



Biology and Disorders of Hair Follicles

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Introduction to the Hair Follicle

1. HF are protein fiber factories
2. Disorders of the hair follicle are not life-threatening to humans or animals
3. Hair follicle disorders may cause discomfort, impact social interactions
4. Hair follicles disorders disrupt the human-animal bond

Introduction to Hair follicles

- 5. HF disorders may alter barrier function
- 6. You are born with all the HF that you will ever have
- 7. HF may change over the lifetime of an individual

Outline

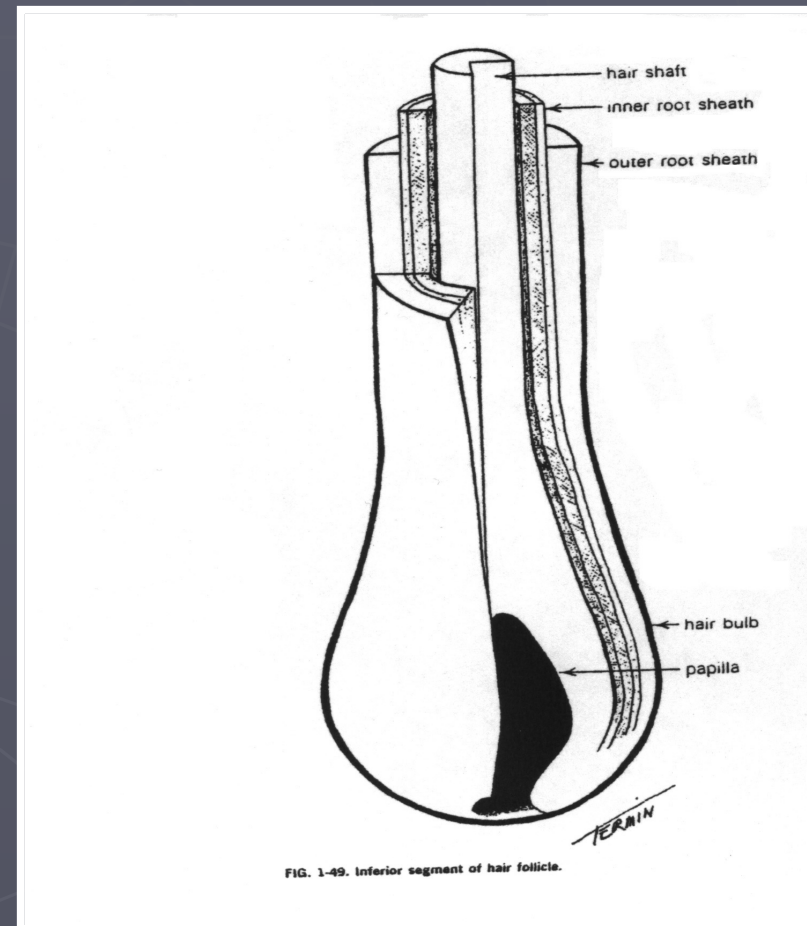
- ▶ Hair follicle anatomy
- ▶ Hair follicle biology
- ▶ Scarring alopecia
- ▶ Nonscarring alopecia
- ▶ Folliculitis classification

Hair Follicle Function

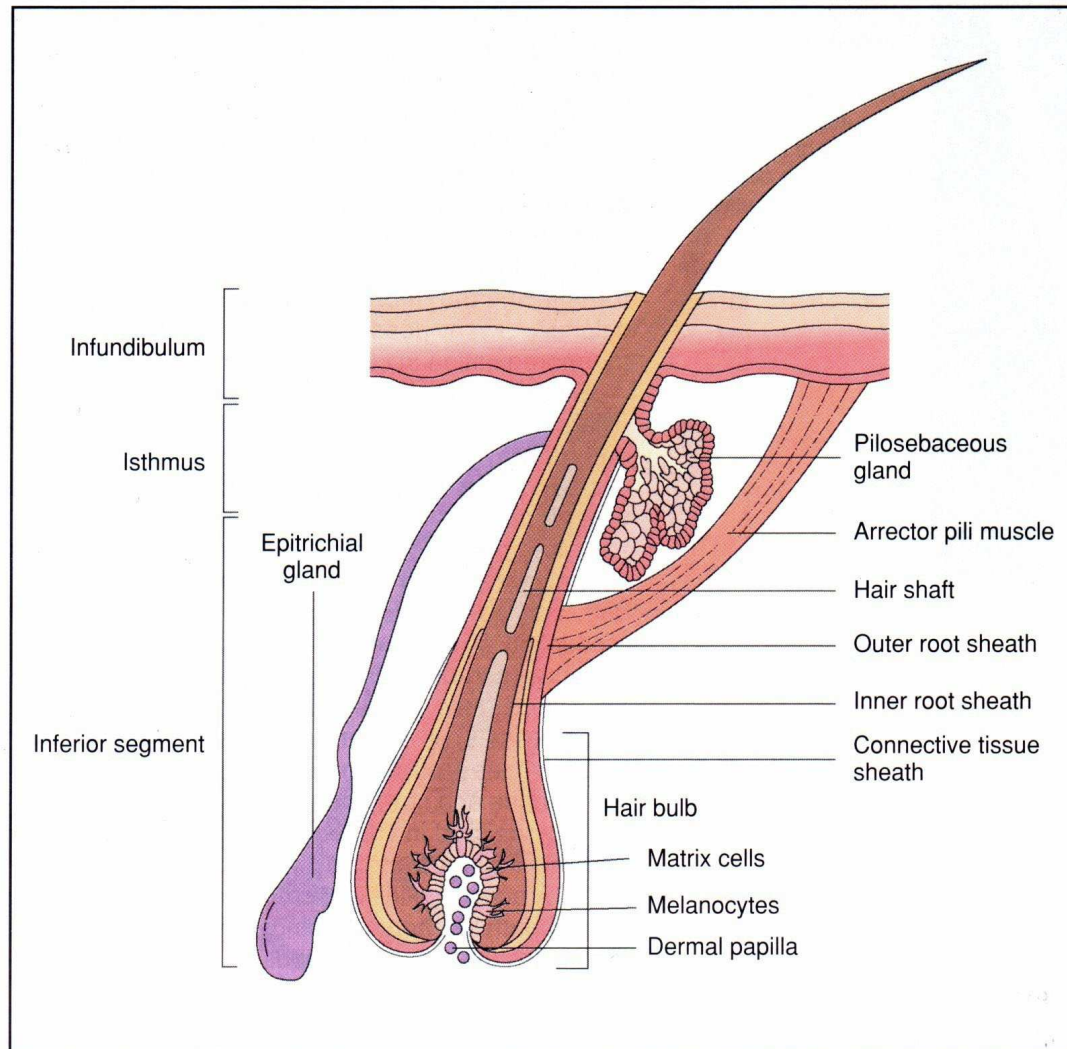
- ▶ Protective barrier
 - Chemical, thermal, microbial, physical
 - Photoprotection
- ▶ Wound repair
- ▶ Social interactions

Structure of Hair

- ▶ Outer root sheath continuous with epidermis.
- ▶ Outer root sheath surrounds an inner tube (inner root sheath).
- ▶ These two tubes surround the hair shaft.
- ▶ Serves as a mold for the developing shaft
- ▶ Hair bulb: base of follicle



Chapter 1 Structure and function of the skin



1.8 The hair follicle and its associated structures. © Anita Patel.



Seven Layers of the HF

- Hair shaft
 - Cuticle
 - Cortex
 - Medulla
- Inner root sheath
 - Huxleys
 - Henleys
- Outer Root Sheath
- Connective tissue sheath

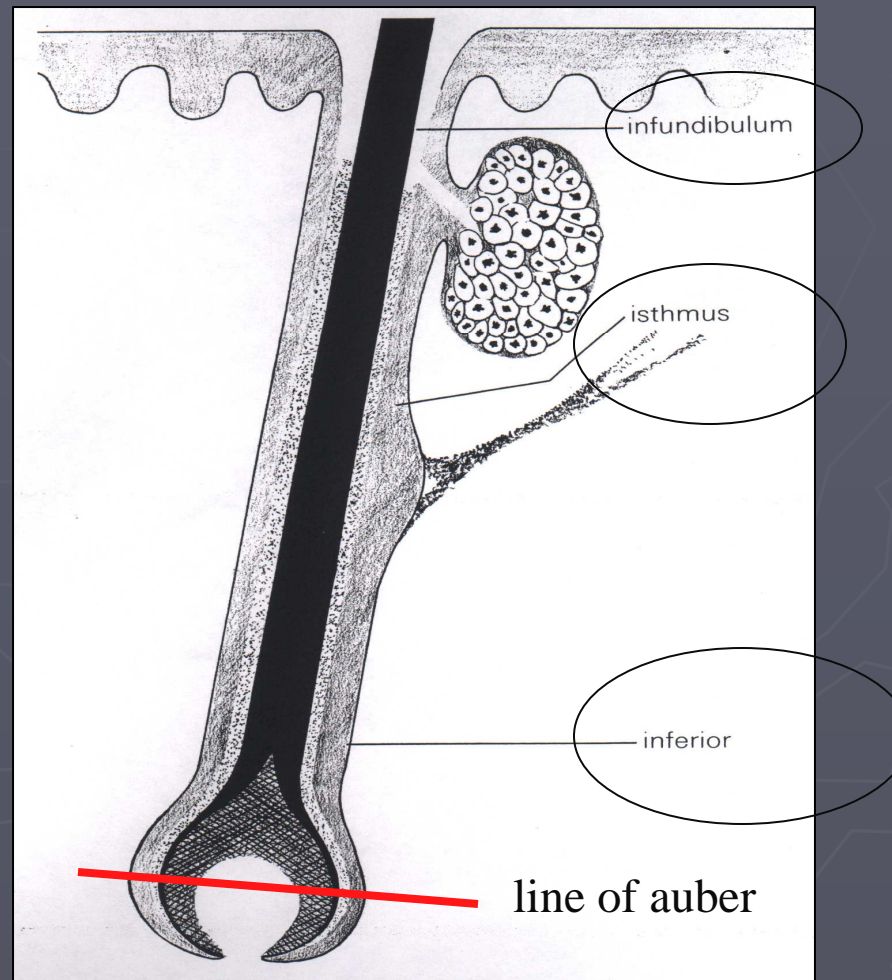


Hair Fiber



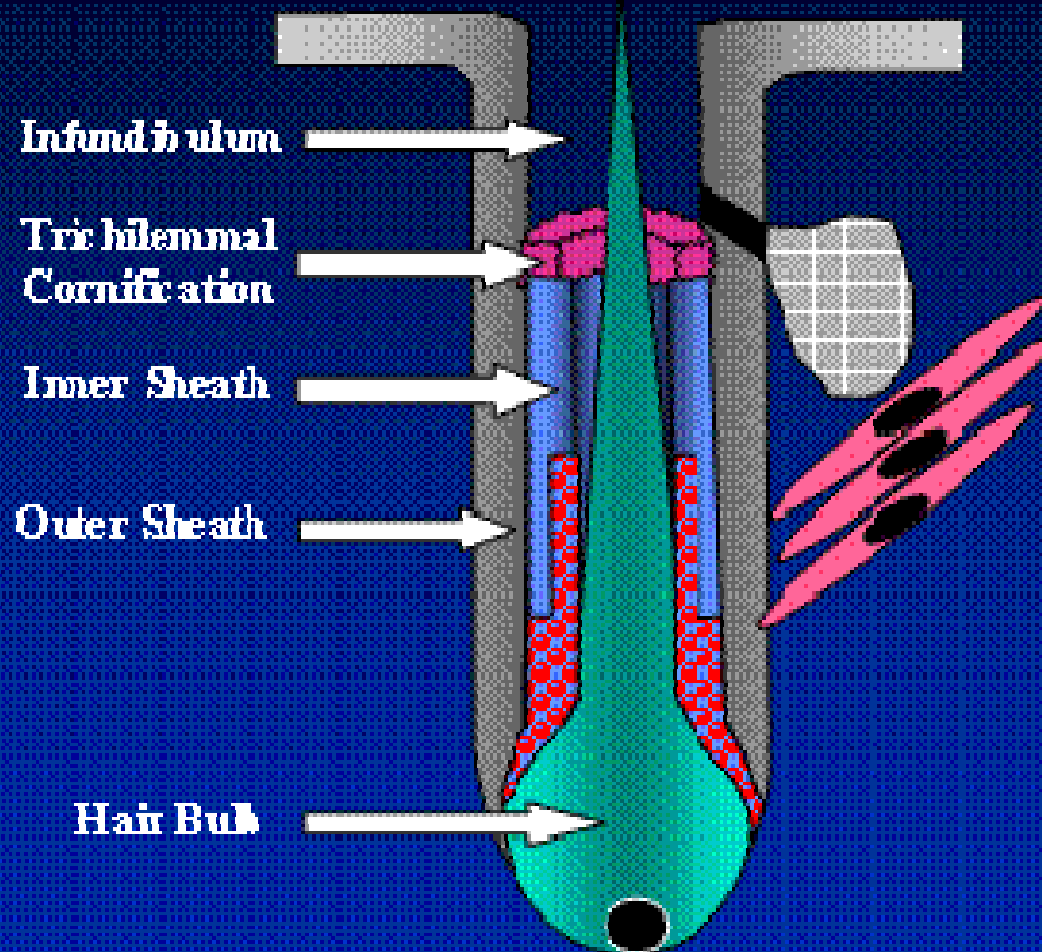
- ▶ “Hard” Keratin
- ▶ Disulfide bonding
 - Sturdy
 - Maintains texture and shape**

Hair Follicle Structure

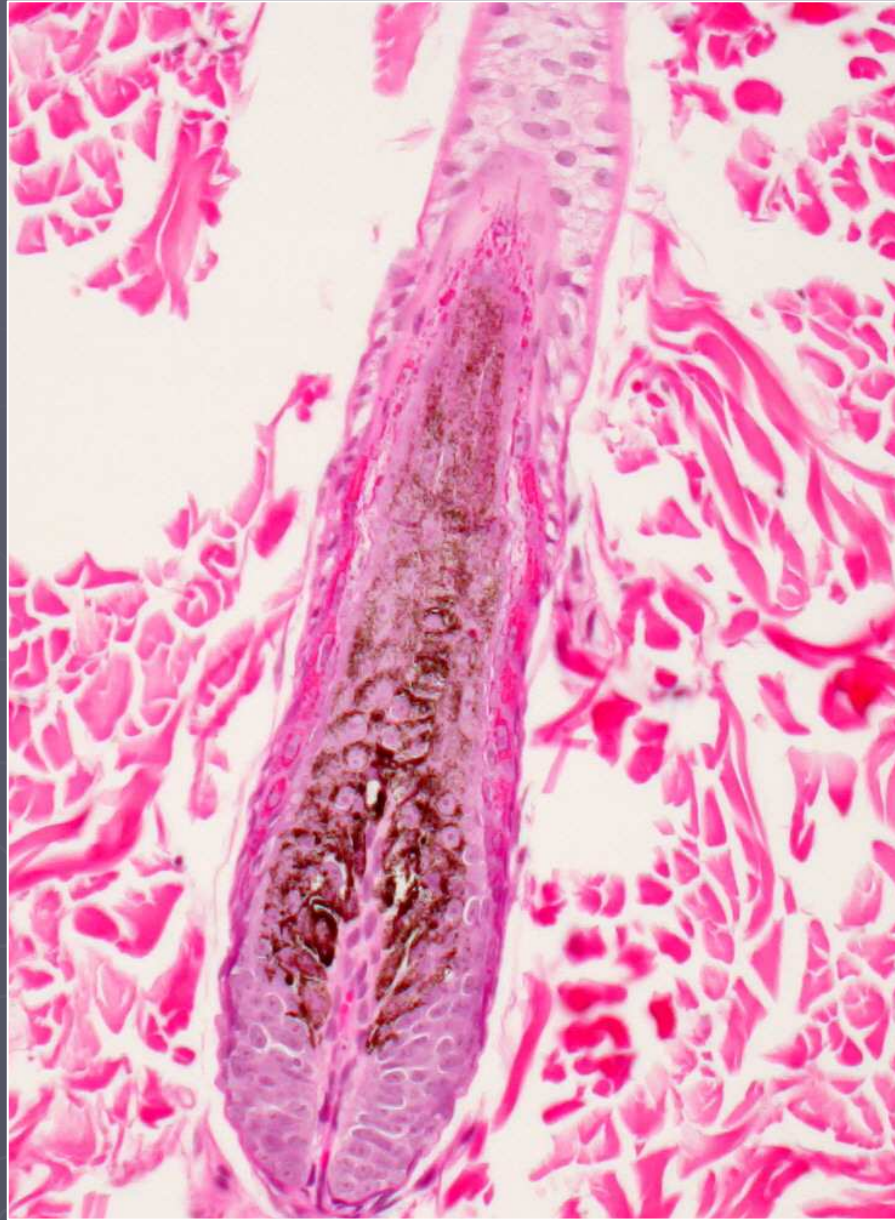


Ackermann 1989

ANAGEN -- [NL, fr. ana- (anew) + L genesis]

