مؤسسة حمد الطبية
Hamad Medical Corporation
HEALTH • EDUCATION • RESEARCH صحة • تعليم • بحوث

In partnership with

Samir Al Hyassat

HMC , Qatar

Dr. Samir Al-Hyassat is a highly regarded senior consultant pathologist with a wealth of experience and expertise in the field. He earned his MBBS degree from The University of Jordan in 1999 and subsequently pursued advanced training and qualifications in the United Kingdom. He obtained the prestigious FRCPath (Fellow of the Royal College of Pathologists) in 2010, as well as the CCT-UK (Certificate of Completion of Training) in the same year.

Dr. Al-Hyassat's passion lies in various subspecialties, including dermatopathology, urological pathology, and gynaecological pathology. His extensive knowledge and keen eye for detail allow him to provide accurate diagnoses and contribute to effective treatment strategies for patients with complex conditions in these areas.

Notably, Dr. Al-Hyassat has embraced the advancements in digital pathology and artificial intelligence, recognizing their potential to revolutionize clinical diagnostic pathology. He has gained significant experience in utilizing digital pathology tools and AI applications in his daily practice, particularly in the analysis of prostate biopsies. Actively engaged in international multicentric AI research projects, he is at the forefront of cutting-edge developments in the field, seeking to enhance diagnostic accuracy and patient outcomes.

Dr. Al-Hyassat's contributions extend beyond his clinical work. He is committed to sharing his expertise through research, academic pursuits, and collaborations with colleagues worldwide. His dedication to advancing the field of pathology and improving patient care is evident in his active involvement in scientific conferences and publications.

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ALOPECIA

Dr Samir Al Hyassat
Senior consultant histopathologist
MBBS, FRCPath, CCT
HMC-Qatar

Conflicts of interest

None

References

Histopathology 2010, **56**, 24–38. DOI: 10.1111/j.1365-2559.2009.03439.x

REVIEW

Histopathology of alopecia: a clinicopathological approach to diagnosis

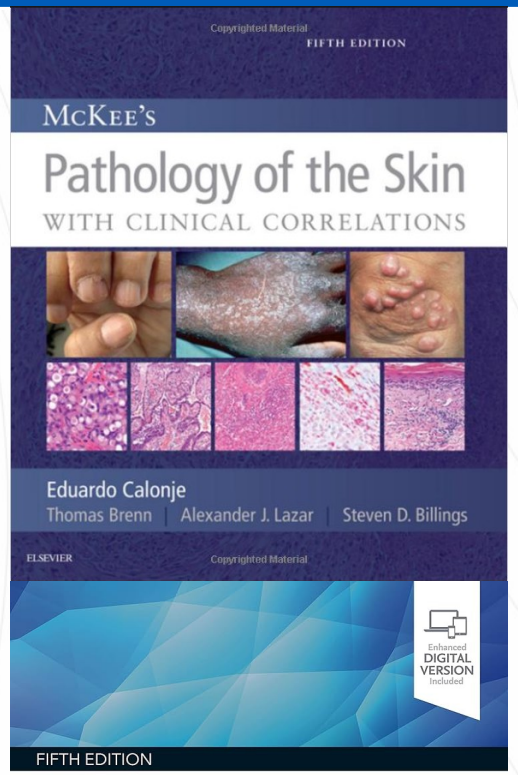
Catherine M Stefanato

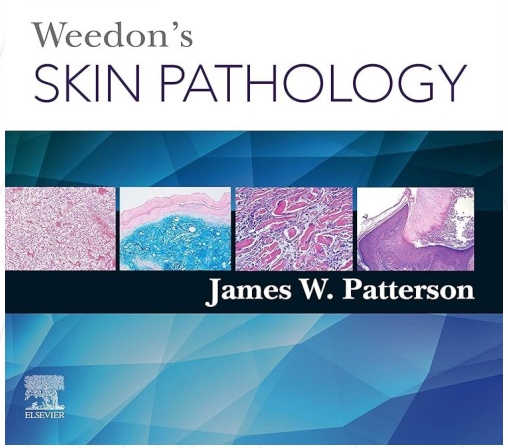
Department of Dermatopathology, St John's Institute of Dermatology, St Thomas' Hospital, London, UK

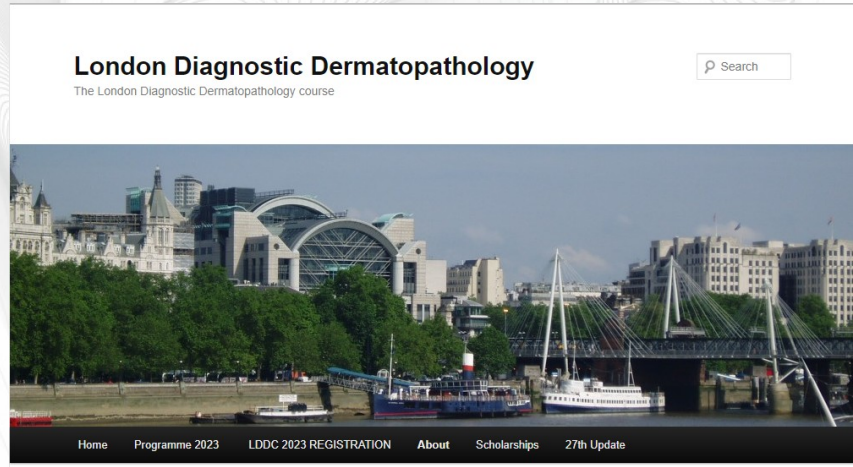
Stefanato C M

(2010) *Histopathology* **56**, 24–38

Histopathology of alopecia: a clinicopathological approach to diagnosis







1. **INTRODUCTION**
2. BIOPSY
   A. WHY IS IT SO DIFFICULT TO INTERPRET A SCALP BIOPSY ?
   B. HOW AND WHERE TO PERFORM A PROPER BIOPSY?
   C. TYPE OF SECTION (VERTICAL, HORIZONTAL, BOTH?)
3. NORMAL HAIR FOLLICLE
   A. ANATOMY
   B. HAIR CYCLE (ANAGEN , CATAGEN, TELOGEN)
4. TERMINAL FOLLICLES / VELLUS HAIR
5. SCARRING ALOPECIAS
6. DIFFERENCES BETWEEN ETHNIC GROUPS

Classification of primary alopecia

Scarring

1. Lymphocytic
2. Neutrophilic
3. Mixed

Non-scarring

1. Androgenic alopecia
2. Telogen effluvium
3. Alopecia areata
4. Trichotillomania
5. Traction alopecia

https://unsplash.com

Scarring Alopecia

Lymphocytic

1. Discoid lupus erythematosus,
2. Lichen planopilaris,
    1. Classic LPP
    2. Frontal fibrosing alopecia
    3. Graham–Little syndrome
3. Central centrifugal cicatricial alopecia
4. pseudopelade of Brocq
5. Alopecia mucinosa
6. Keratosis follicularis spinulosa decalvans,

Neutrophilic

1. Folliculitis decalvans,
2. Dissecting cellulitis/ folliculitis (perifolliculitis capitis abscedens et suffodiens)

Mixed

3. Folliculitis (acne) keloidalis
4. Folliculitis (acne) necrotica
5. Erosive pustular dermatosis

Secondary scarring alopecia

1. Aplasia cutis congenita
2. Cicatricial bullous pemphigoid
3. Infectious (kerion, staphylococcal)
4. Neoplastic (primary, metastasis)
5. Connective tissue disease (morphea)
6. Trauma (burn)
7. Metabolic (amyloid, mucin)
8. Granulomatous (sarcoid)

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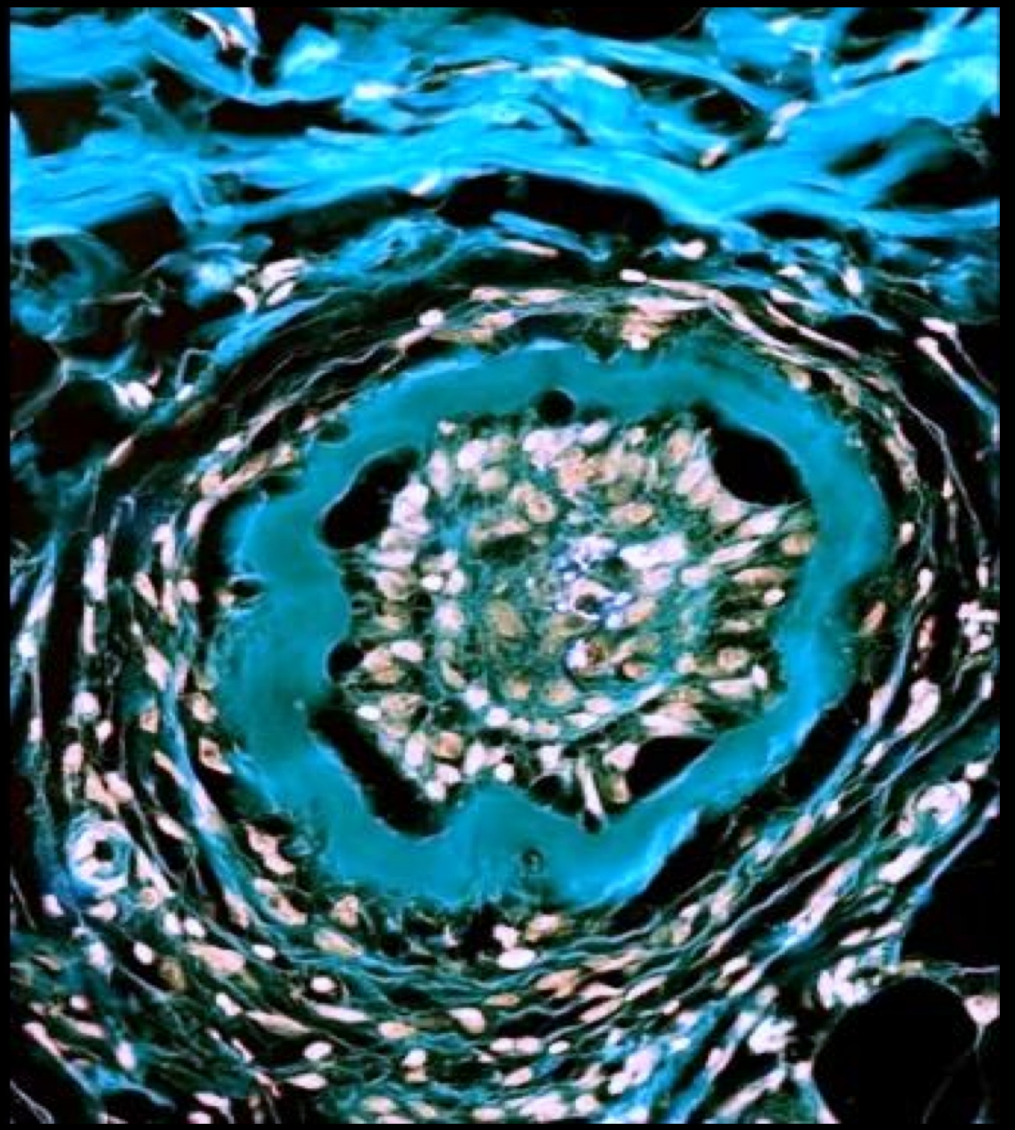

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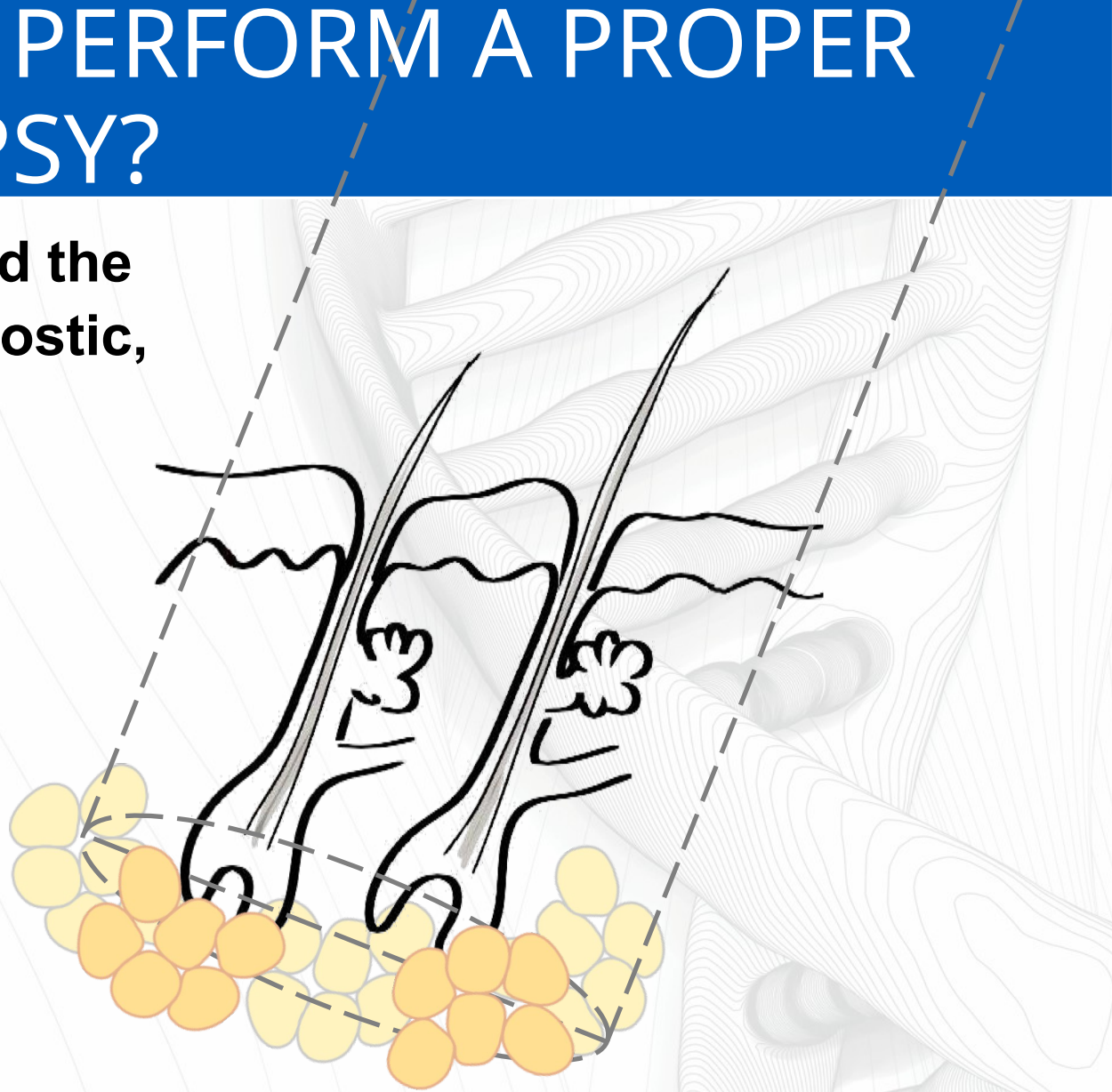
HOW AND WHERE TO PERFORM A PROPER BIOPSY?

4 mm punch biopsy is considered the Ideal technique to obtain a diagnostic, full-thickness skin specimen

The biopsy is taken following the direction of the hair with the intention of minimizing tangential sections

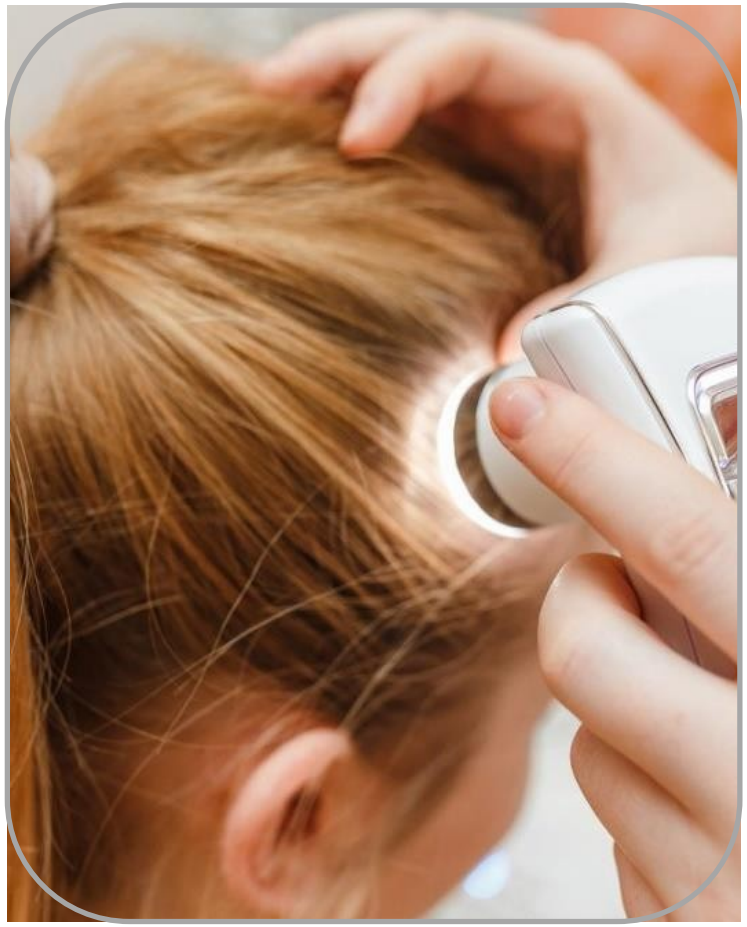
It should include a generous amount of subcutaneous tissue



Selecting the biopsy site is a crucial part of the process.

Two punch biopsies 4 mm in diameter should be obtained for comparison from different sites: from the affected area and from the unaffected scalp in the periphery

Dermoscopy guided scalp biopsy is an accurate way to identify affected follicles, mainly in cicatricial alopecia.



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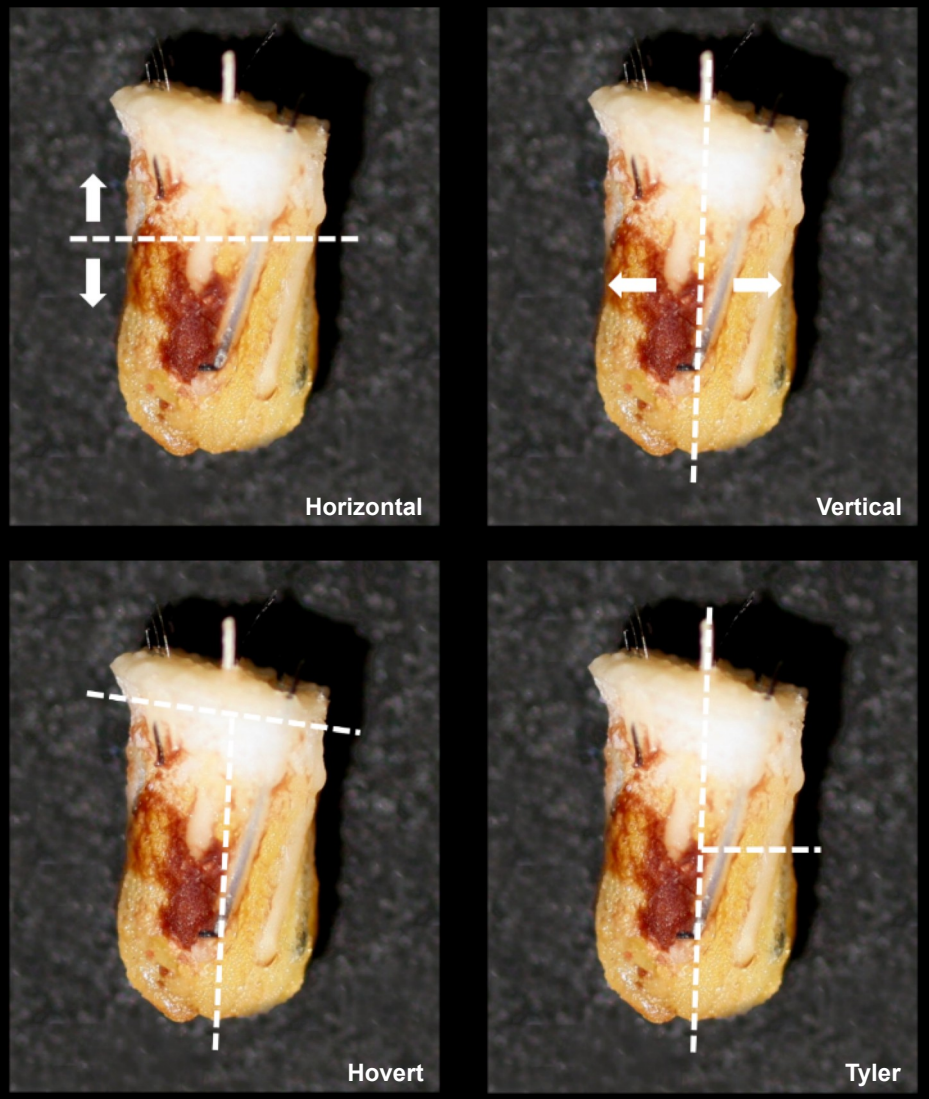


Alopecia protocol (HMC):

Staining:

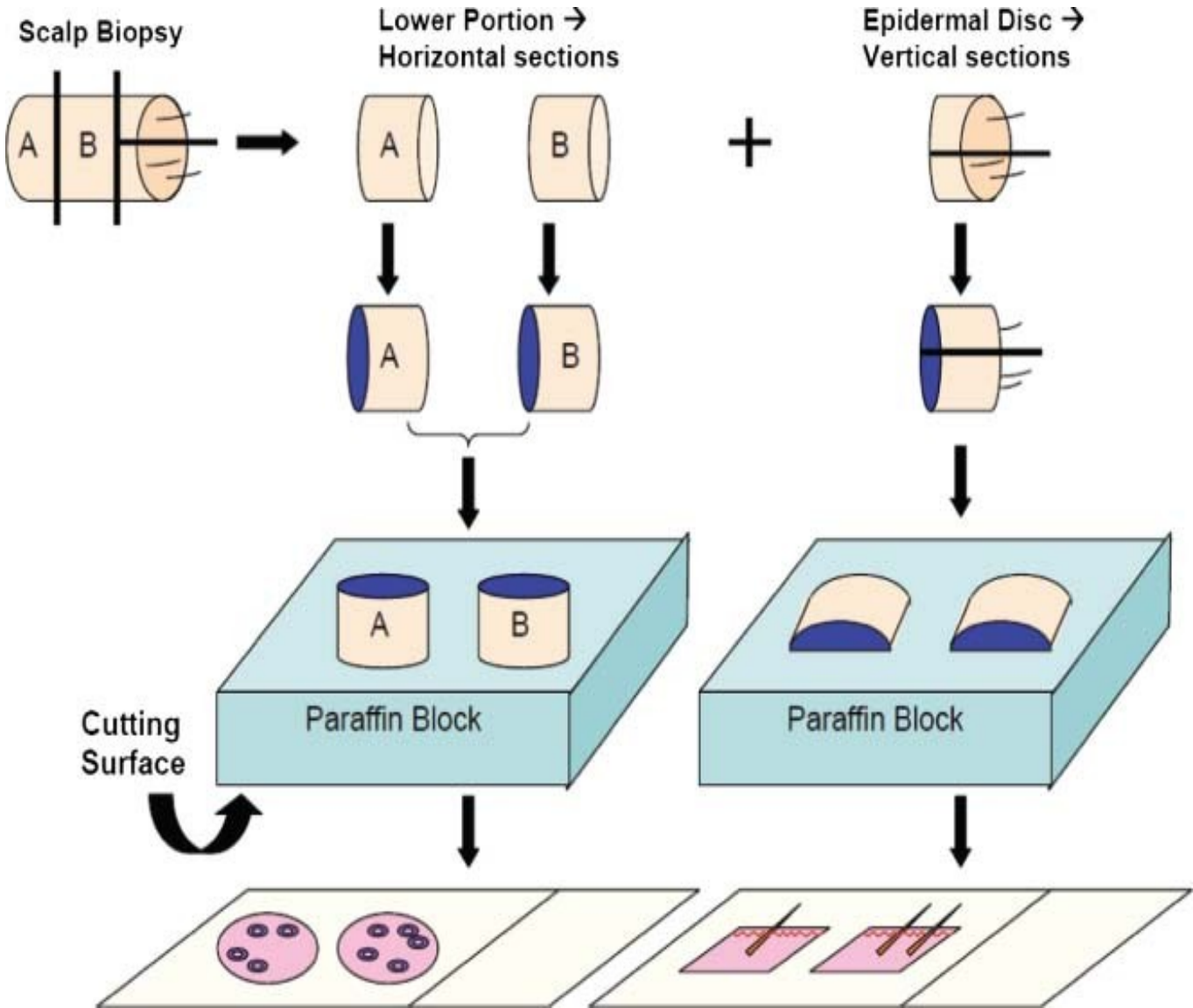
For all techniques and all blocks: H&E ×6 (initial) + PAS + Alcian blue + EVG.

Alopecia protocol (HMC):

Grossing:

If a single biopsy of adequate size is received, then use protocol on right >>>>>>>>>

If the biopsy is very small to process, then embed vertically (for scarring alopecia) or horizontally (for non-scarring alopecia).



If 2 punch biopsies are received

Scarring alopecia

Both taken at the peripheral edge

One in formalin, second for IF+ vertical

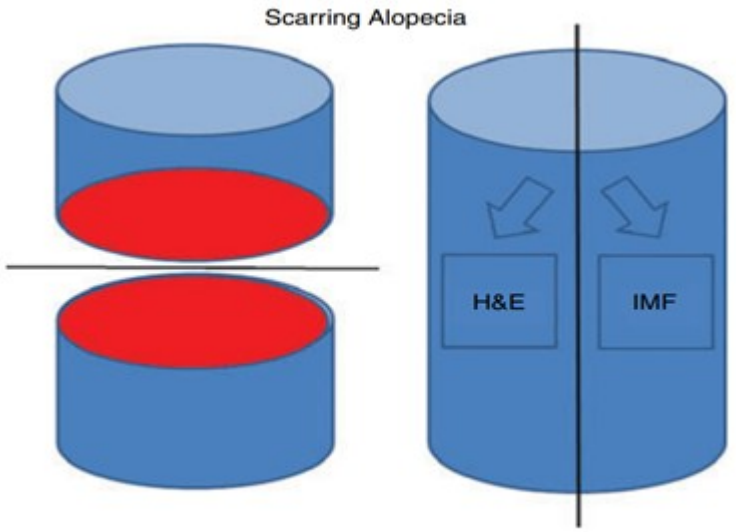


Figure 2. Schematic diagram of the St John's scarring alopecia protocol.

Non-scarring alopecia

One from involved area and the other from uninvolved area

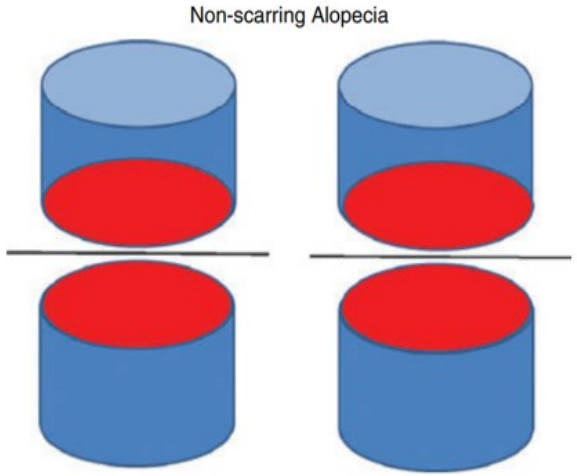


Figure 3. Schematic diagram of the St John's non-scarring alopecia protocol.

