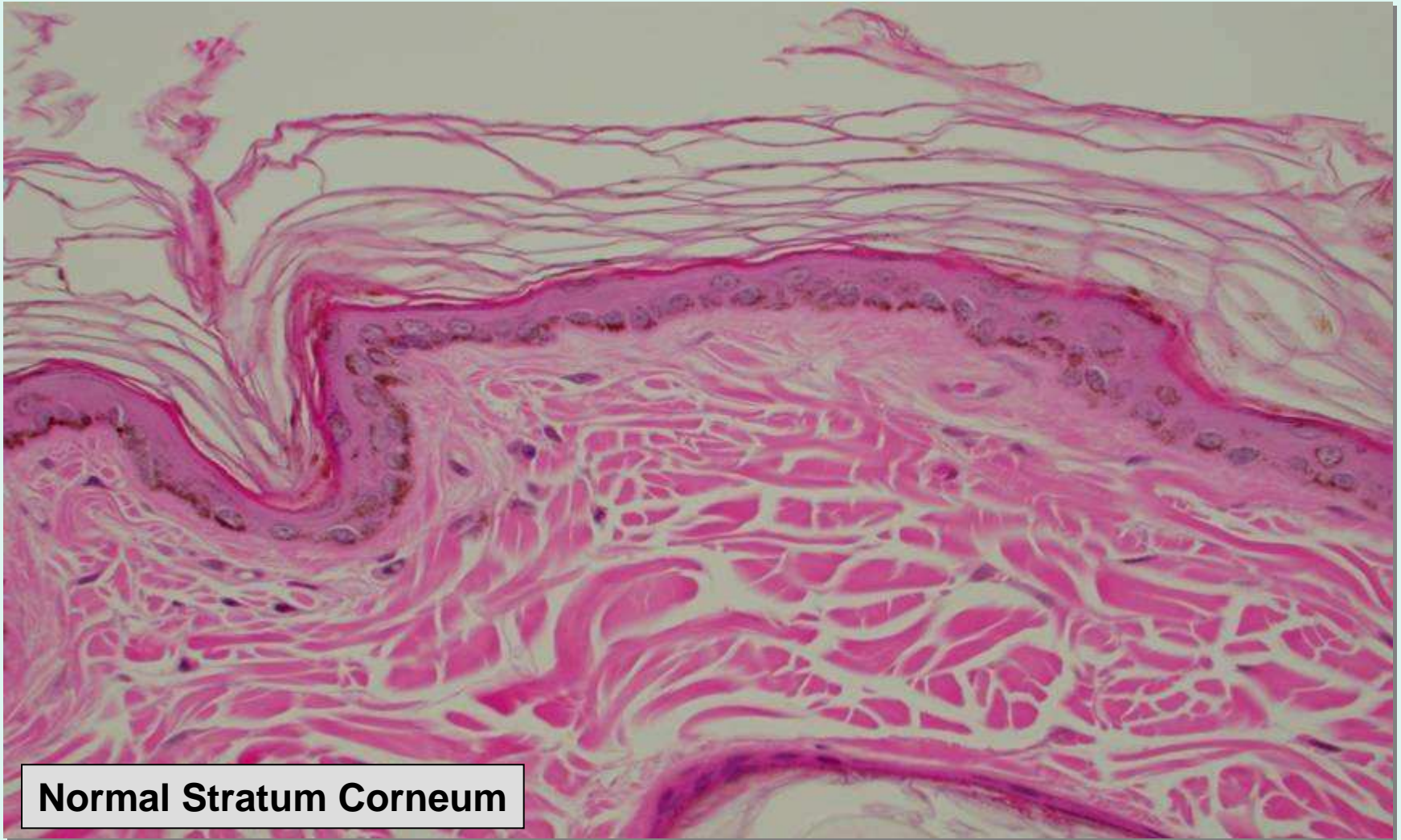
Zinc-responsive



GR Ichthyosis



NME



Normal Stratum Corneum

Evolving Stratum Corneum Concepts

1. Unimportant, desquamation (up to 1960)
2. Tough, impermeable “plastic wrap” (up to 1975)
3. Structural/biochemical “mortar and bricks” (current)
4. Persistent metabolic activity “living” (current)
5. Interactive with underlying tissue (current)
 - Metabolic responses
 - Signaling cascades
 - Biosensor