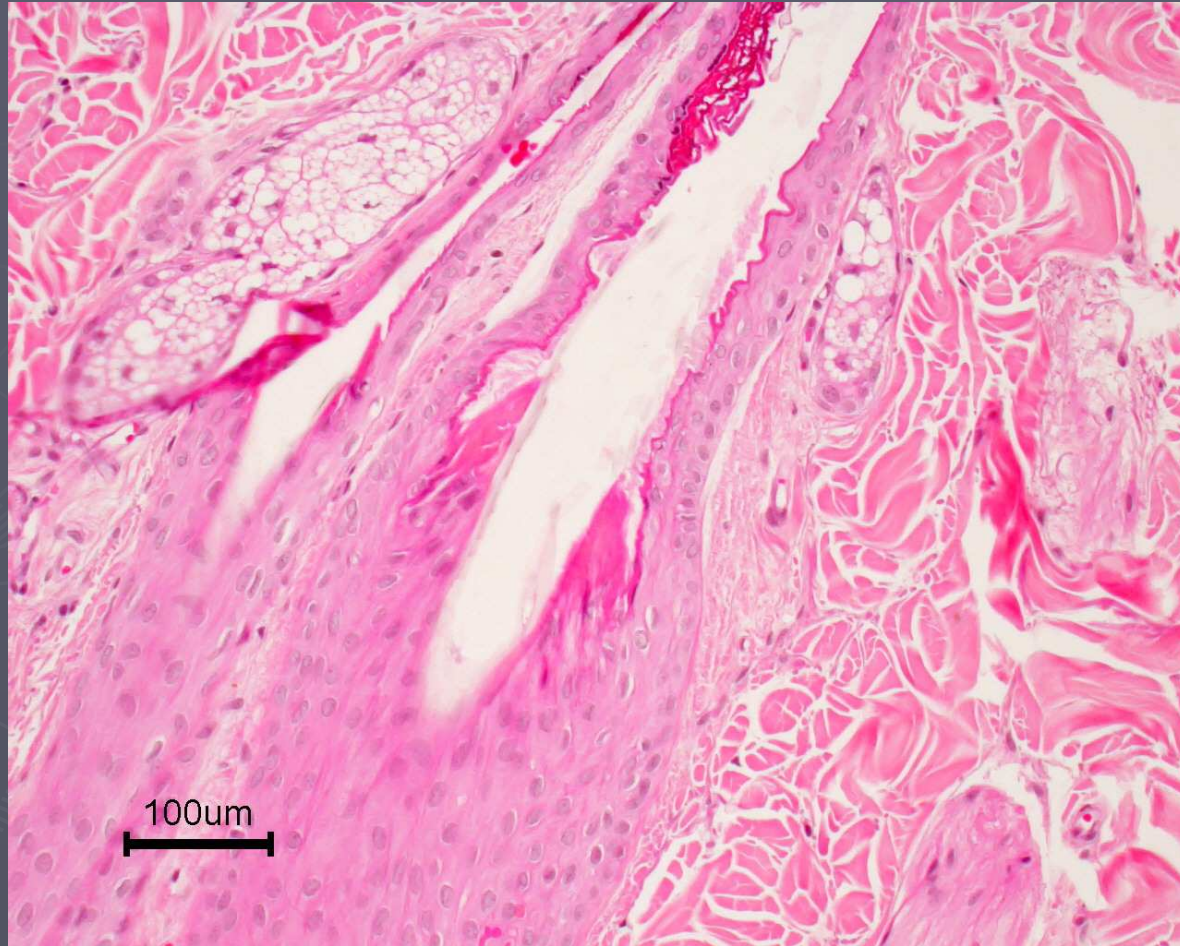


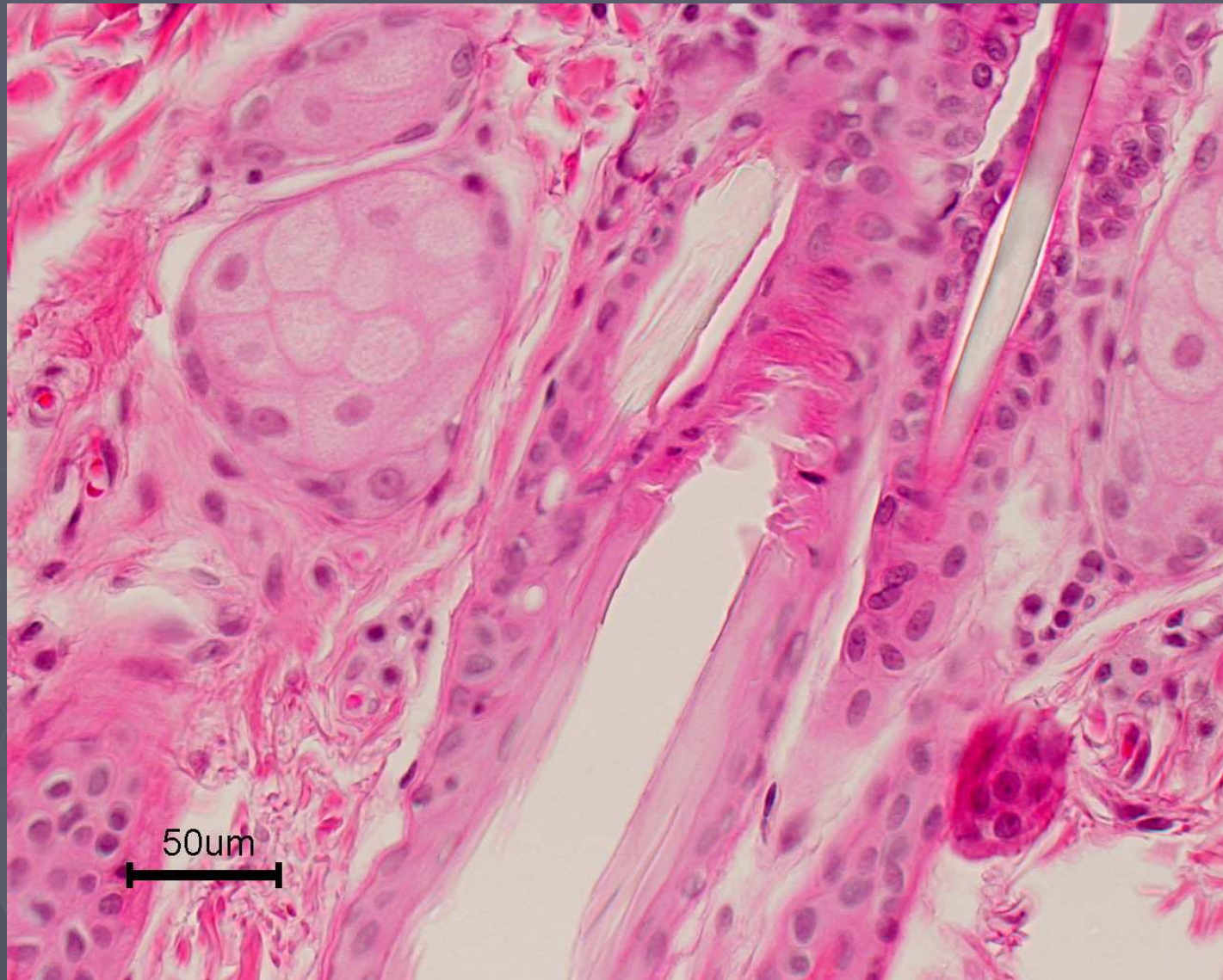
Slide courtesy of R. Dunstan

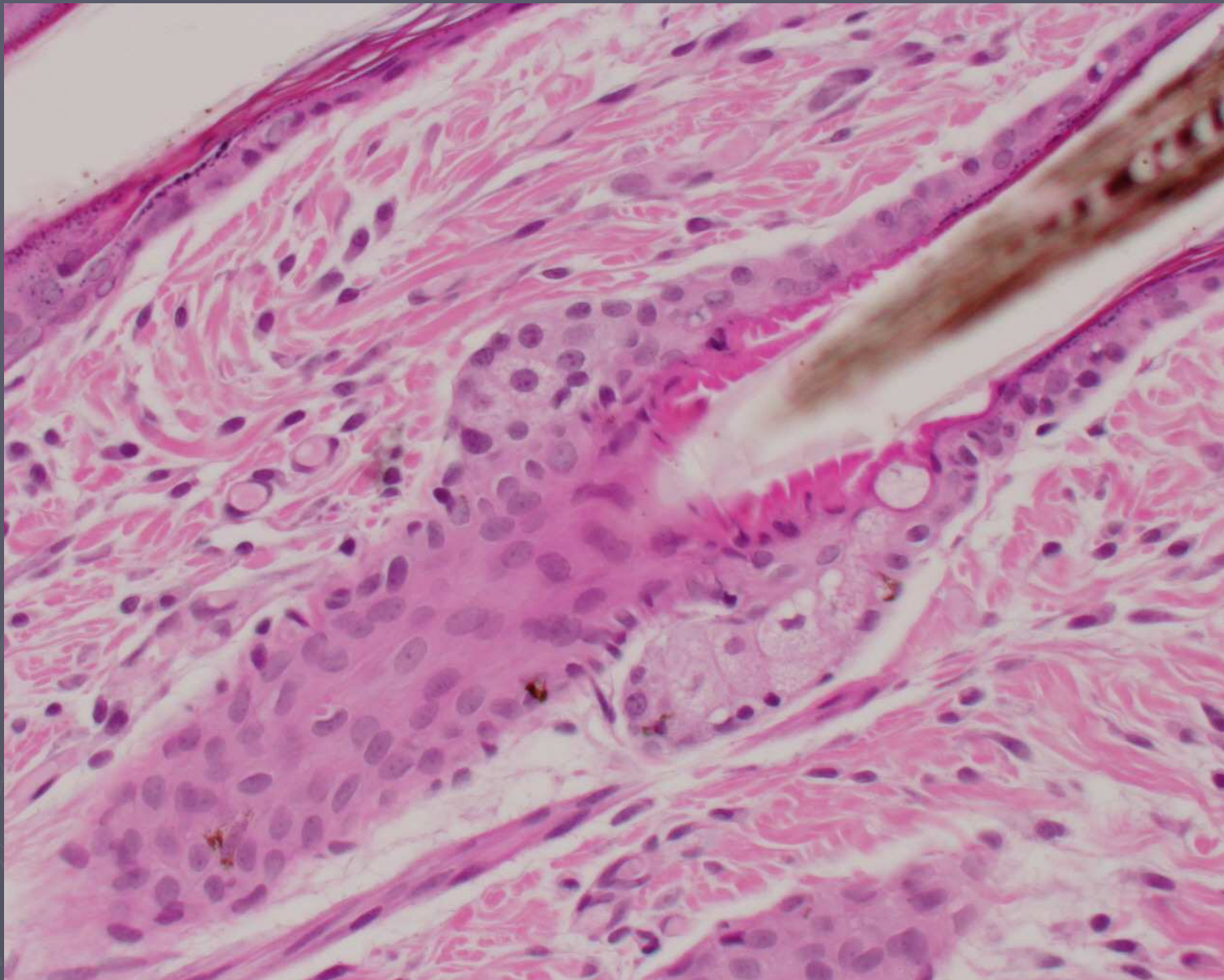




Adamson's Fringe







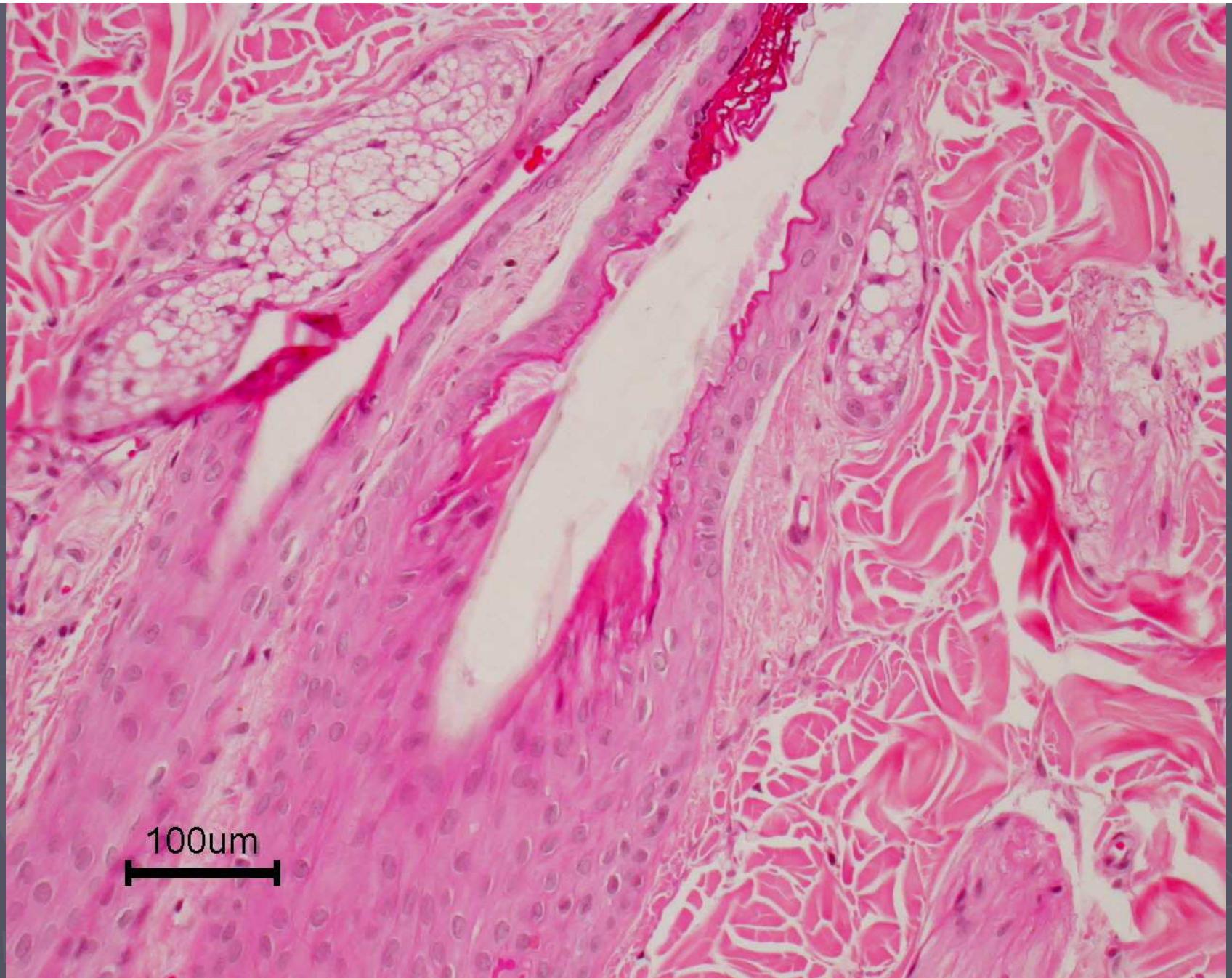
Canine HF (Adamson's fringe)

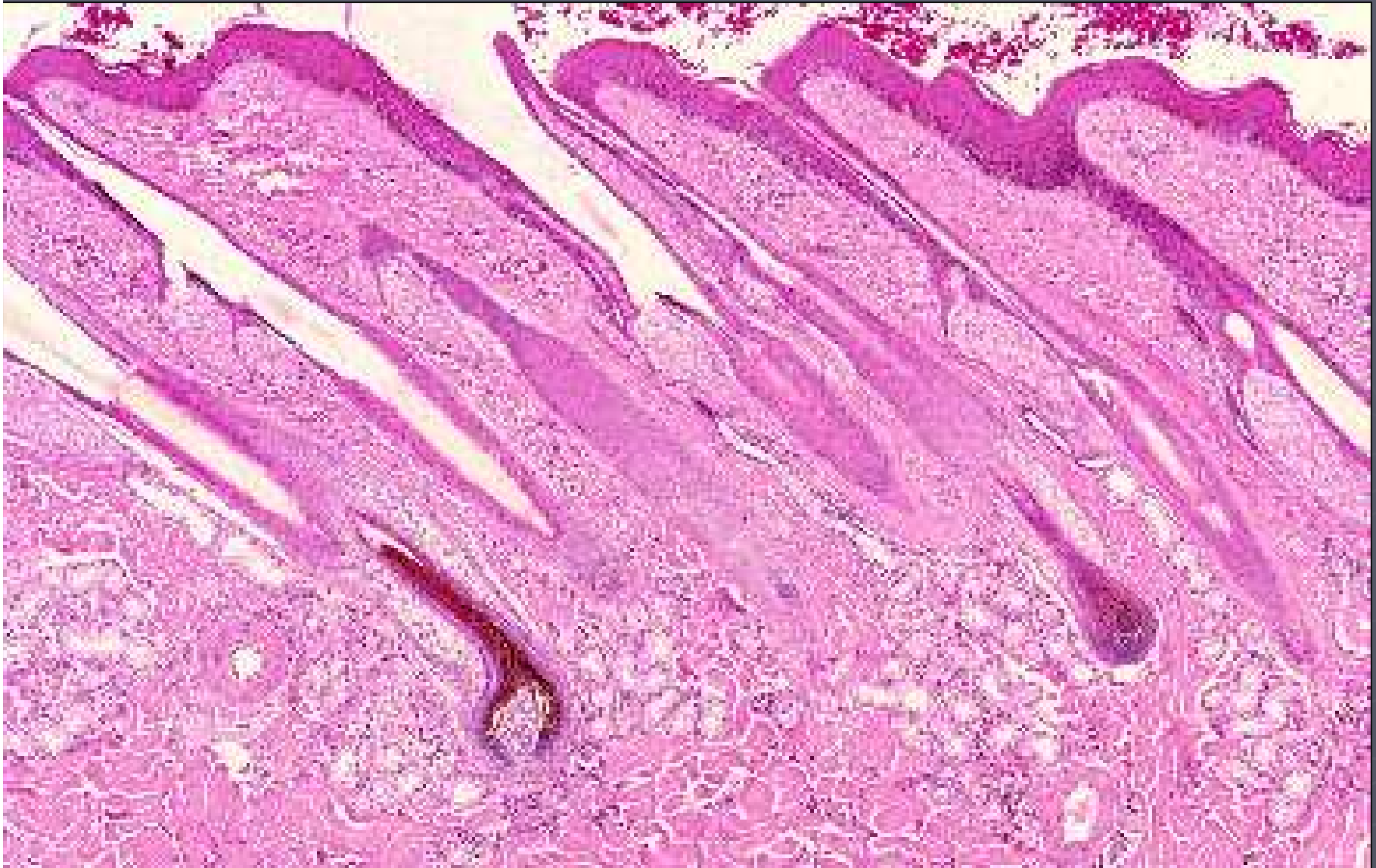
Types of Follicles

- ▶ **Simple follicles**
- ▶ **Compound follicles**
- ▶ **Sinus hair** (whiskers, vibrissae)
- ▶ **Tylotrich hair**

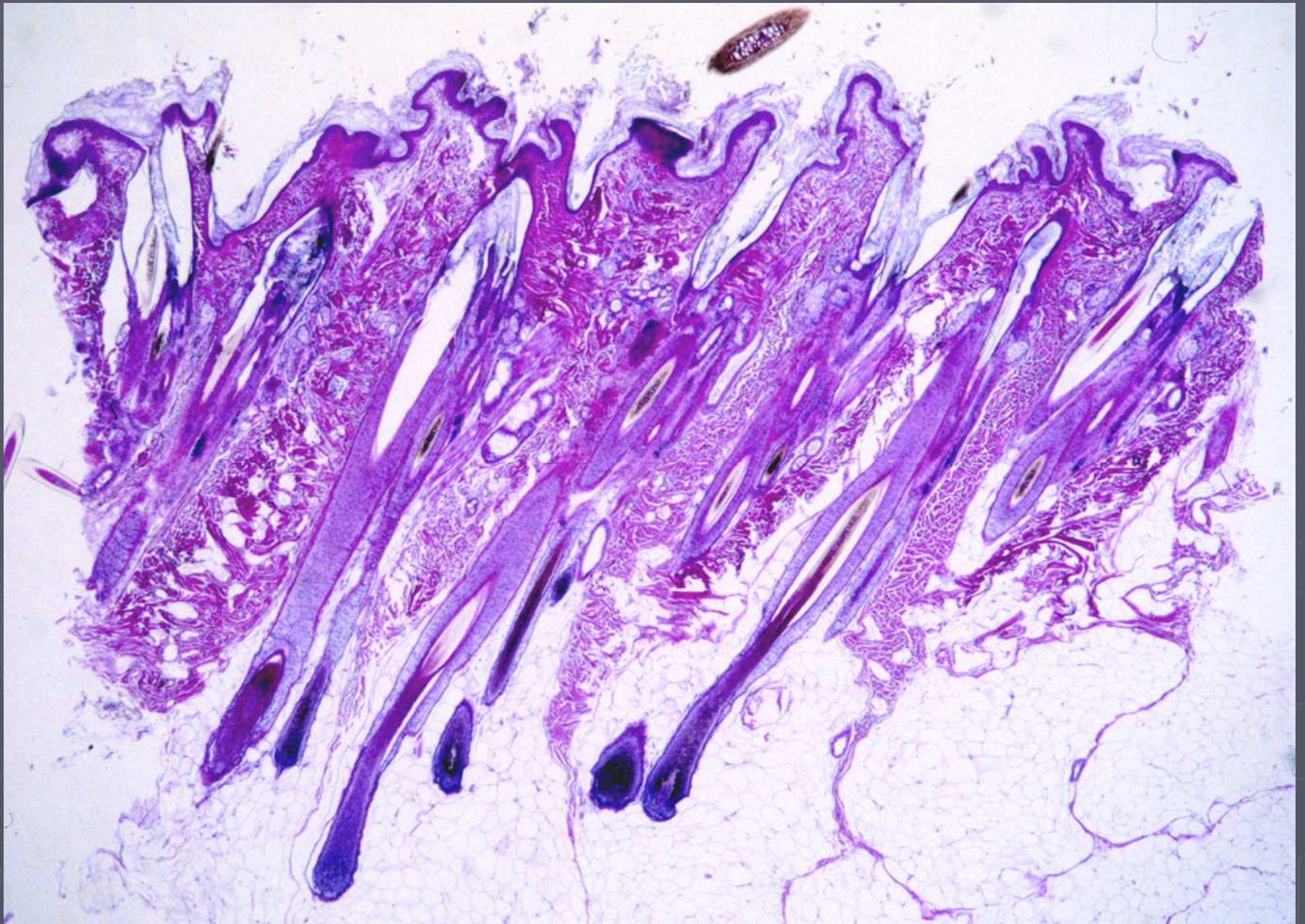


Sinus hair





Equine normal skin



Canine normal skin

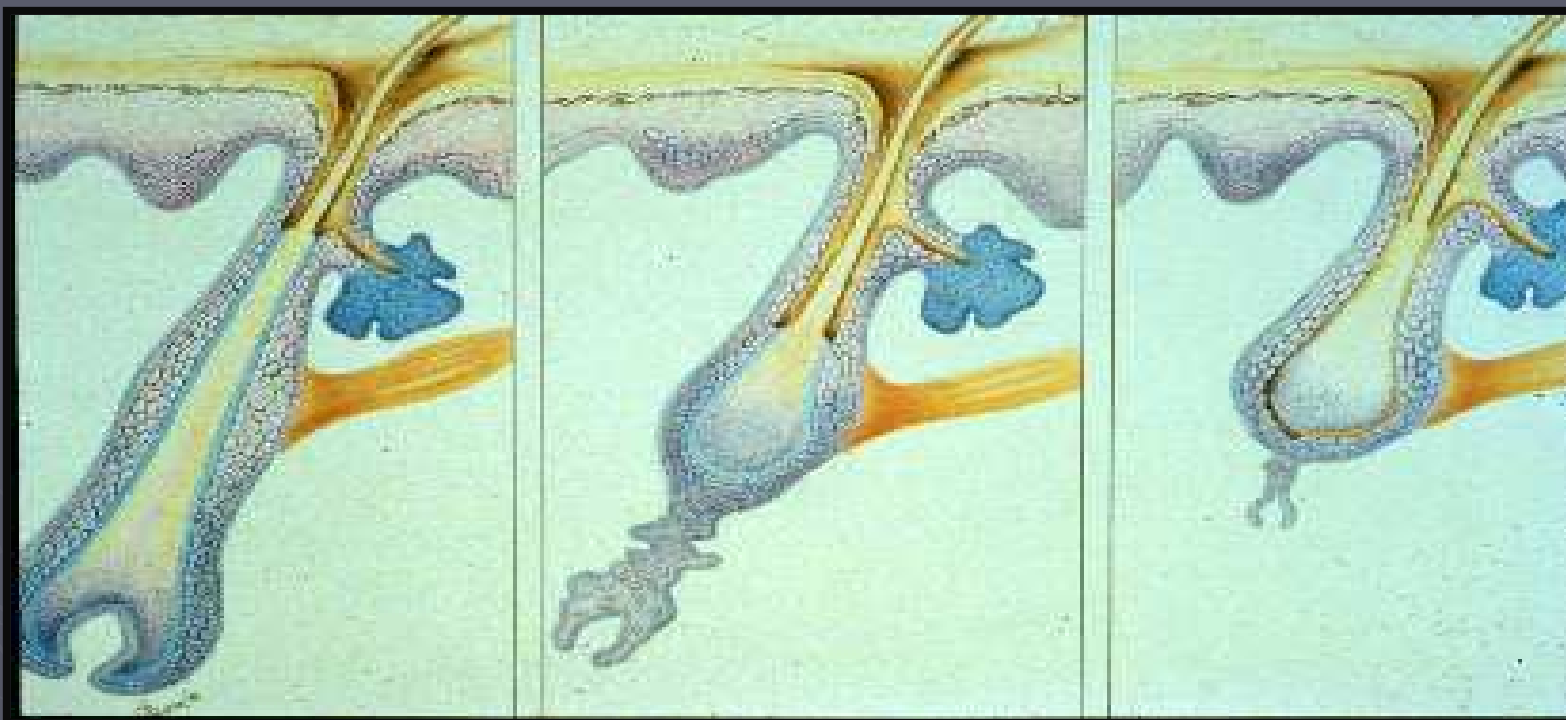
- The hair follicle is the only organ in the mammalian organism that undergoes life-long cycles of rapid growth (anagen), regression (catagen) and resting periods (telogen)

Krause, The biology of the hair follicle: the basics, Sem Med Surg, 2006.