COMMON CAUSES OF SCARRING AND NON-SCARRING ALOPECIAS

NON-SCARRING ALOPECIAS	SCARRING ALOPECIAS
• Androgenic alopecia • Telogen effluvium • Traction alopecia (early) • Trichodystrophy • Alopecia areata	• Central centrifugal cicatricial alopecia • Lichen planopilaris/frontal fibrosing alopecia • Traction alopecia (late) • Dissecting cellulitis • Chronic cutaneous lupus • Pseudopelade of Brocq • Alopecia mucinosa

CAUSES OF NON - SCARRING & SCARRING ALOPECIA - MNEMONIC

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NON - SCARRING ALOPECIA

MNEMONIC - **THATS STD**

- **T**inea capitis(Non Inflammatory Type)
- **H**ormonal - Hypothyroidism, Androgenetic alopecia
- **A**nagen effluvium, Alopecia areata
- **T**richotillomania
- **S**econdary syphilis (moth eaten alopecia)
- **S**LE
- **T**elogen effluvium
- **D**eficiency of Zinc, Iron

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SCARRING ALOPECIA

MNEMONIC - **STD DVL**

- **S**cleroderma
- **T**inea capitis(Inflammatory Type - Kerion
- **F**olliculitis Decalvans
- **D**LE
- **L**upus Vulgaris
- **L**ichen Planopilaris

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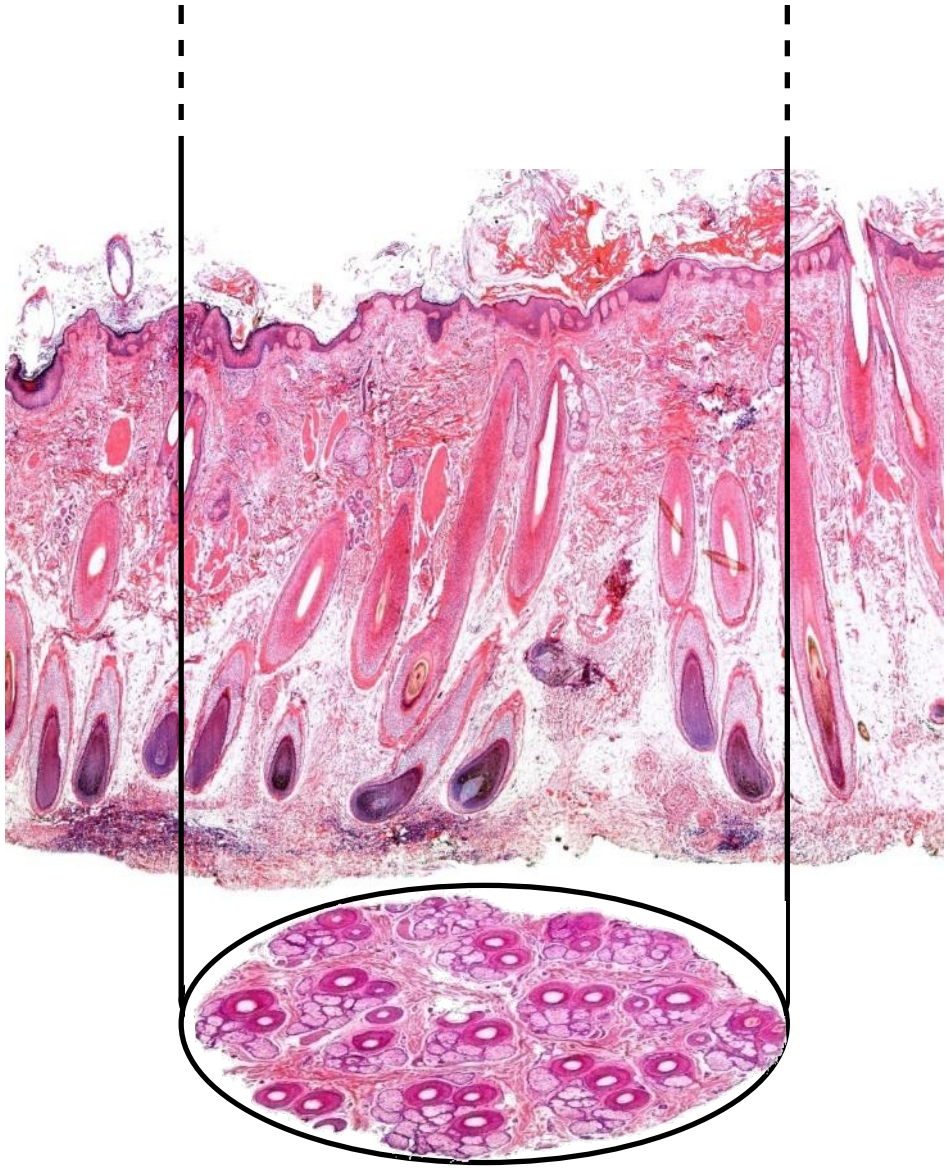
Note

Clinical information will significantly impact the away we should process specimens, and consequently impact on the ability to interpret the biopsy and give proper diagnosis.

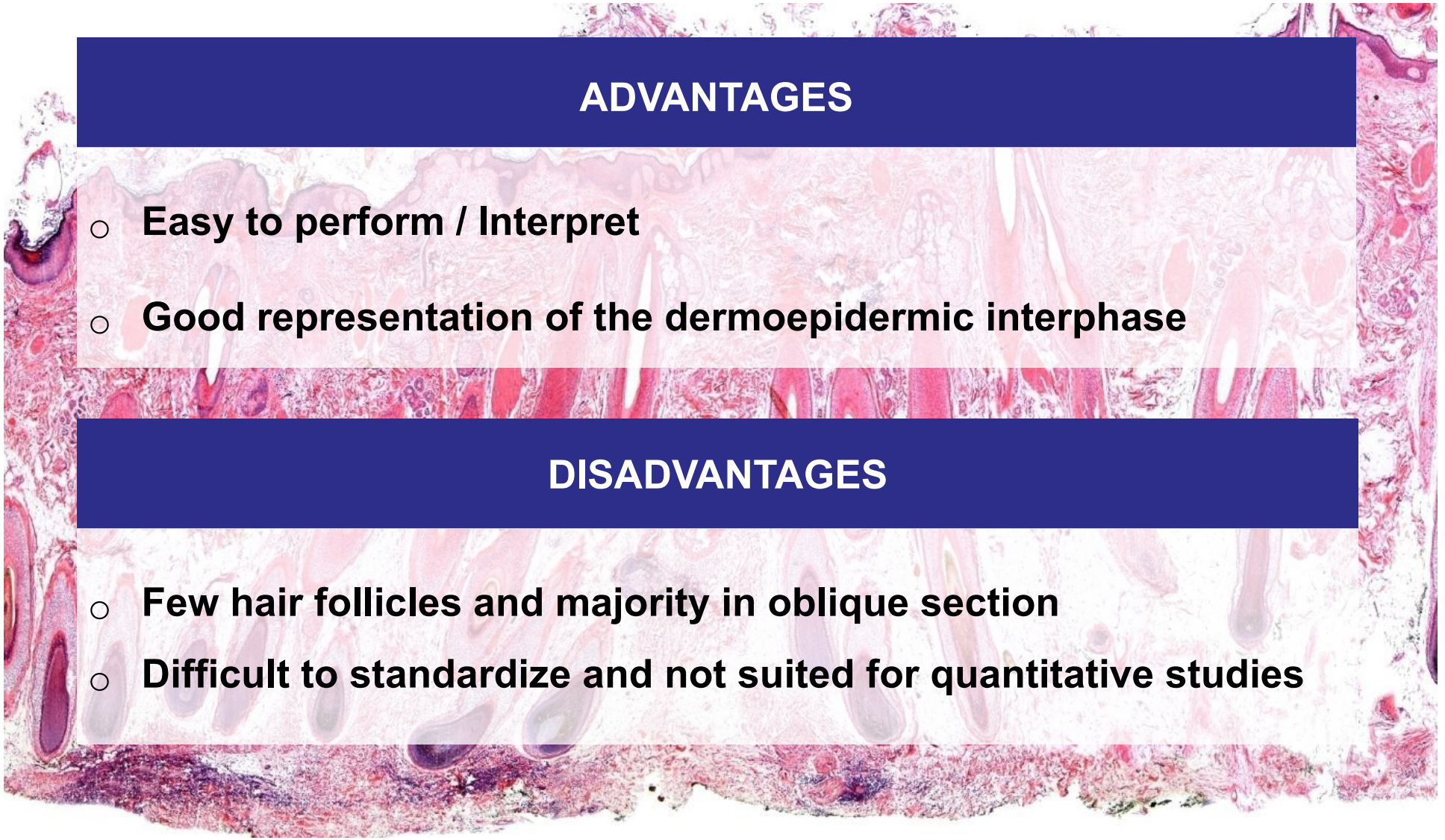
Communication with dermatology colleagues essential.

WHAT IS THE BEST TYPE OF SECTION TO USE?



Transverse sectioning of the scalp (Headington technique)

VERTICAL SECTION



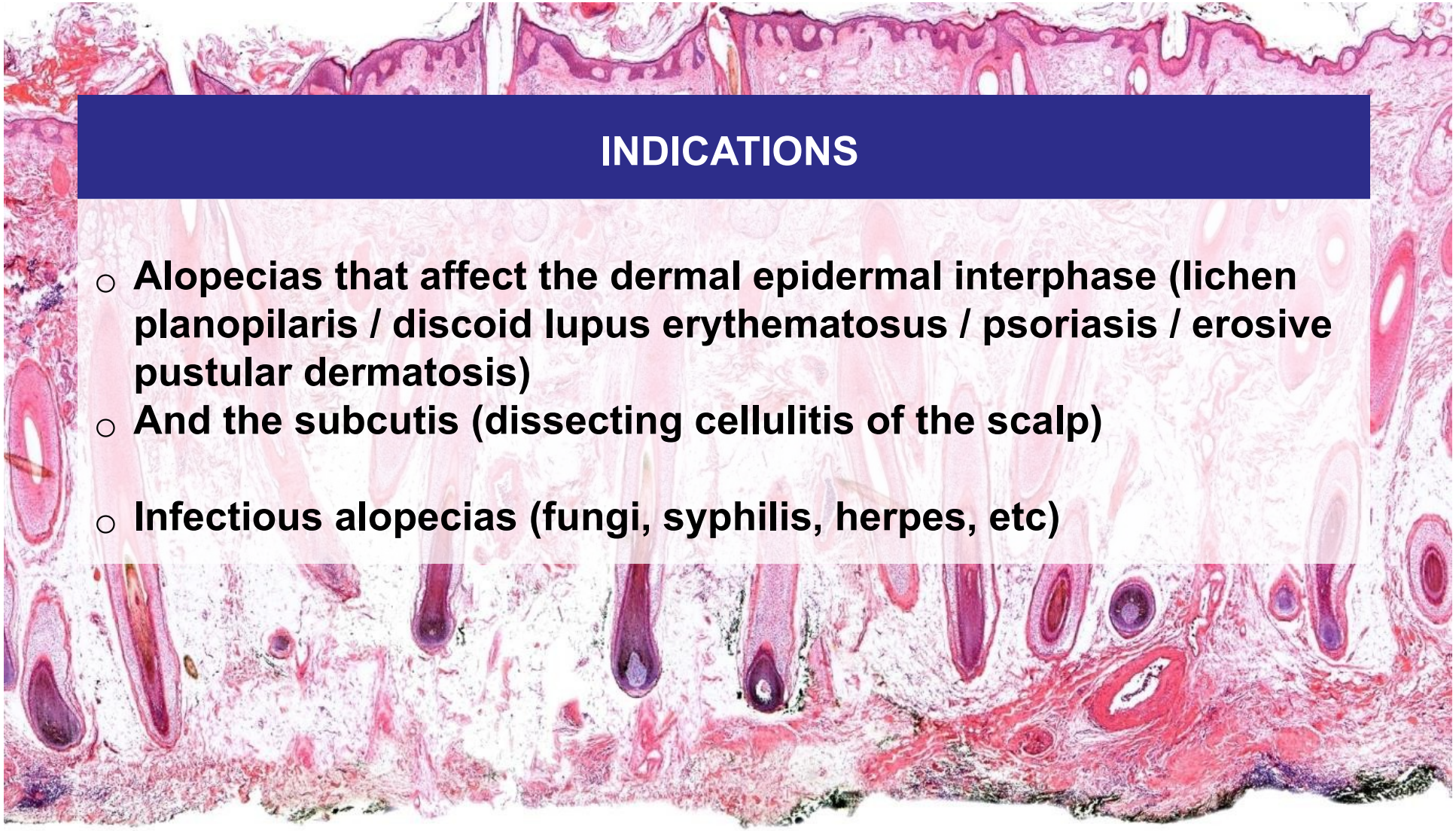
ADVANTAGES

- Easy to perform / Interpret
- Good representation of the dermoepidermic interphase

DISADVANTAGES

- Few hair follicles and majority in oblique section
- Difficult to standardize and not suited for quantitative studies

WHEN IS IT BEST TO USE A VERTICAL SECTION?

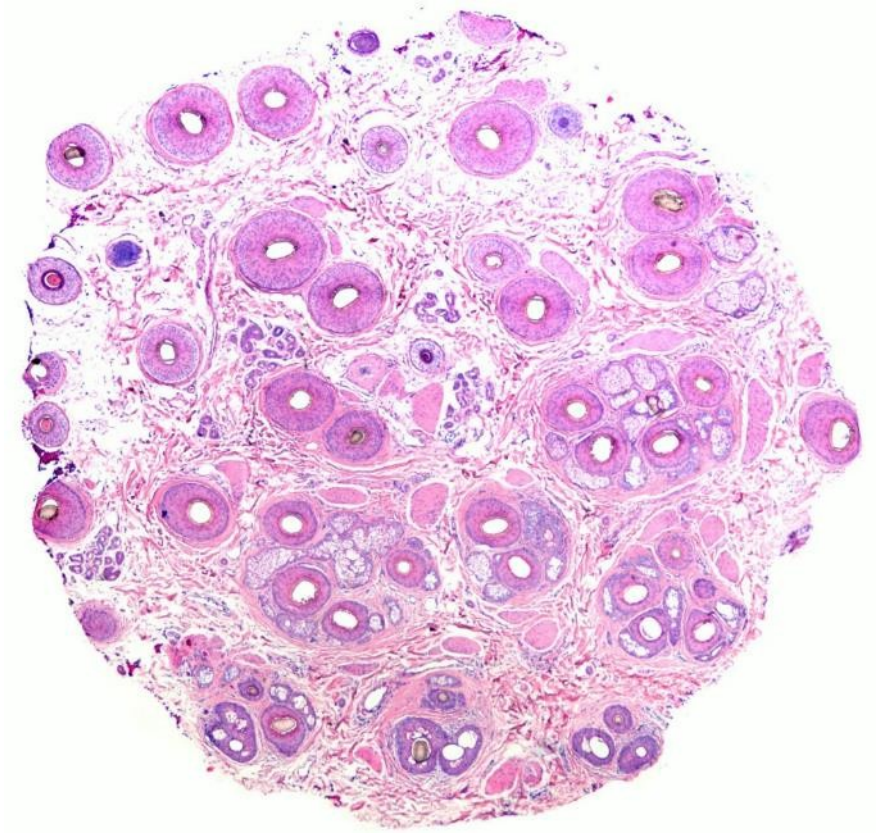


INDICATIONS

- Alopecias that affect the dermal epidermal interphase (lichen planopilaris / discoid lupus erythematosus / psoriasis / erosive pustular dermatosis)
- And the subcutis (dissecting cellulitis of the scalp)

- Infectious alopecias (fungi, syphilis, herpes, etc)

HORIZONTAL (TRANSVERSAL) SECTION



ADVANTAGES

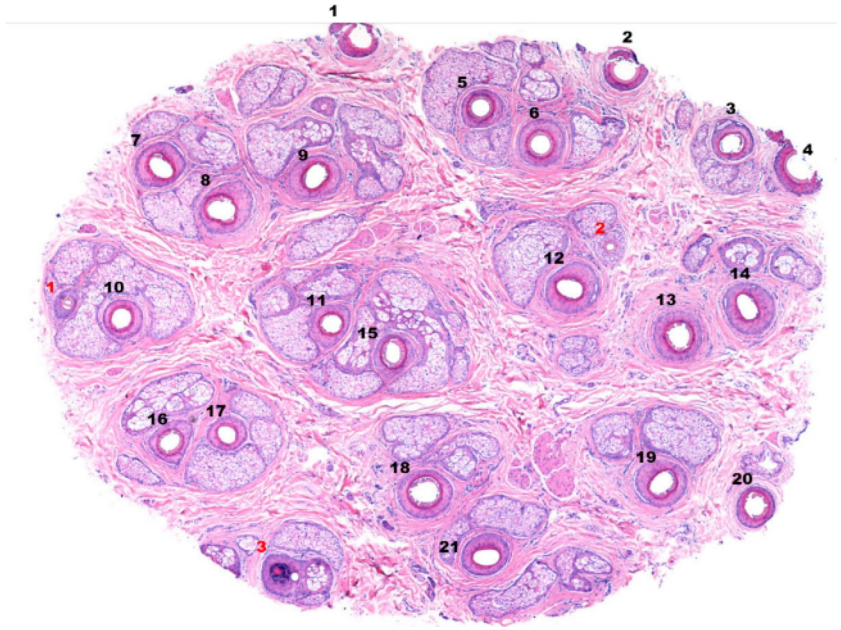
All follicles are seen on only one plane

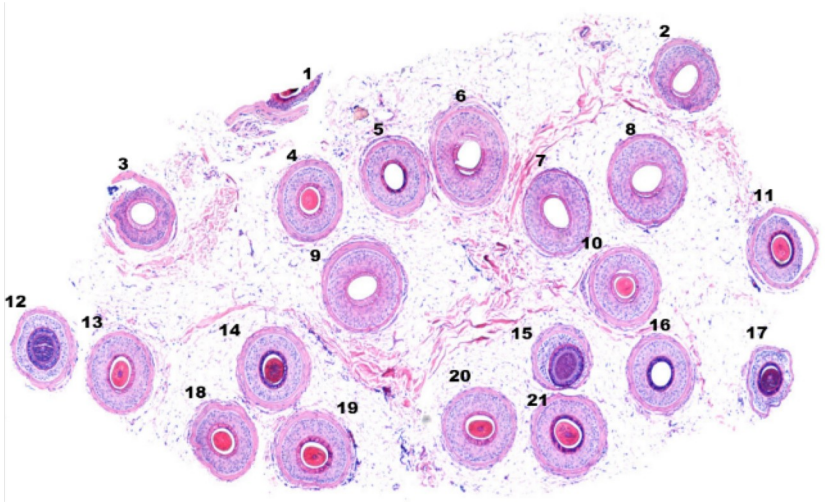
Easy to standardize and useful for morphometric studies

DISADVANTAGES

Difficult to perform and interpret

Poor representation of the dermal epidermal junction



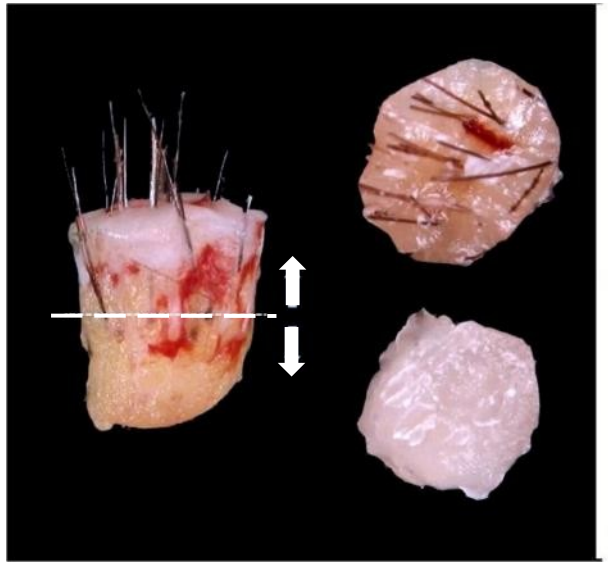


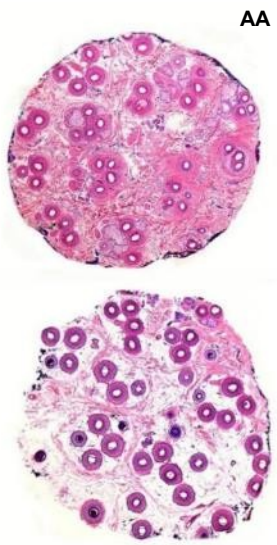
INDICATIONS

Morphometric studies that require quantitative and comparative analysis such as:

- **Androgenetic alopecia**
- **Chronic telogen effluvium**
- **Alopecia Areata**

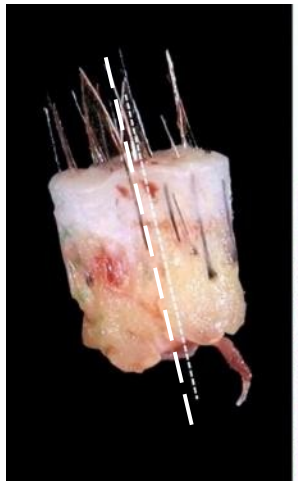
SUMMARY

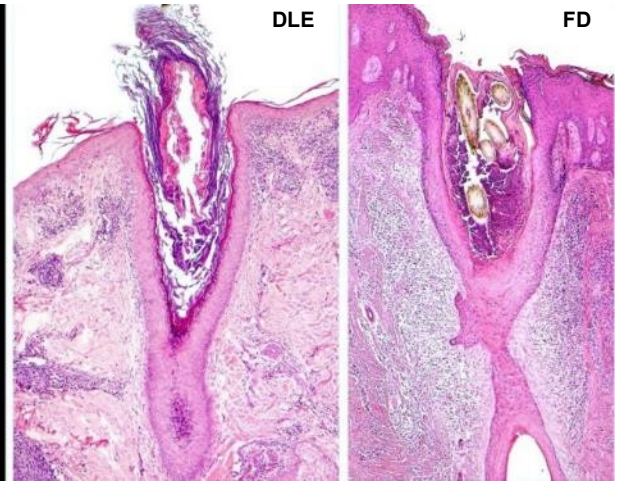




- Androgenetic alopecia
- Telogen effluvium
- Alopecia areata

USE HORIZONTAL SECTIONS





- Scarring alopecias
- Infectious type alopecias

USE VERTICAL SECTIONS OR BOTH

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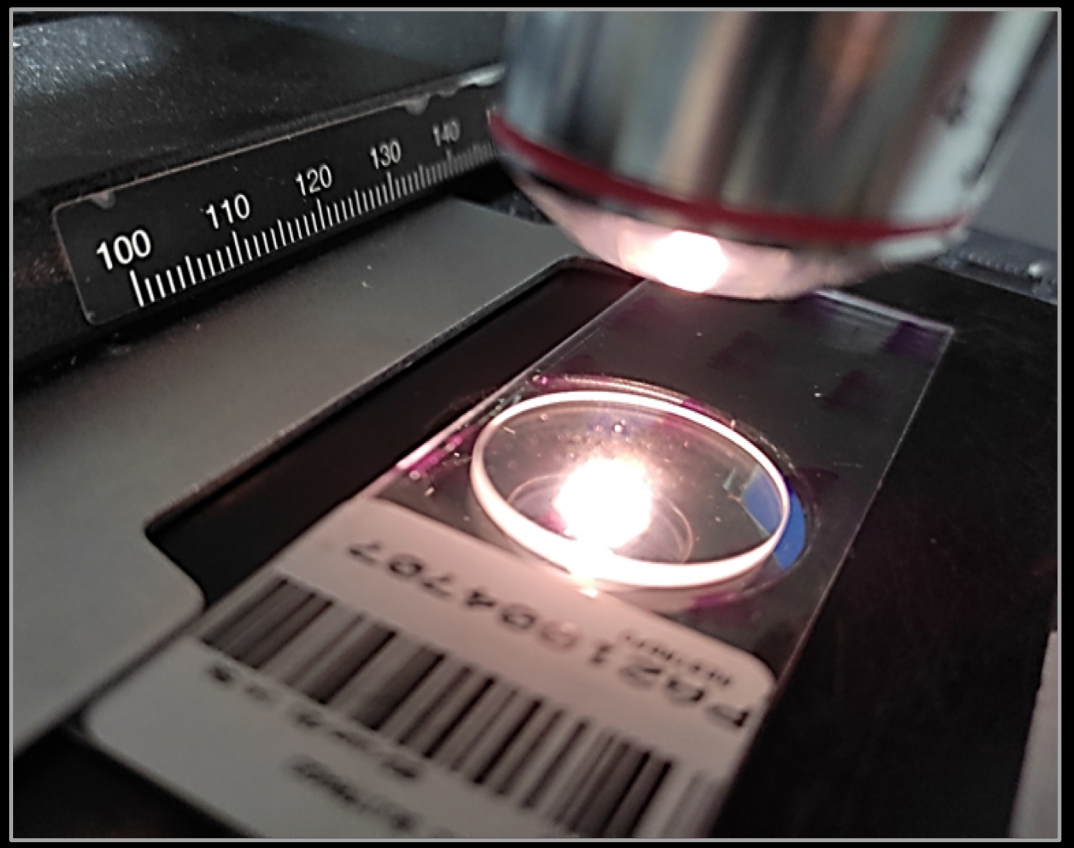
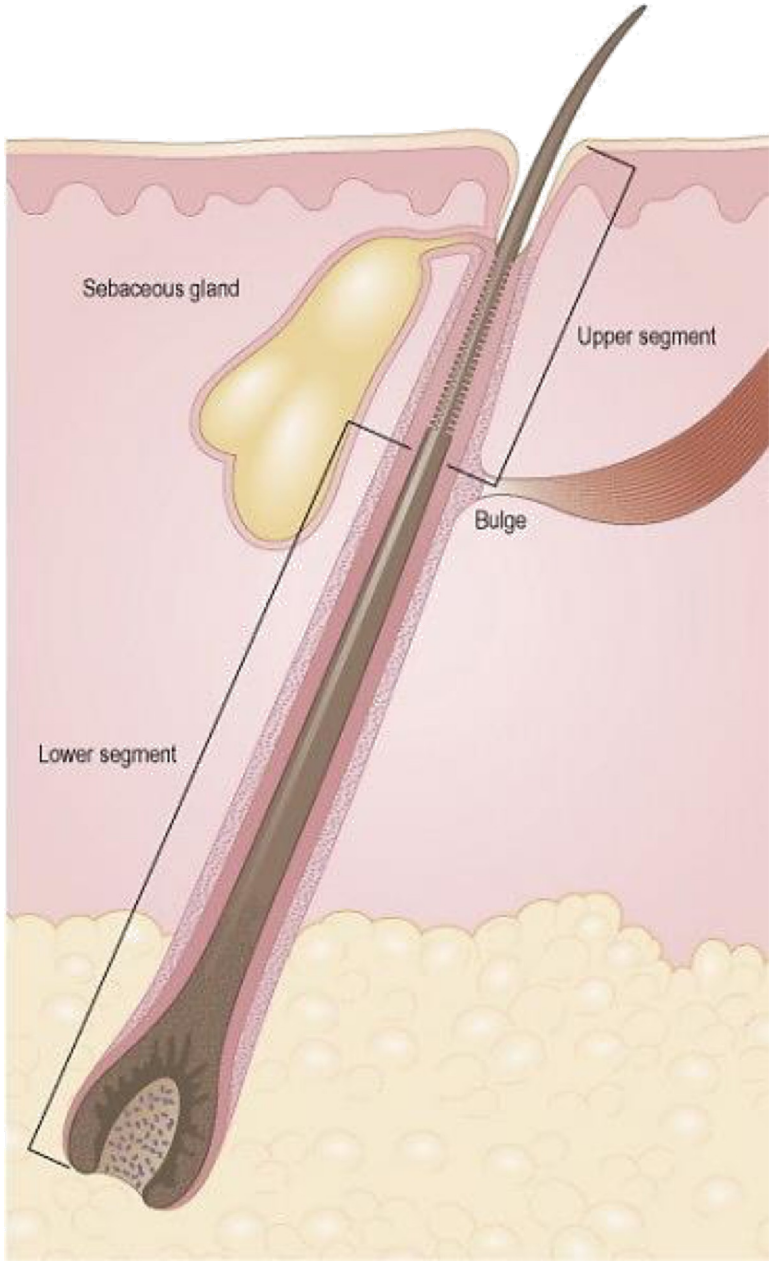


NORMAL HAIR FOLLICLE ANATOMY

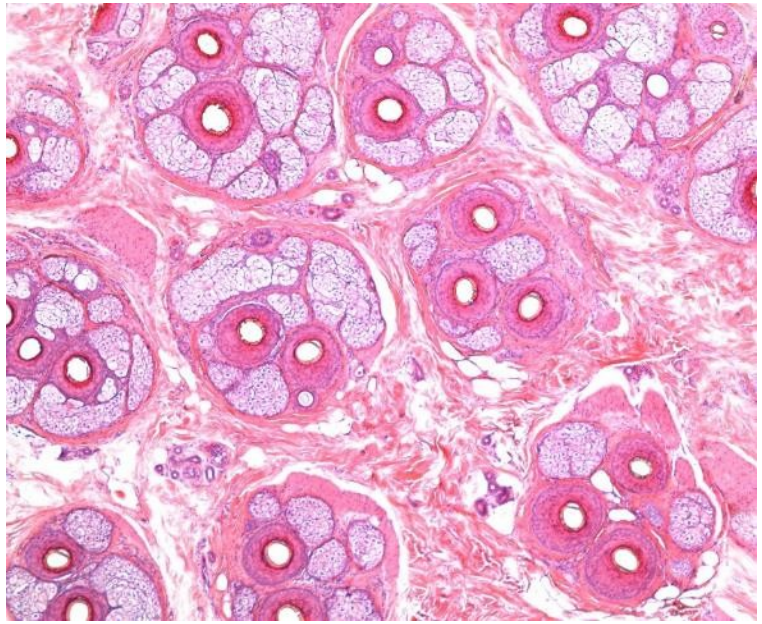


UPPER AND LOWER SEGMENTS

The hair follicle can be divided into two distinct segments.