Interface with the ambient environment

Protective Functions

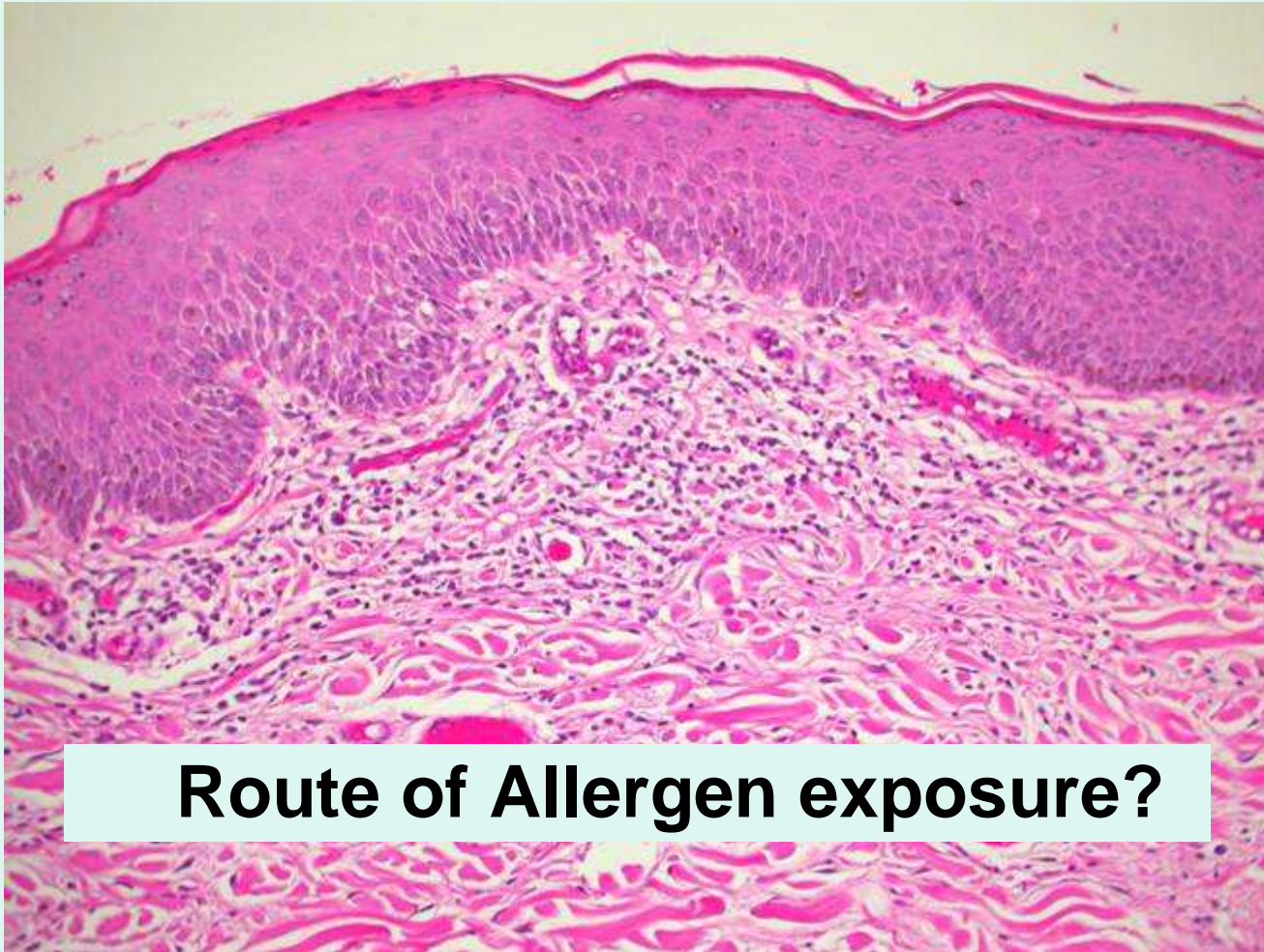
- Integrity and resilience
- Inhibit contact with noxious substances, xenobiotics and allergens
- Antimicrobial defense
- Prevent water loss
- UV protection



Evolving Concepts.....