Hair Follicle Development

- ▶ Cyclical periods of growth → Anagen
- ▶ Regression → Catagen
- ▶ Resting → Telogen
- ▶ Shedding → Exogen

Hair Cycle



Anagen

Catagen

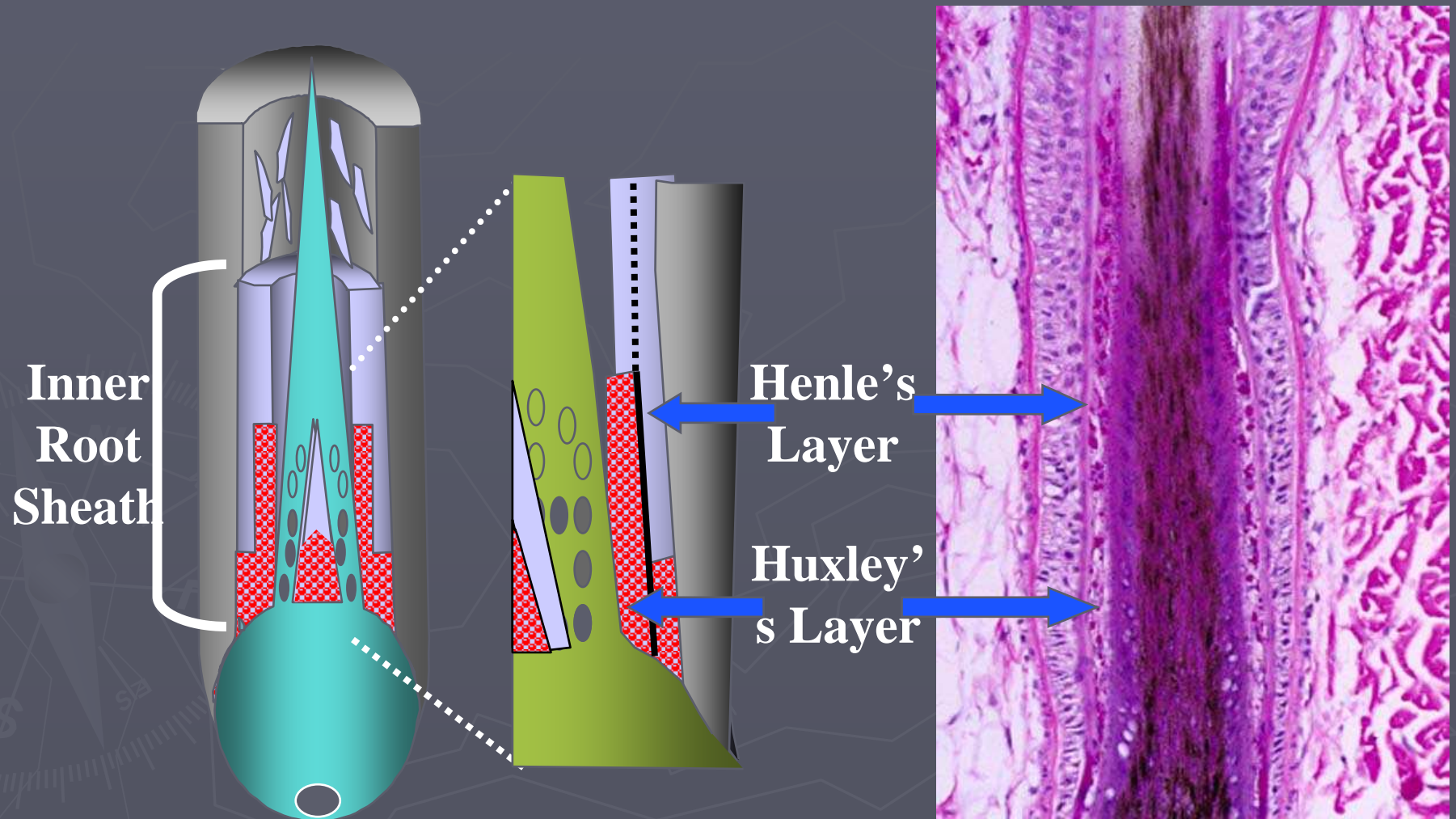
Telogen

Klein, LM from Fitzpatrick's Dermatology in General Medicine, 2003.

*The following slides
were composed and generously
provided by
Dr. Bob Dunstan*



The Inner Root Sheath

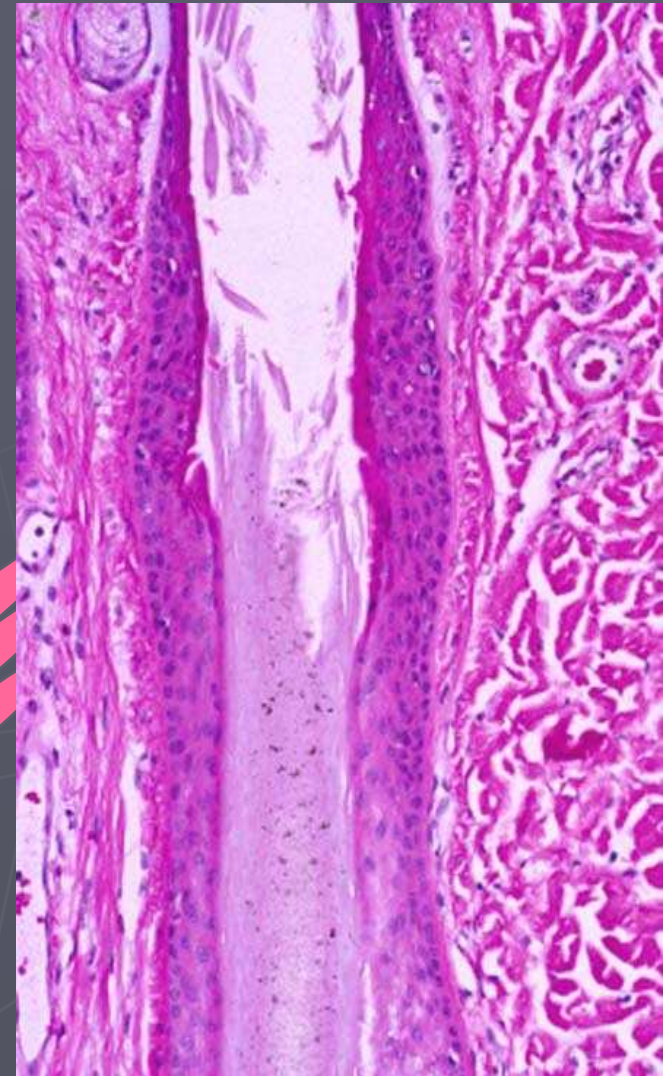
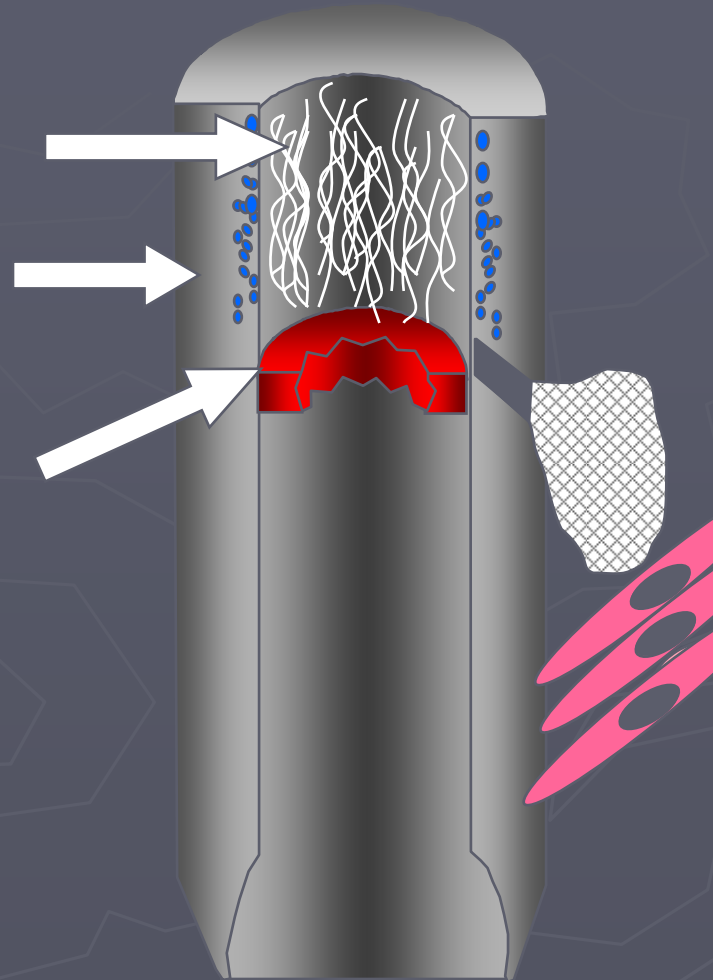


Cornification Patterns of the Outer Root Sheath

**Infundibular
Cornification**

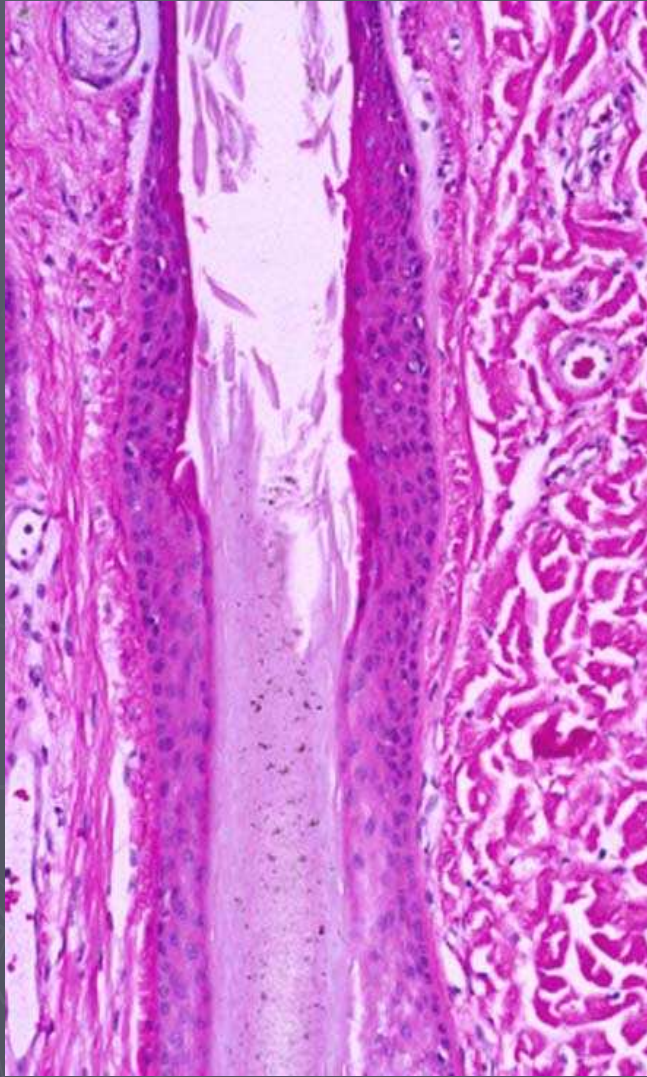
**Keratohyaline
Granules**

**Trichilemmal
Cornification**



R. Dunstan

Cornification Patterns of the Outer Root Sheath

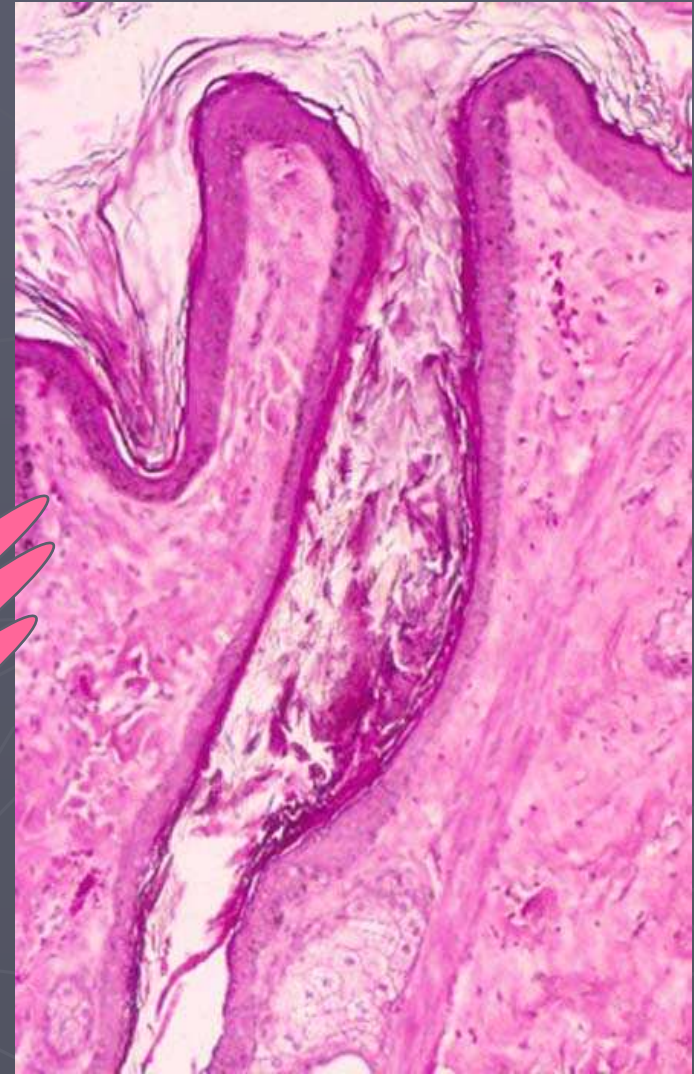
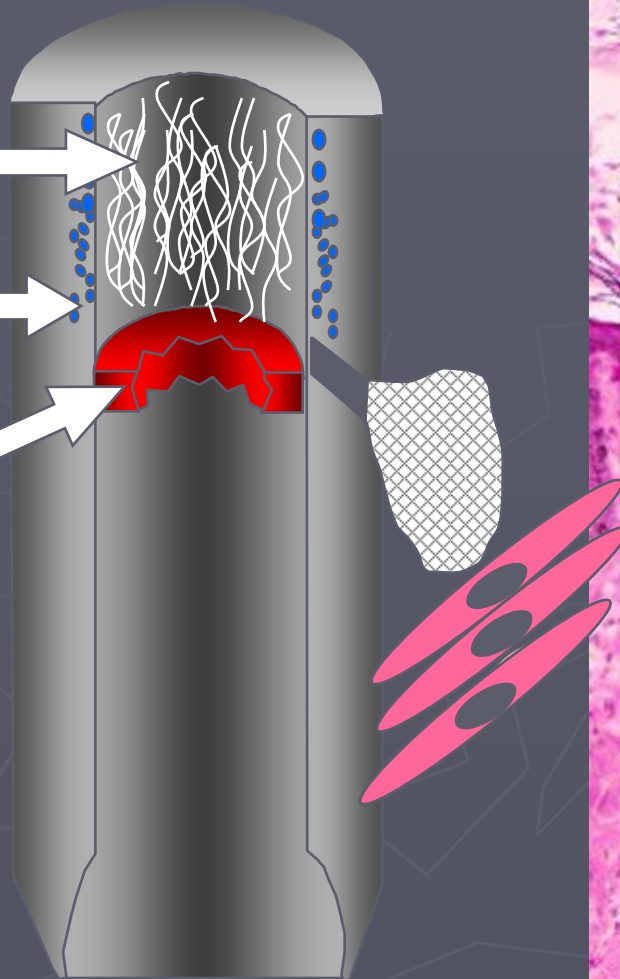


Cornification Patterns of the Outer Root Sheath

**Infundibular
Cornification**

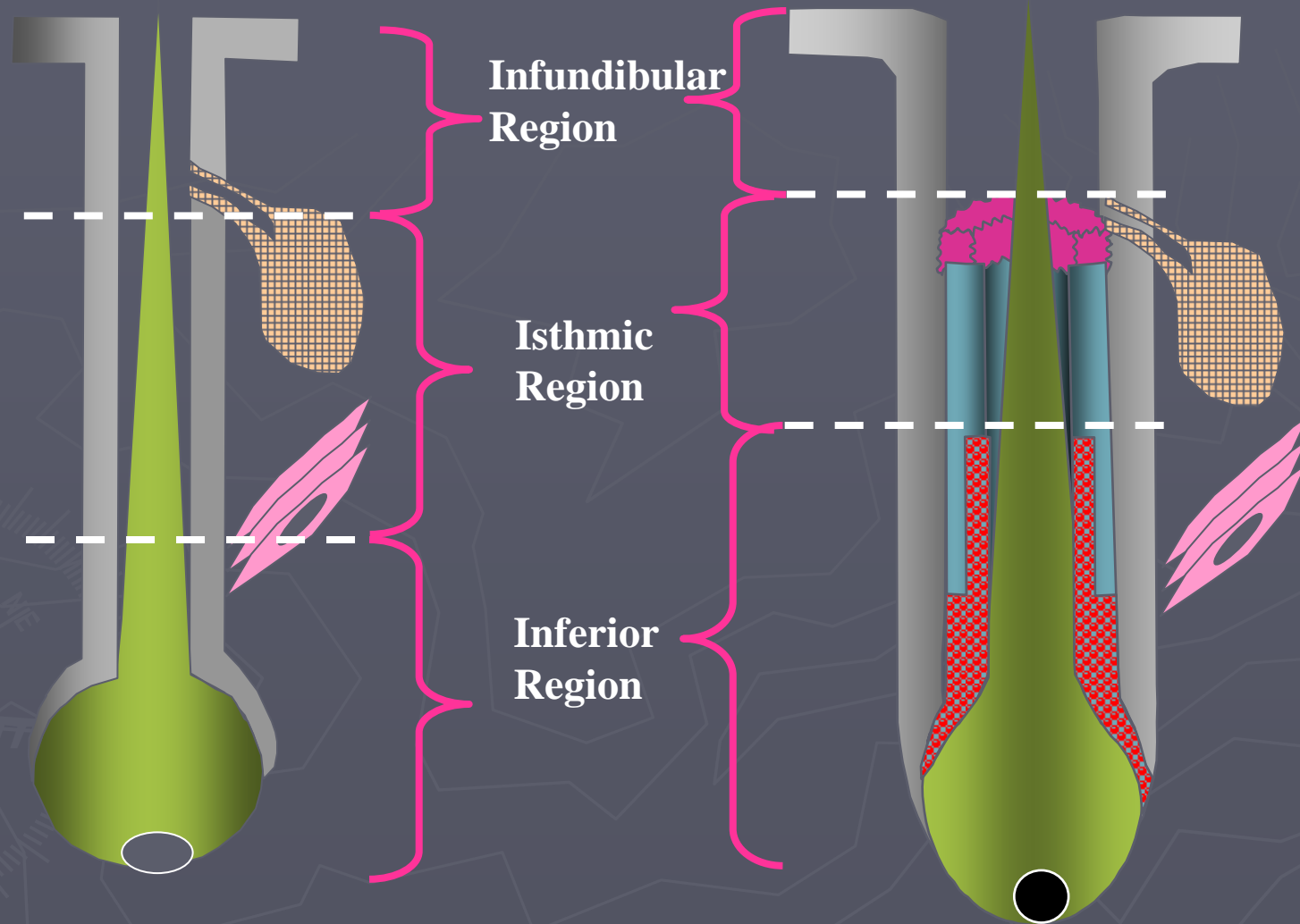
**Keratohyaline
Granules**

**Trichilemmal
Cornification**



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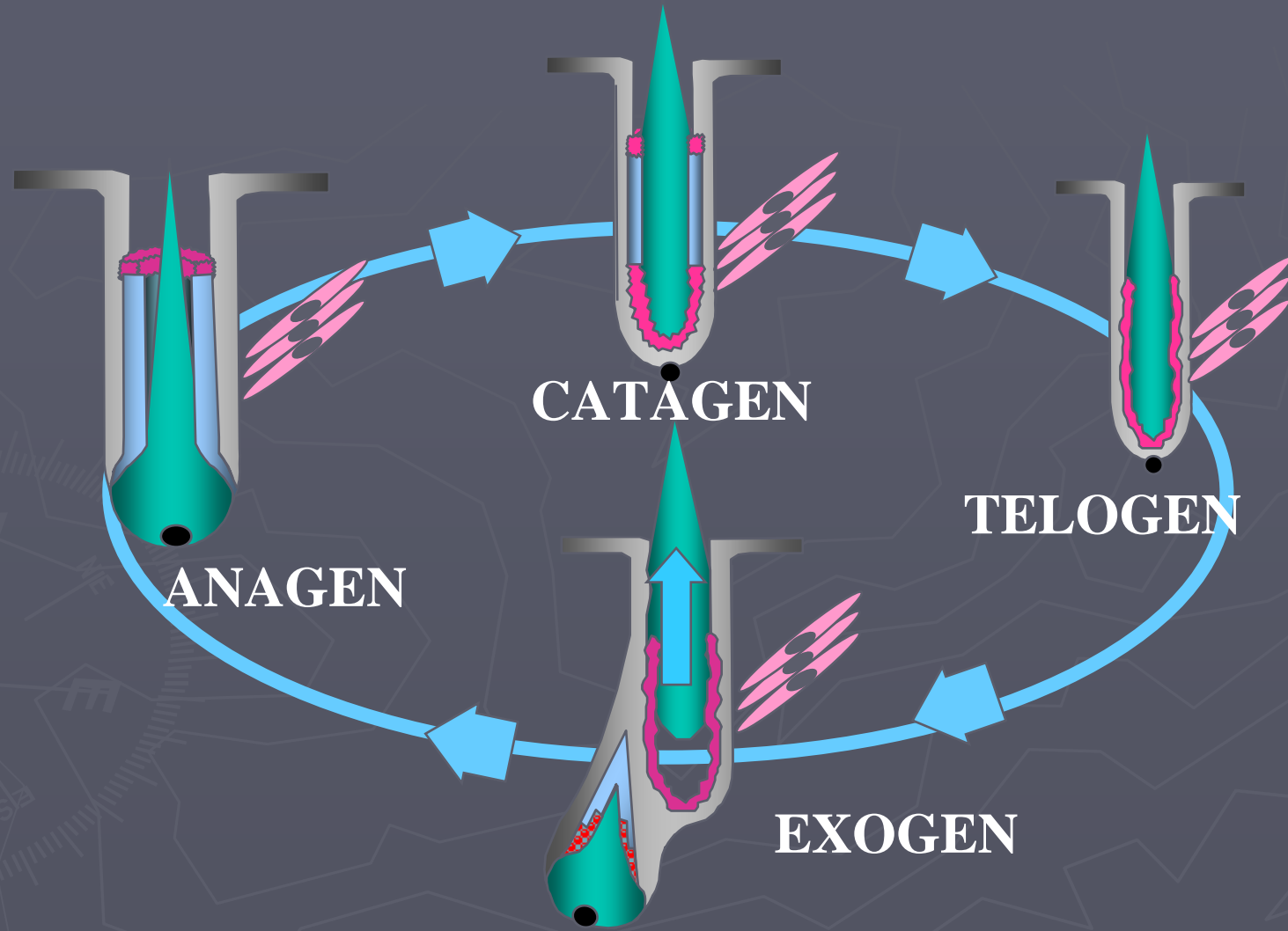
Divisions of the Anagen Follicle