- **The upper portion is very stable.**
- **The lower portion undergoes considerable morphological change according to its stage in the hair cycle.**

NORMAL HAIR FOLLICLE ANATOMY

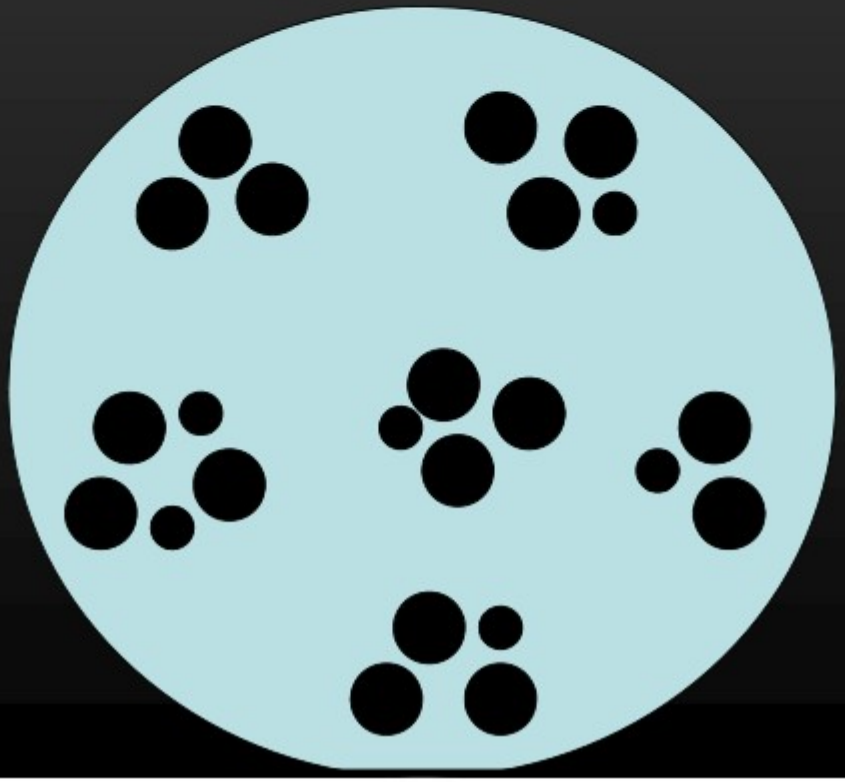


UPPER SEGMENT

FOLLICULAR UNITS

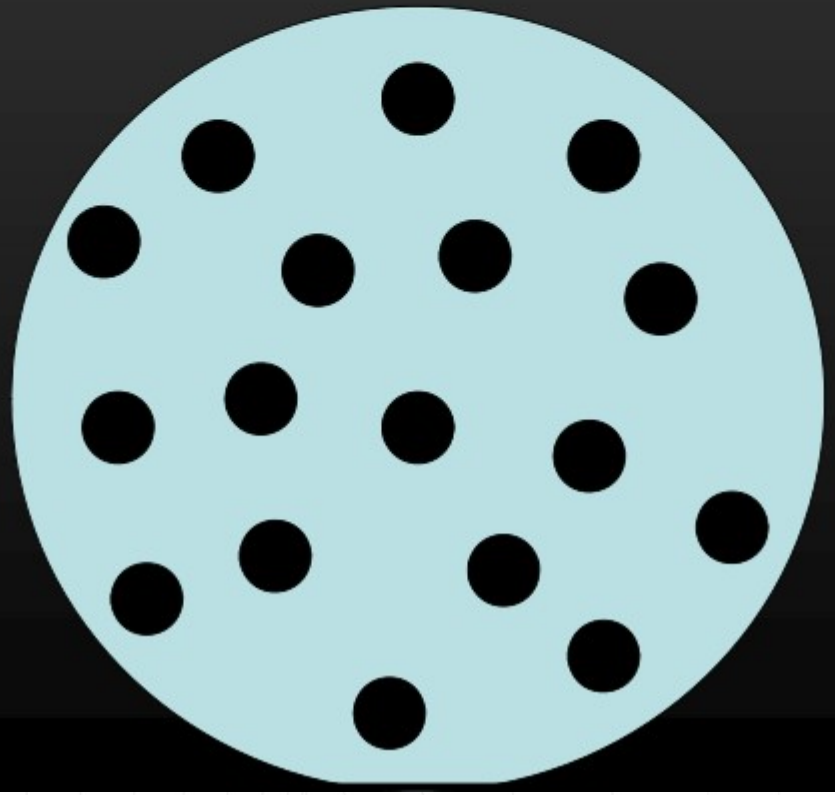
Horizontal sections of the upper segment show that hair follicles are grouped forming anatomic structures known as follicular units, which are composed of hairs, sebaceous glands, and arrector pili muscles.

- In the mid and upper dermis, groups of follicles become segregated into *follicular units*.
- Each follicular unit contains about 2-5 terminal hairs and 0-2 vellus hairs.



Follicular units

- In the superficial fat and lower dermis, the follicles are spaced apart fairly evenly.



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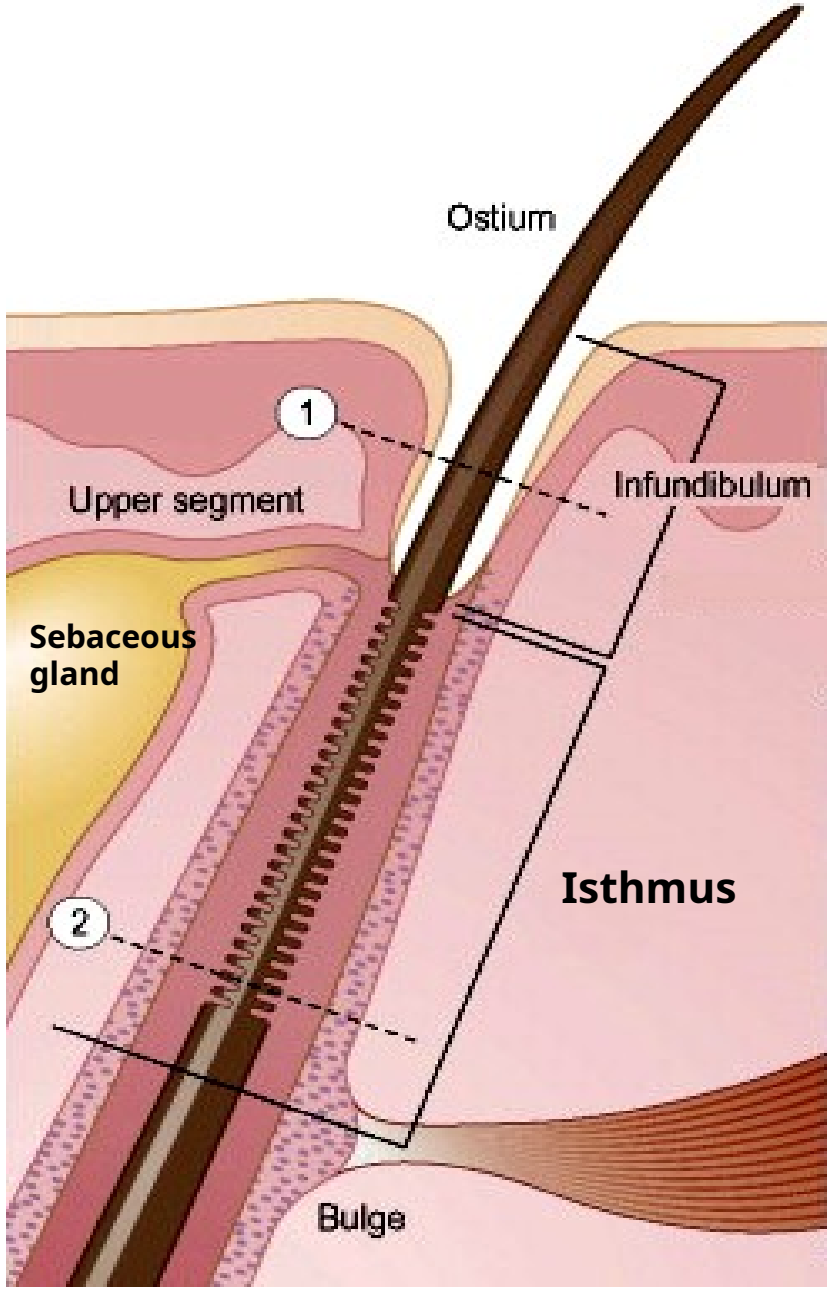


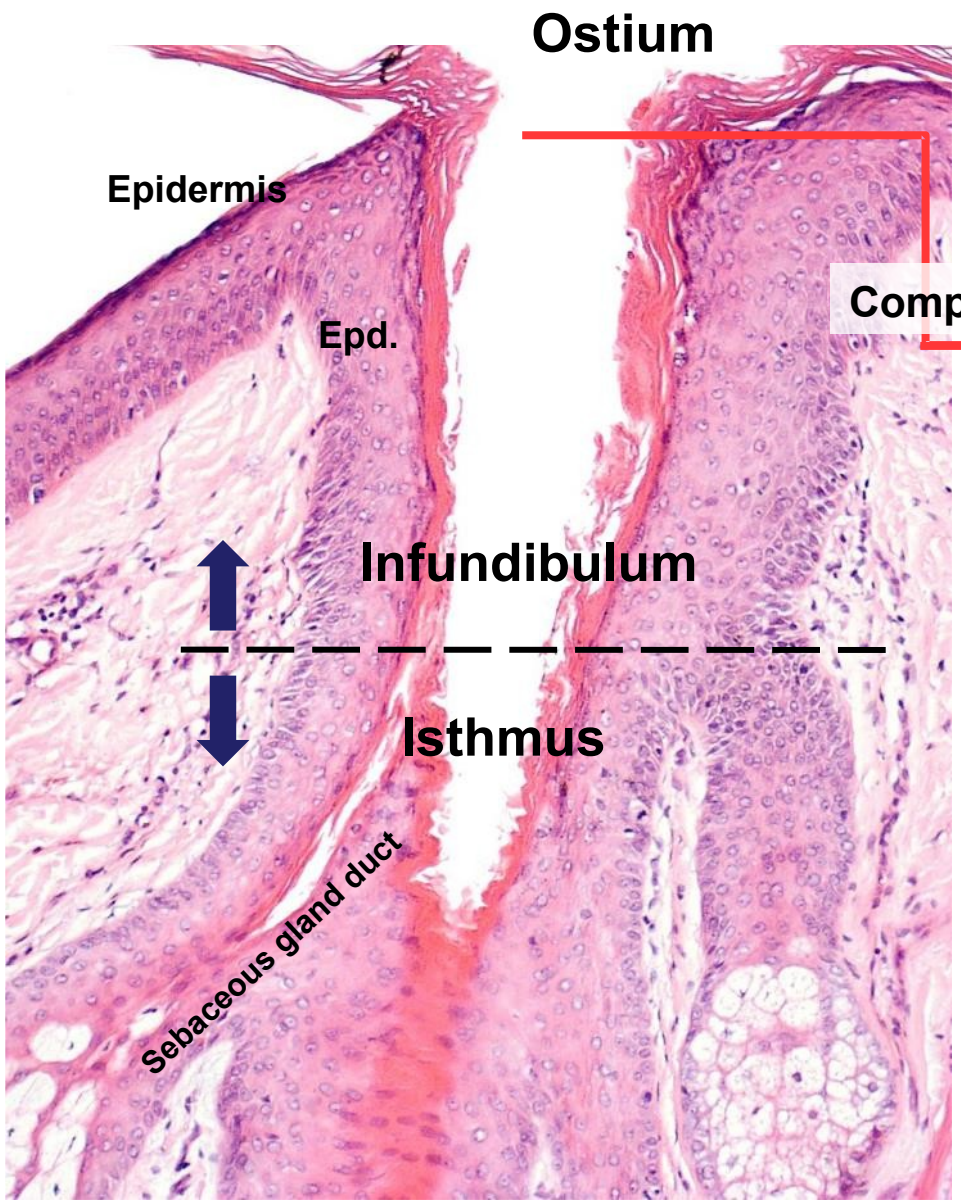
UPPER SEGMENT OSTIUM, INFUNDIBULUM & ISTHMUS

The upper segment of the hair follicle consists of 2 parts:

- **The infundibulum extends from the ostium downwards to the opening of the sebaceous gland duct.**
- **The isthmus continues from the opening of the sebaceous gland duct to the site of attachment to where the arrector pili muscle attaches to the bulge.**

UPPER SEGMENT -- OSTIUM AND INFUNDIBULUM

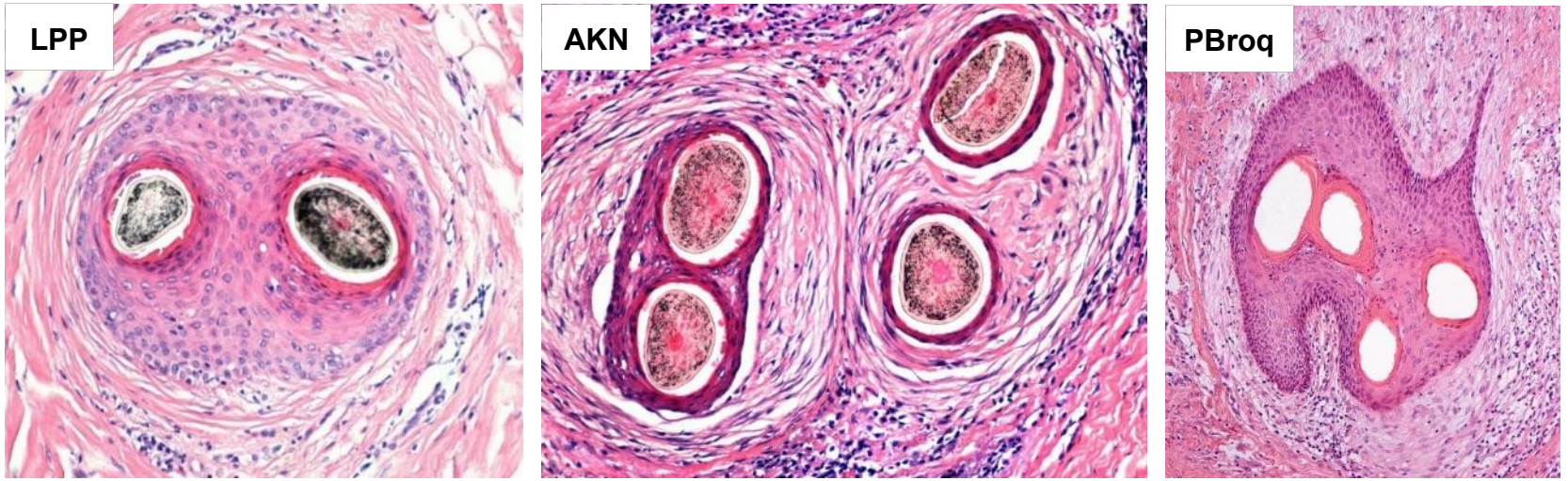
NORMAL HAIR FOLLICLE ANATOMY



Compound follicles

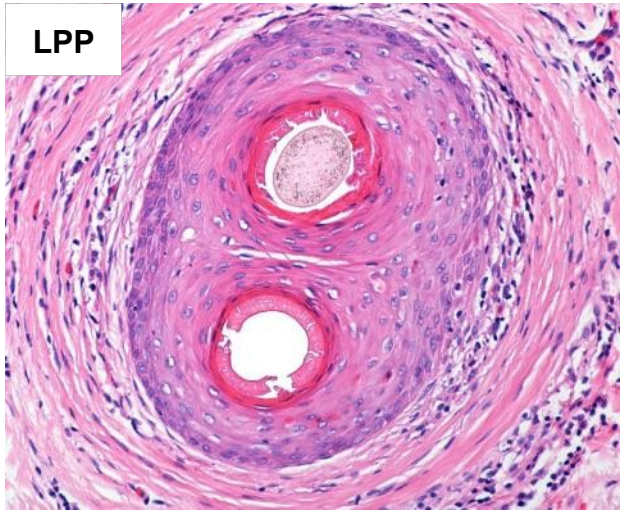
NORMAL COMPOUND FOLLICLES. INFUNDIBULUM.

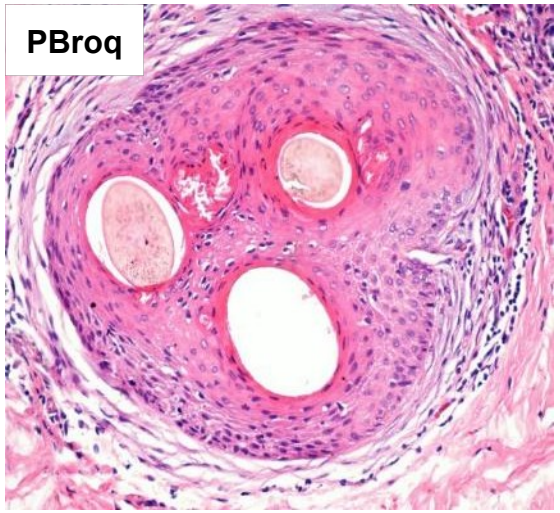
COMPOUND FOLLICLES IN CICATRICIAL ALOPECIA – ISTHMUS.

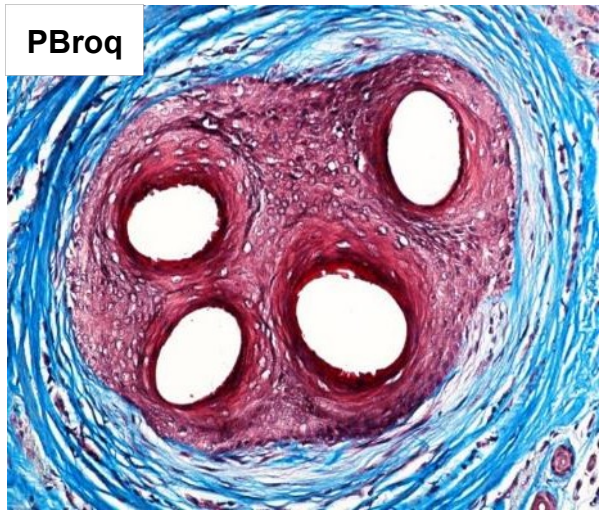


COMPOUND FOLLICLES IN LYMPHOCYTE-MEDIATED PRIMARY CICATRICIAL ALOPECIA

LYMPHOCYTE-MEDIATED PRIMARY CICATRICIAL ALOPECIA







COMPOUND FOLLICLES IN NEUTROPHIL-MEDIATED PRIMARY CICATRICIAL ALOPECIA

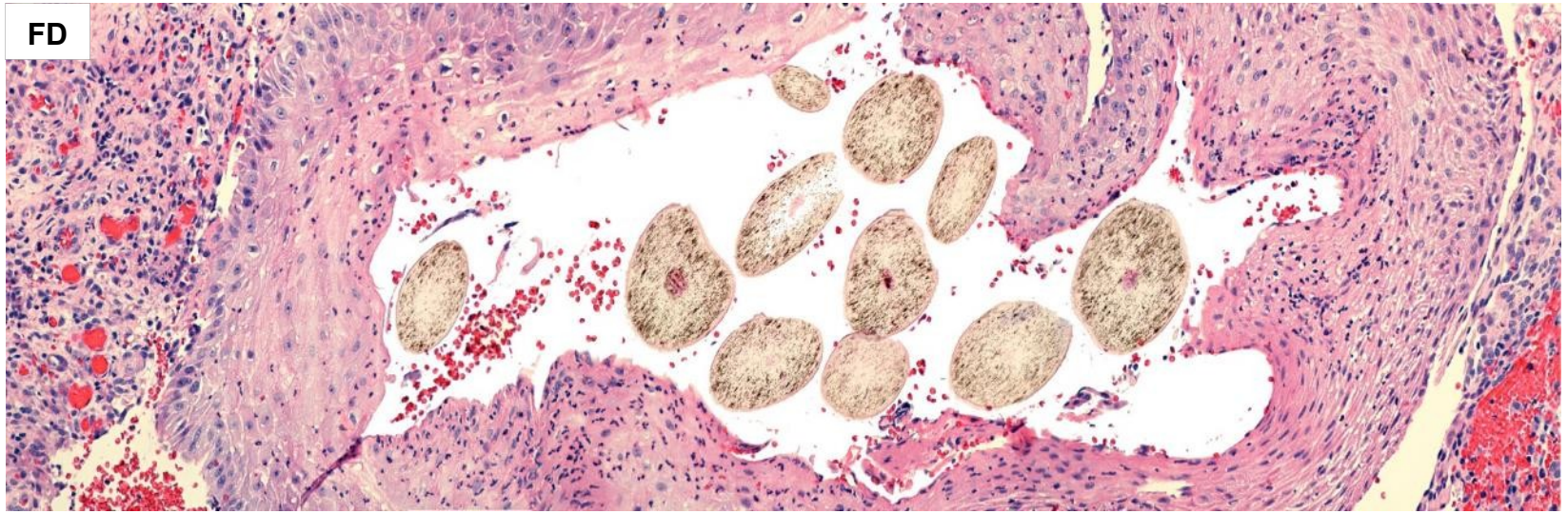
FD

NORMAL HAIR FOLLICLE ANATOMY

AKN

NEUTROPHIL-MEDIATED PRIMARY CICATRICIAL ALOPECIA

FD



COMPOUND FOLLICLES IN CICATRICIAL ALOPECIA

Other diagnostic clues are:
- **'Goggles' in CCA**
- **'Owl eyes' in LPP/FFA**

NORMAL UPPER SEGMENT – INFUNDIBULUM.
COMPOUND FOLLICLES

NORMAL COMPOUND FOLLICLES

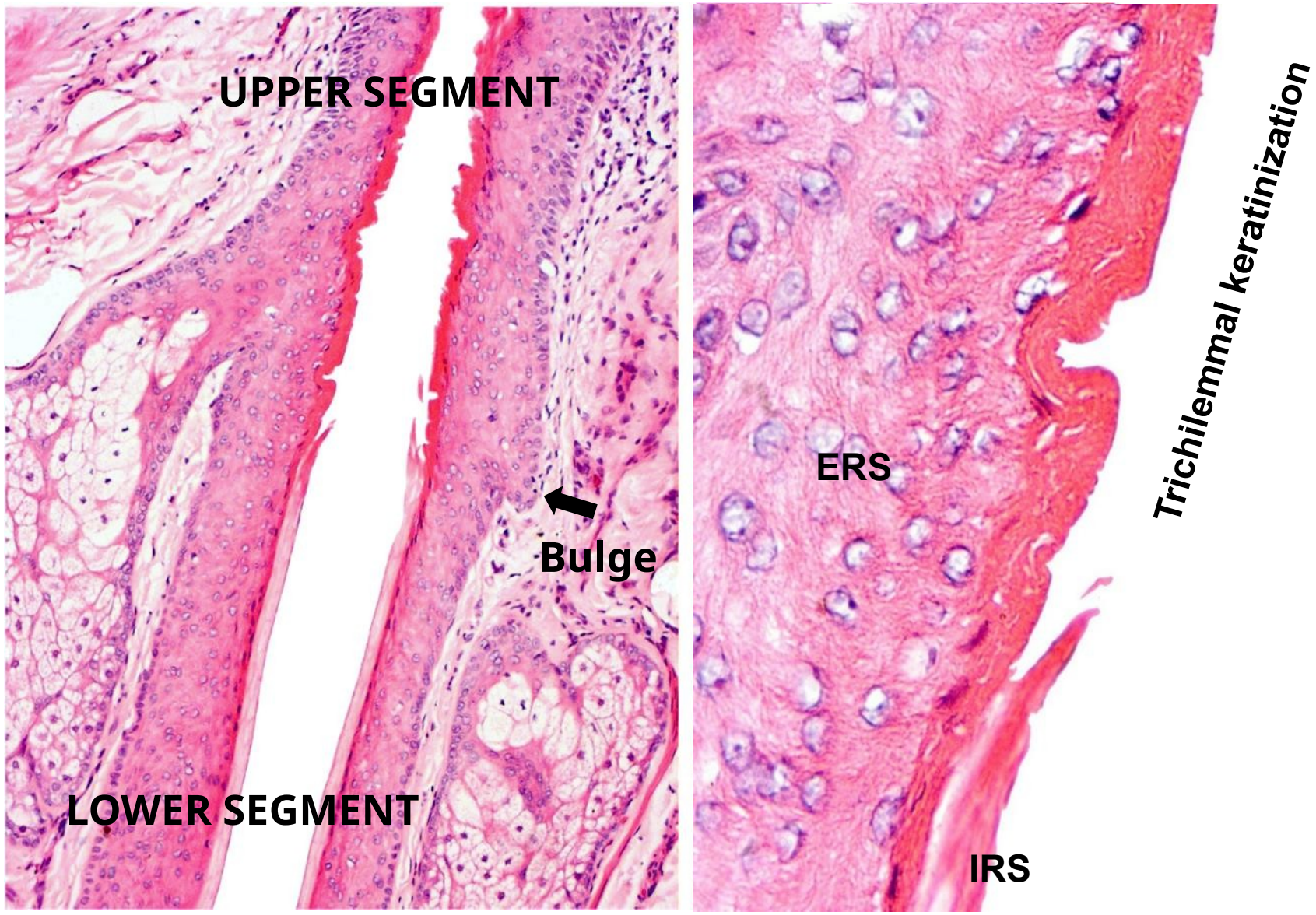
SUMMARY

Always keep in mind that these histopathological clues should not be evaluated at the infundibulum level because it may be confused with normal infundibula, which at this plane of section often forms compound structures.

They always should be evaluated at isthmus or deeper level.