Stratum Corneal abnormalities →
altered barrier function

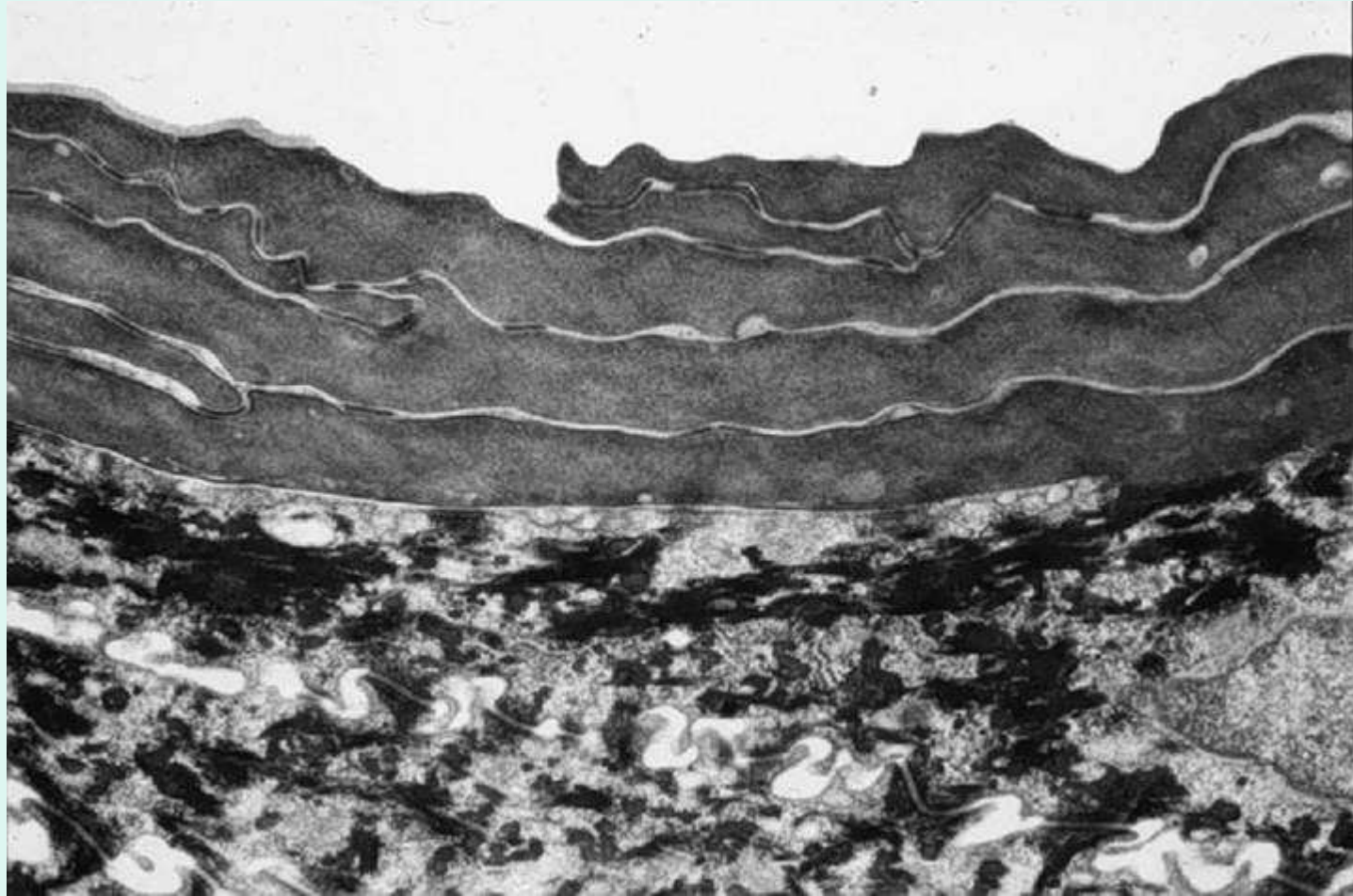
- Loss of integrity/elasticity
- Water loss
- Inflammation
- Pathogen entry



Route of Allergen exposure?

Evolving Concepts.....

- Could a genetically impaired skin barrier