Anagen Follicle

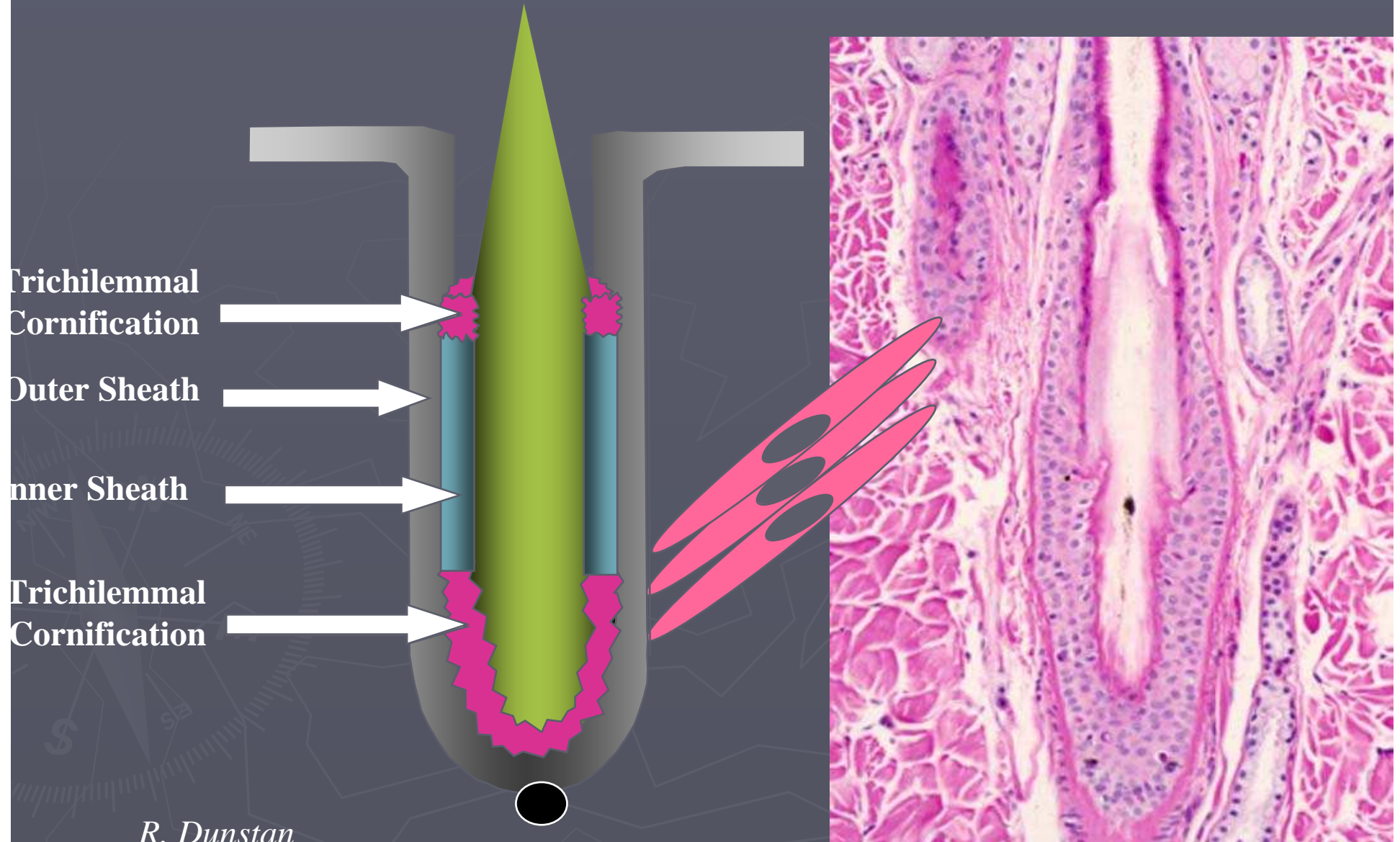
What Do All Hair Follicles Have in Common?

All hair follicles cycle

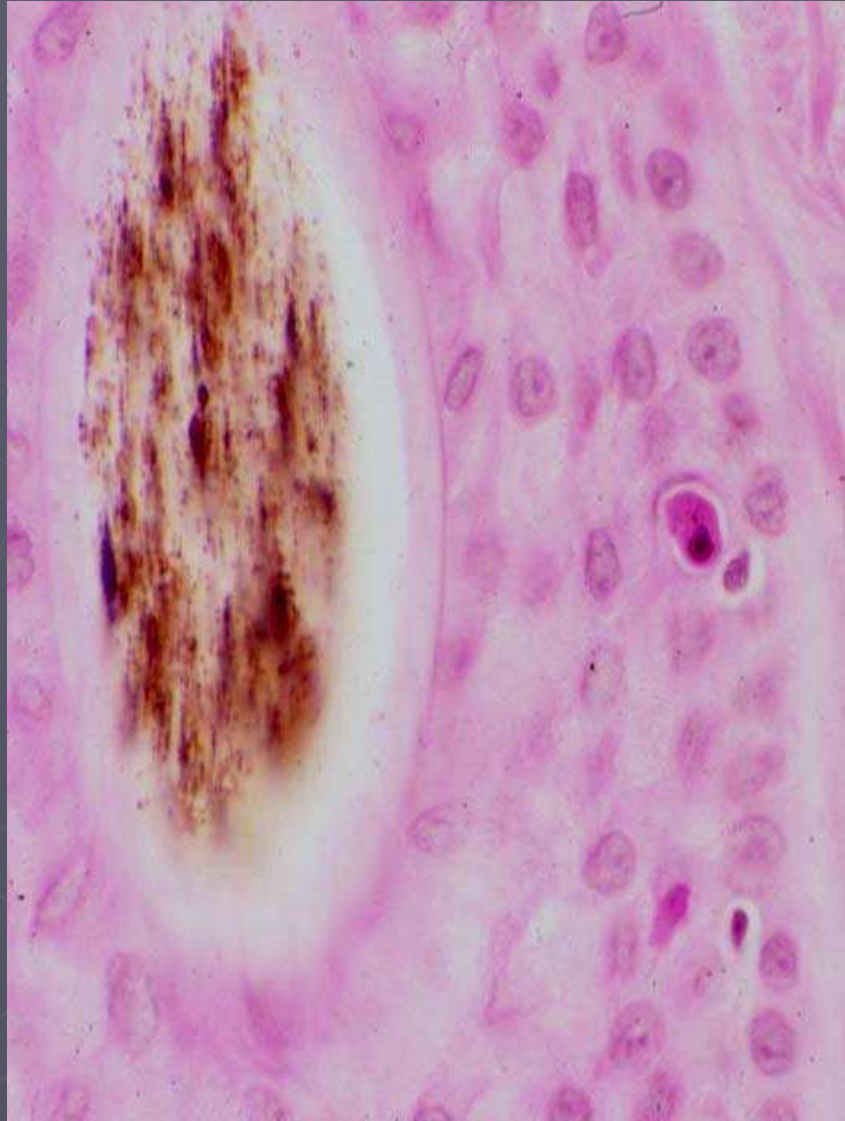


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CATAGEN--[Gr. kata- (down) + L genesis]

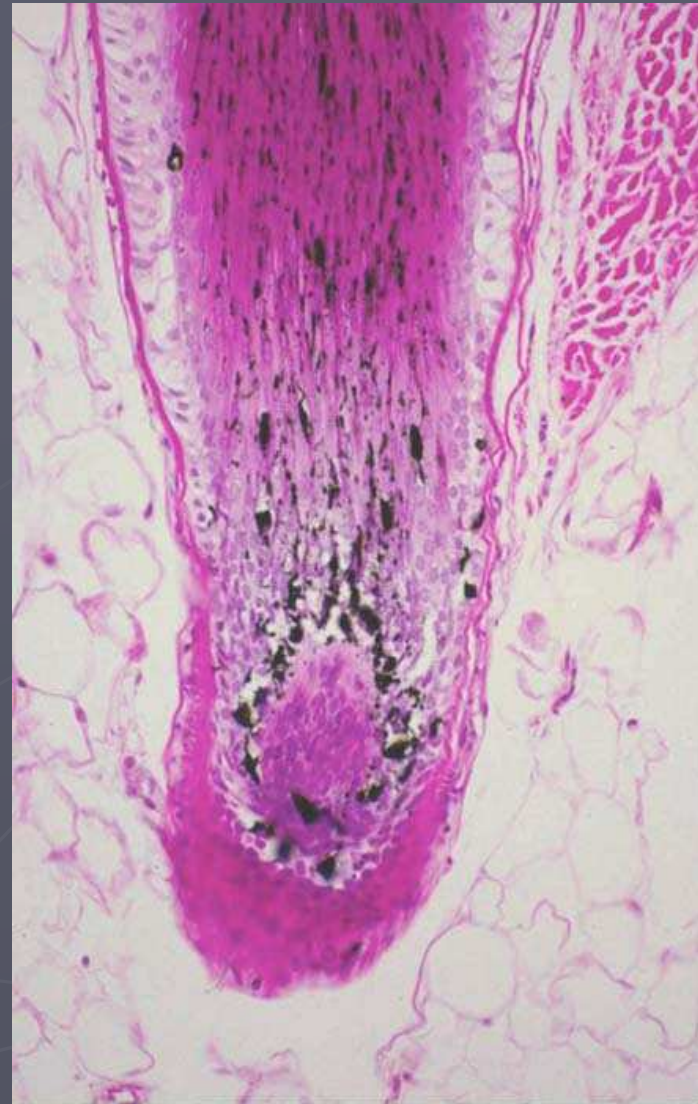
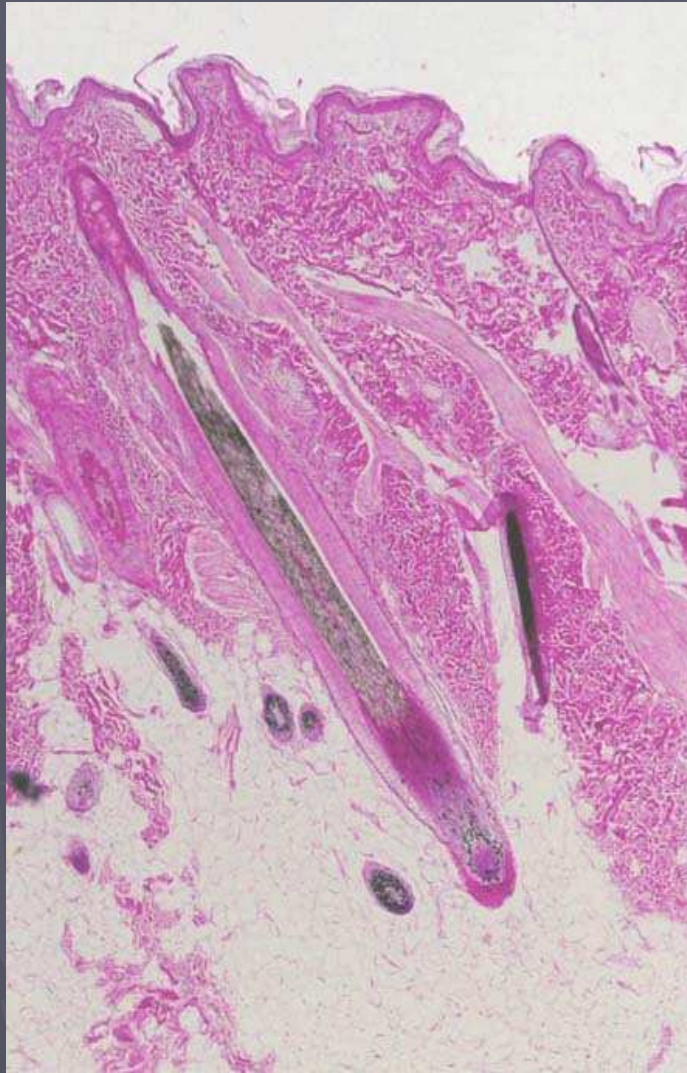


CATAGEN --[Gr. kata- (down) + L genesis]



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CATAGEN --[Gr. kata- (down) + L genesis]



Hints in the hair follicle

What is the hint?



R. Dunstan

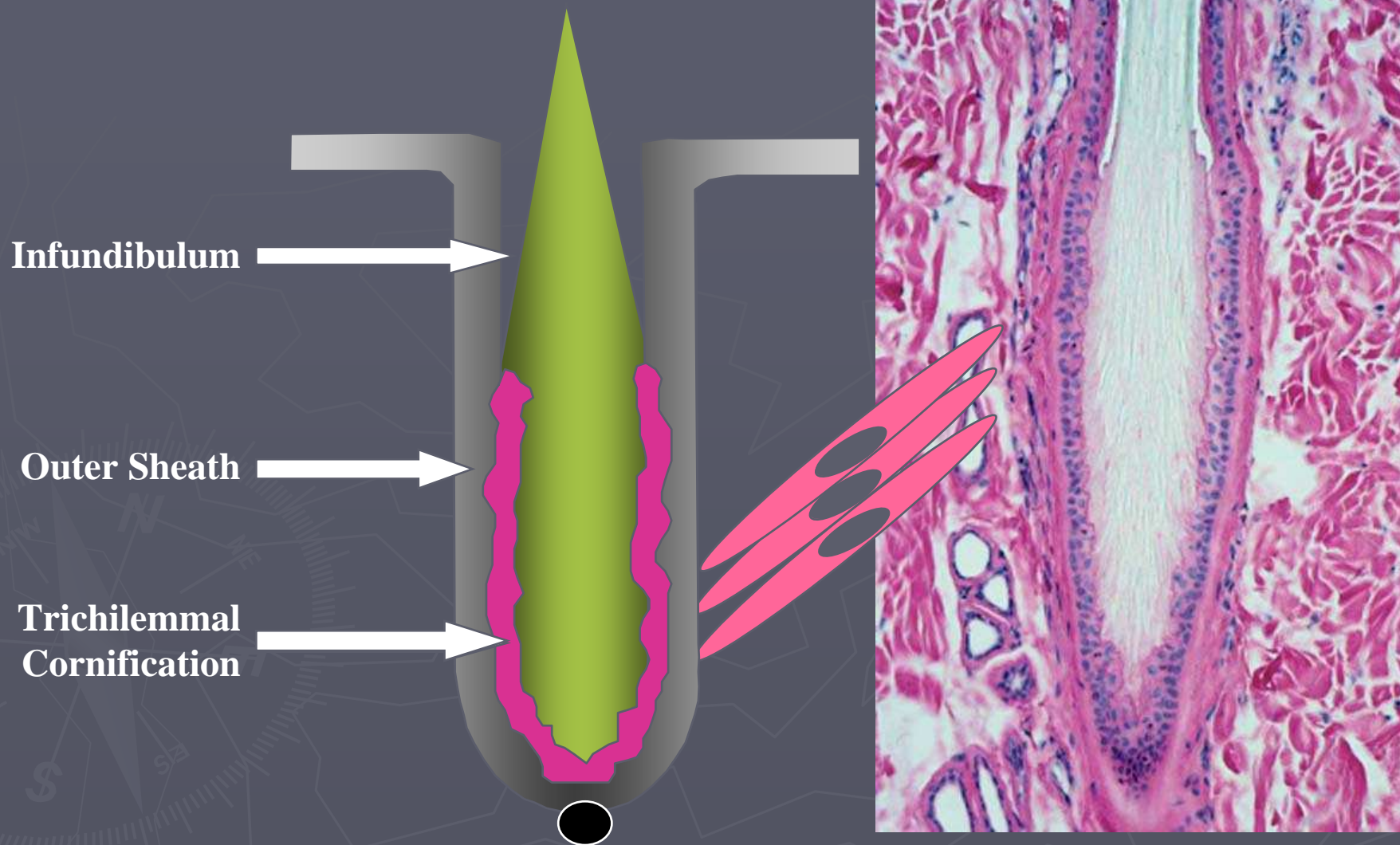
Hints in the hair follicle

If you see a follicle with both inner root sheath and trichilemmal cornification you are looking at a catagen hair.



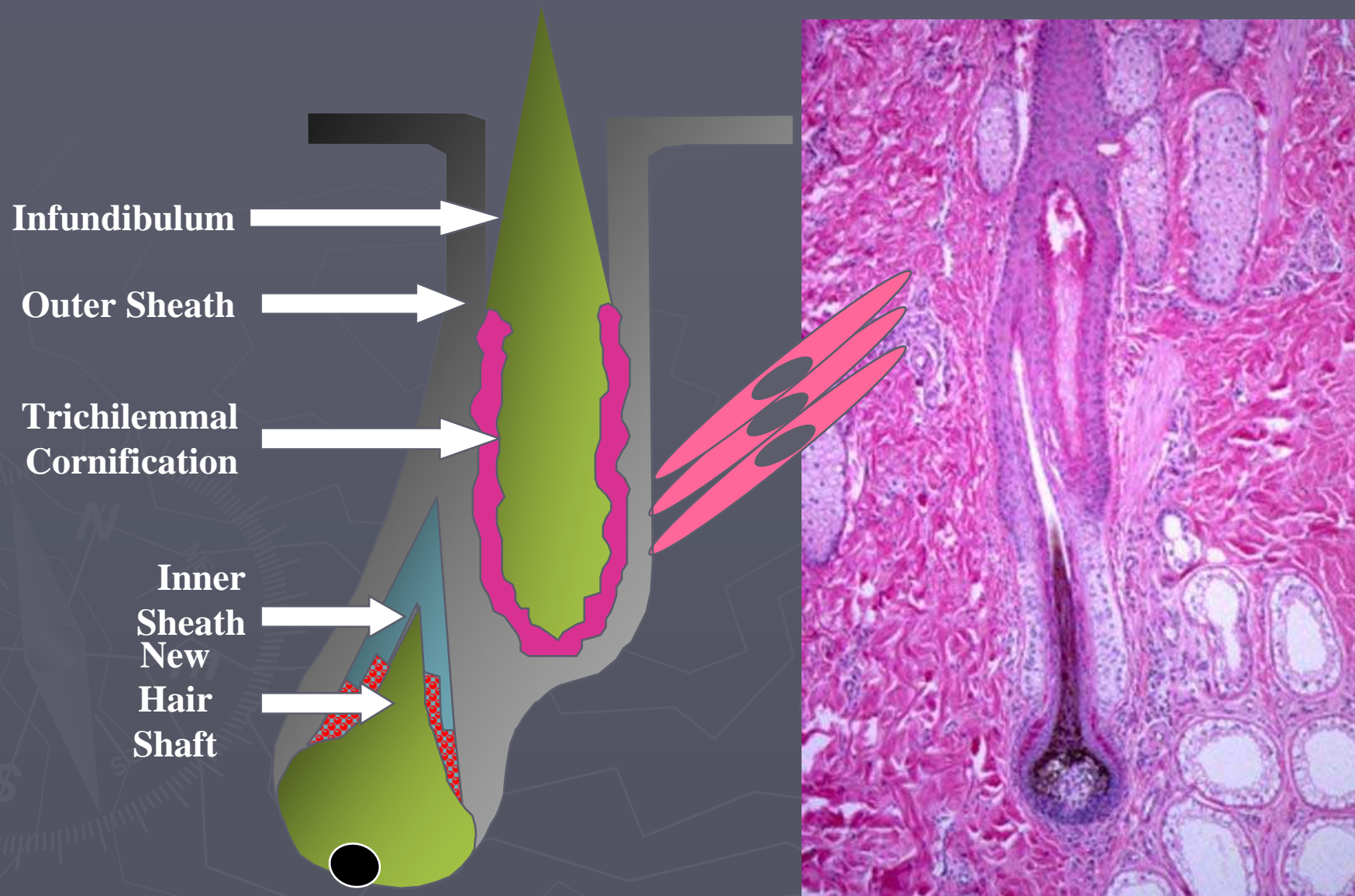
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HAired TELOGEN-[Gr. telos- (end) + genesis]



R. Dunstan

TELOGEN TO ANAGEN (EXOGEN)



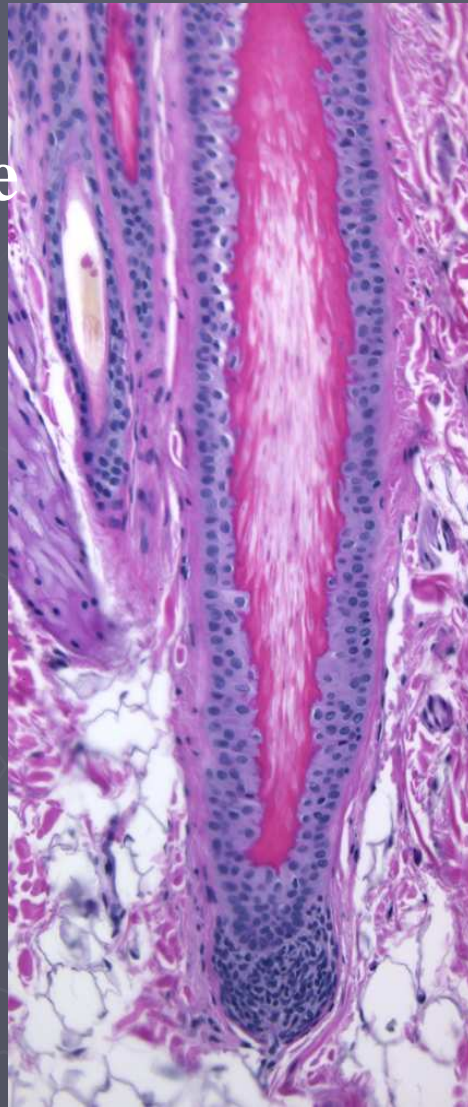
Hints in the hair follicle



Anagen

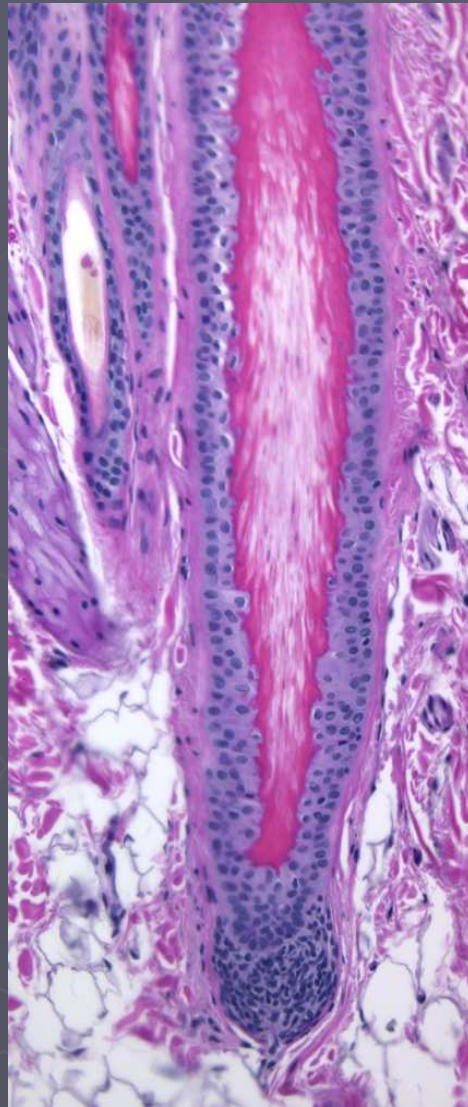
Hints in the hair follicle

What is stage of the hair cycle?