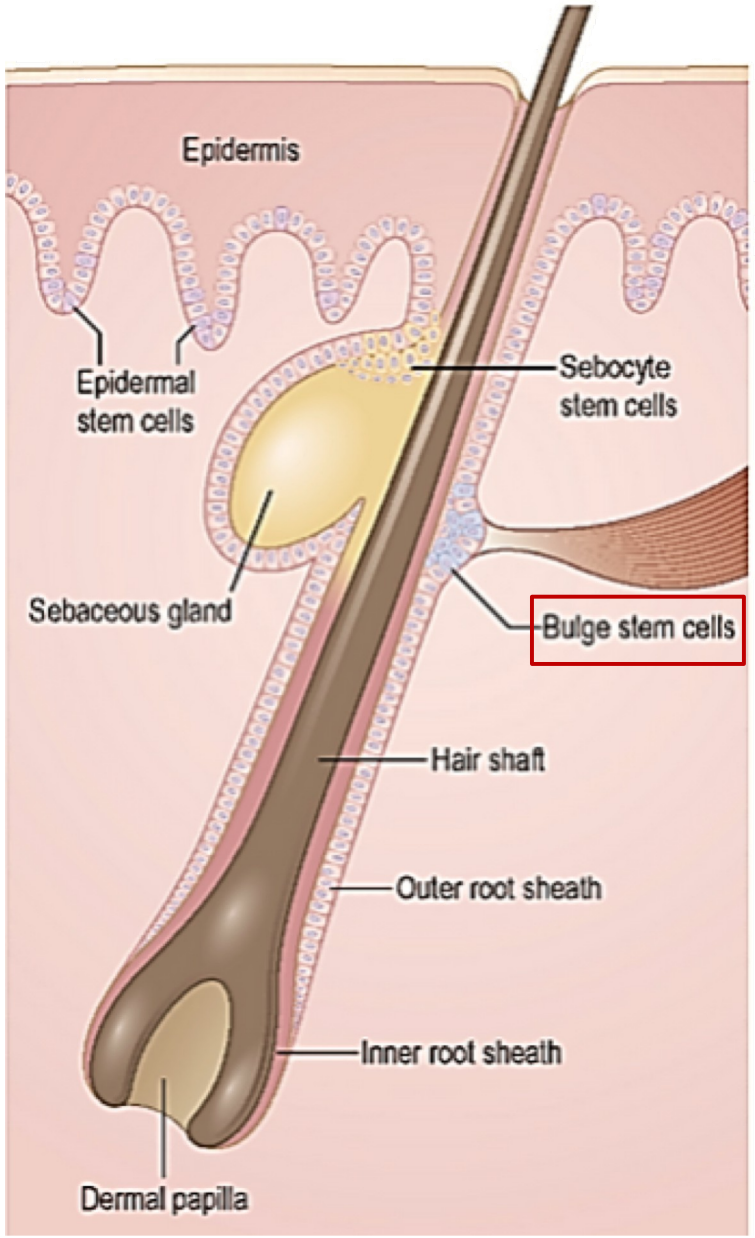
UPPER SEGMENT -- ISTHMUS

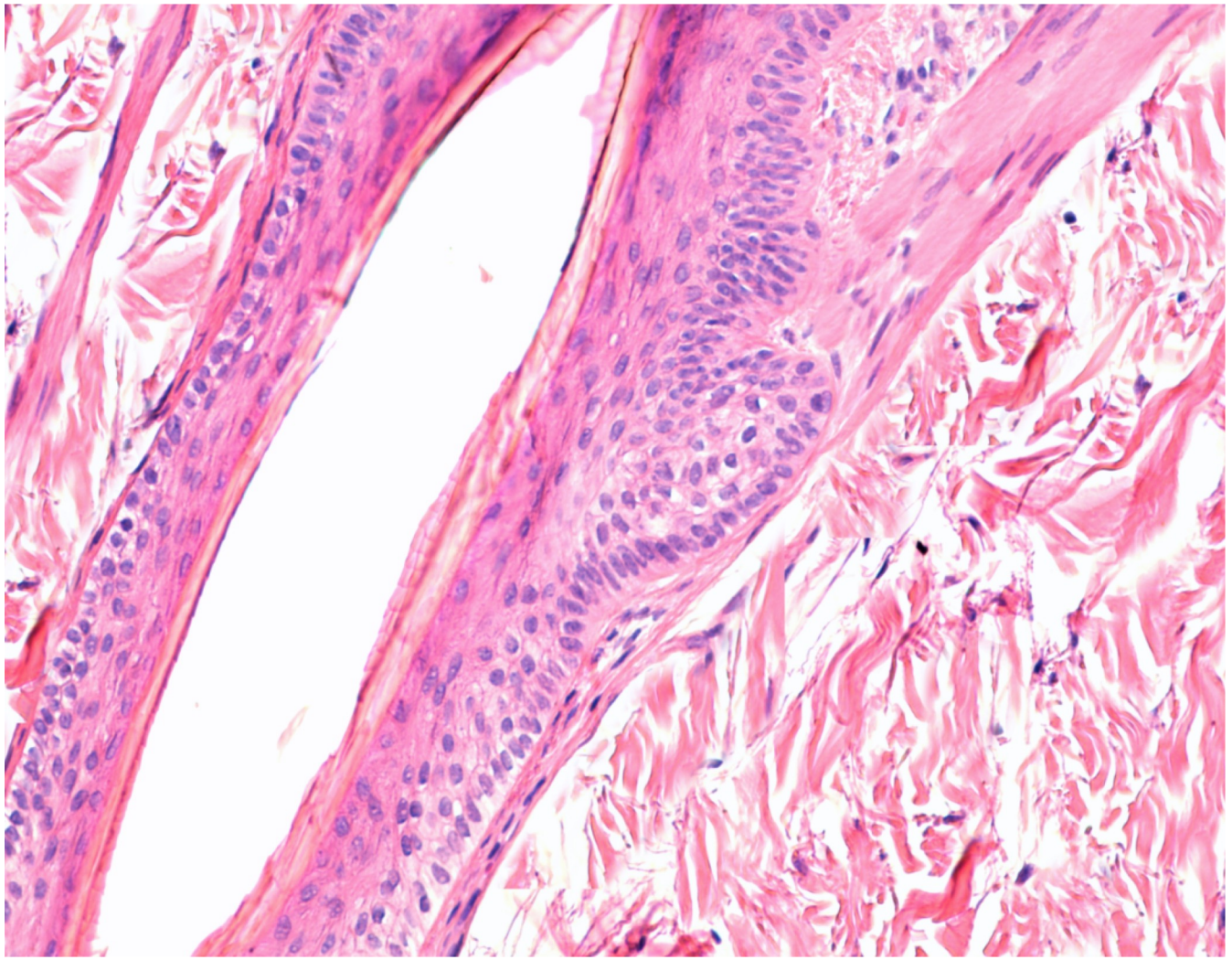
NORMAL TRICHILEMMAL KERATINIZATION - ANAGEN



UPPER SEGMENT – THE BULGE

STEM CELLS

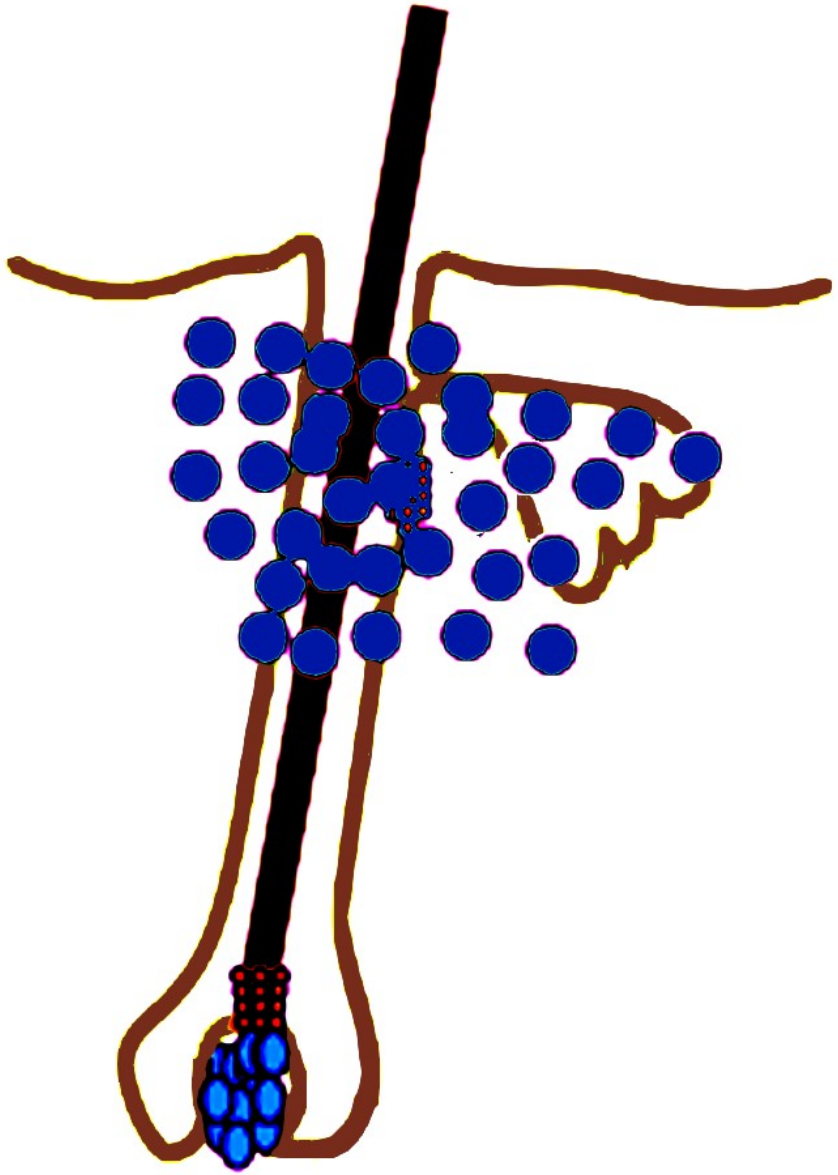




The demarcation between the upper portion and lower portion is the insertion of the arrector pili muscle into the bulge.

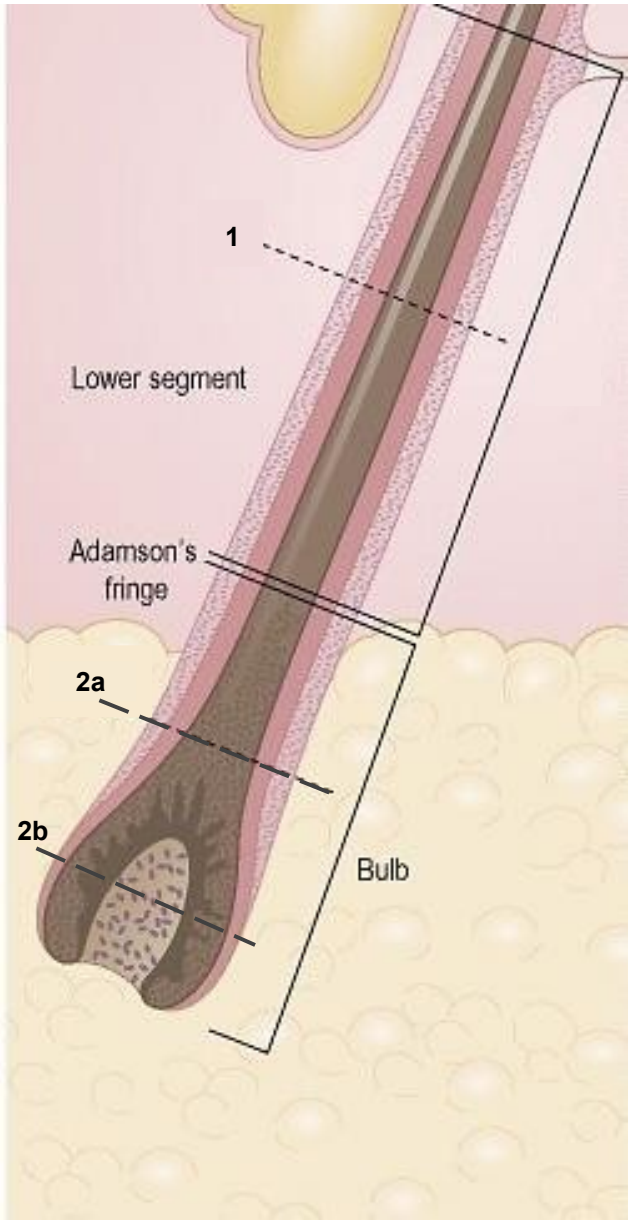
UPPER SEGMENT – THE BULGE

STEM CELLS AND SCARRING ALOPECIA

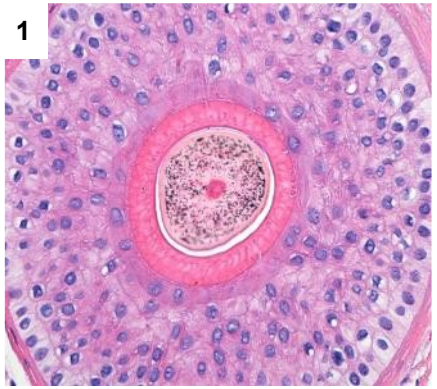


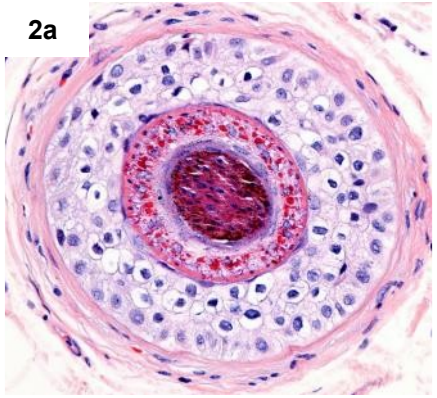
The histopathological hallmark of almost all scarring alopecias are usually the presence of an inflammatory infiltrate surrounding the bulge and isthmus region with loss of stem cells.

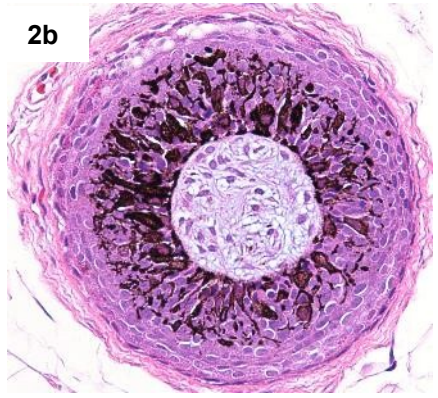
LOWER SEGMENT – STEM AND BULB

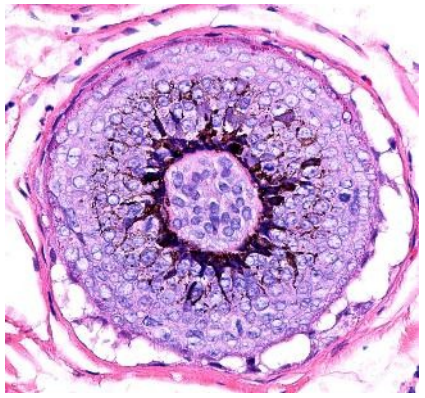


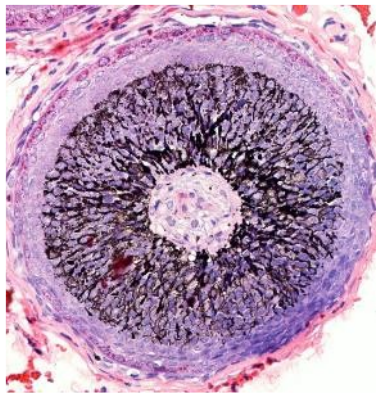
Vertical



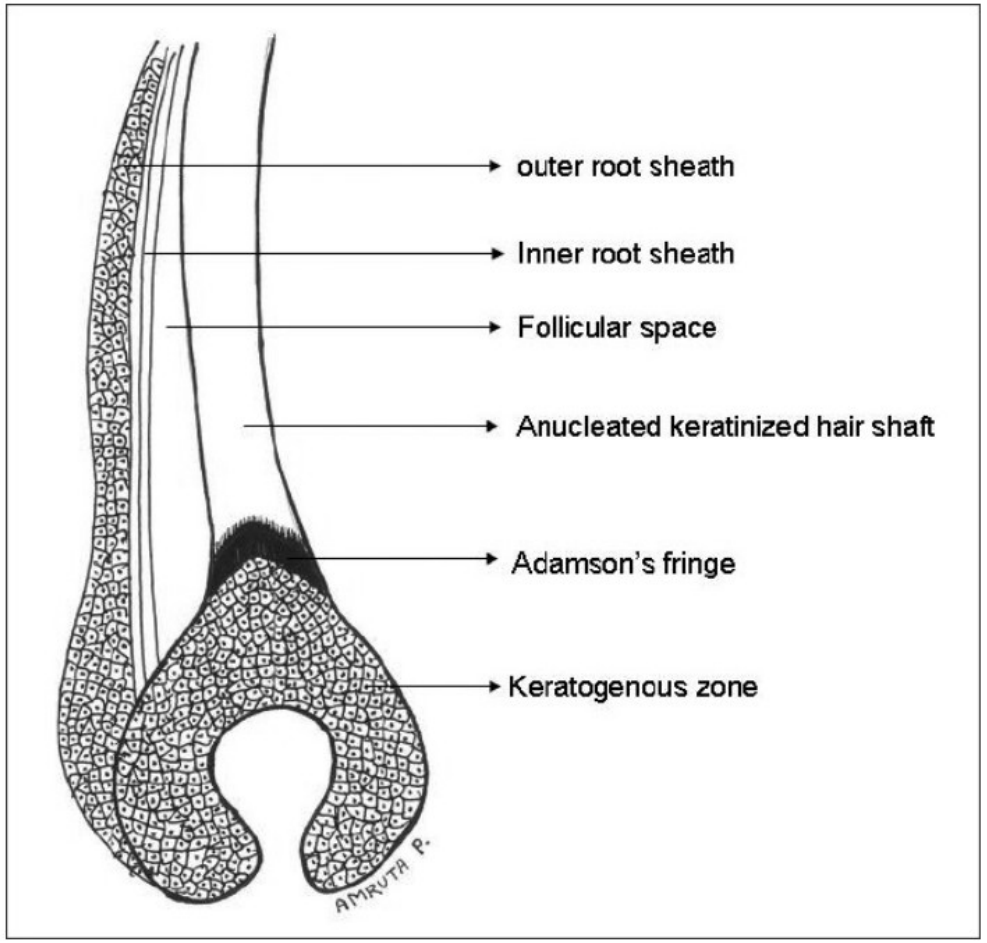








Horizontal



Diagrammatic representation of LS of hair follicle showing Adamson's fringe

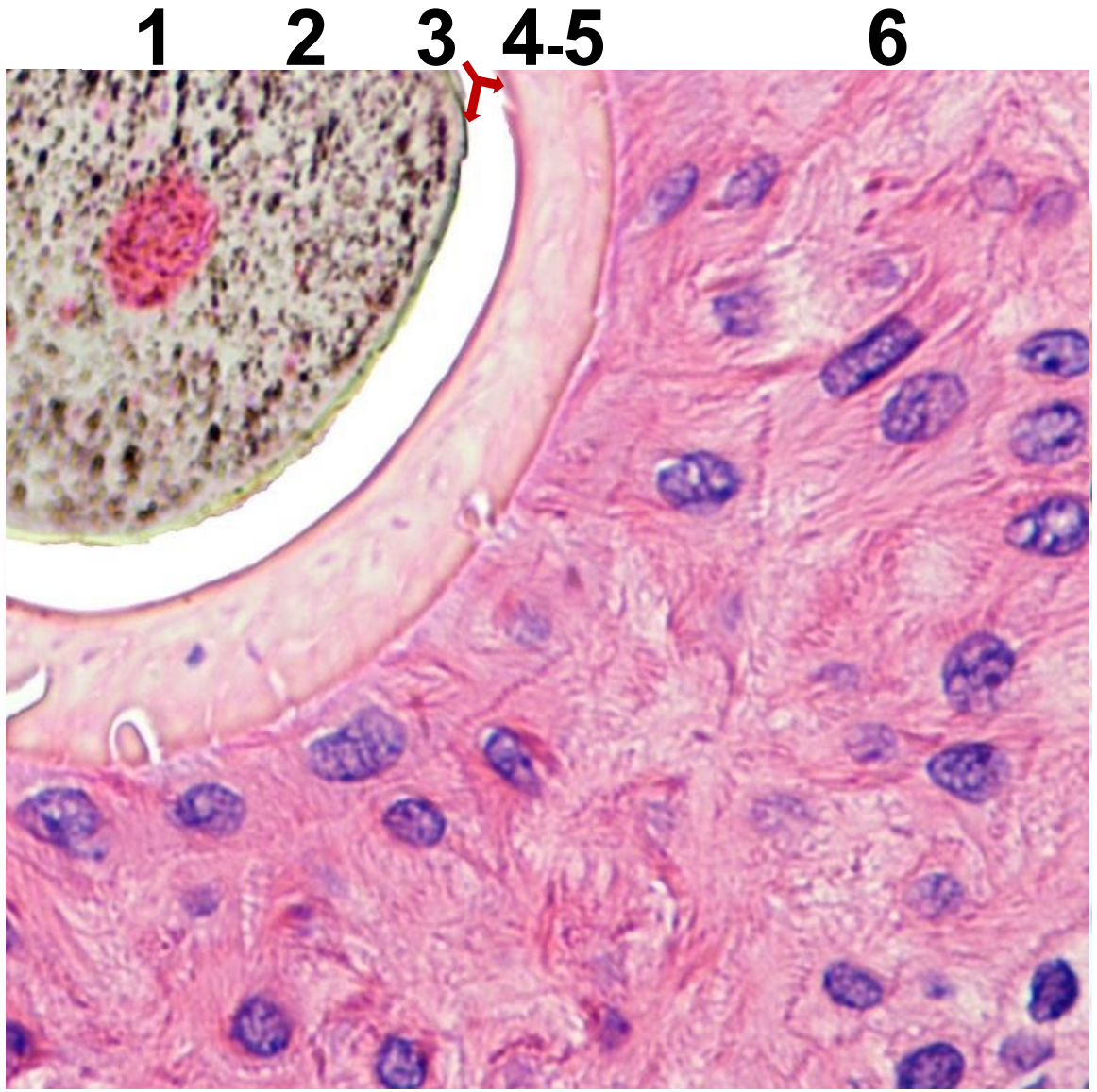
Adamson's fringe is located at the upper margin of the keratogenous zone of the hair follicle where the nucleated hair shaft cornifies completely and gets converted to hard anucleated keratin. It marks also the area of complete keratinization of the cuticle and Henle's layer of the inner root sheath and the beginning of the stem of the follicle.

https://www.researchgate.net/publication/51502290_Adamson%27s_Fringe_Horatio_George_Adamson_and_Kligman%27s_Experiments_and_Observations_on_Tinea_Capitis

LOWER SEGMENT – ABOVE ADAMSON'S FRINGE

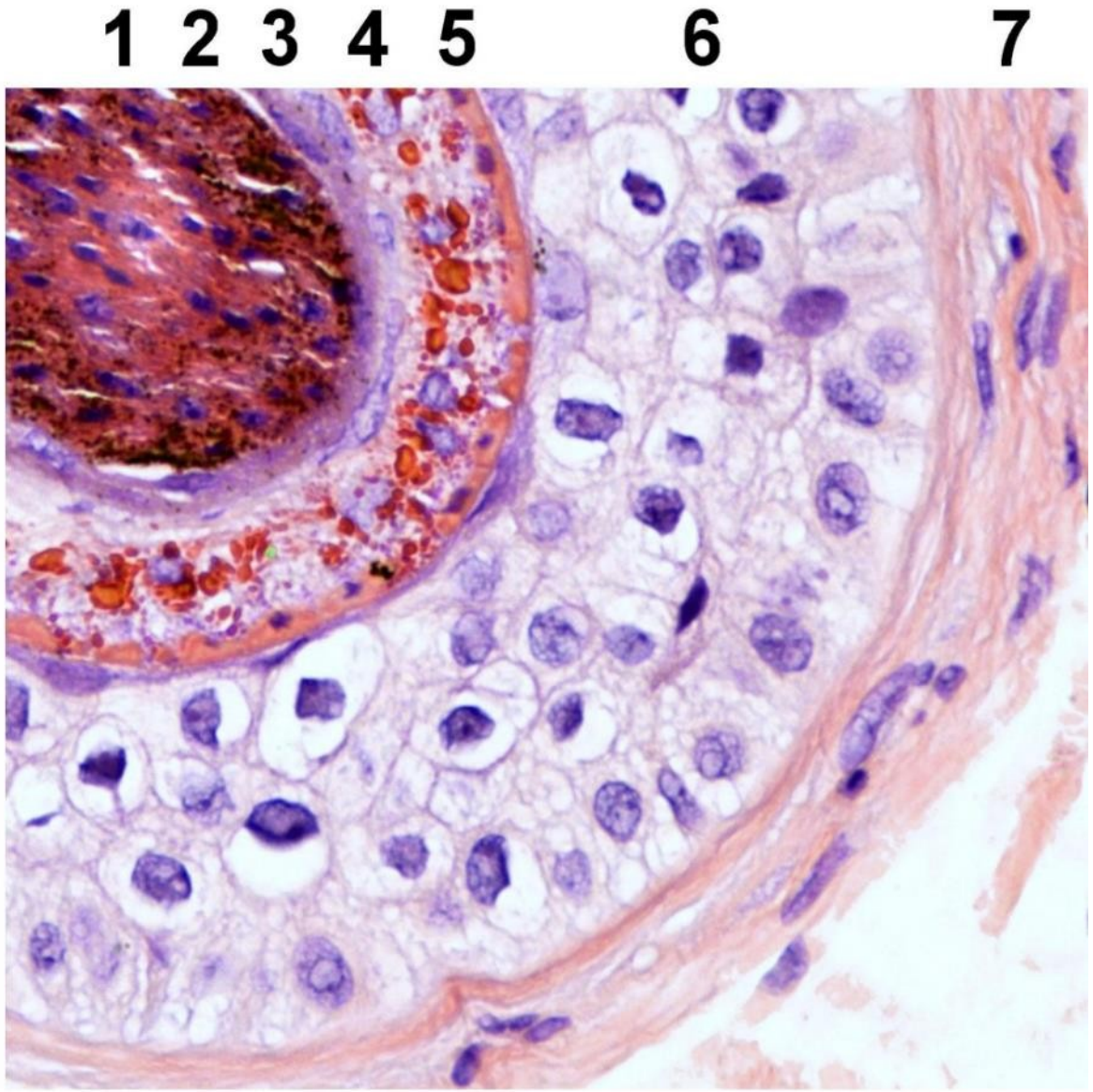
NORMAL HAIR FOLLICLE ANATOMY

1. Medulla
2. Hair shaft cortex
3. Hair shaft and inner root sheath cuticle
4. Inner root sheat
5.
6. Outer root sheath

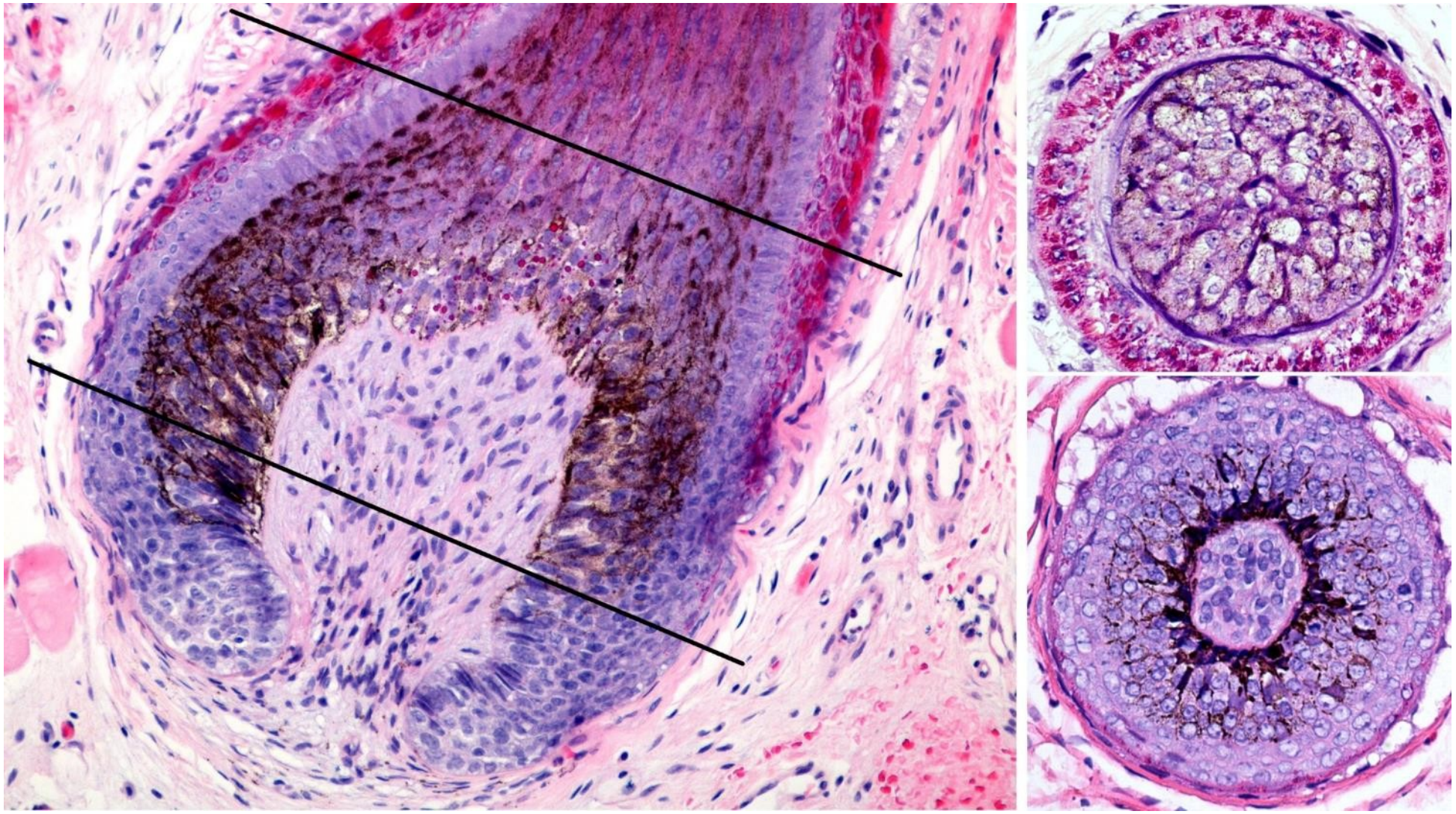


LOWER SEGMENT – BELOW ADAMSON'S FRINGE

1. Medulla
2. Hair shaft cortex
3. Hair shaft and inner root sheath cuticle
4. Huxley's layer
5. Henle's layer
6. Outer root sheath
7. External fibrous layer



LOWER SEGMENT – HAIR BULB



LOWER SEGMENT – HAIR BULB

ALOPECIA AREATA

httpwww.ecodiy.orgimagesbee%20swarm.JPG

LOWER SEGMENT – HAIR BULB

ALOPECIA AREATA. LATE STAGE

In late alopecia areata stages there could be a remarkable increase in catagen (C), telogen (T), nanogem (N) and miniaturized follicles (MF), with a sparse or absent peribulbar lymphocytic infiltrate (PLI).