lead to systemic sensitization to allergens through the skin?
- Could skin barrier dysfunction contribute to the rapid increase in atopy and allergic asthma in the past three decades?



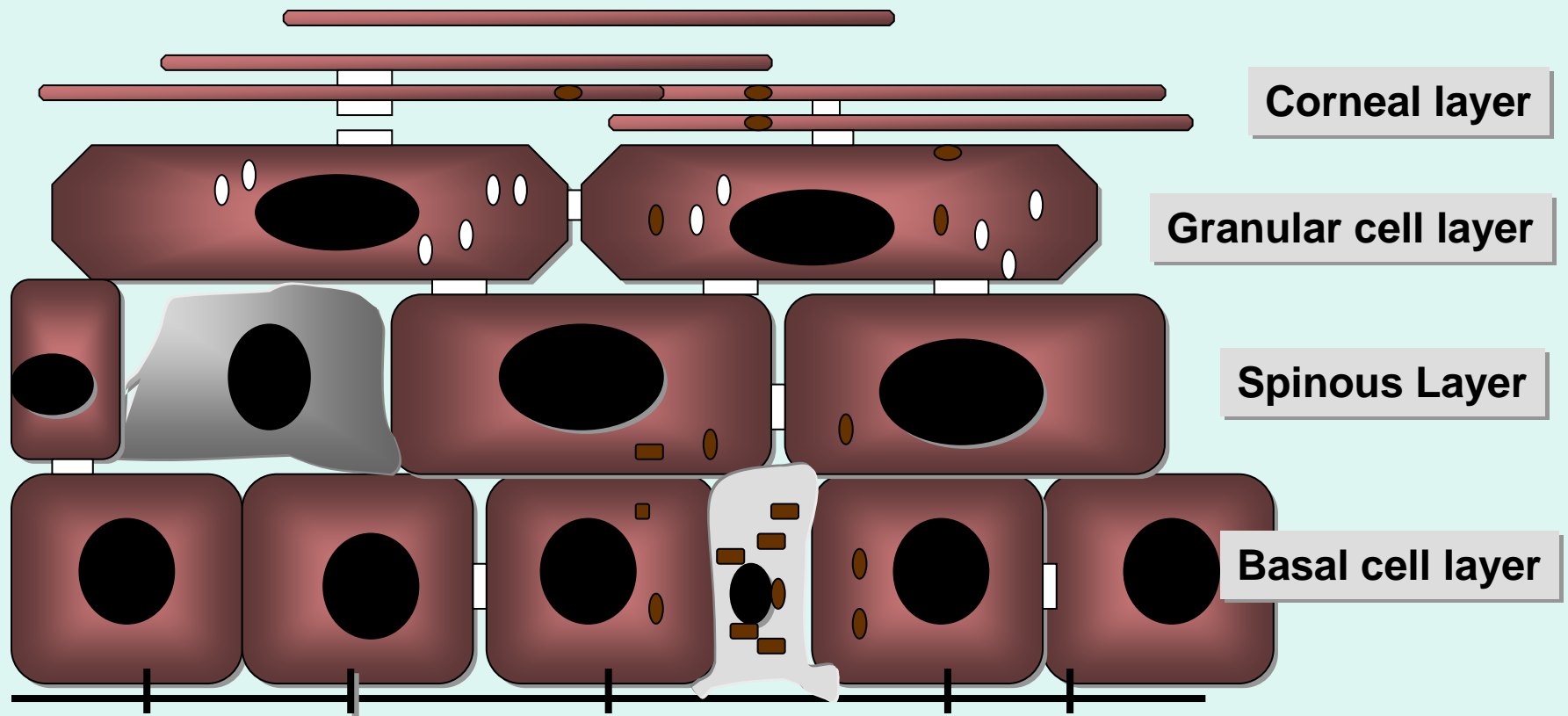
Corneal Function: Restrict water movement