R. Dunstan

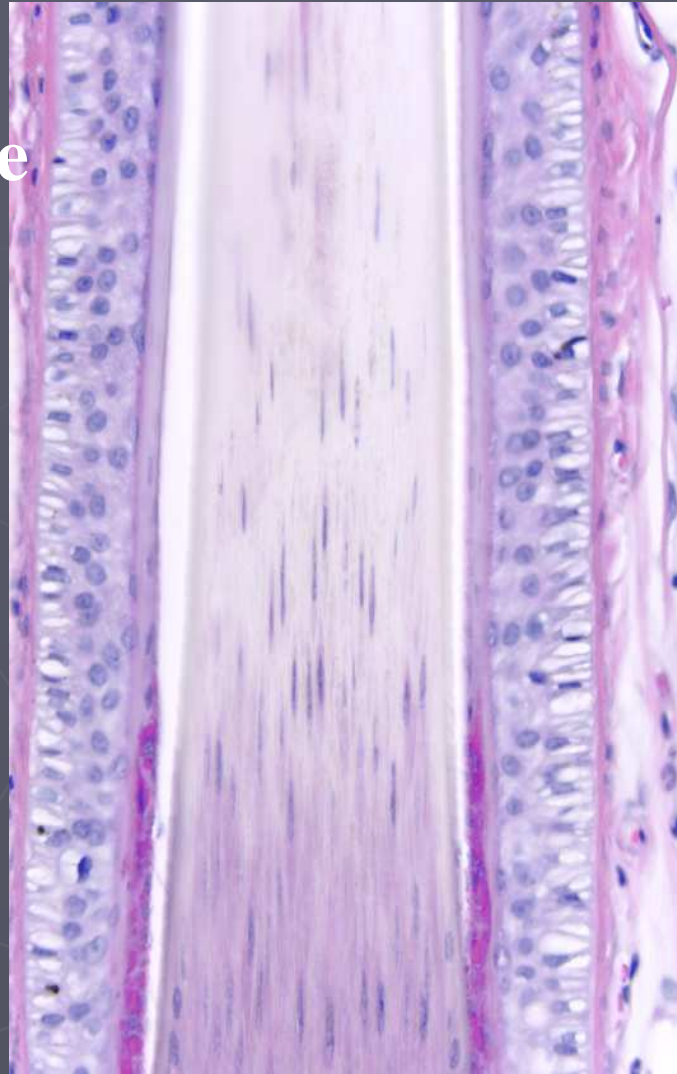
Hints in the hair follicle



Telogen

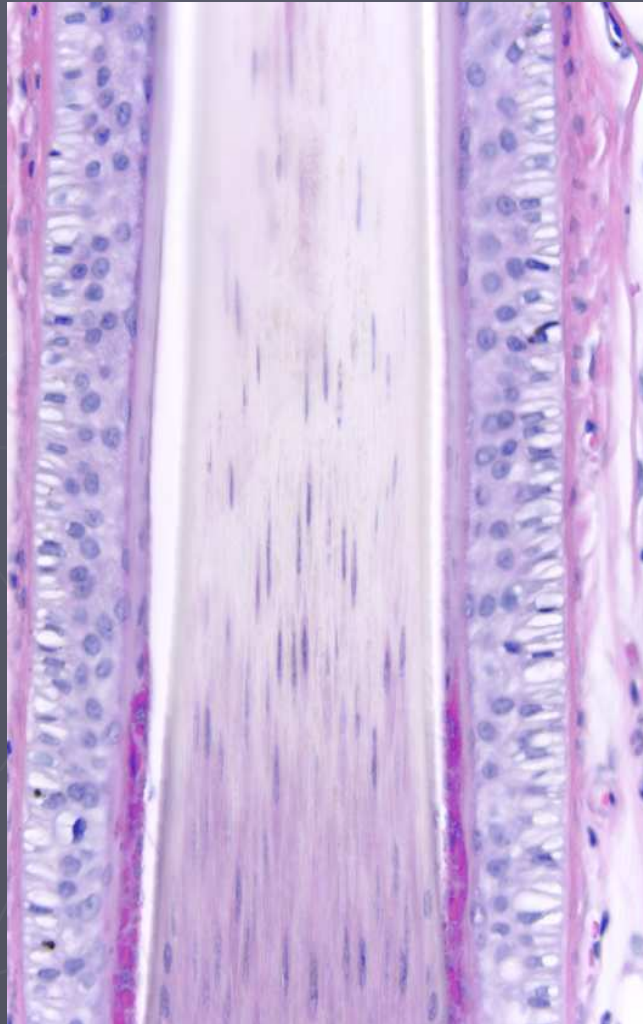
Hints in the hair follicle

What is stage of the hair cycle?



Hints in the hair follicle

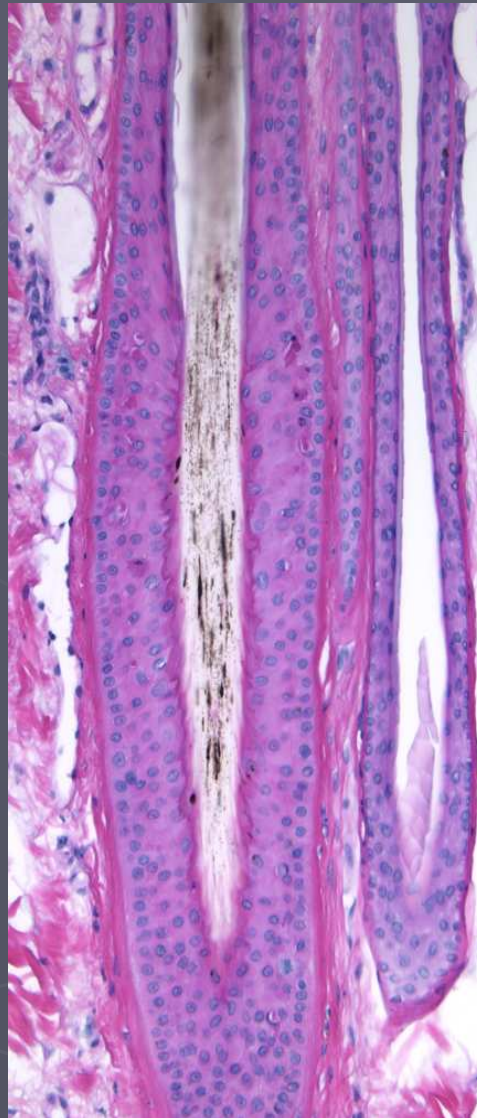
What is the hint?



Anagen

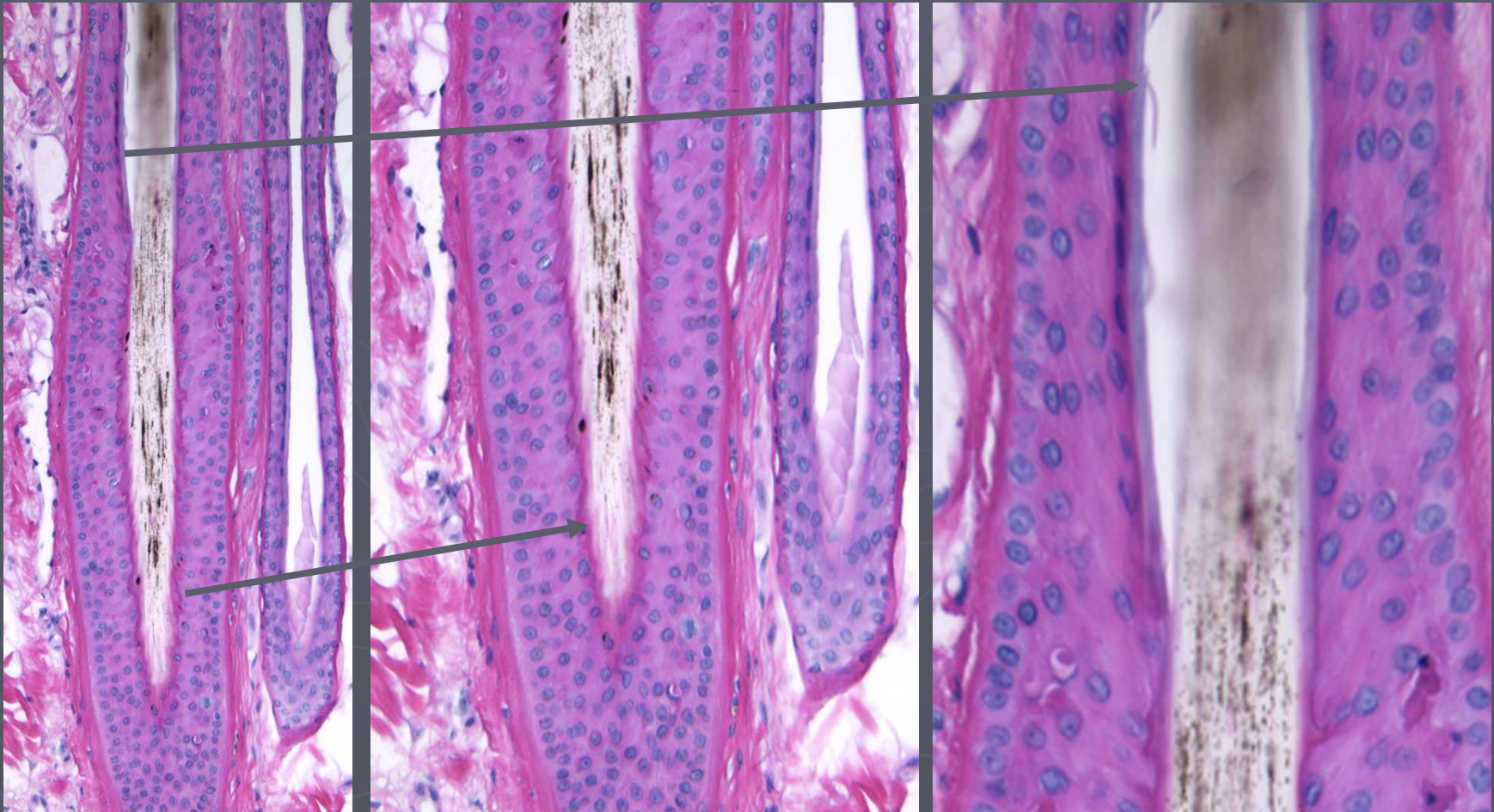
Hints in the hair follicle

What is the hint?

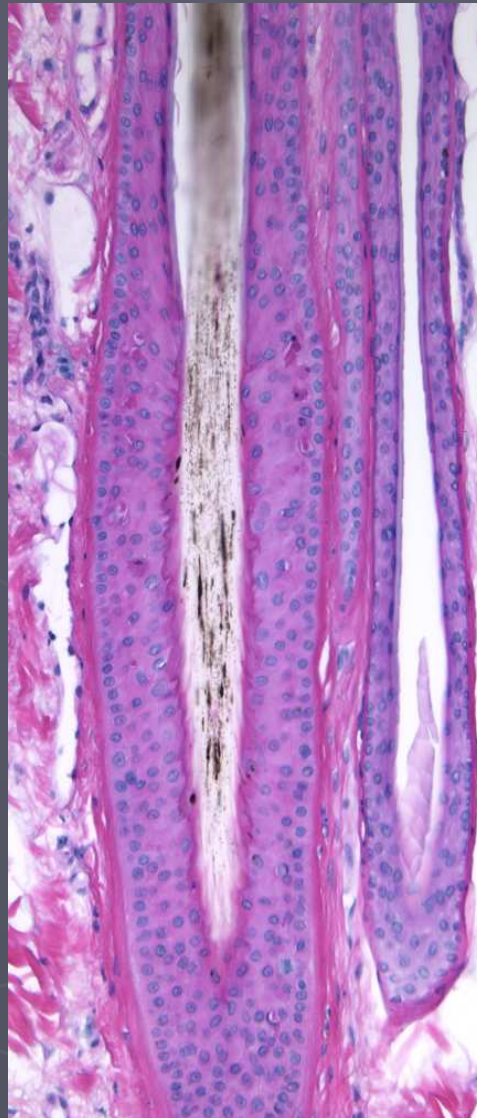


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Hints in the hair follicle

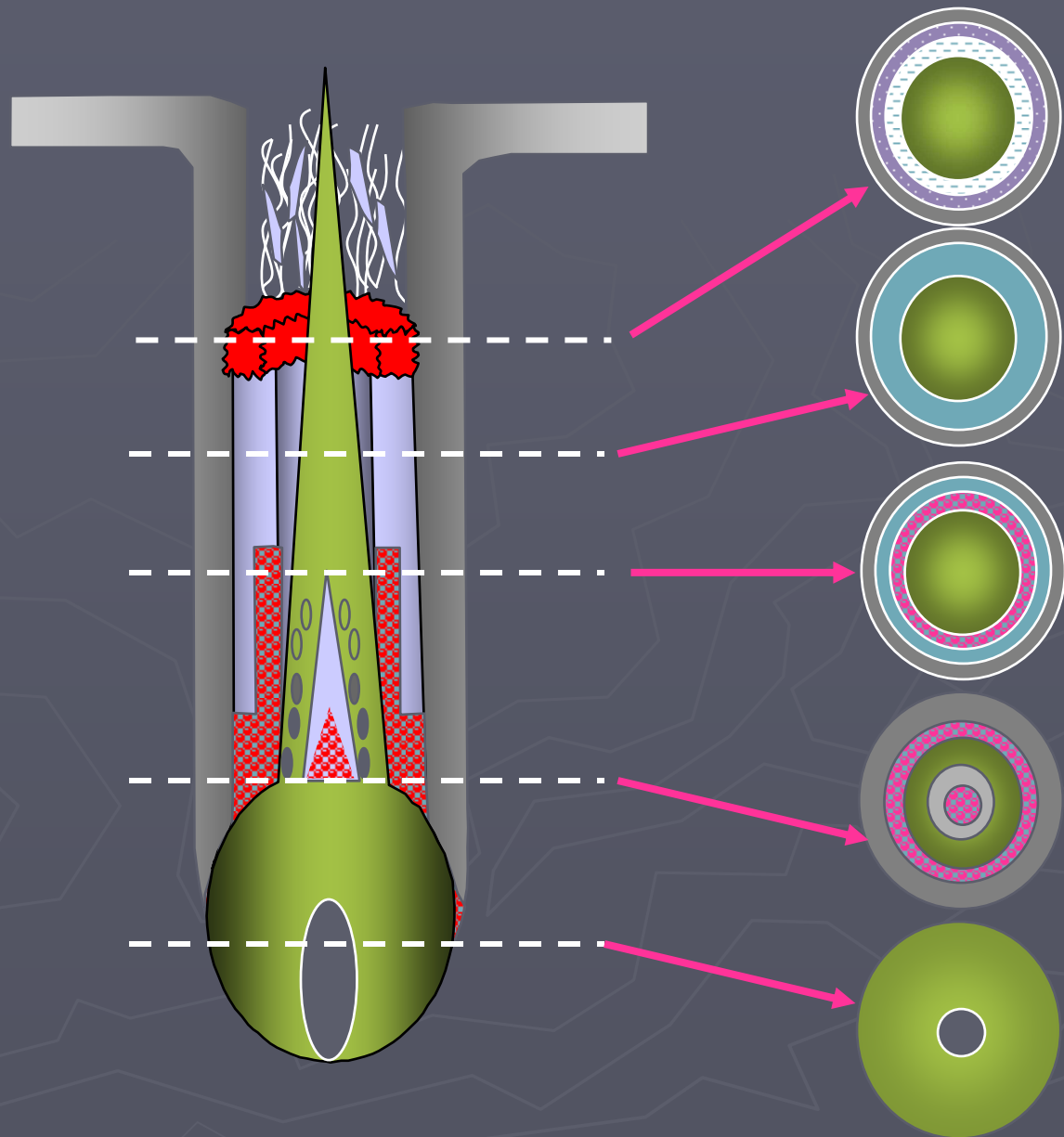


Hints in the hair follicle



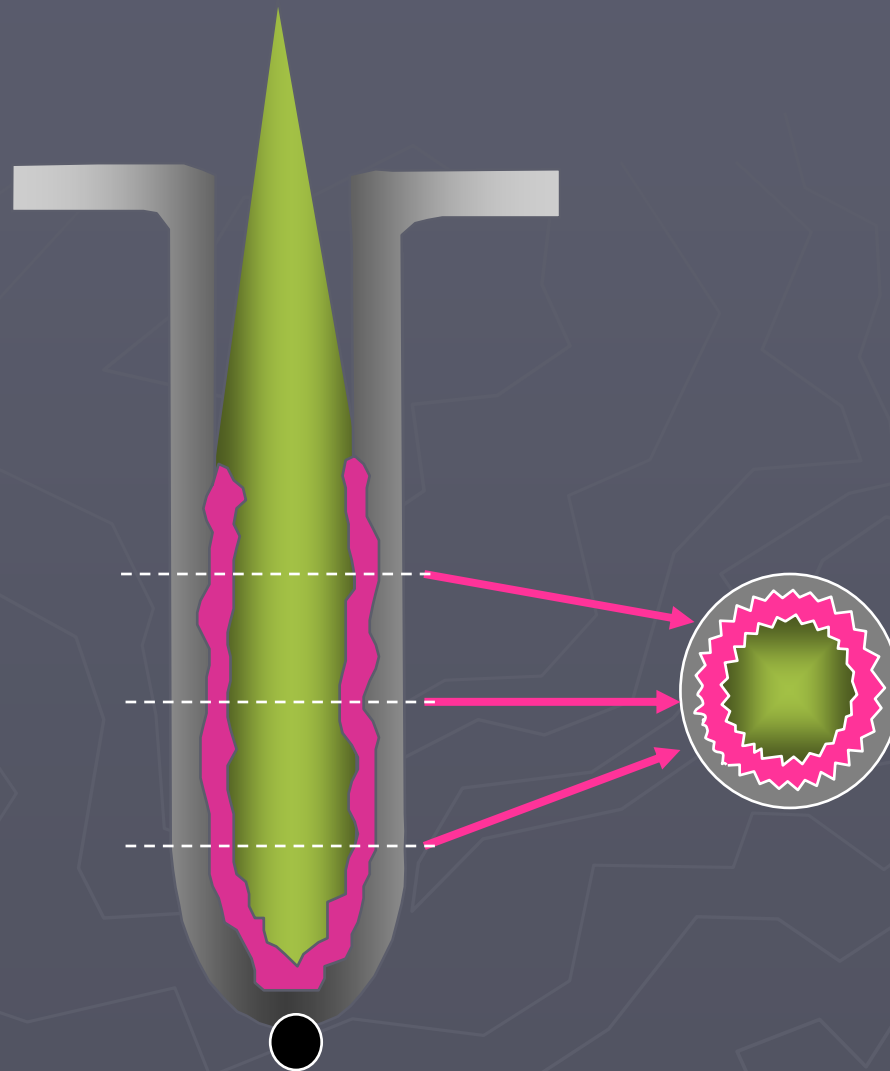
Catagen

The anagen hair in cross section



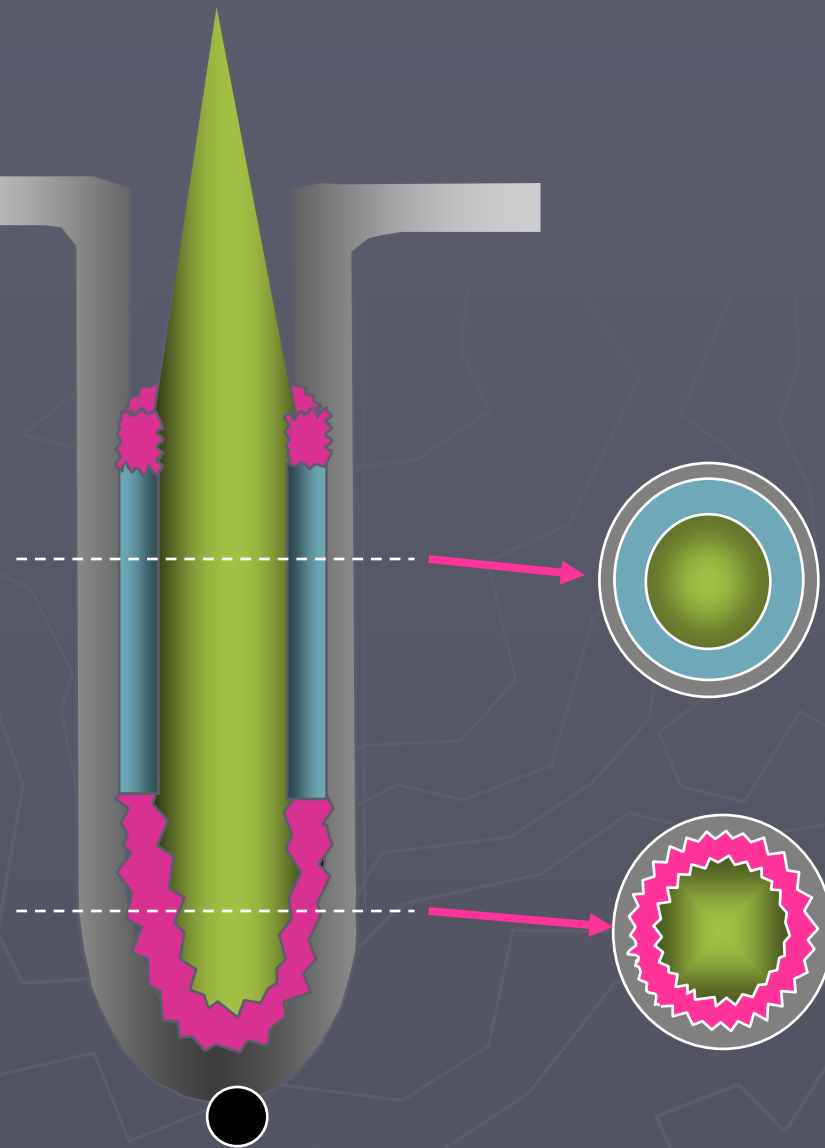
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The telogen hair in cross section