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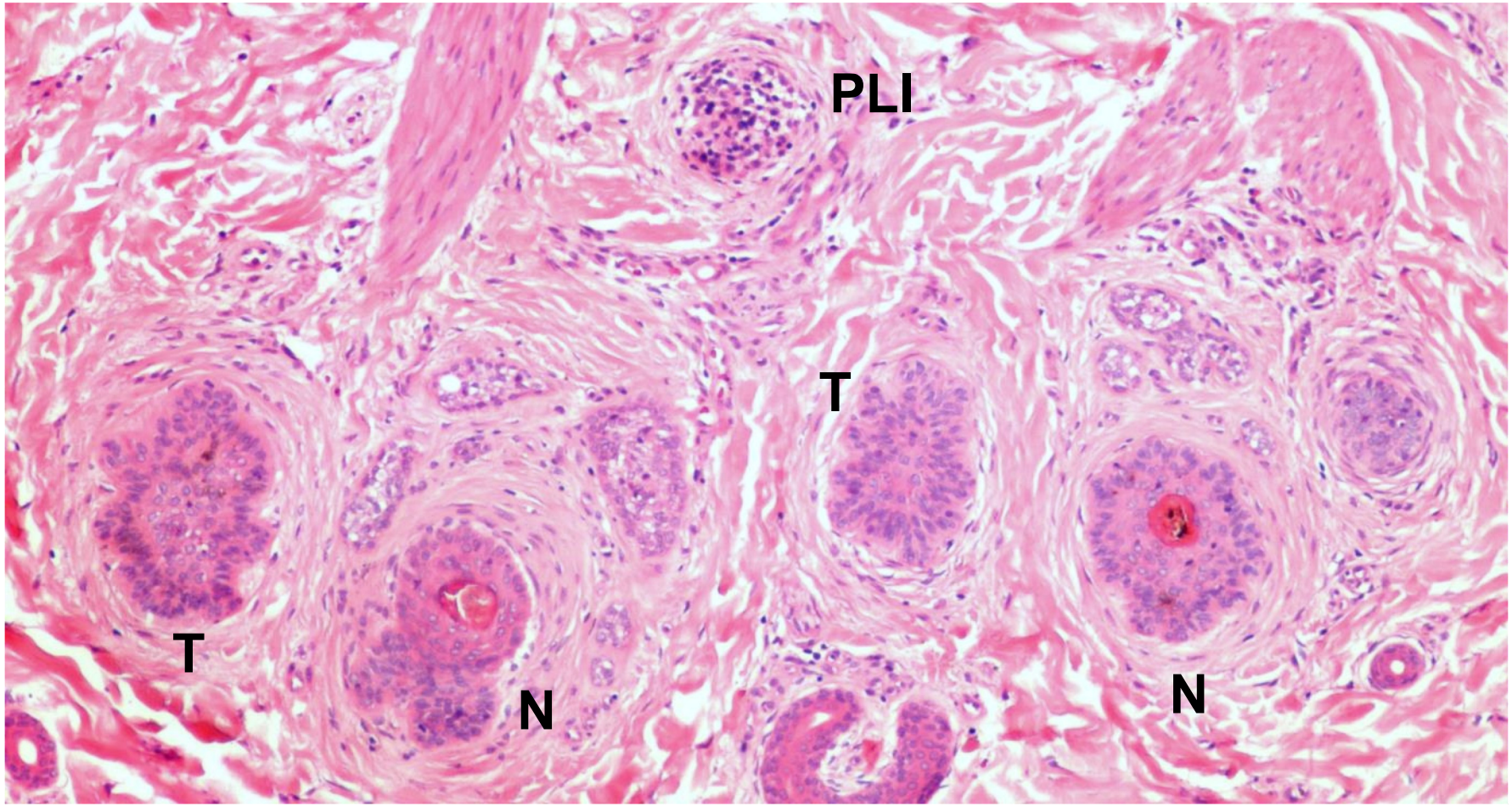

LOWER SEGMENT – HAIR BULB

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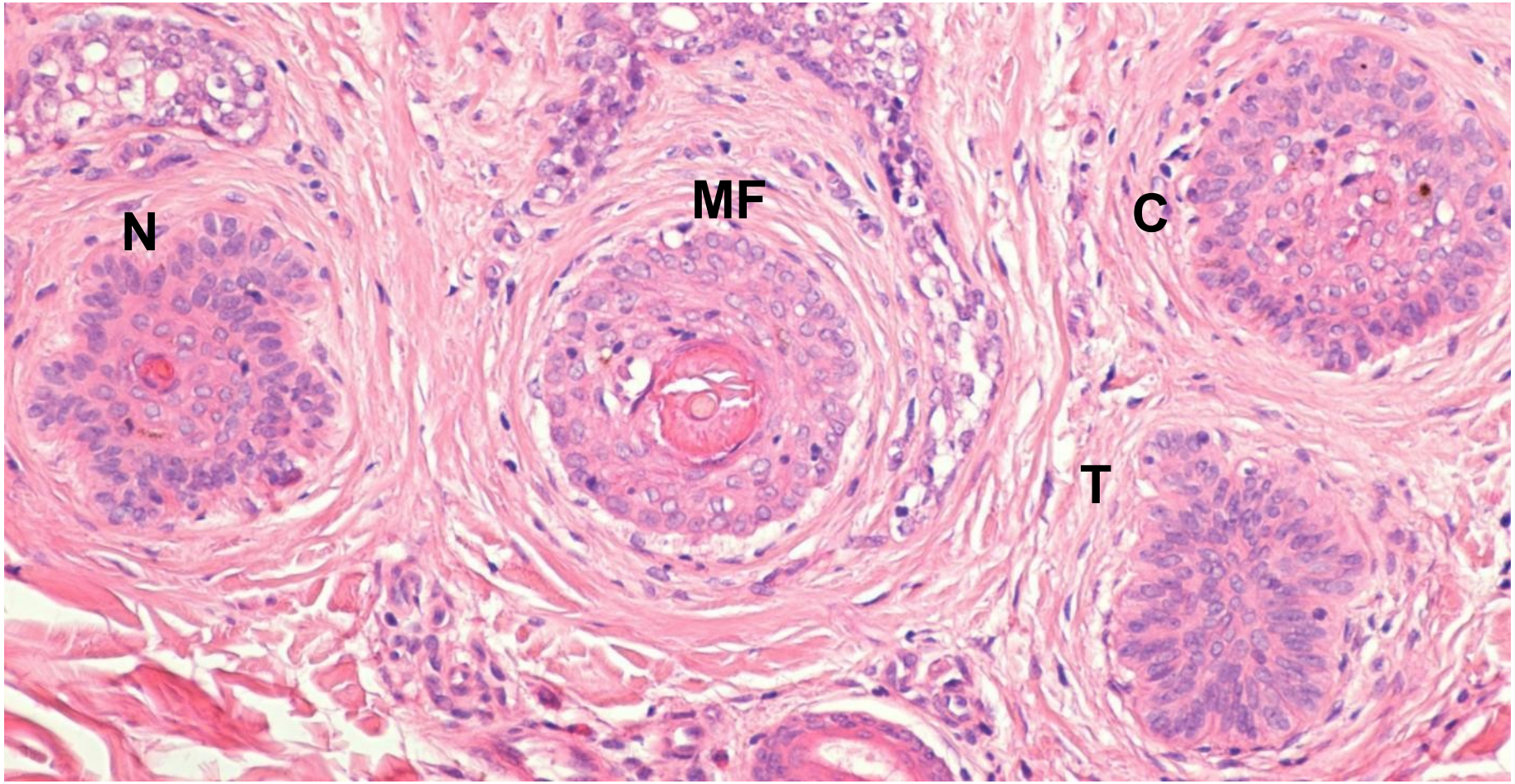

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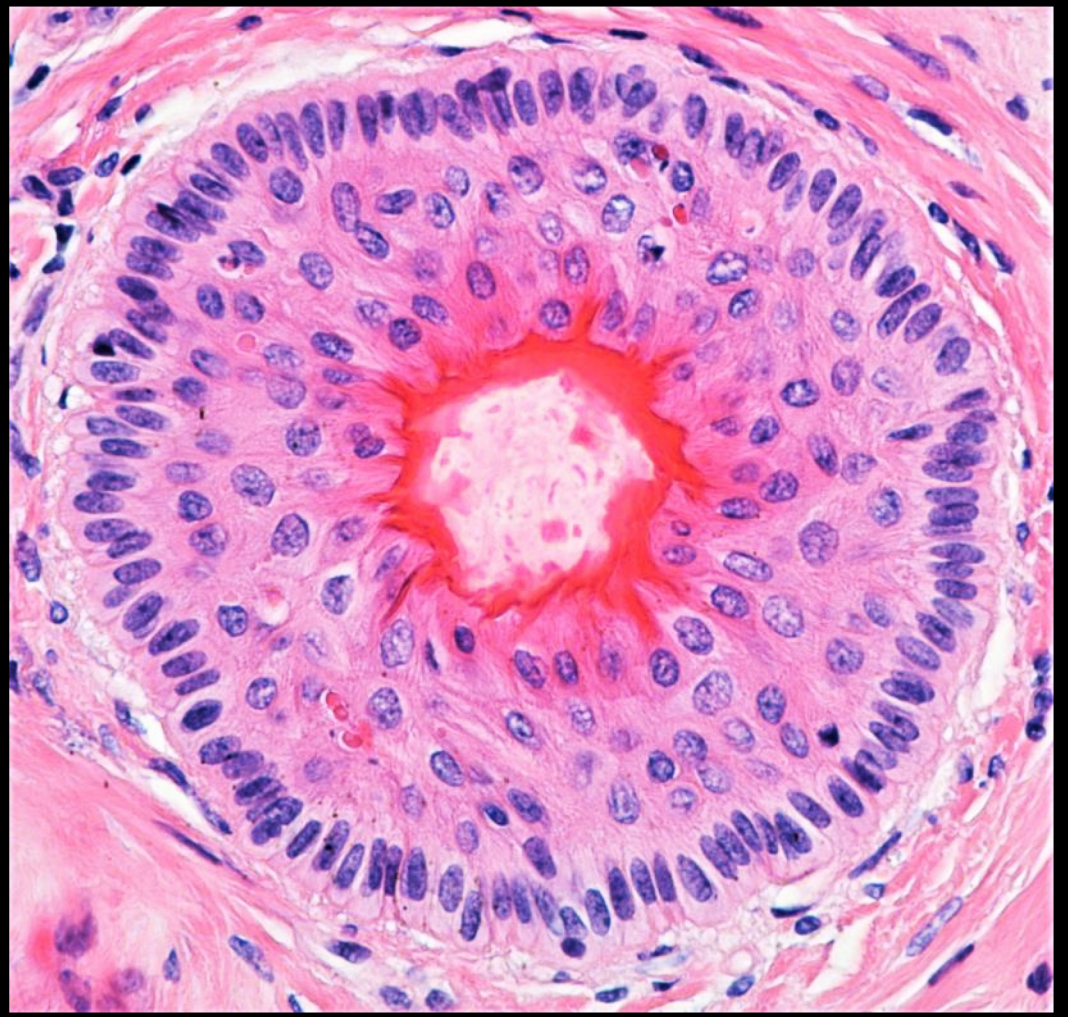
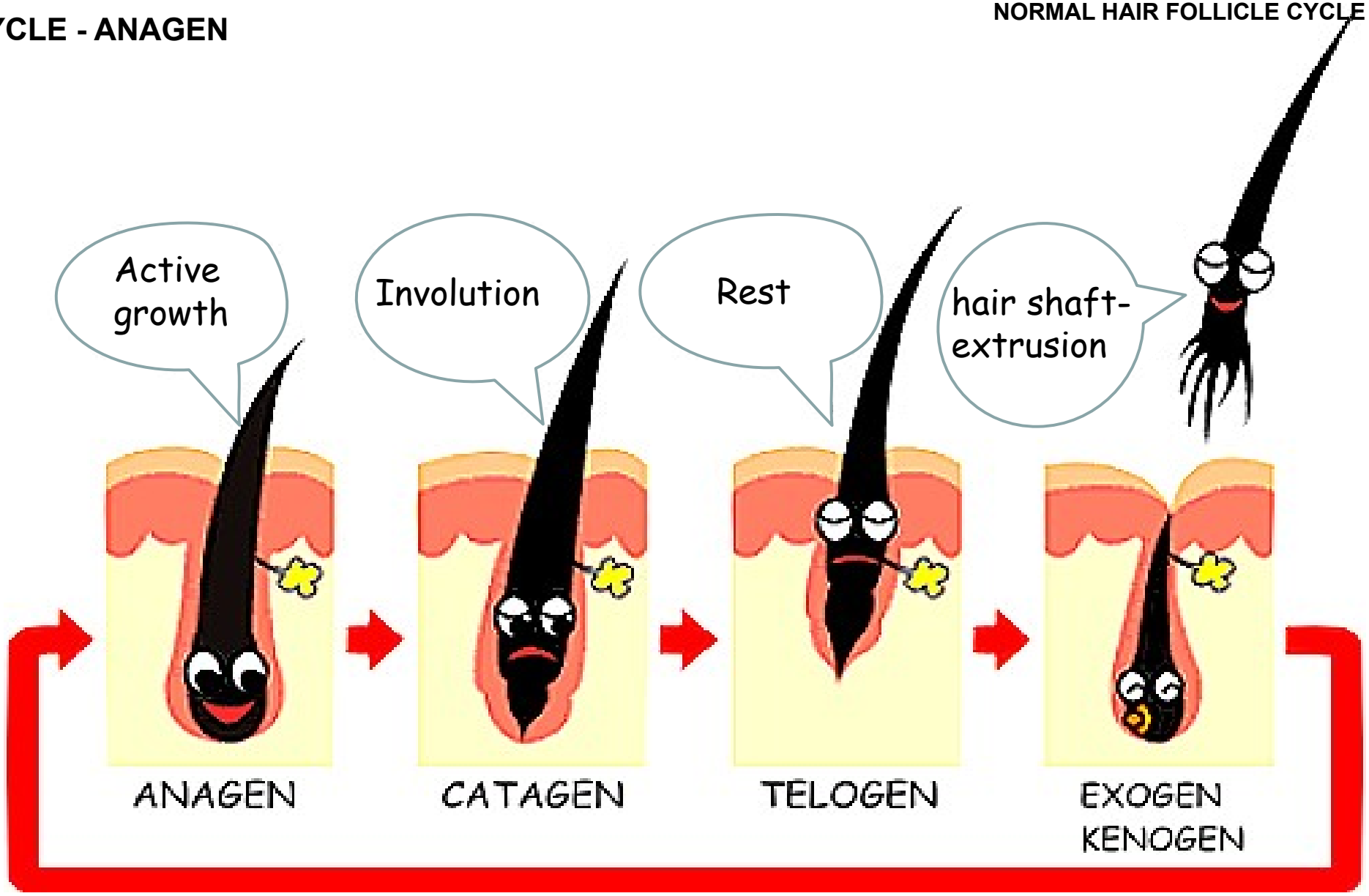


HAIR CYCLE - ANAGEN

NORMAL HAIR FOLLICLE CYCLE



80 to 100%
2 - 7 years

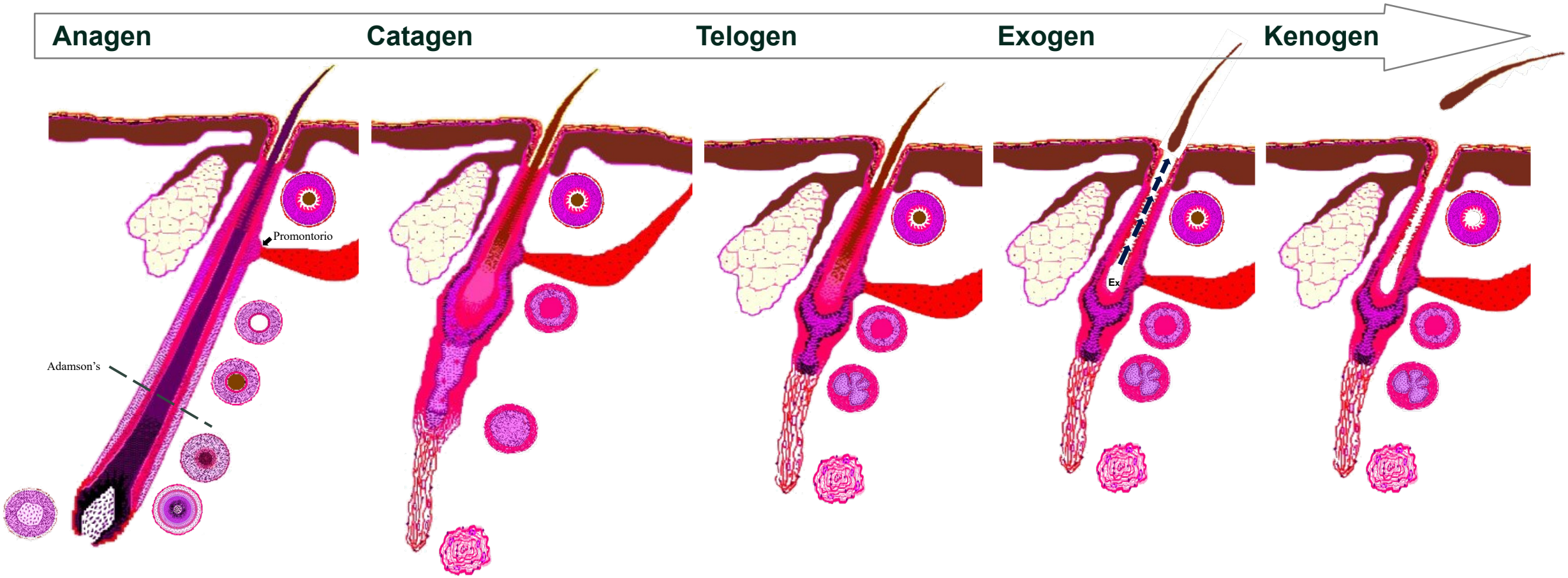
0 to 1%
2 - 3 weeks

0 to 20%
100 days

http://www.reve21.co.jp/eng/tips/img/il_column_10.gif

HAIR CYCLE - ANAGEN

NORMAL HAIR FOLLICLE CYCLE



HAIR CYCLE - ANAGEN

Anagen lasts from 2 to 7 years and is characterized by continuous growth, giving place to a long and pigmented pilar stem, which is easily visible.

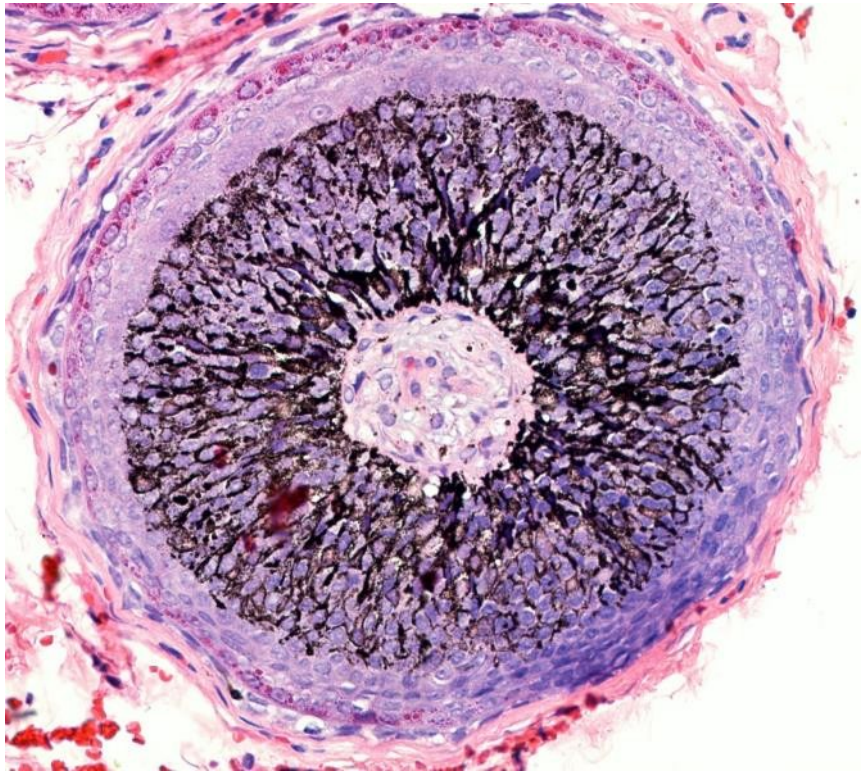
➡ **To the naked eye, the visible hair is terminal and in anagen**

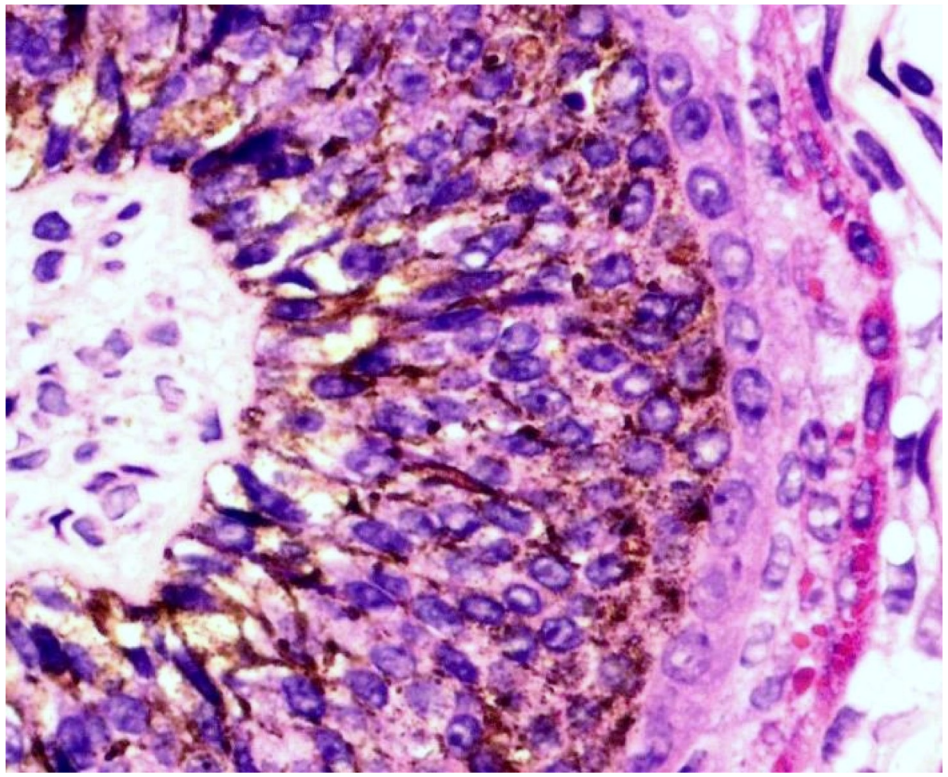
HAIR CYCLE - ANAGEN

Humans have the longest anagen phase among all mammals (2-7 Y)

HAIR CYCLE - ANAGEN

- Pigmentation of the hair occurs in anagen.
- Melanogenesis of hair follicle is coupled to the anagen phase.
- Cyclic reconstruction of the hair follicle pigmentary unit occurs during the first 10 hair cycles, i.e., until approximately 40 years of age.