- Lipid content
- Injury → “leaky” → water loss → xerosis
- Xerosis typical of AD in humans
 - Conflicting studies in dogs

Corneal Function: Antimicrobial

- Continuous desquamation
- Antimicrobial peptides
- pH
 - Hydrolases
 - Urocanic acid
 - Phospholipids → free fatty acids
- pH in dogs

Cornification



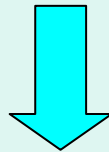
Steps in Cornification

Lipid formation

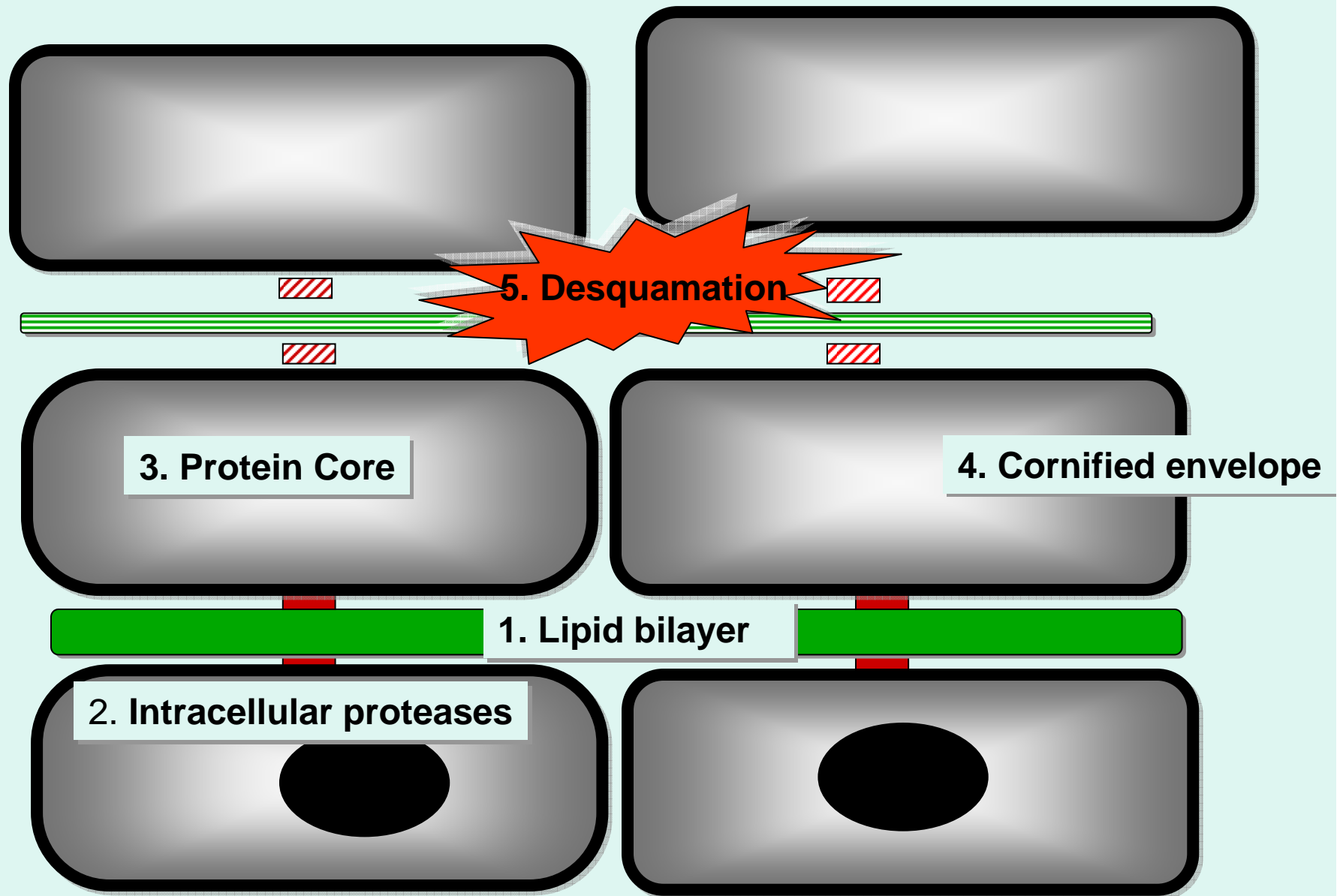
Dissolution of nucleus and organelles

Aggregation of intermediate filaments

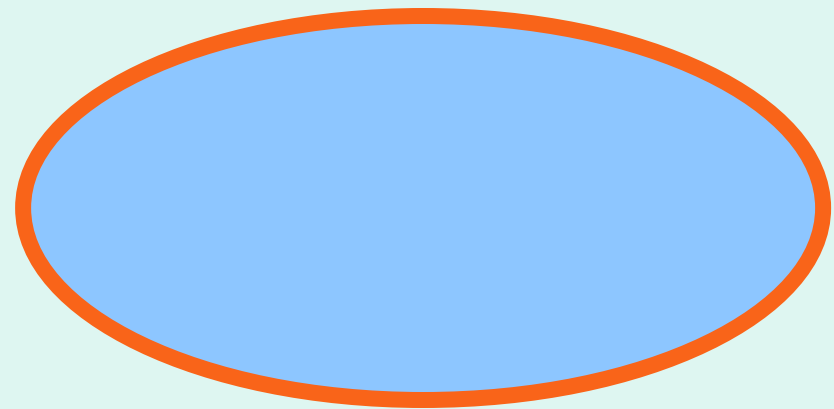
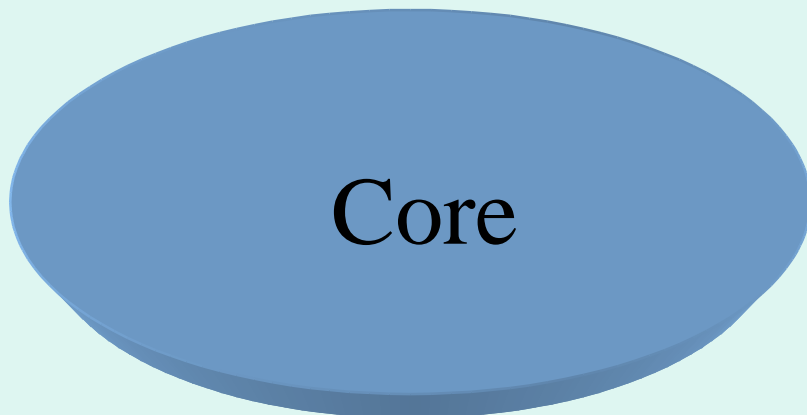
Formation of the cornified envelope



Desquamation



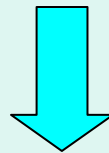
Mentos Model of Cornification



Candy-coating= CE

Steps in Cornification

1. Lipid formation
2. Dissolution of nucleus and organelles
3. Aggregation of intermediate filaments
4. Formation of the cornified envelope