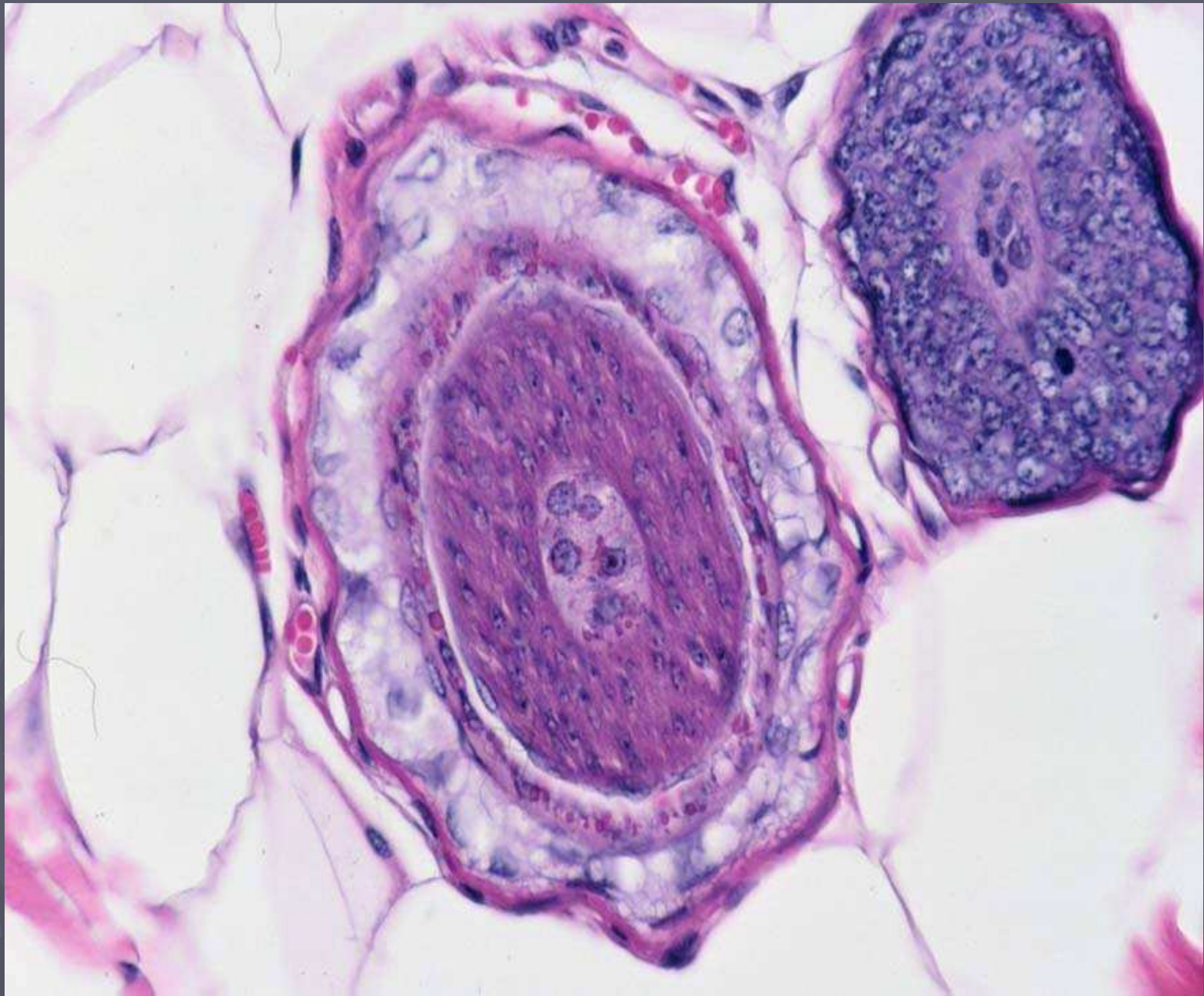


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The catagen hair in cross section



R. Dunstan



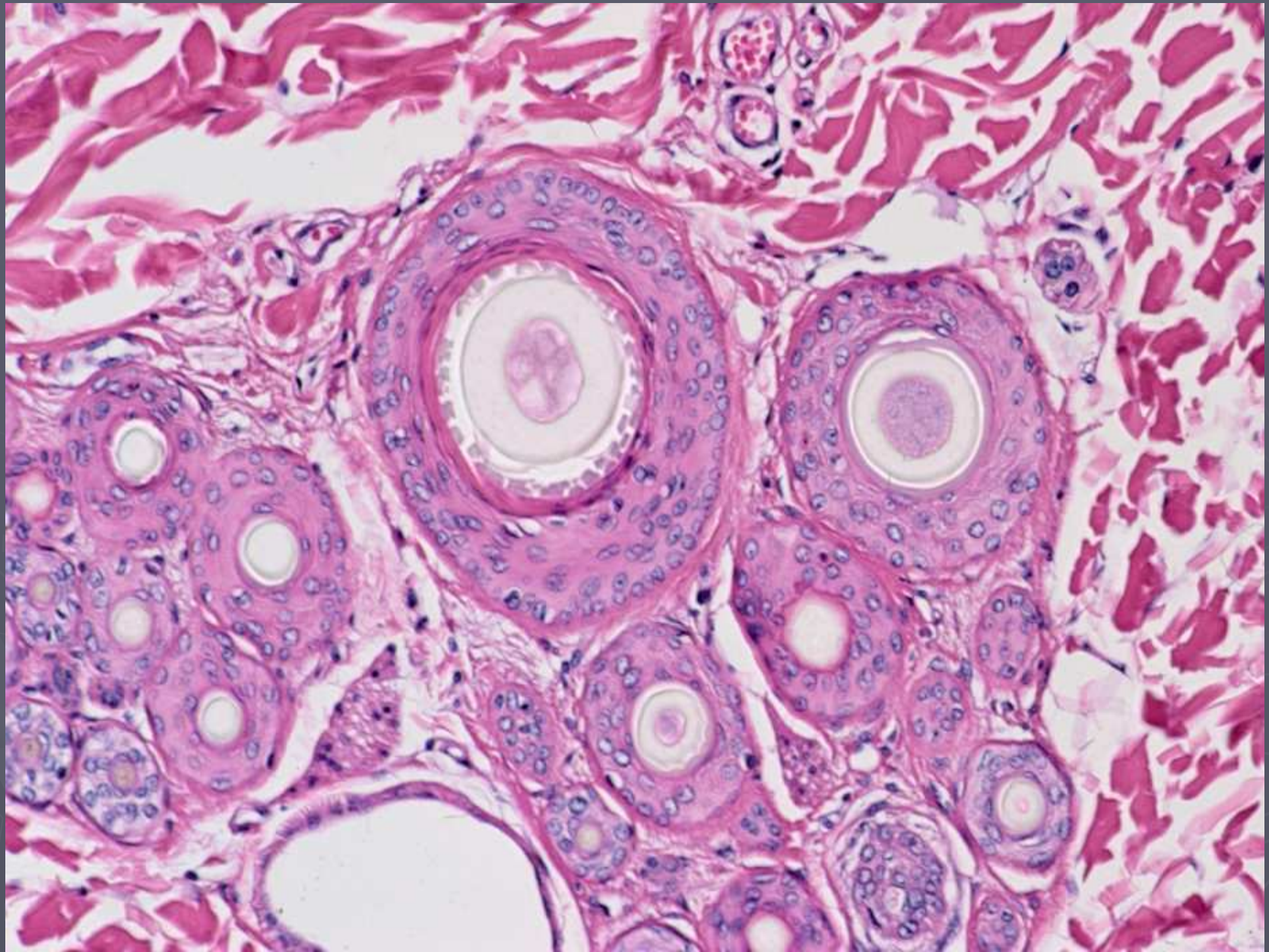
R. Dunstan

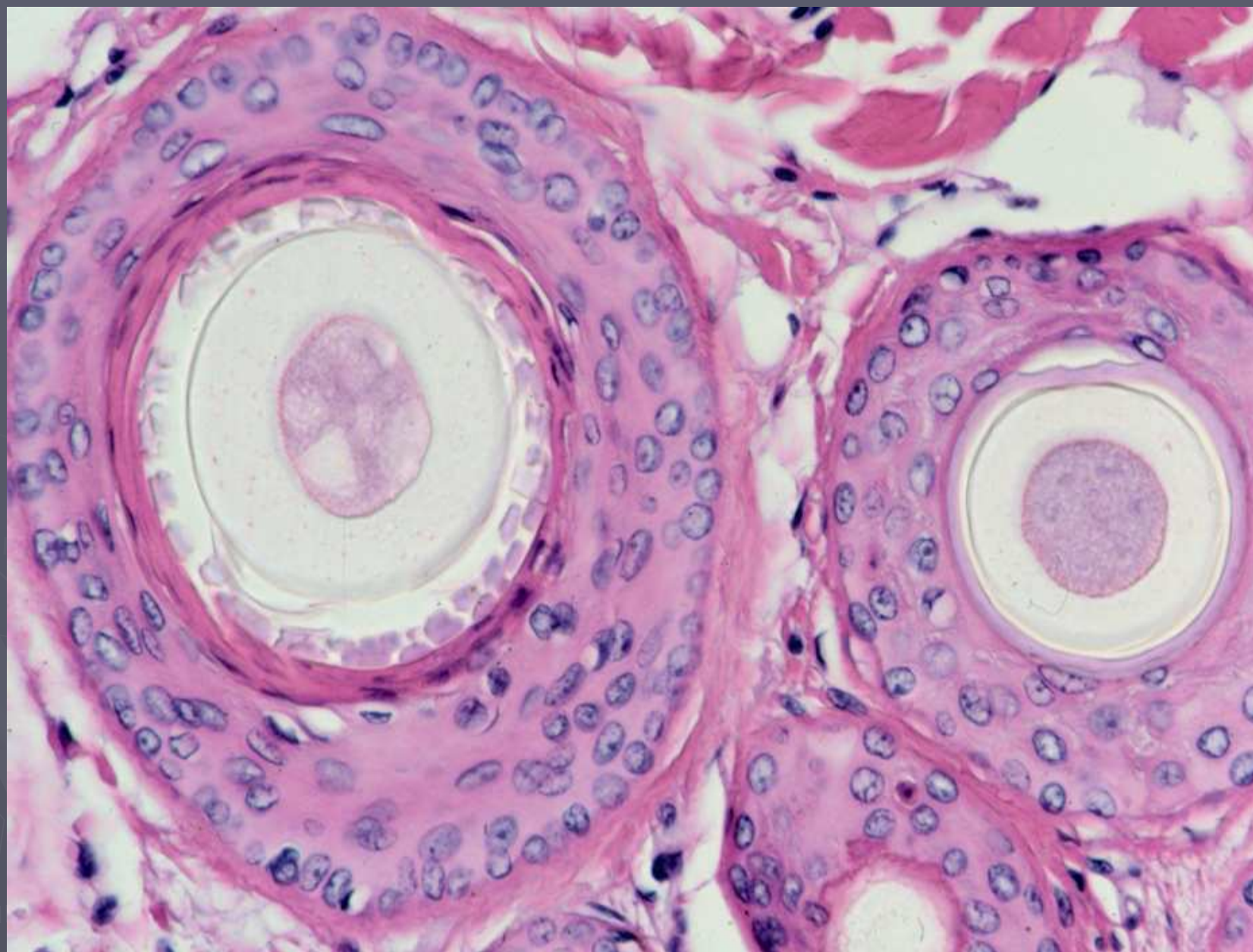


R. Dunstan



R. Dunstan

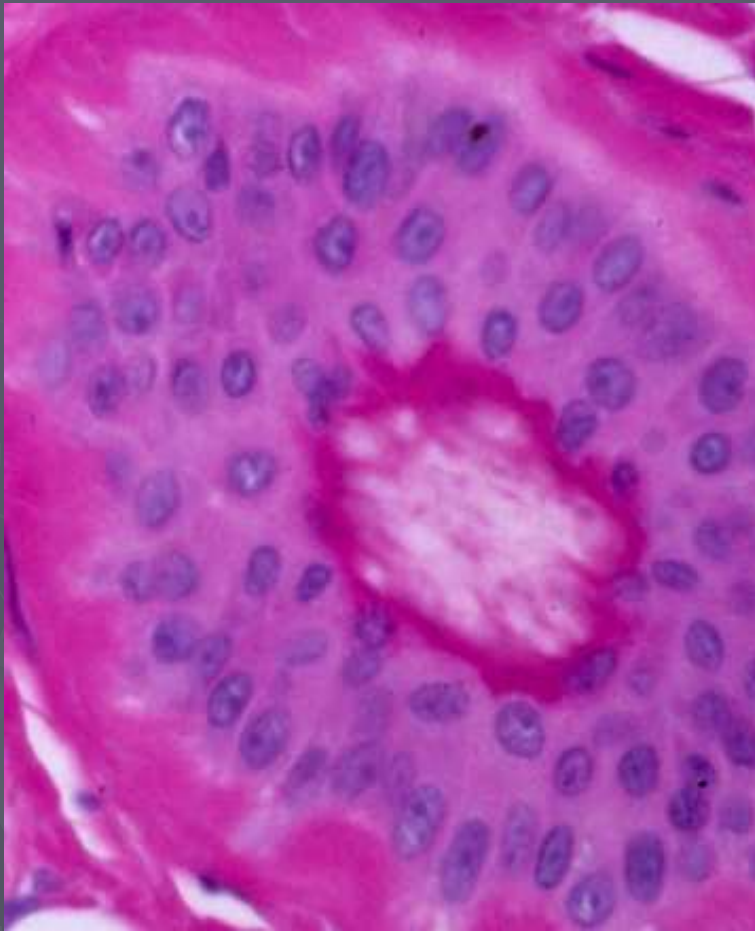




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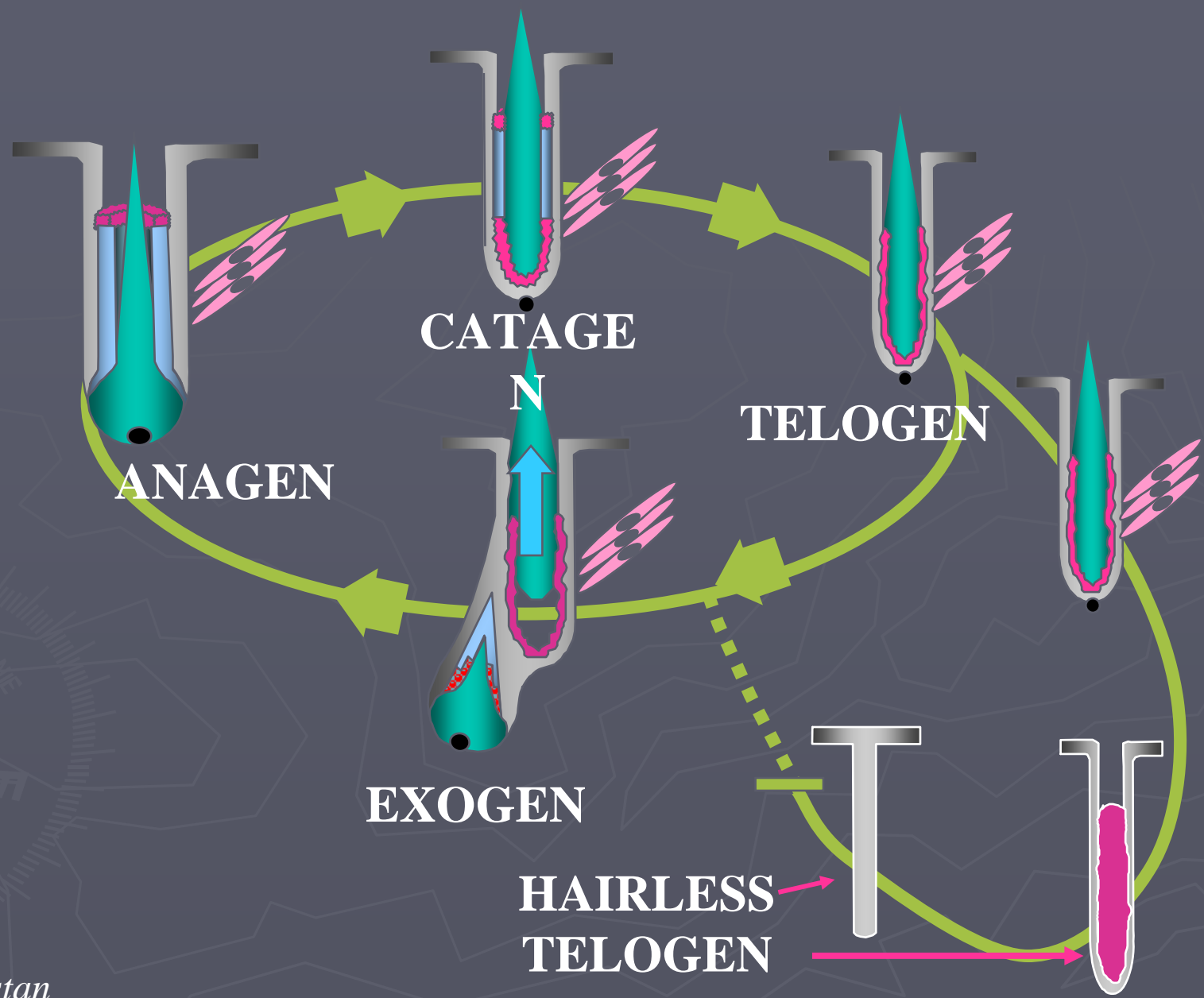
Is upper and lower trichilemmal cornification the same?