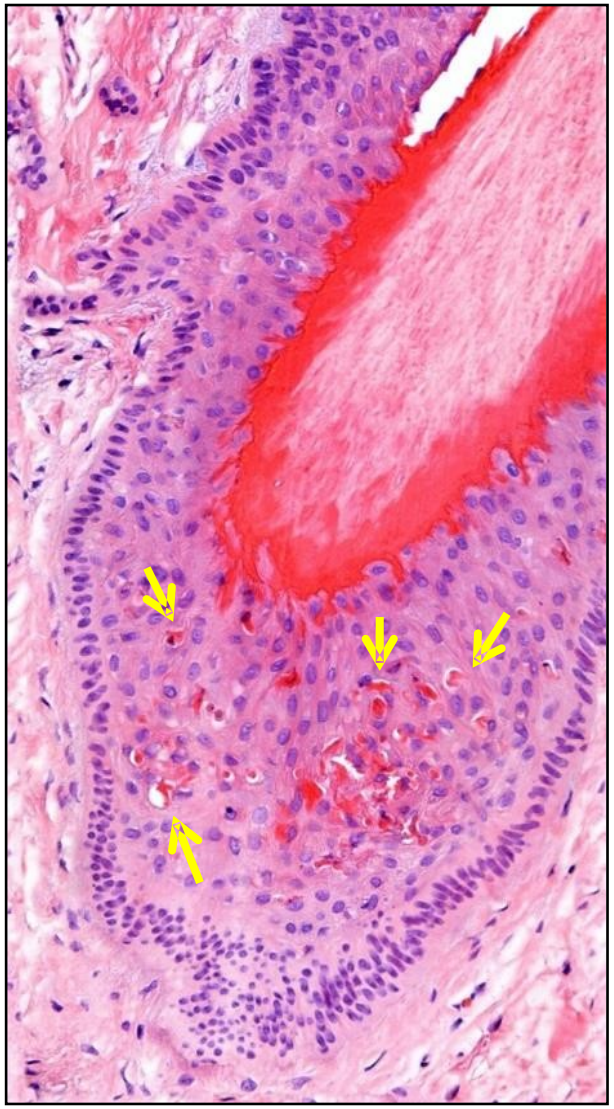


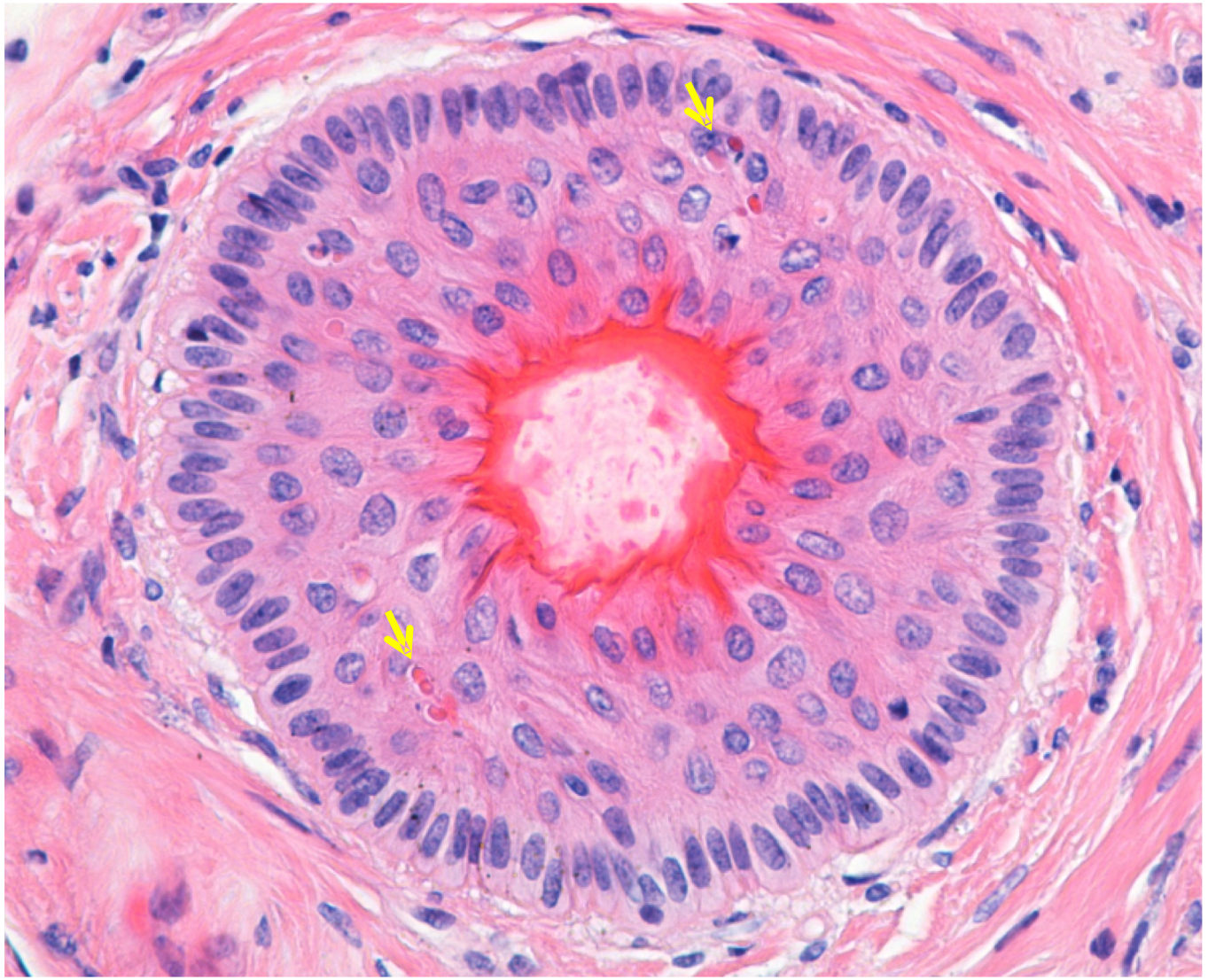
Between 80% - 100% of the hair follicles are in anagen at any given time

Anagen phase

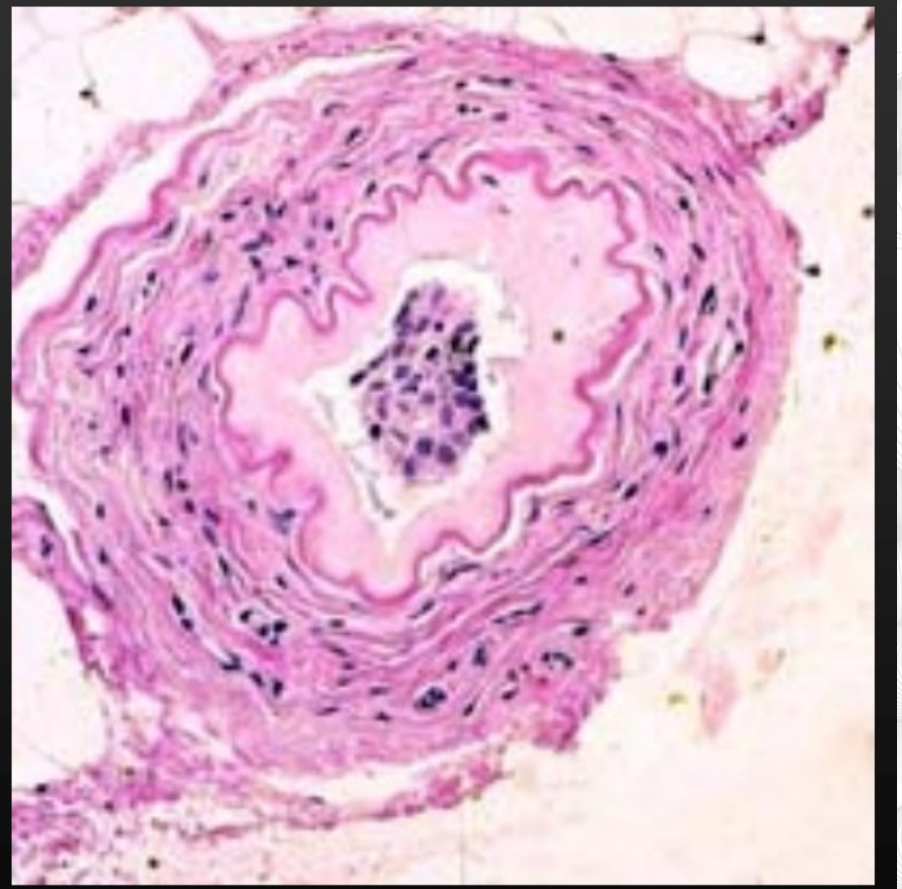
HAIR CYCLE - CATAGEN

There is involution of the follicle and trichilemmal keratinization, highlighted in deep red around the club hair shaft. The outer root sheath shows marked apoptosis.



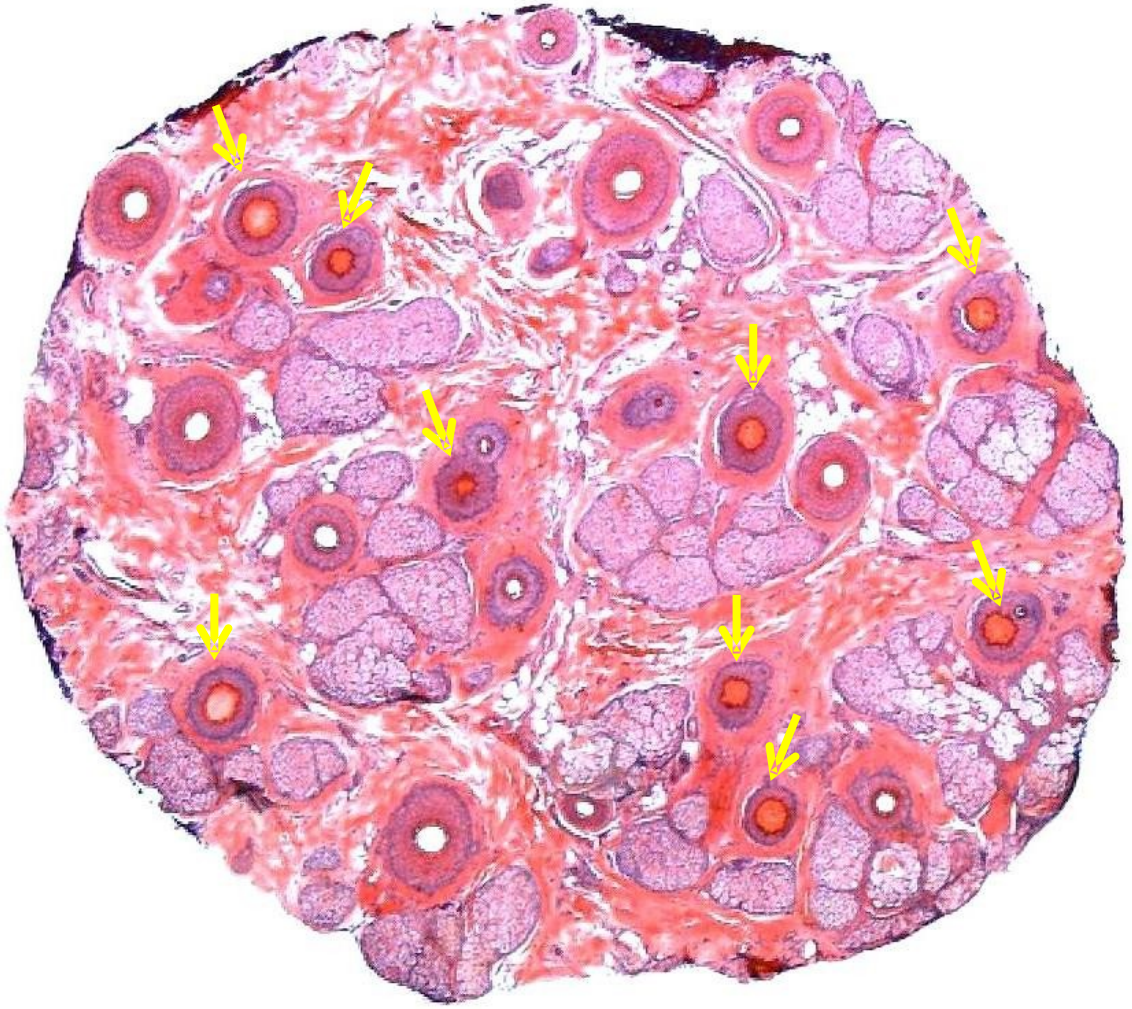


catagen phase



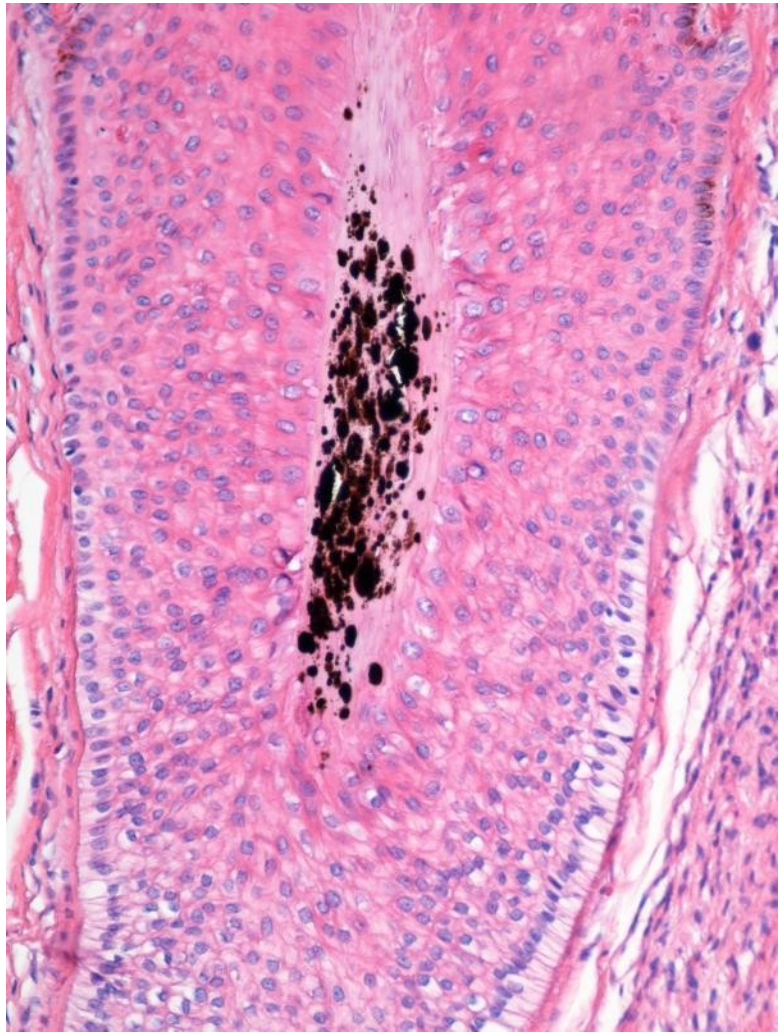
HAIR CYCLE – CATAGEN - TRICHOTILLOMANIA

This phase lasts from 2 to 3 weeks and only 1% to 2% of the follicles are in catagen. Catagen follicles ↘ are frequent in trichotillomania



HAIR CYCLE – CATAGEN - TRICHOTILLOMANIA

Pigment casts (left) and the ‘hamburger sign’ are anohers clues in the diagnosis of trichotillomania, the last due to vertically oriented split within the hair shaft



HAIR CYCLE - TELOGEN

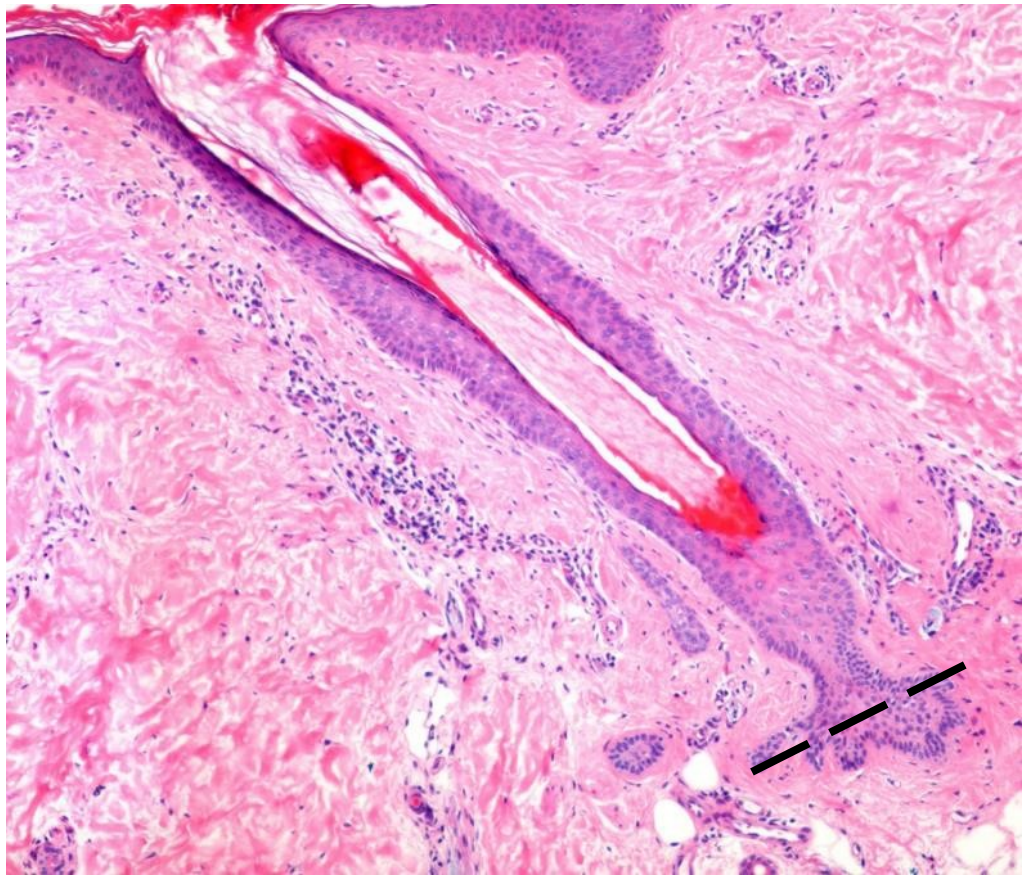
Telogen lasts 100 days

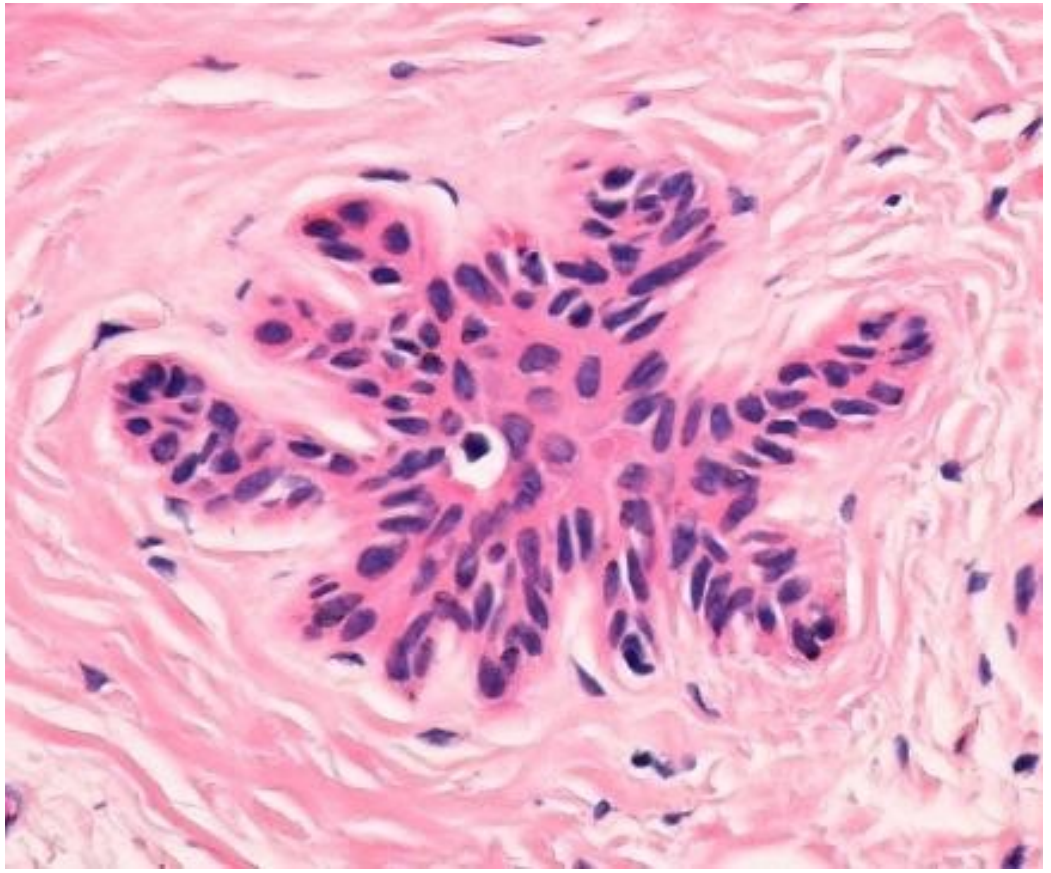
Residual apoptotic cells are present in the central part of the secondary germ (Telogen germinal unit).

A hair follicle in telogen represents the final stage of involution of the lower segment.

Around 100 telogen hairs are shed per day

HAIR CYCLE - TELOGEN

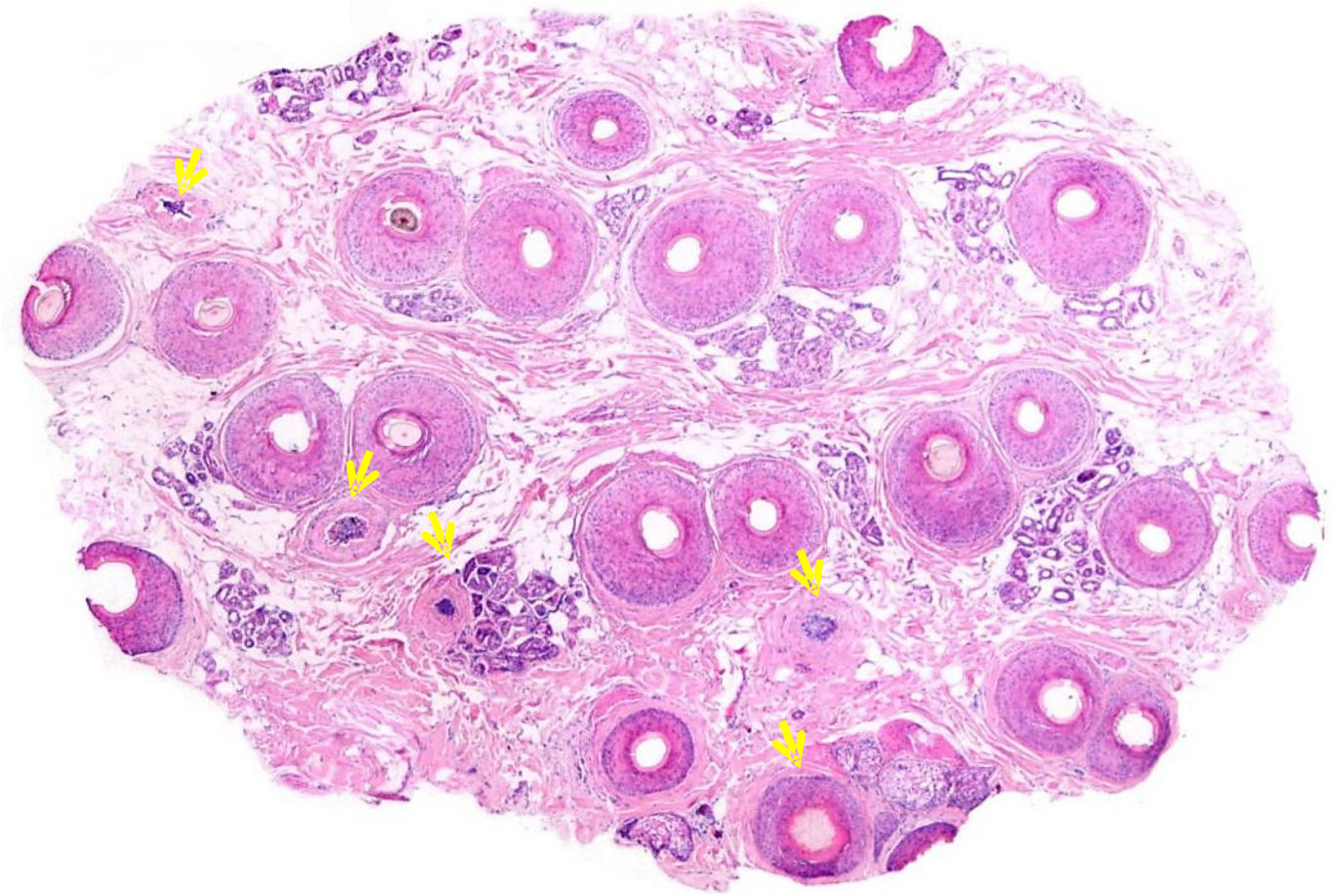


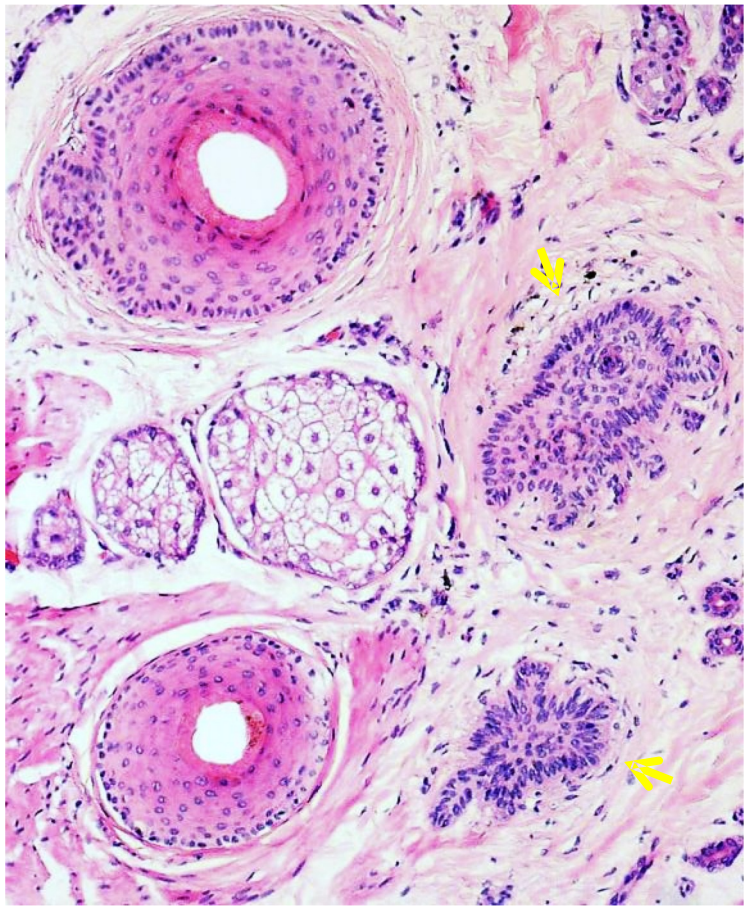


The hair papilla is present under the area of insertion of the arrector pili muscle and in a horizontal section appears as an aggregate of basaloid cells (secondary germ or telogen germinal unit)

HAIR CYCLE - TELOGEN / TELOGEN - TELOGEN EFFLUVIUM

NORMAL HAIR FOLLICLE CYCLE

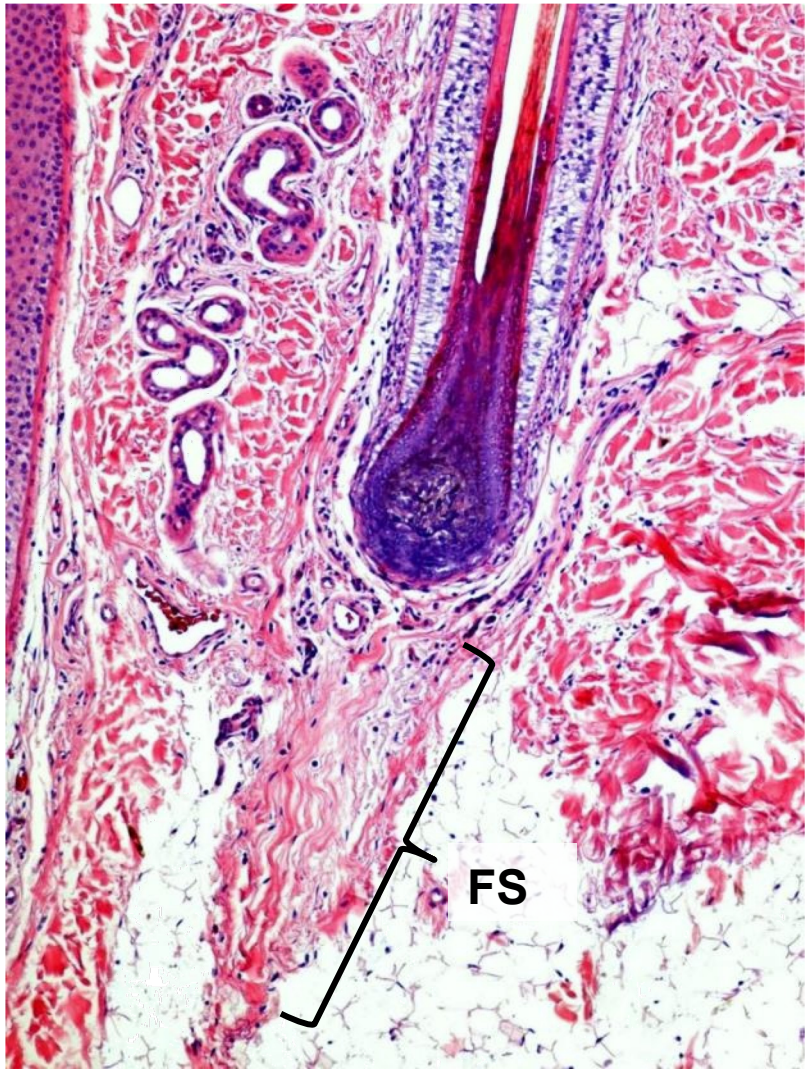


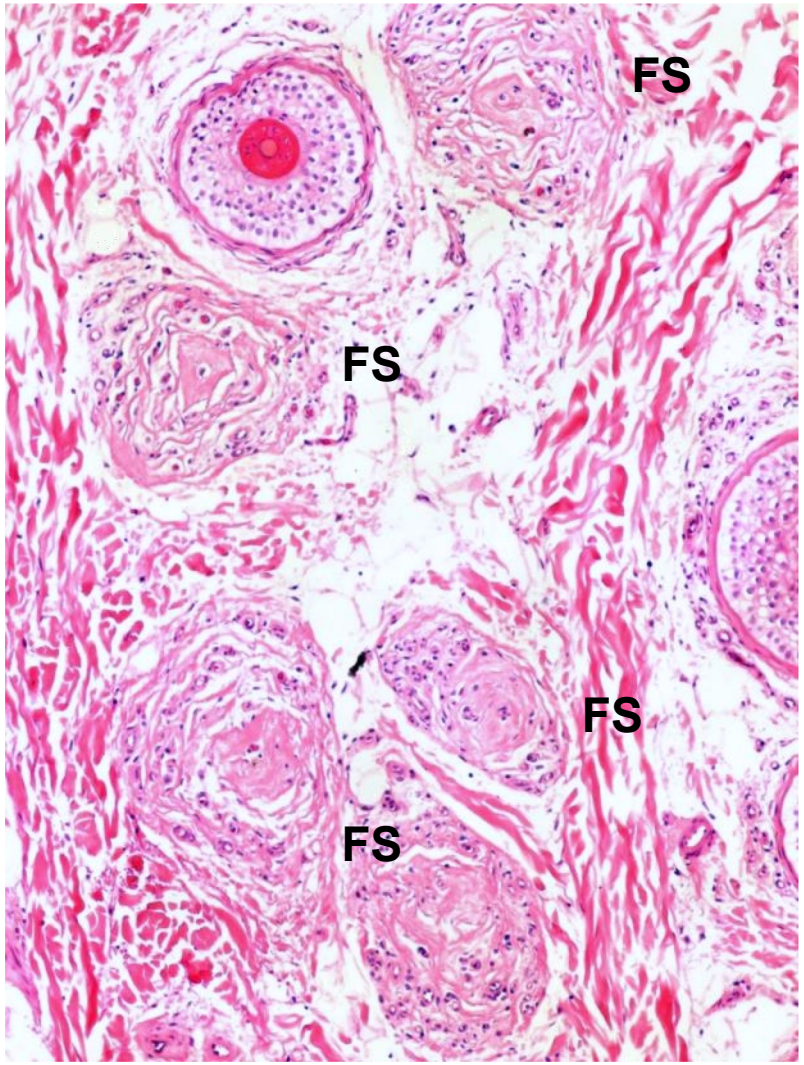


There are an increase in number of telogen germinal unit, telogen hair follicle, and follicular stellae , with a normal number of hair follicles and absence of inflammatory infiltrate or follicular miniaturization