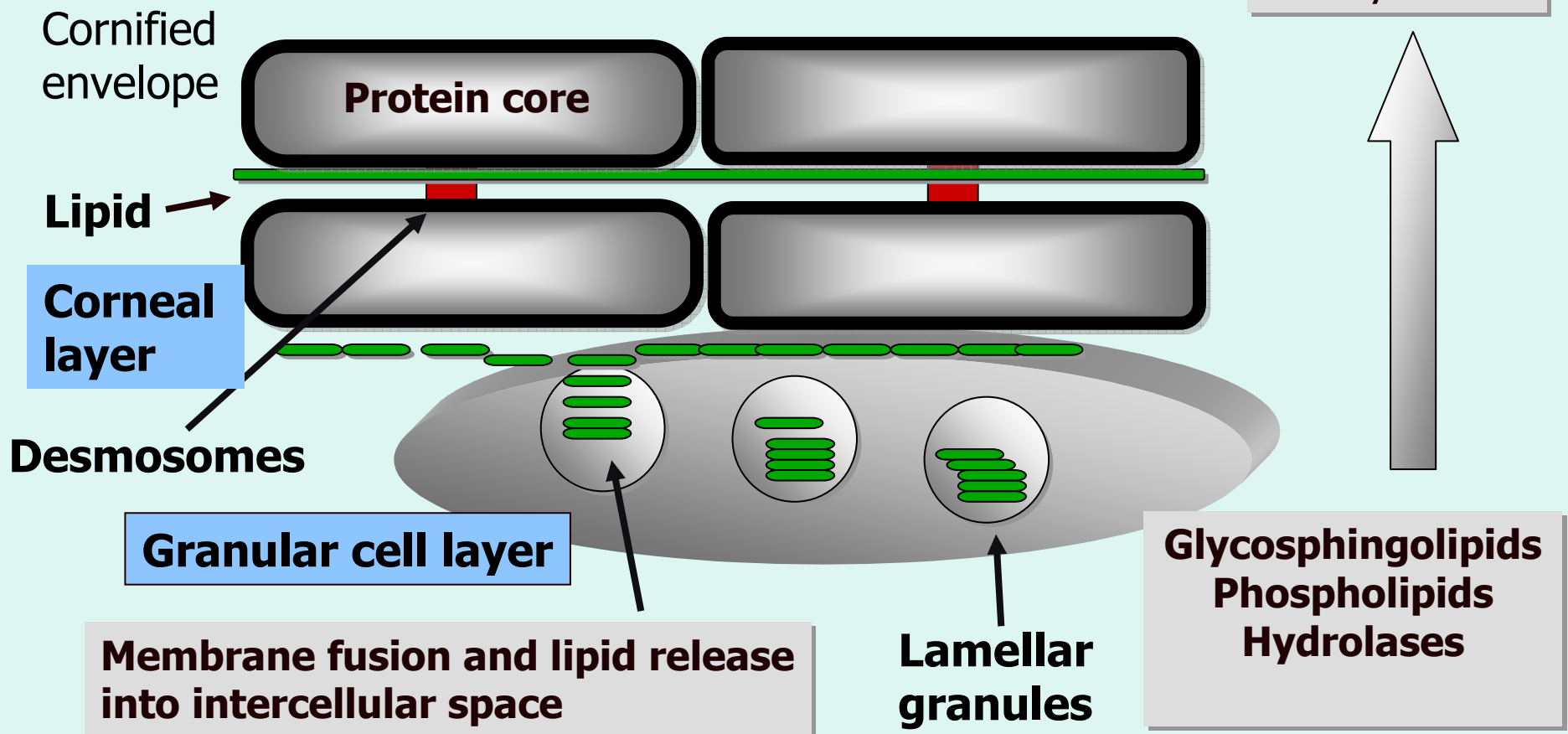
5. Desquamation

1. Lipid Formation

Lamellar bodies

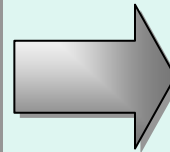
- Ellipsoidal organelles- similar to lysosomes
- Form in basal cell layer
- Most concentrated in SG
- Fuse with cell membrane at SG/SC junction
- Supply lipids and enzymes to SC

Corneal Lipid Formation



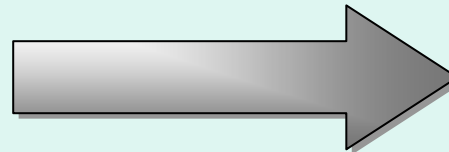
Lamellar Granule Content

Glycosylceramides → Ceramides
Sphingomyelin → Ceramides
Phospholipids → FFA
Cholesterol →



- Cohesion
- Hydration
- Antimicrobial action
- Chemical defense

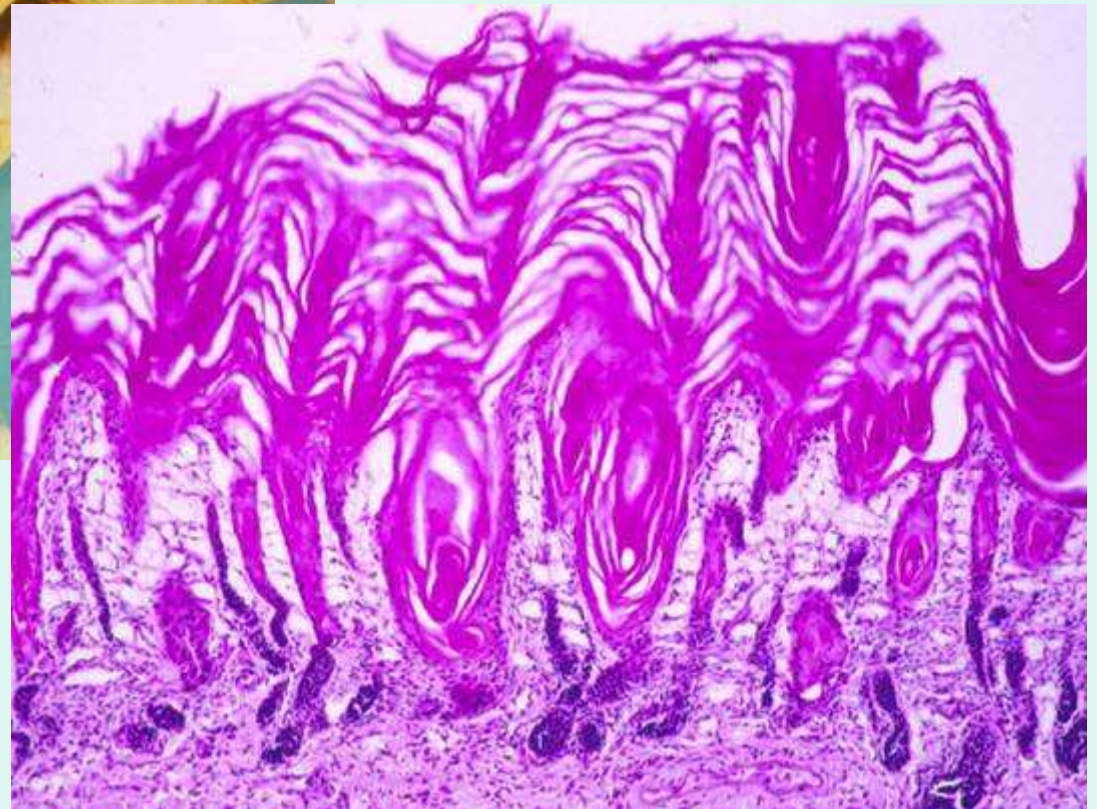
Proteases, lipases,
acid phosphatase,
glycosidases