Lower



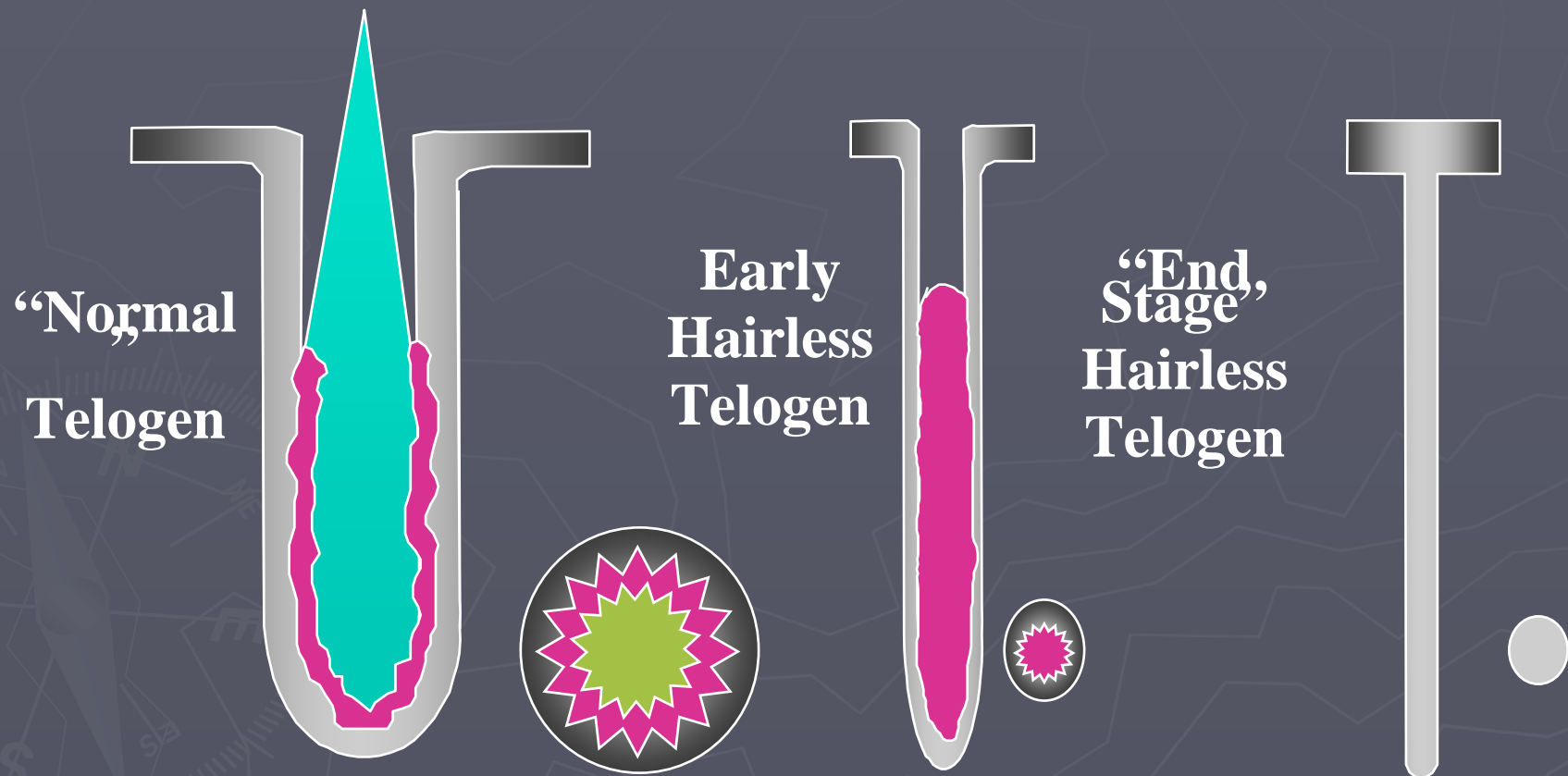
Upper





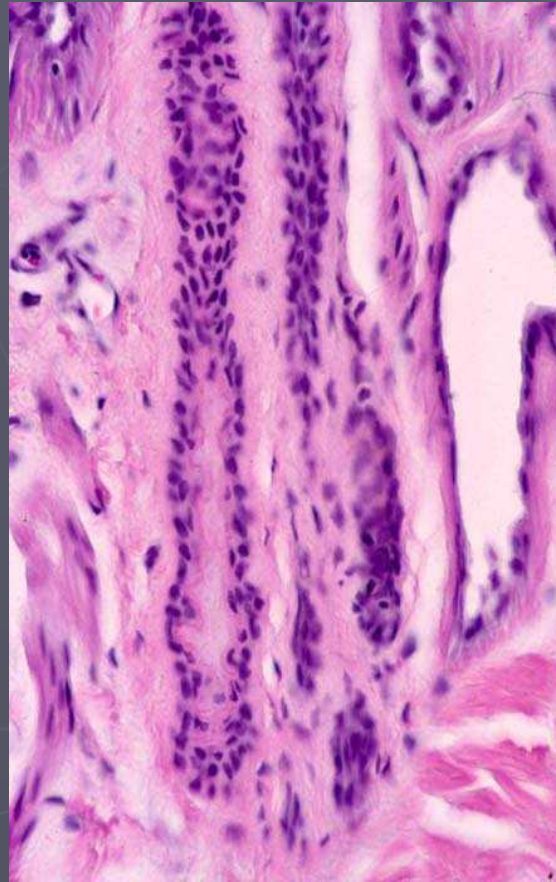
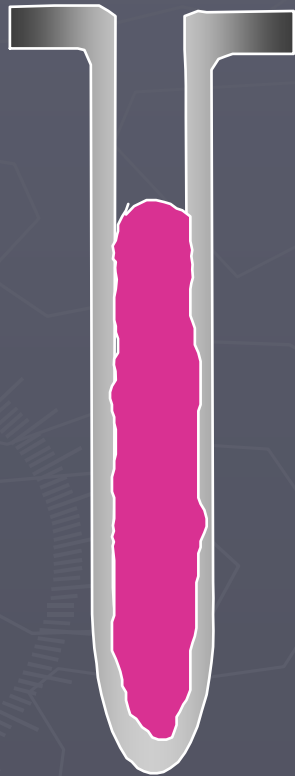
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Morphologic Features of Telogen: Longitudinal and Transverse Sections

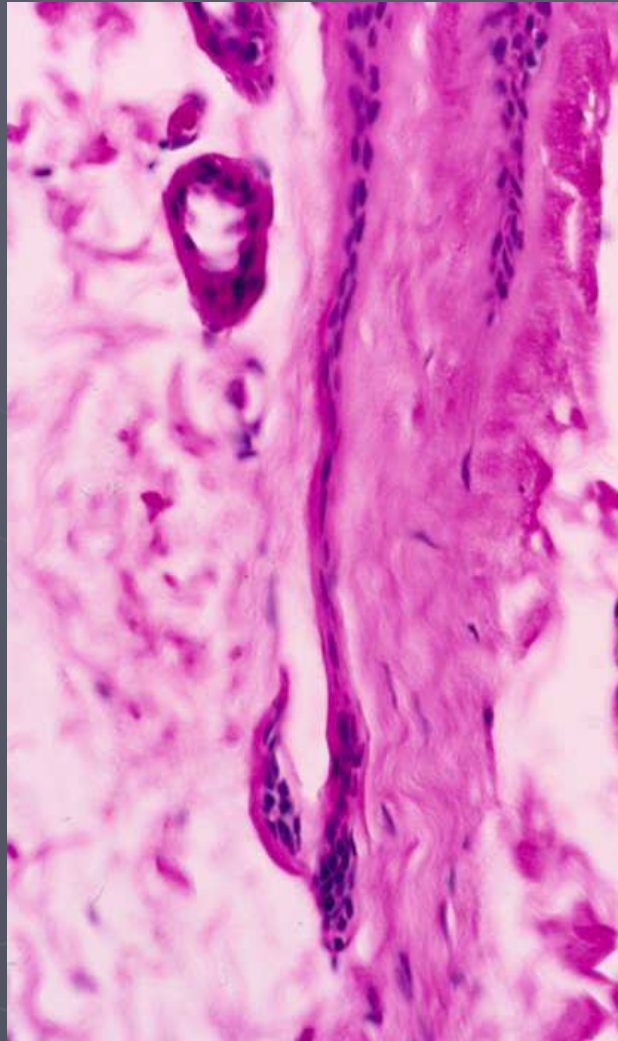


R. Dunstan

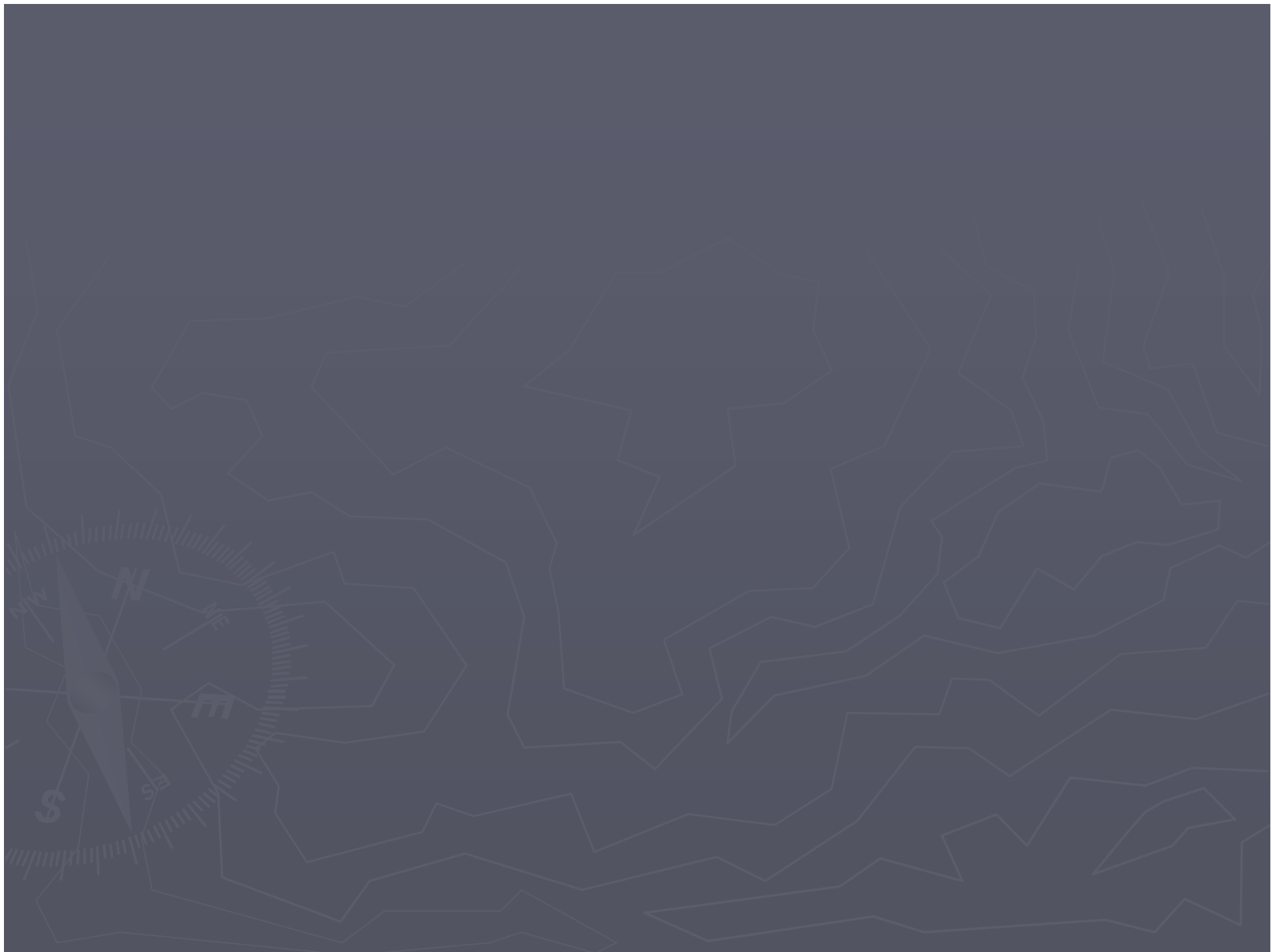
Early Hairless Telogen



Late Hairless Telogen



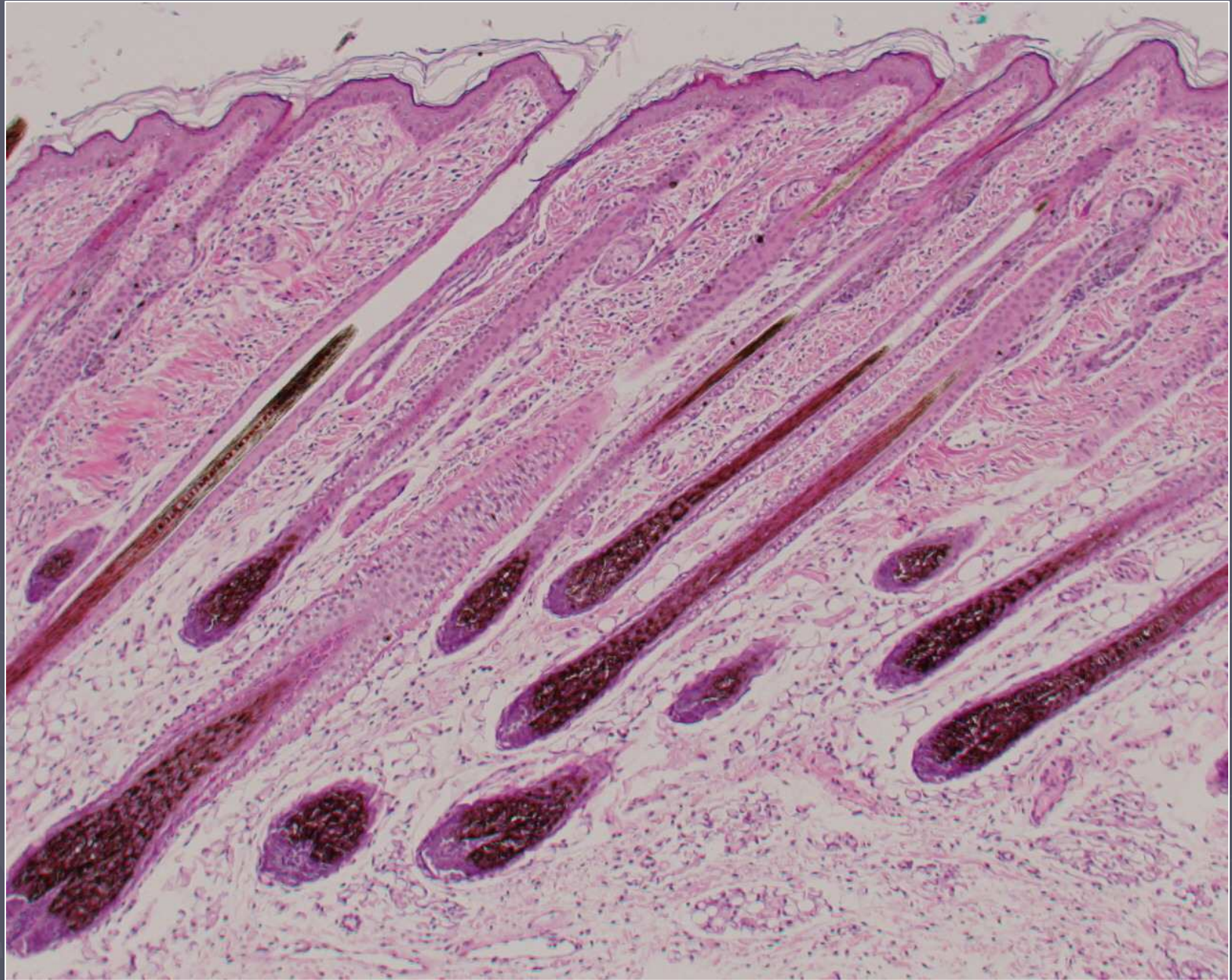
R. Dunstan



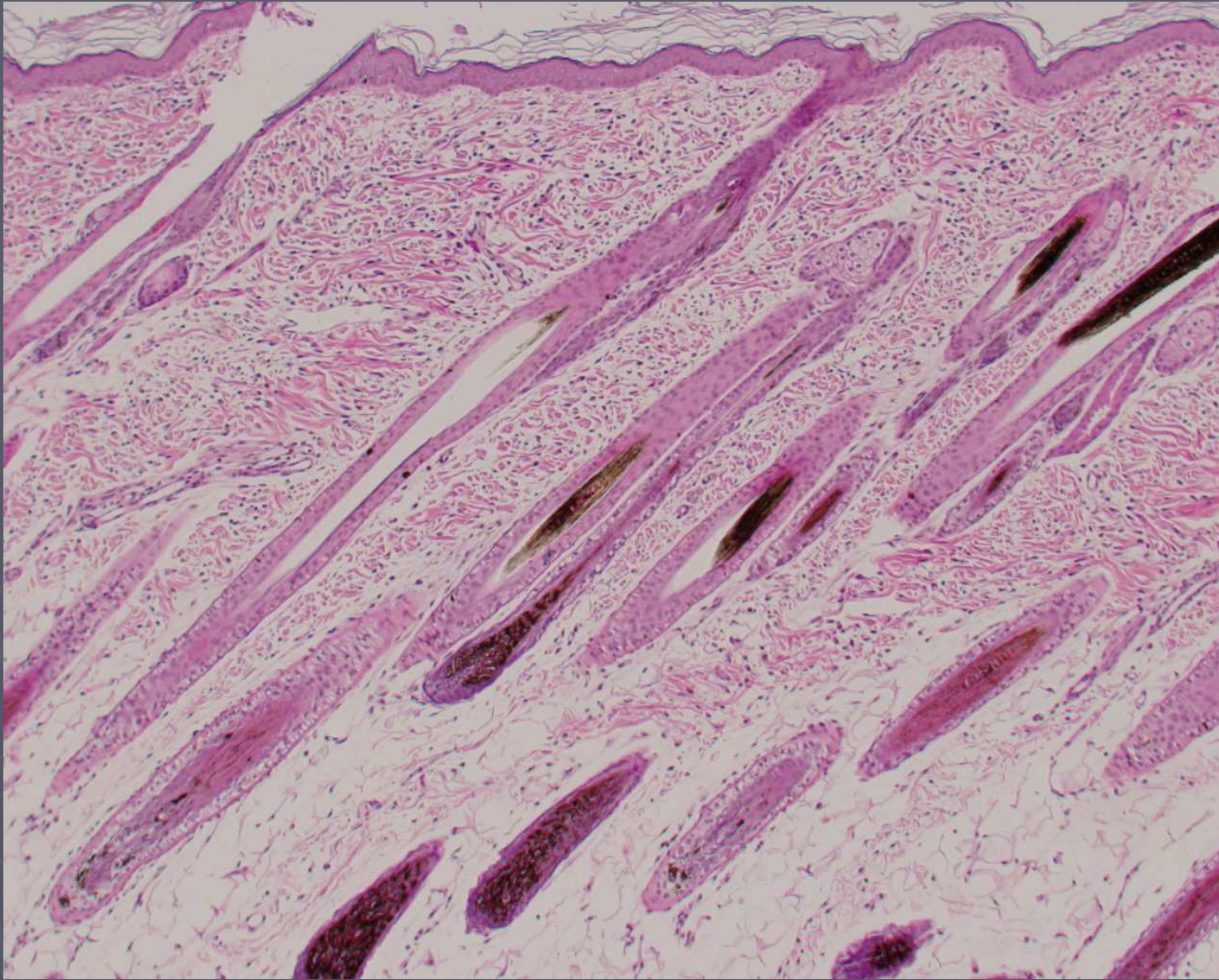
Hair Follicle Development

- ▶ Only during embryogenesis
- ▶ Dogs gain an adult coat rather than lose a puppy coat!

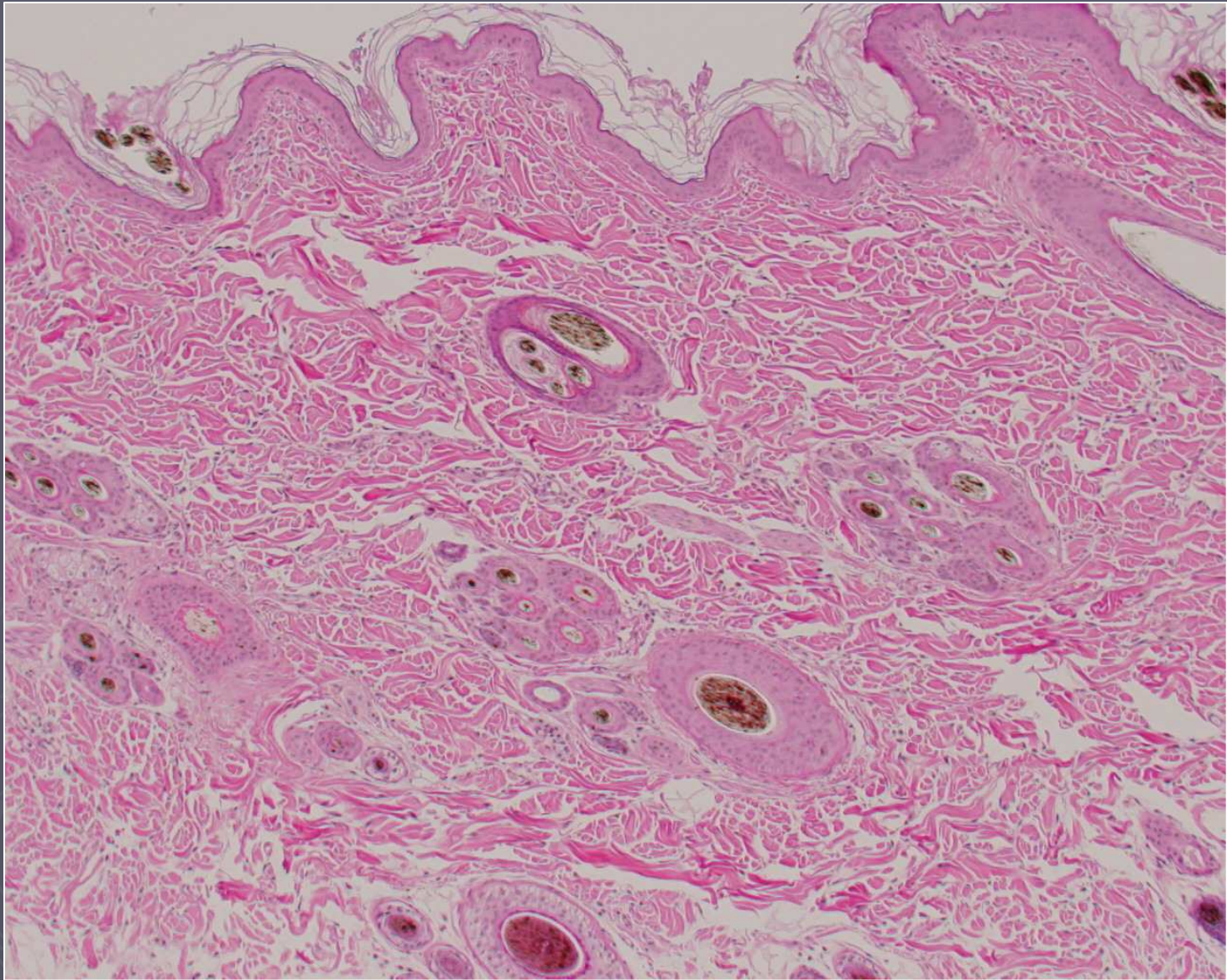
Secondary follicles branch from primary follicles



Two-day old puppy



Two-week old puppy



10 week old puppy

Embryologic HF Development

Epithelial mesenchymal interactions

- ▶ **Wnt pathway**– cross talk b/w epidermis and dermis
 - ▶ Regulate HF development and growth
 - Embryogenesis and initiate anagen phase
- ▶ **SHH signalling**
 - Paracrine- one cell produces it→ the next cell uses it
 - Regulates HF embryogenesis and cycling later than Wnt→ may play role in HF tumors
- ▶ **Notch signaling/Noggin**
 - Transmembrane receptor
 - Hair shaft medulla formation
- ▶ **EGF/TGF- α**

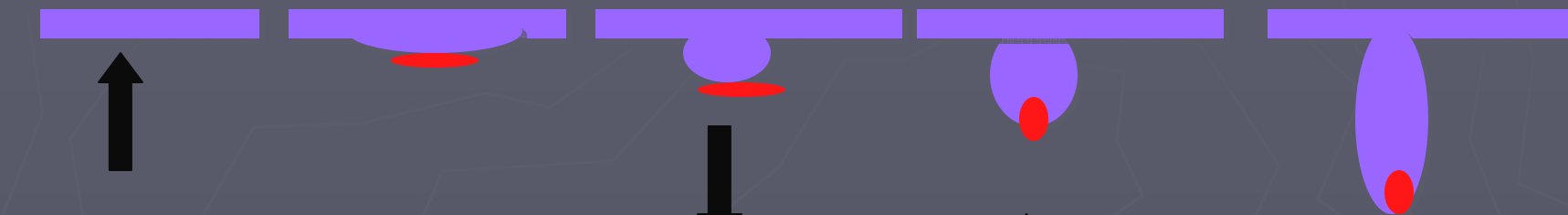
Undifferentiated
epithelium

Placode

Germ

Peg

Bulbous peg



Form an appendage

Form dermal
papilla

Form a
hair follicle



Pathways to HF Development

Series of signals b/w cells of epithelium and dermis

- ▶ First signal from dermis to epidermis
 - Form an Appendage!
 - ▶ Regular spaced thickenings of epidermis (Placodes)
 - ▶ activities of inducing and regressing molecules
- ▶ Epithelial signal from placode causes clustering of mesenchymal cells → “dermal condensate”
 - Promotion of papilla sonic hedgehog and PDGF-A
- ▶ Second signal from dermis to epidermis-
 - Make a Hair follicle!
 - ▶ Placode cells grow downward and surround mesenchymal cells
 - Formation of IRS and hair shaft

First Dermal Signal- Make an appendage, any appendage!