FOLLICULAR STELLA

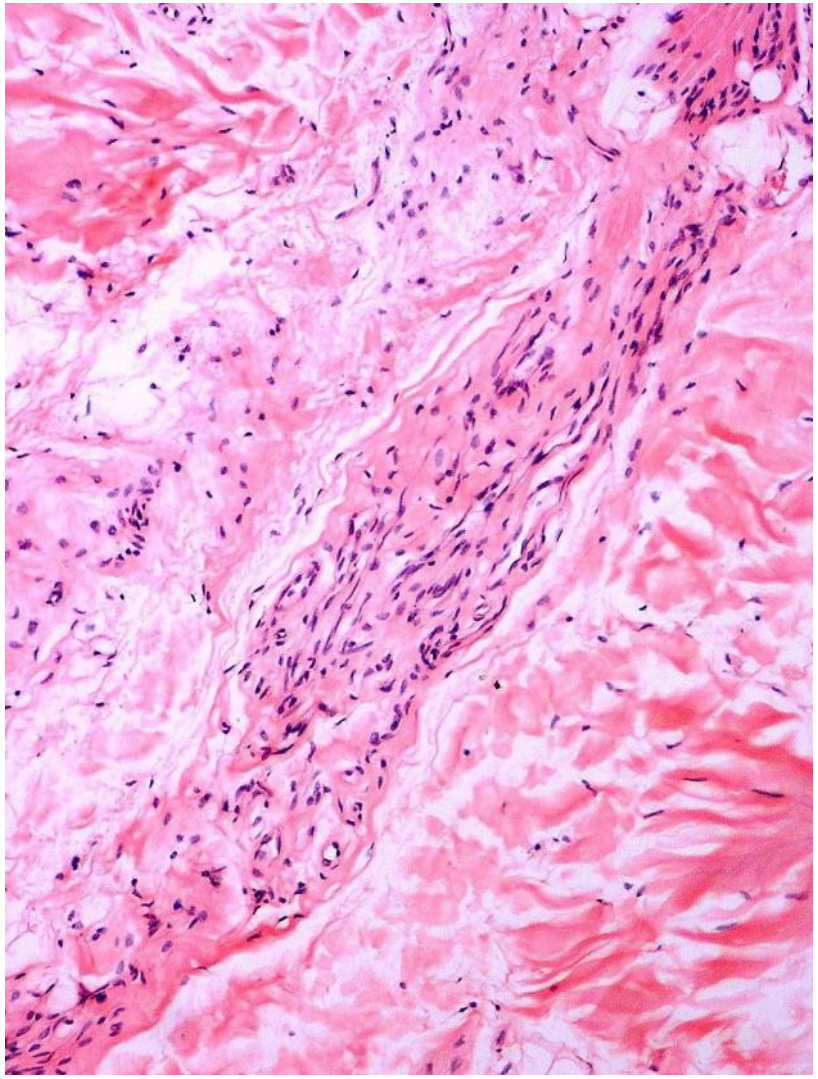
NORMAL HAIR FOLLICLE ANATOMY

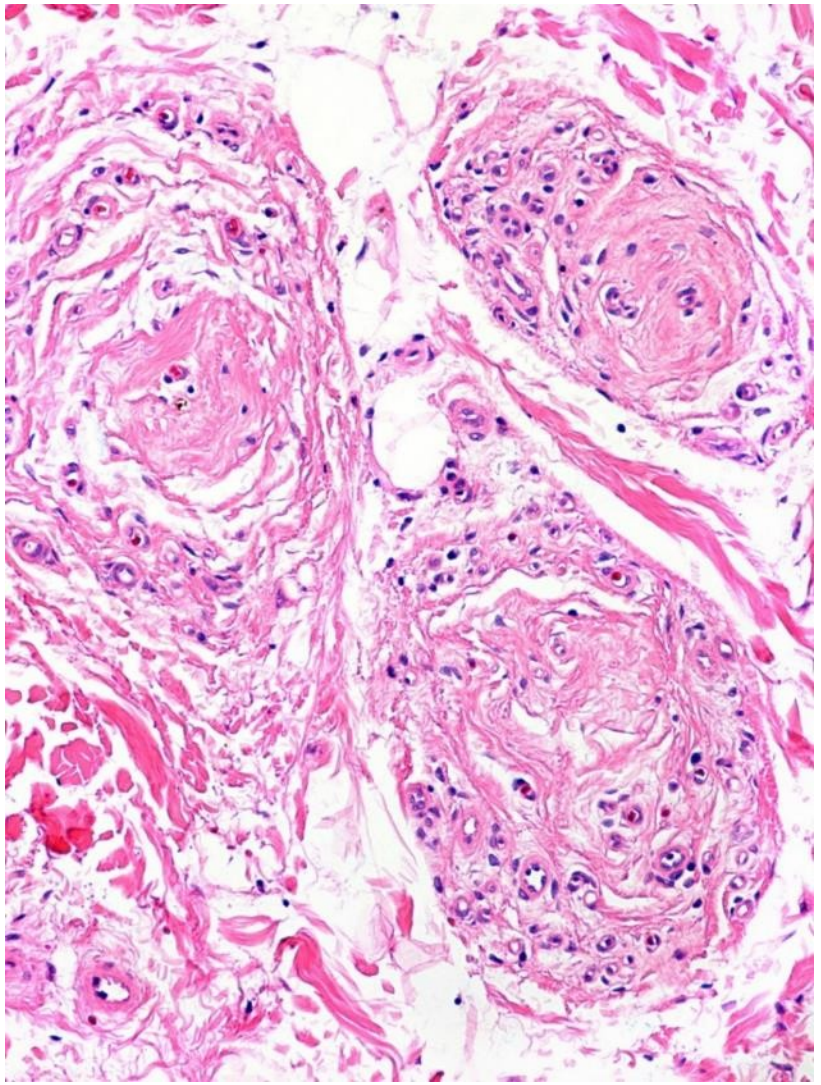




In telogen and in miniaturized hairs, the lower segment of the hair follicle involutes completely, leaving only a structure called a follicular stella.

FOLLICULAR STELLA





The follicular stellae is in relation to telogen or vellus hairs in the subcutaneous fat

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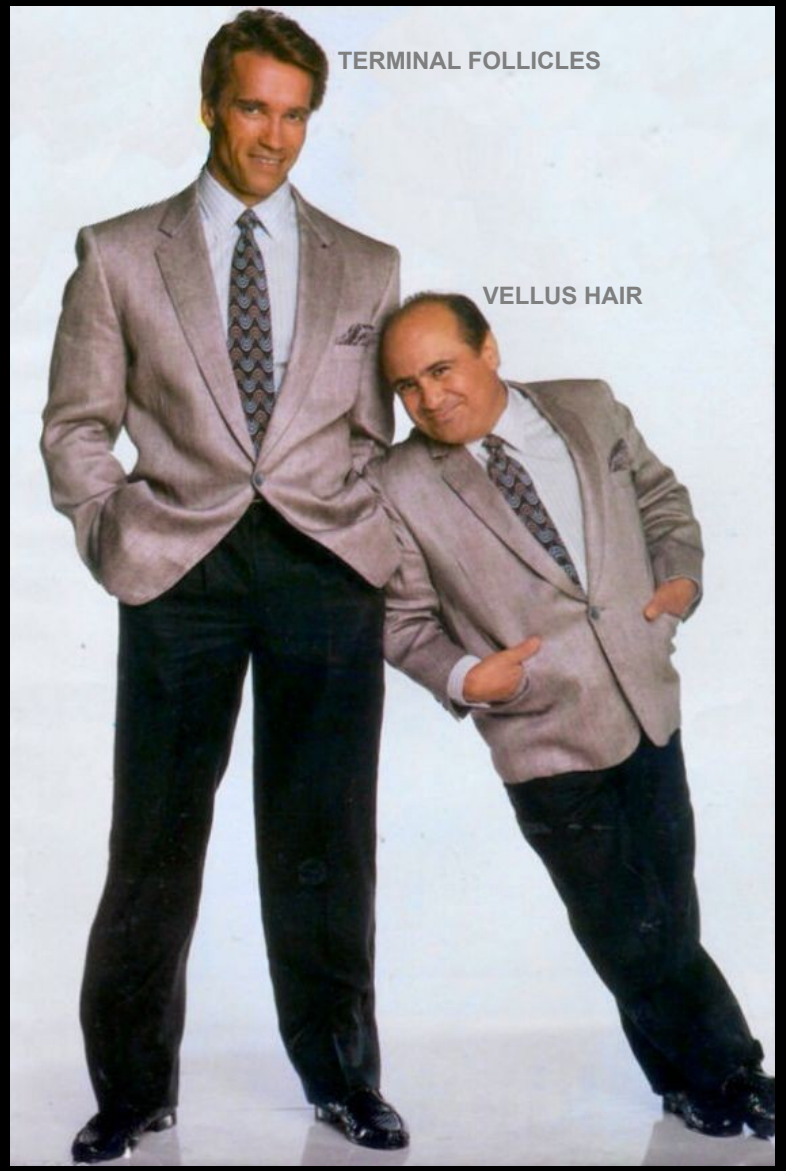
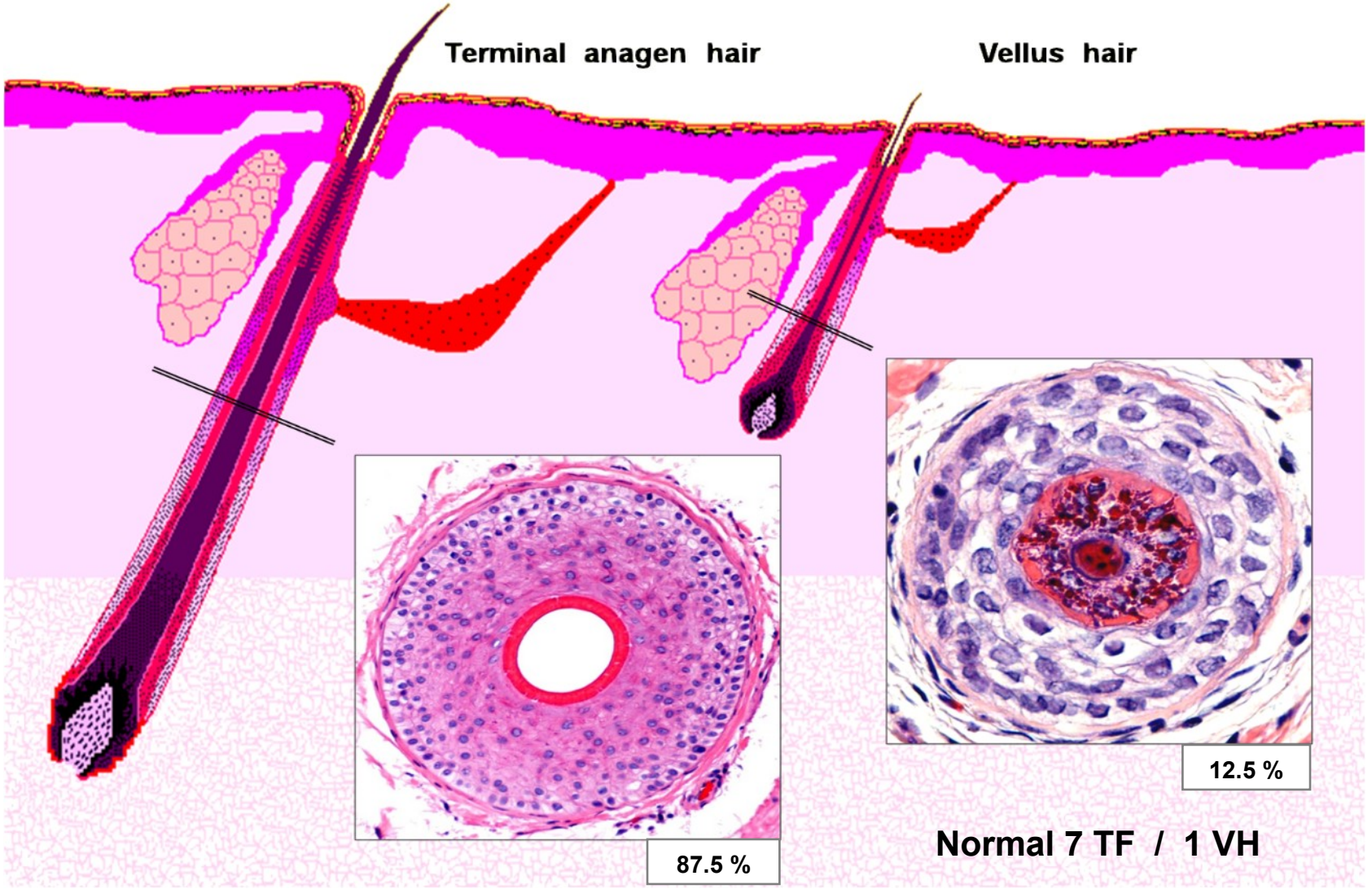


https://ar.pinterest.com/pin/636485359816507542/

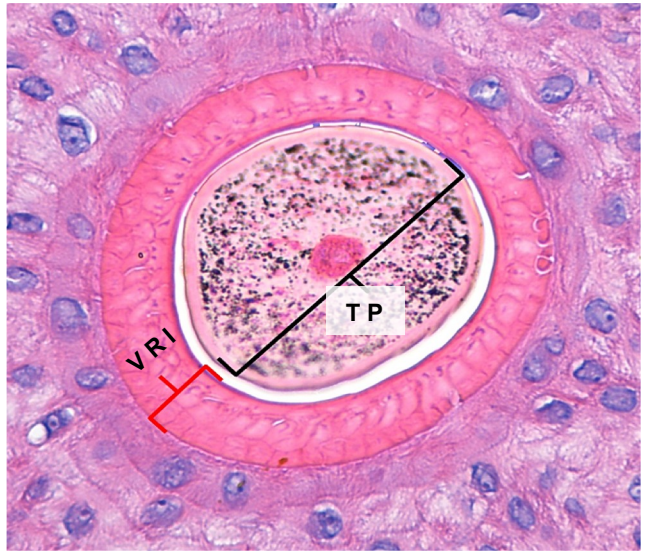
TERMINAL FOLLICLES AND VELLUS HAIR

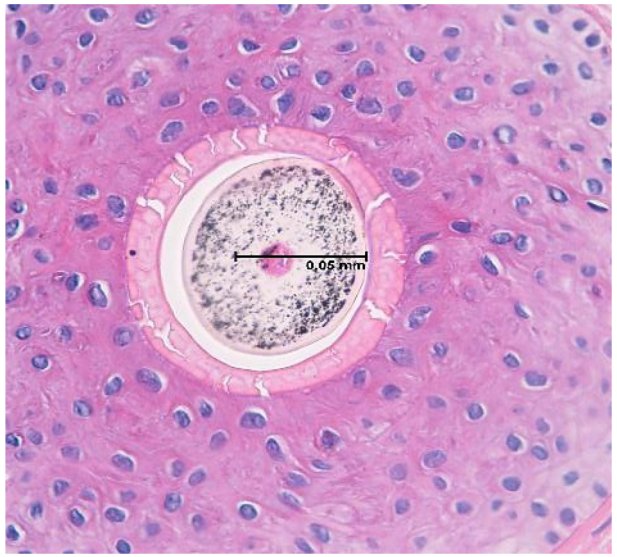
The terminal anagen follicles (TF) reach the fat. The vellus hairs and miniaturized follicles (VH) are located in the deep dermis.



TERMINAL FOLLICLES AND VELLUS HAIR

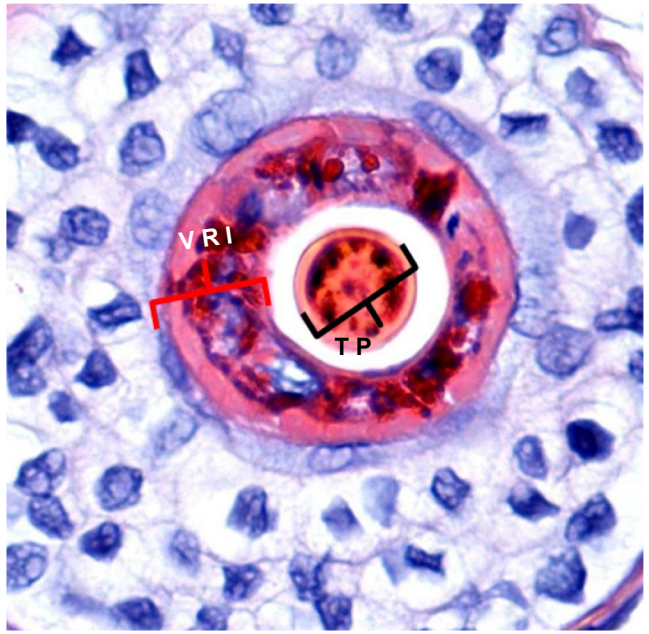
TERMINAL FOLLICLES

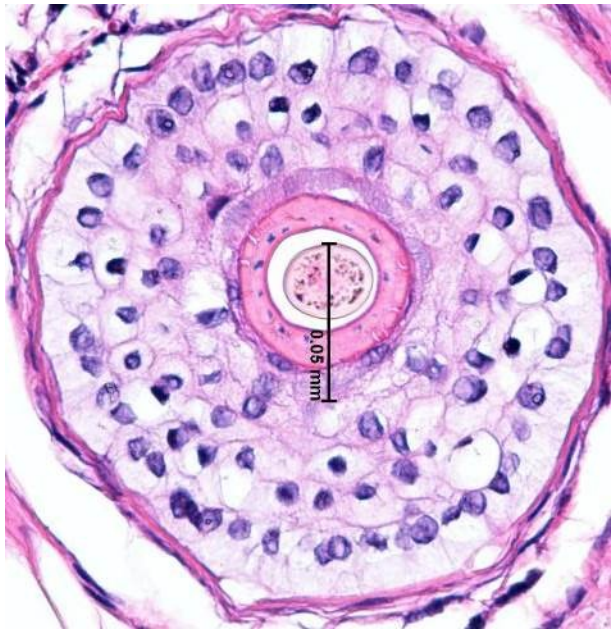




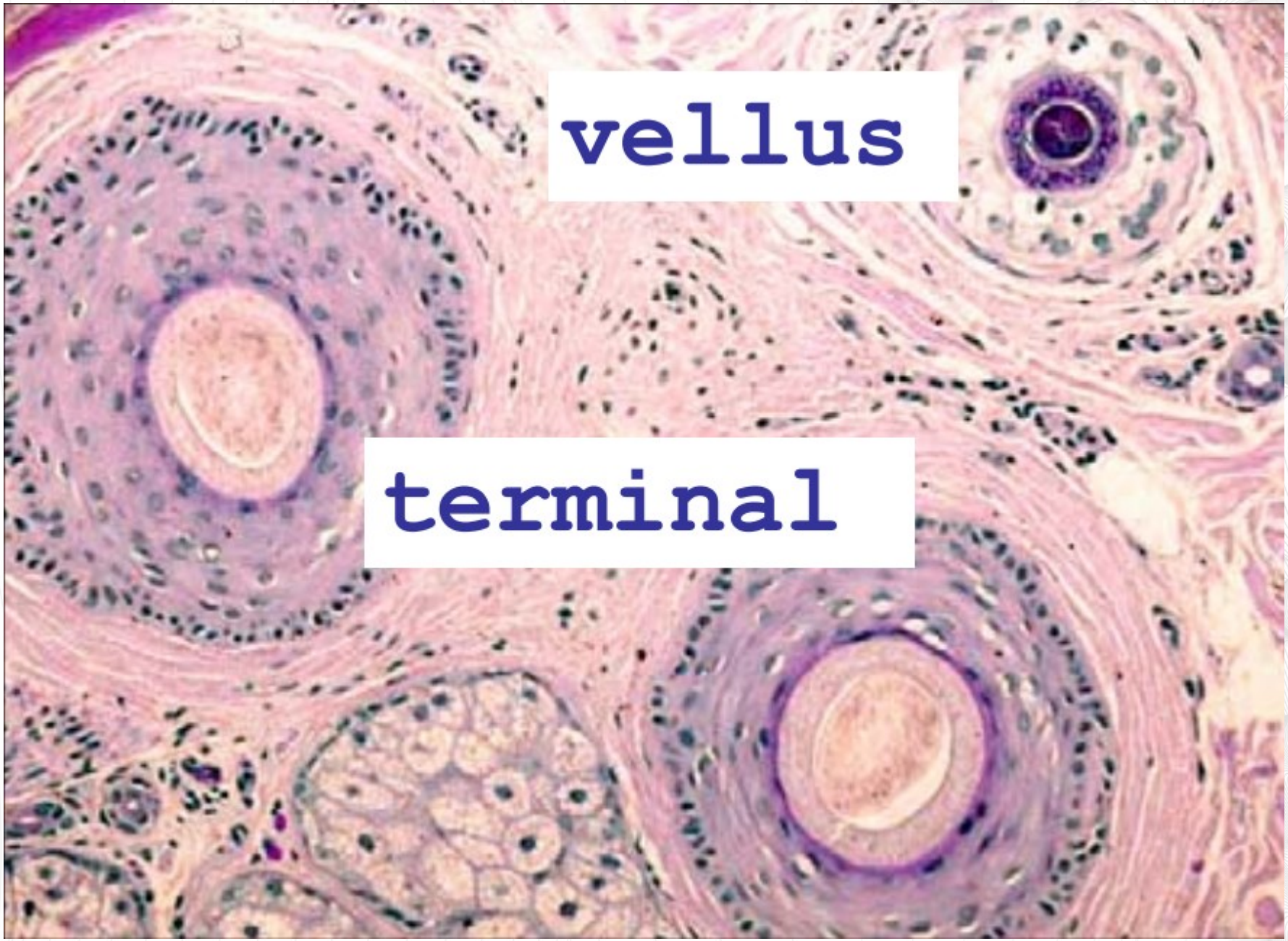
- **Terminal follicles** have been defined as hairs with a hair shaft diameter 0.06mm-0.03 mm.
- The hair shaft is bigger than its inner root sheath

VELLUS HAIR AND MINIATURIZED FILLICLES





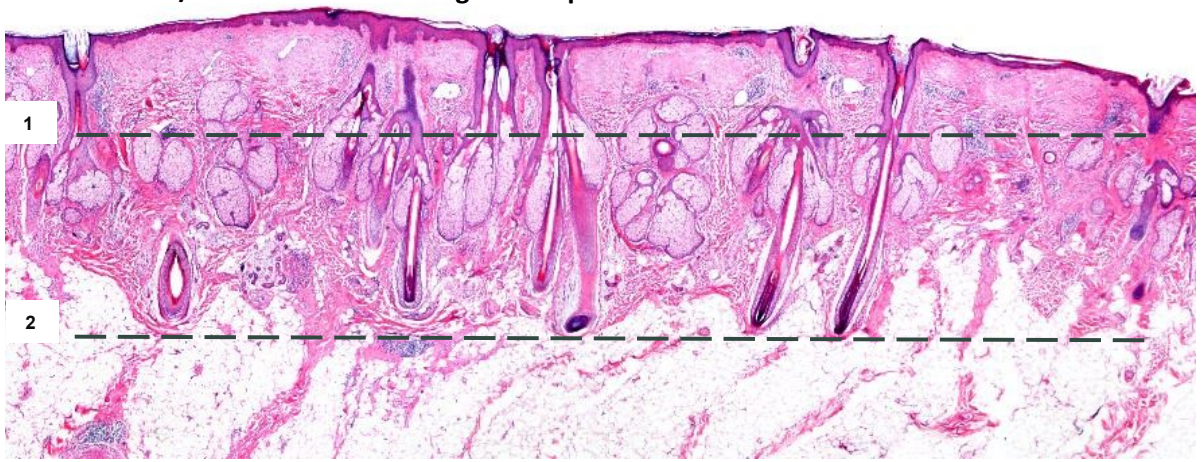
- **Vellus-like follicles** have been defined as hairs with a hair shaft diameter ≤ 0.03 mm and thinner than its inner root sheath. The shaft lacks pigment and medullary cavity.
- All hairs are counted as vellus-like hairs whether primary or secondary to miniaturization from any cause.


vellus
terminal

TERMINAL FOLLICLES AND VELLUS HAIR

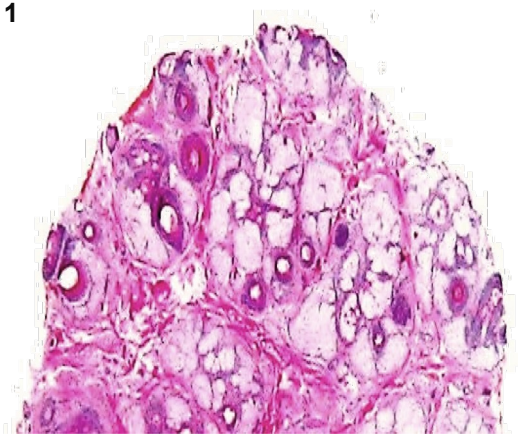
Frontal – AGA / FAGA : Female Androgenic Alopecia

Vertical



Horizontal /Transversal

1



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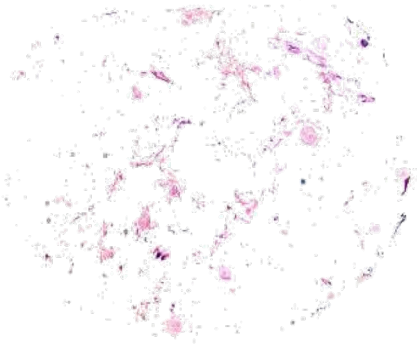
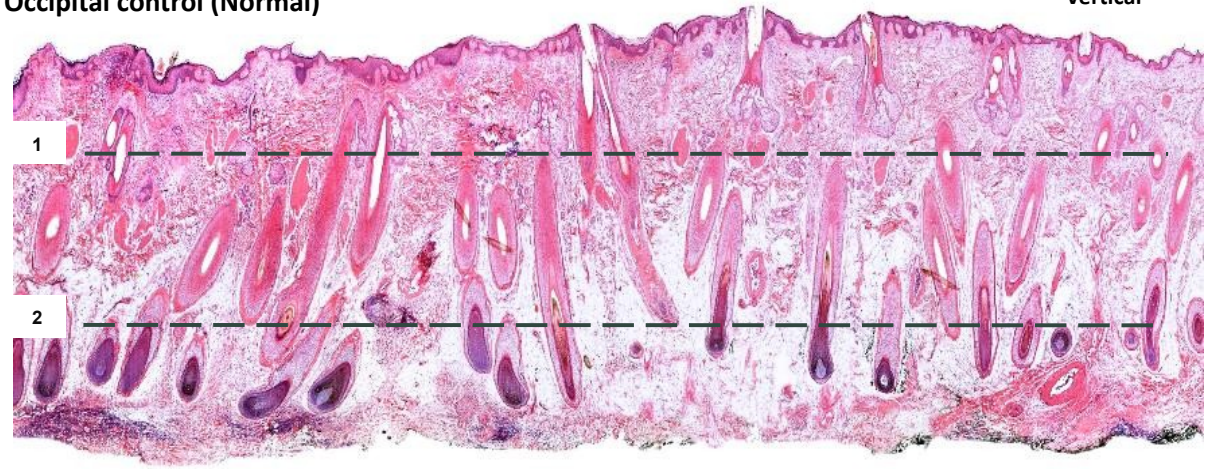


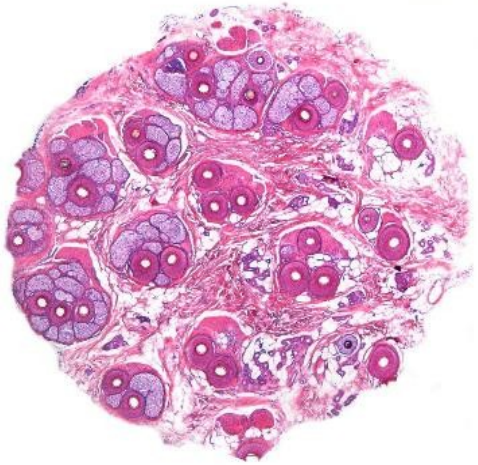
Occipital control (Normal)

Vertical



Horizontal /Transversal

1



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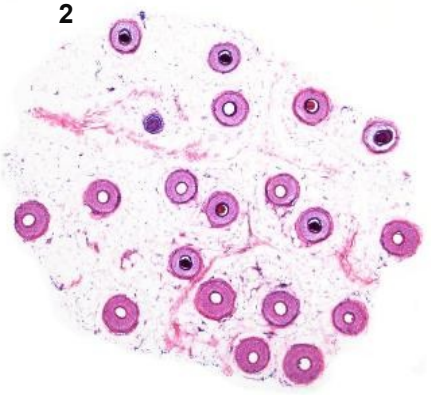


ANDROGENIC ALOPECIA (AA)

Distinguishing between terminal and vellus hair follicles (V) is critical for the diagnosis of AnA.