Decreased in AD

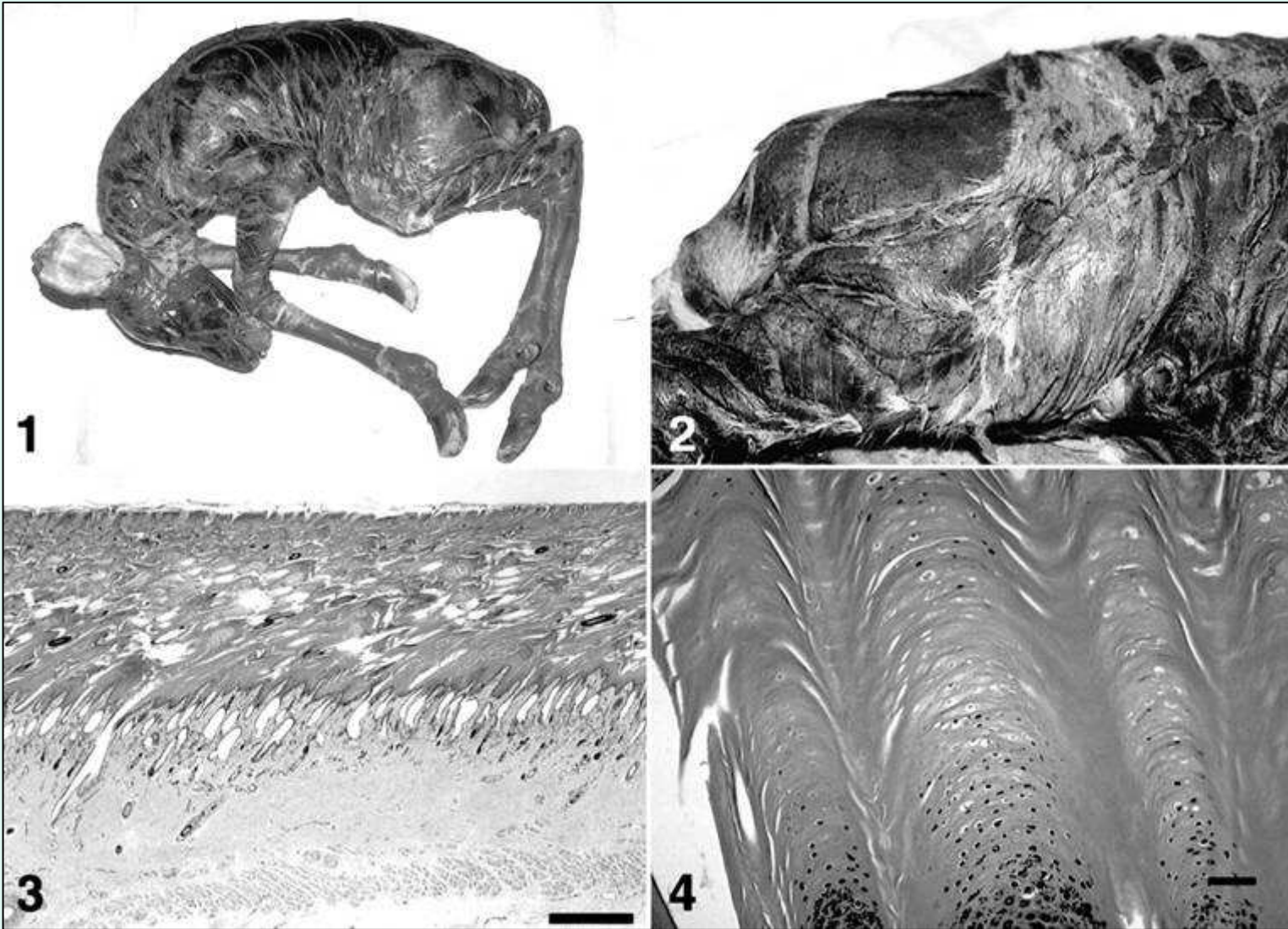
Defects in Lipid Formation

- Harlequin ichthyosis
- Atopic dermatitis?
 - Decreased ceramide
 - Defective lamellar body extrusion
 - Defects in enzymes that modify lipids
 - Abnormal lipid in dogs?