► Form a Placode!

- **Wnt signaling pathway**
- Wnt signalling--> leads to the appearance of diffuse **b-catenin** in dense dermis

In mice if you inhibit wnt (ie dickkopf-1)

- **NO PLACODES DEVELOP ALOPECIC MICE!!**

Undifferentiated
epithelium

Placode

Germ

Peg

Bulbous peg



Form an appendage



Form dermal
papilla



Form a
hair follicle



First epithelial signal!

Formation of the dermal papilla

- ▶ **Wnt and PDGF** induces formation of dermal condensate by paracrine signalling
- ▶ Competition b/w factors +/- placode formation
 - Inhibition: **BMPS** (bone morphogenic proteins)
 - Antagonists of BMPs: **Noggin** bind bmp2
- ▶ **Inhibition of epithelial BMP's** → first mesenchymal inductive message for hair follicle formation
- ▶ **Sonic hedgehog** acts later in follicular development but is dependent on Wnt signalling

Undifferentiated
epithelium

Placode

Germ

Peg

Bulbous peg



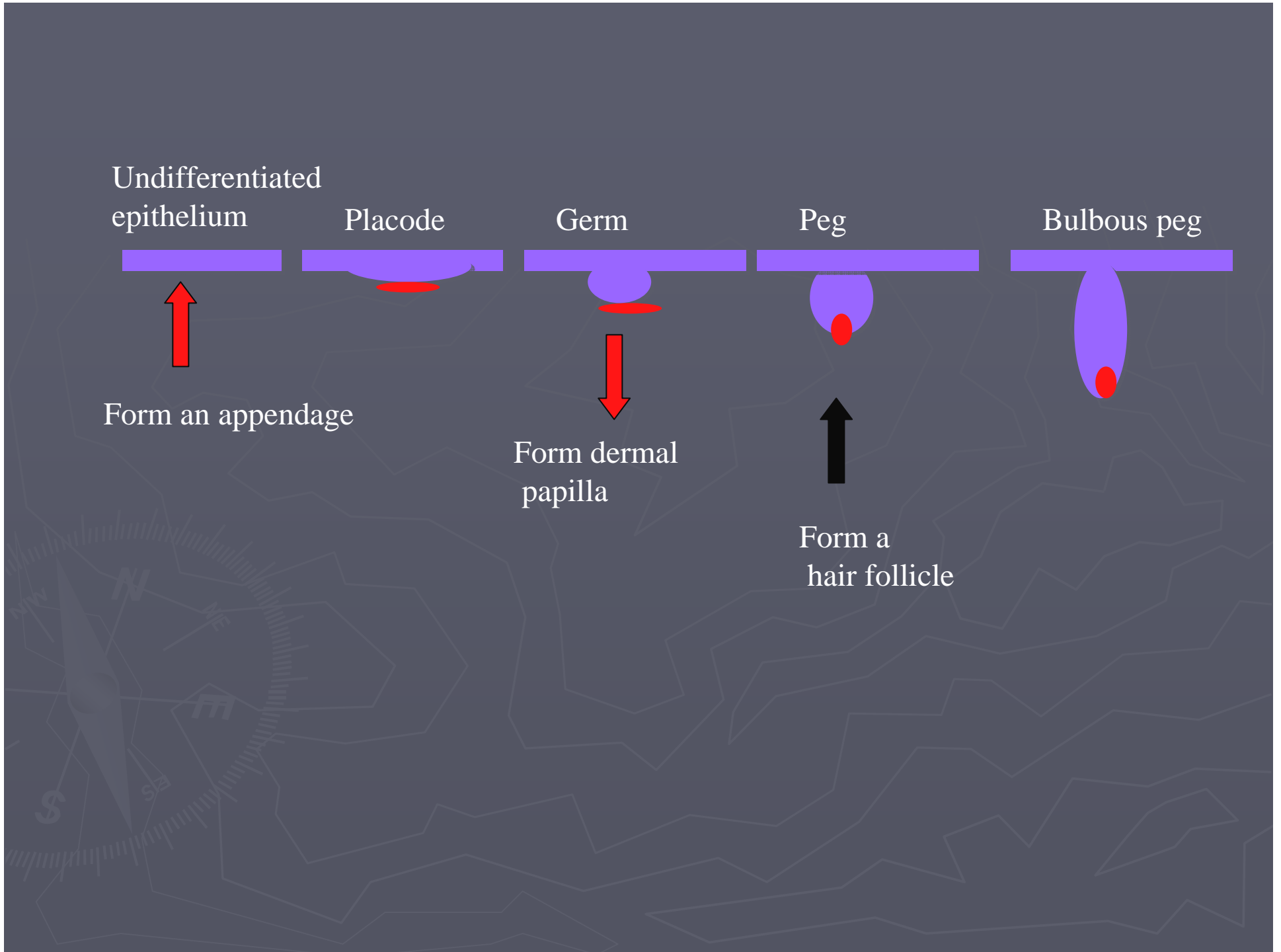
Form an appendage



Form dermal
papilla



Form a
hair follicle



Second Dermal signal

- Make a Hair follicle!
 - ▶ Placode cells grow downward and surround mesenchymal cells = **dermal papilla**
 - ▶ Formation of IRS and hair shaft

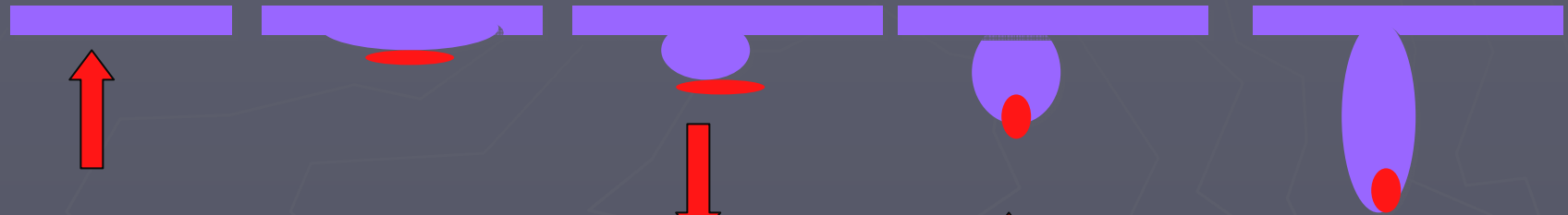
Undifferentiated
epithelium

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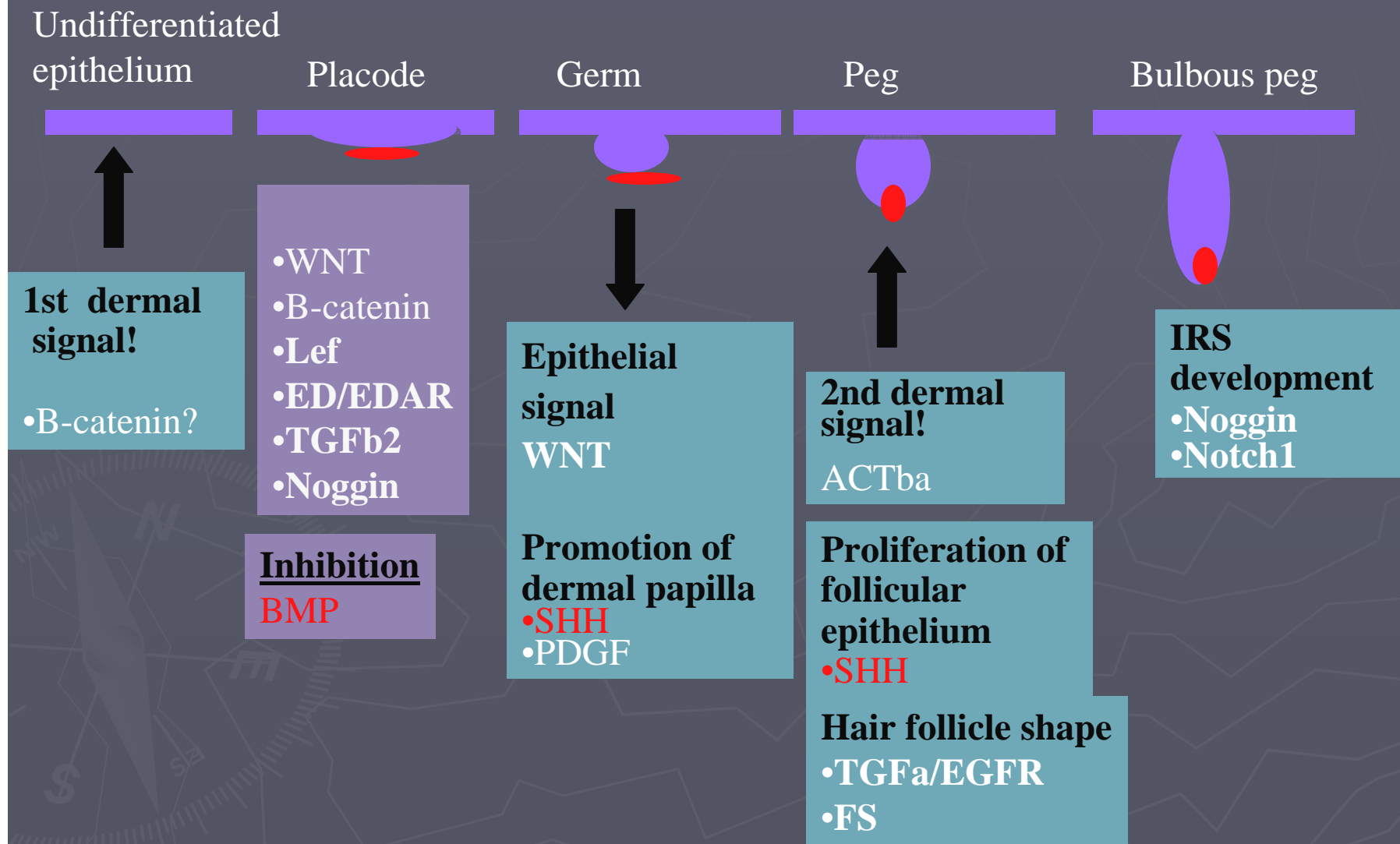
Bulbous peg



Form dermal
papilla

Form a
hair follicle

Summary of Pathways involved in Embryogenesis



Adapted from Cotsarelis and Miller. *Trends* 2001

Ectodysplasin

- ▶ Ectodysplasin and receptor (EDAR)
Ectodysplasin (ED1/ED2)—TNF family encoded by an X-linked gene
- ▶ Ectodysplasin activates transcription factor (NF κ B/REL)→ stimulate expression of Wnt ?? → cell proliferation/placode formation
- ▶ Models in mice and model in dog
- ▶ Spontaneous disease in dogs

Hypohidrotic Ectodermal Dysplasia

- ▶ **Triad of lesions**
 - Hypodontia/malformed teeth
 - Patterned hypotrichosis
 - Eccrine gland aplasia
- ▶ **Spontaneous mutation ED1**
- ▶ **Colony established**



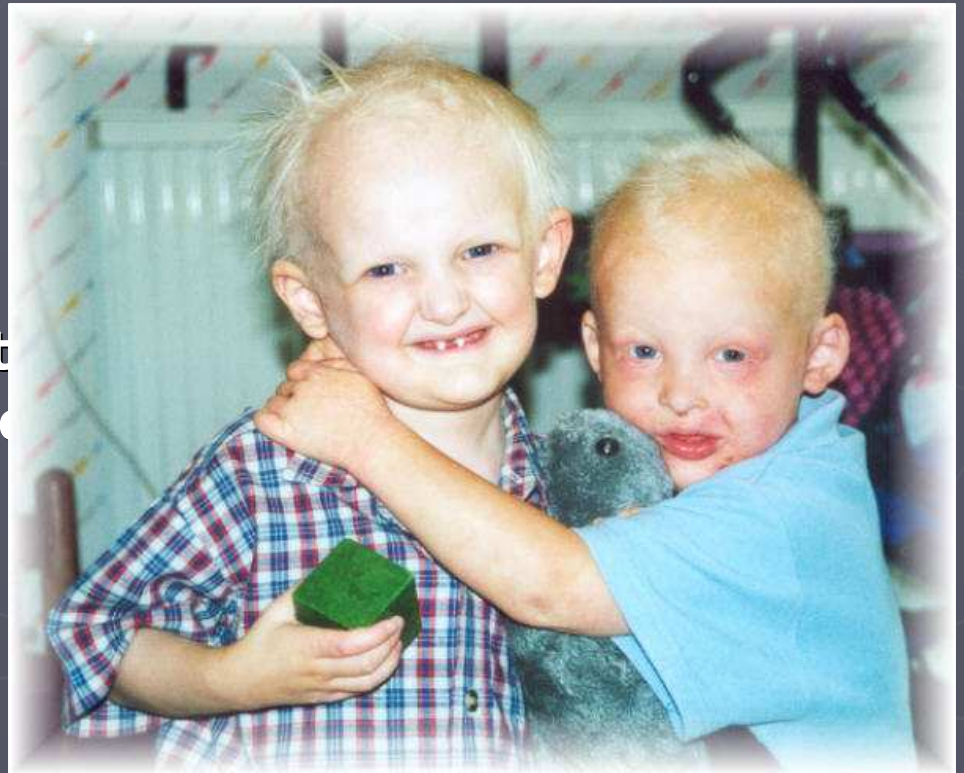
Casal J *Heredity*, 1997

Ectodermal dysplasia

- ▶ **Ectodysplasin- trimeric, transmembrane, protein with extracellular TNF-like signaling domain**
 - Embryologic mesenchymal/epithelial interactions: adnexa, tooth buds
 - May also signal through Wnt→ placode development
- ▶ **X-linked hypohidrotic ectodermal dysplasia most common form of ED**
 - Mutation in ectodysplasin 1 gene

Human XHED

- ▶ **Triad of lesions:**
 - **Hypodontia/peg-shaped teeth**
 - **Eccrine gland aplasia/hypoplasia,**
 - **Alopecia**
- ▶ **Failure to thrive**
- ▶ **Hyperthermia (30% mortality)**
- ▶ **Recurrent respiratory infections**
- ▶ **Dry eye**
- ▶ **Atopic disease**
- ▶ **Self confidence issues**



Mouse Models of ED

- ▶ Phenotypes of tabby, downless, sleek and crinkled mutant mice are similar
- ▶ **Tabby mice** lack functional ligand **ecotdysplasin-1**
 - Downless and sleek (ED1 receptor)
 - Crinkled (ED1 receptor-associated death domain)
- ▶ Developmental defects in ectodermal organs

Canine XHED

- ▶ ↑ morbidity/mortality due to respiratory infections
- ▶ Decreased weight gain
- ▶ Respiratory infections → ↓ mucociliary clearance*
- ▶ Keratoconjunctivitis sicca
- ▶ Signs of atopic disease



* Casal et al, *Vet Immunol Immunopathol*, 2005

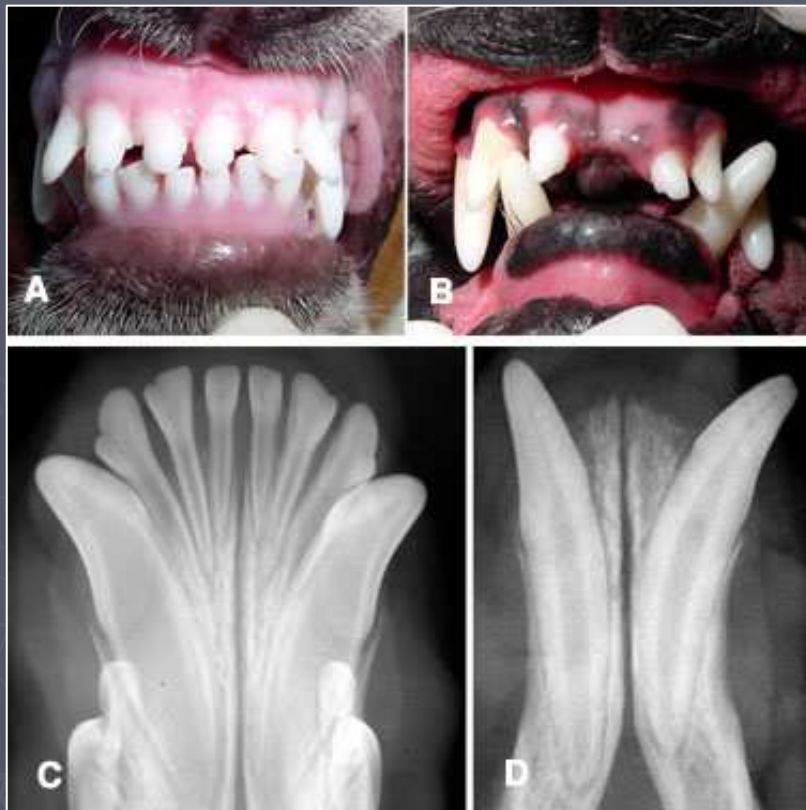


- ▶ **Breeding studies confirmed X-linked inheritance**
- ▶ **Some carriers mild hypotrichosis → lyonization**
- ▶ **UPENN- frame shift mutation ED1 → premature stop codon → truncates translation of both isoforms (EDA-1, EDA-2) → absence of TNF-like receptor binding site**

Casal et. al. *Mammalian Genome* 2005

XHED dogs have missing teeth and conically-shaped teeth

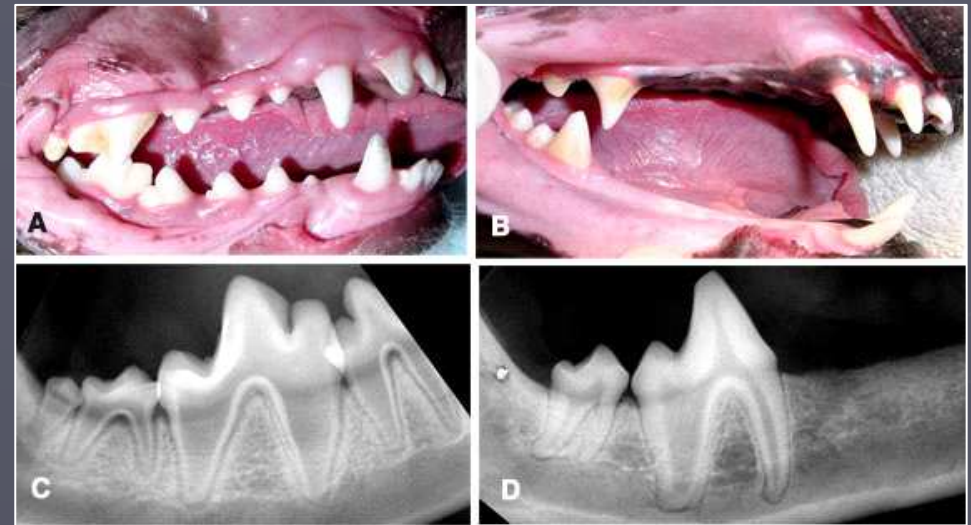
Incisors and Canines



Normal

Affected

Premolars and Molars



Normal

Affected