Harlequin ichthyosis

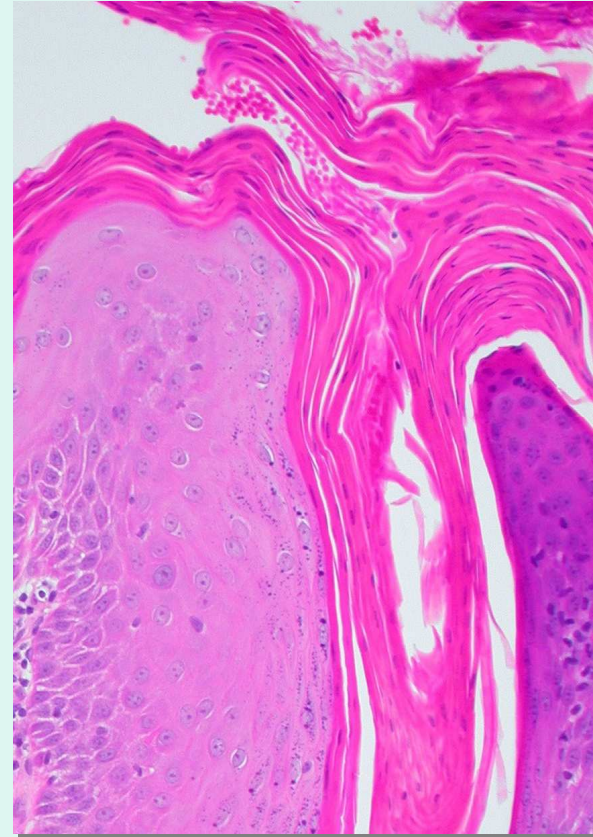
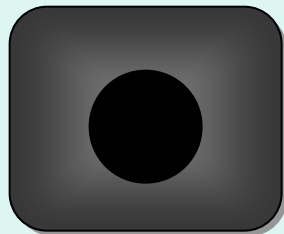
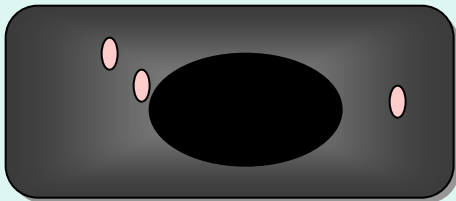
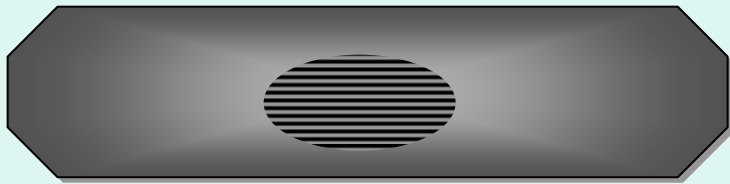
Courtesy of R. Dunstan



HI in Greater Kudu calves

Chittick, *Vet Pathol.* 2002

2. Release of Proteases



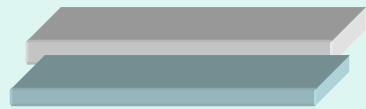
Retained nuclei- parakeratosis

3. Aggregation of keratin filaments

Keratohyalin granules

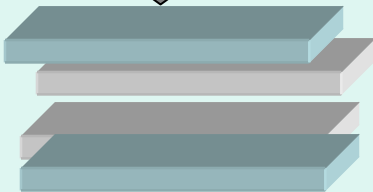
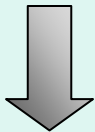
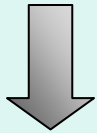
- Profilaggrin → Filaggrin
 - Aggregates keratin intermediate filaments
 - Forms the protein core
- Filaggrin → histidine → Urocanic acid
 - Contribute to pH
 - UV function

Keratins

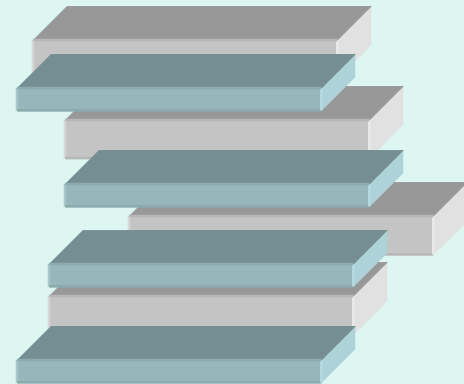


Type 1 acidic K10-K20

Type 2 basic K1-K9



Protofilament



Profibrils

Intermediate Filaments

- Type 1
 - Acidic
 - Smaller kd
 - 9-23
- Type 2
 - Basic
 - Larger kd
 - 1-8