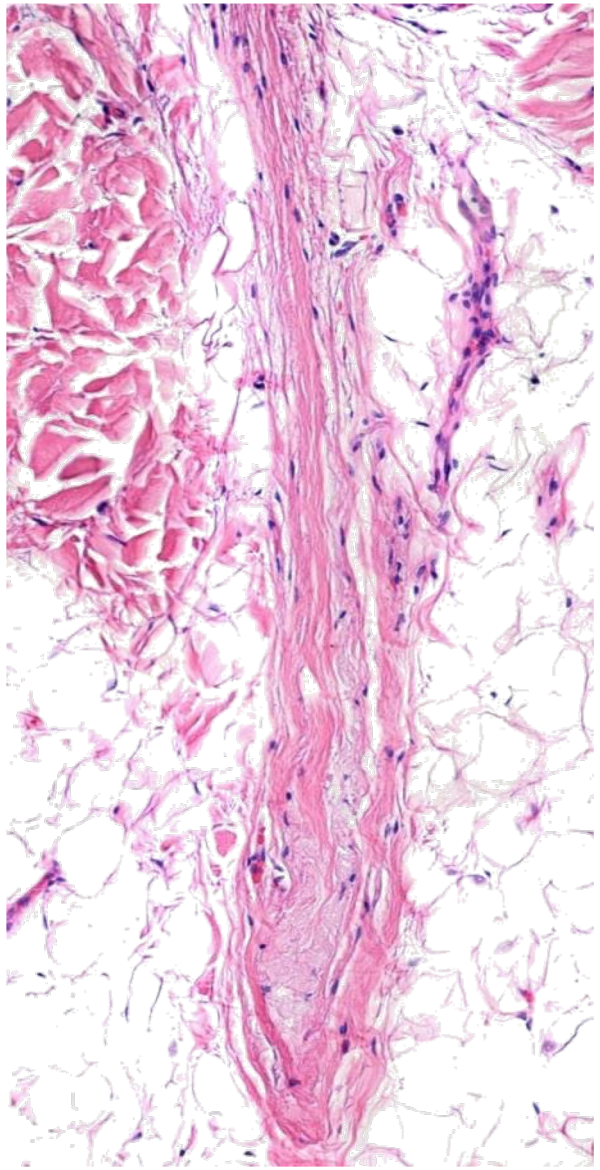
AnA results from a progressive decrease in the size of hair follicles and their transformation into vellus forms.

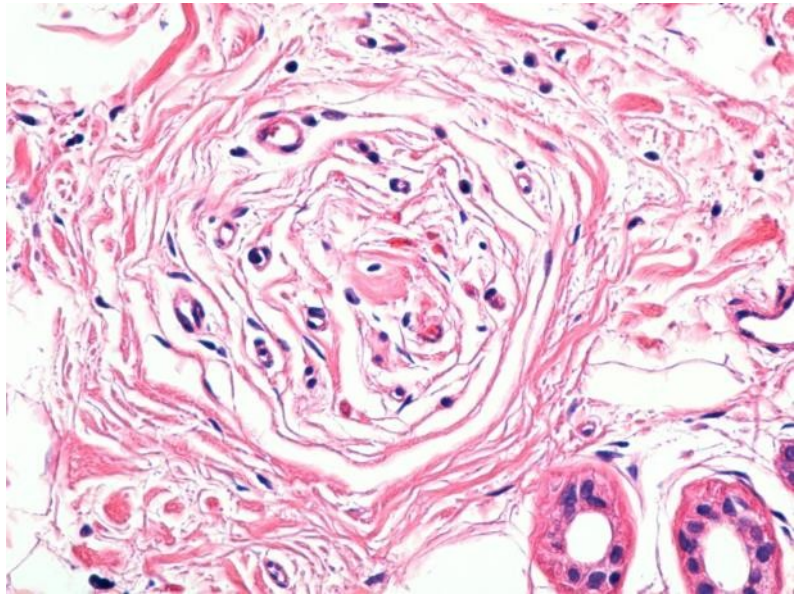
The normal ratio between terminal and vellus hairs is approximately 7:1.

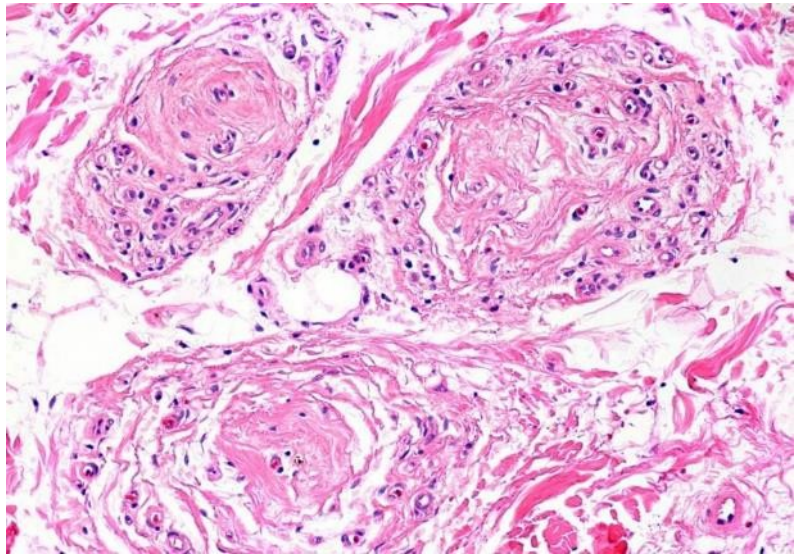
A ratio of 4:1 or less suggests androgenetic alopecia.

ANDROGENIC ALOPECIA

FOLLICULAR STELLA IN ANDROGENIC ALOPECIA

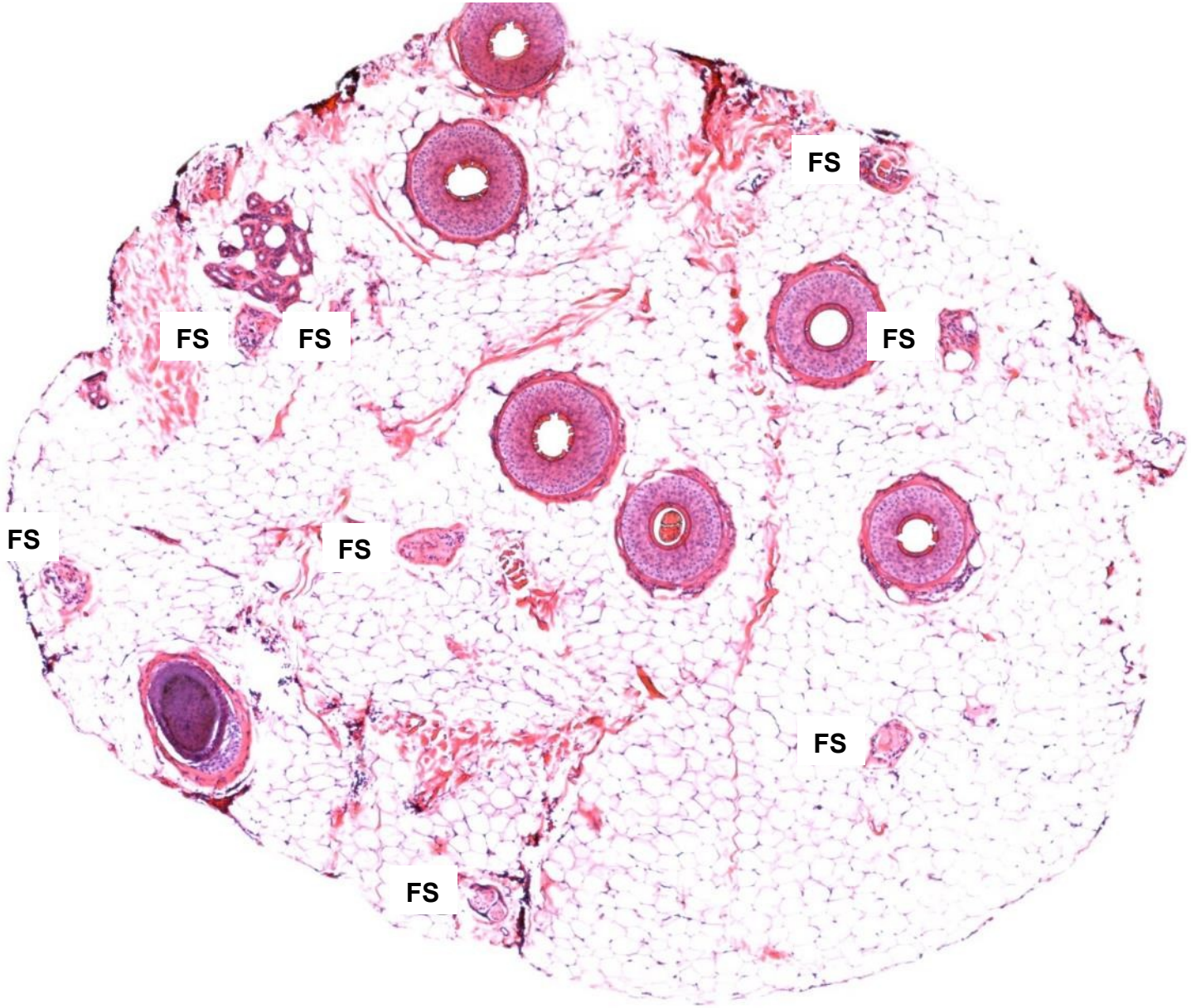






ANDROGENIC ALOPECIA

FOLLICULAR STELLA (FS) IN ANDROGENIC ALOPECIA

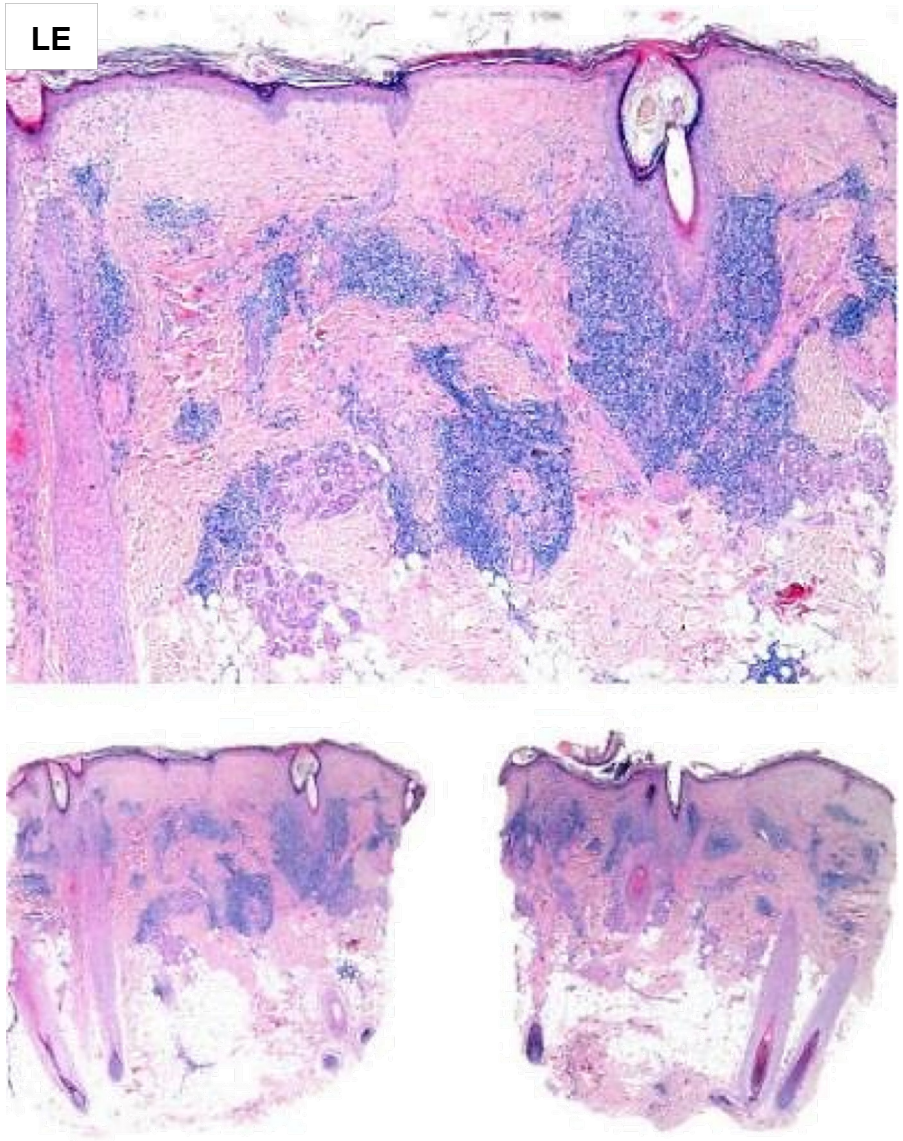


1. INTRODUCTION
2. SCALP BIOPSY
   - WHY IS IT SO DIFFICULT TO INTERPRET A SCALP BIOPSY ?
   - HOW AND WHERE TO PERFORM A PROPER BIOPSY?
   - TYPE OF SECTION (VERTICAL, HORIZONTAL, BOTH?)
3. NORMAL HAIR FOLLICLE
   - ANATOMY
   - HAIR CYCLE (ANAGEN , CATAGEN, TELOGEN)
4. TERMINAL FOLLICLES / VELLUS HAIR
5. **SCARRING ALOPECIAS**
6. DIFFERENCES BETWEEN ETHNIC GROUPS

SCARRING ALOPECIA

- **Scarring alopecia constitutes one of the most difficult and complex areas in the study of hair disease.**
- **It includes a wide variety of nosological entities with different etiologies and distinctive clinical features.**
- **Dermoscopy and scalp biopsy is the most important test to achieve the diagnosis.**

SCARRING ALOPECIA AND STEM CELLS



The histopathological hallmark of scarring alopecias are:

- **Presence of an inflammatory infiltrate surrounding the bulge and isthmus region with loss of stem cells.**

SCARRING ALOPECIA AND STEM CELLS

FD

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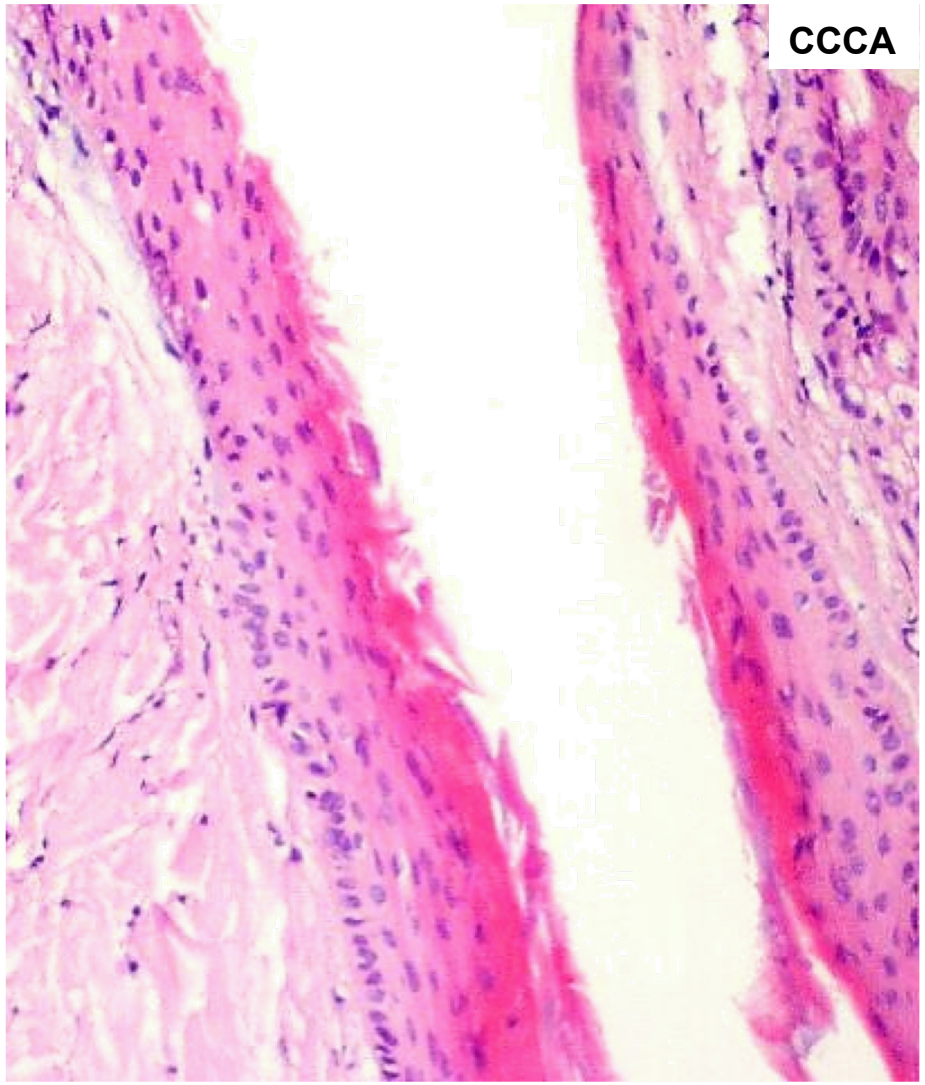
- **Presence of an inflammatory infiltrate surrounding the bulge and isthmus region with loss of stem cells.**
- **Loss of sebaceous glands.**

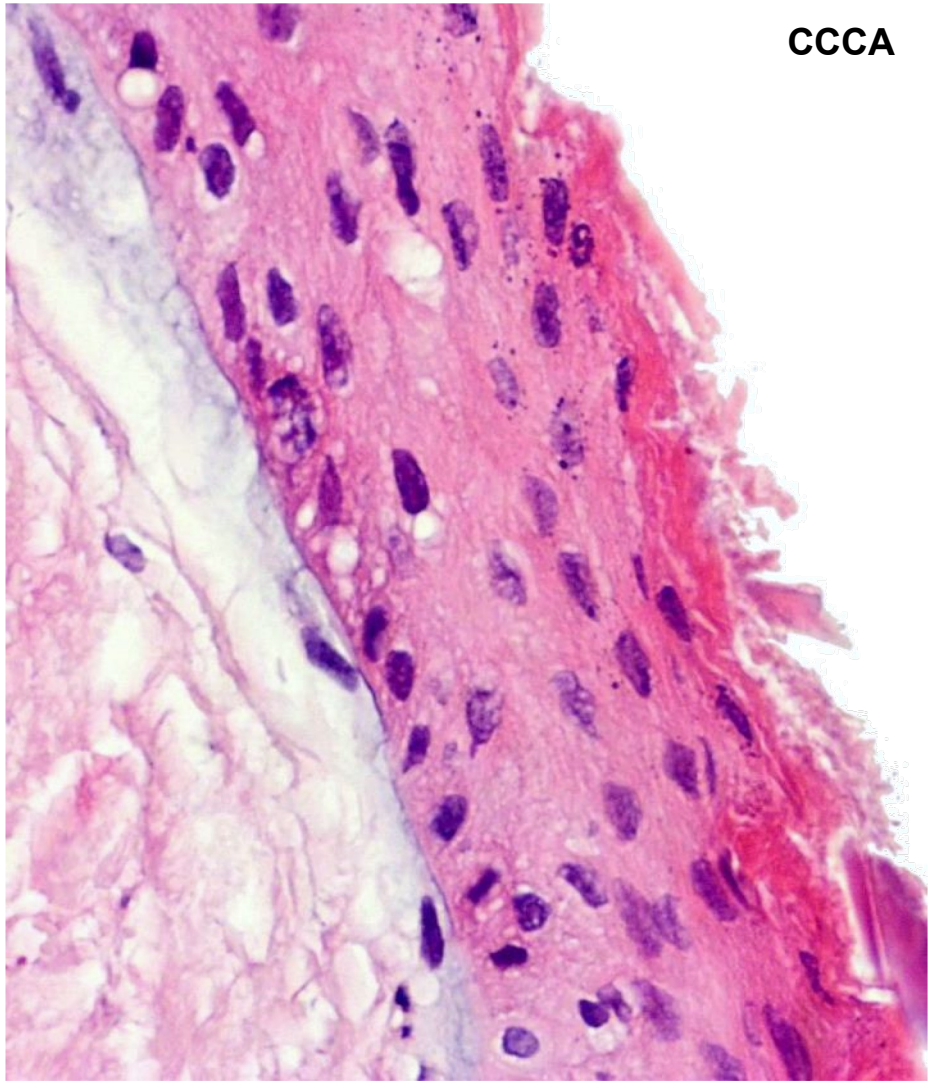
SCARRING ALOPECIA AND STEM CELLS



The histopathological hallmark of scarring alopecias are:

- **Presence of an inflammatory infiltrate surrounding the bulge and isthmus region with loss of stem cells.**
- **Loss of sebaceous glands.**
- **Premature desquamation of the internal root sheath.**

SCARRING ALOPECIA AND STEM CELLS



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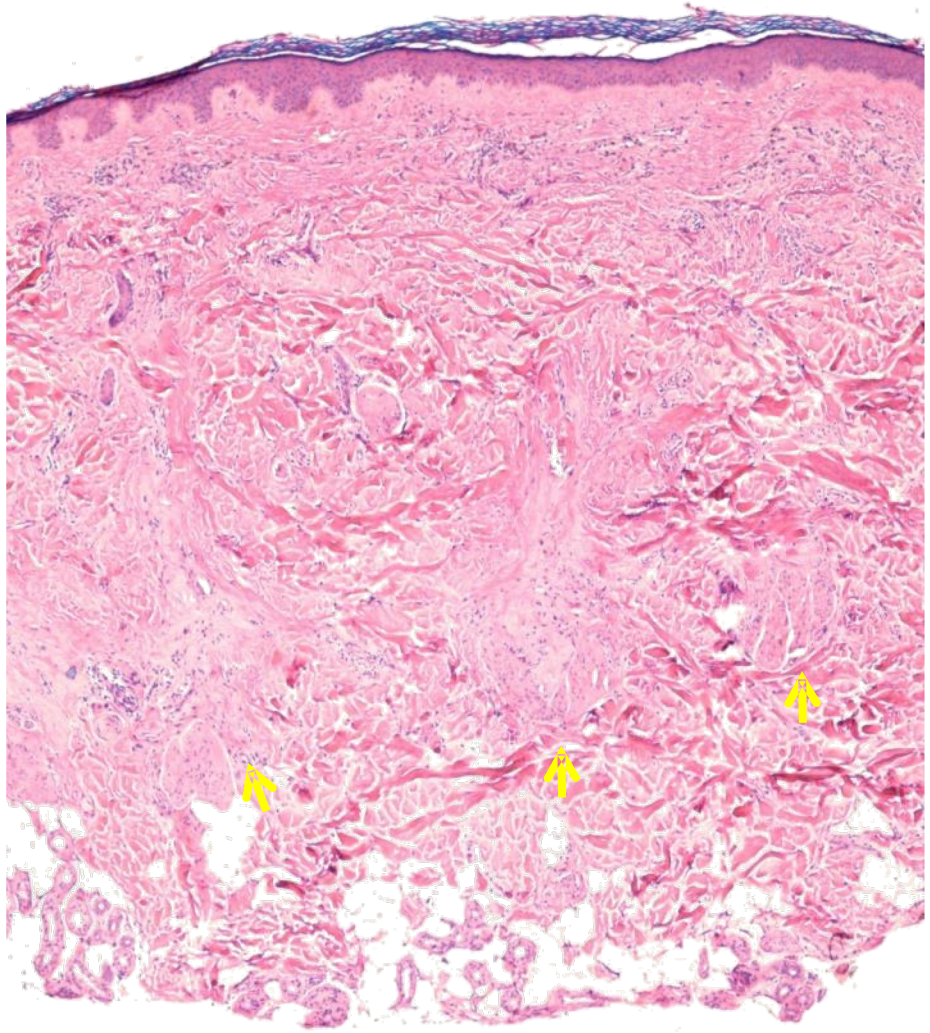
SCARRING ALOPECIA AND STEM CELLS



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SCARRING ALOPECIA AND STEM CELLS

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- **Positive birefringence in the area of follicular scar**

SCARRING ALOPECIA AND STEM CELLS

The histopathological hallmark of scarring alopecias are:

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- **Loss of sebaceous glands.**
- **Premature desquamation of the internal root sheath.**
- **Formation of a scar.**
- **Positive birefringence in the area of follicular scar**
- **Formation of compound follicles with lamellar fibrosis and inflammatory infiltrate**

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5. NON SCARRING ALOPECIAS
6. SCARRING ALOPECIAS
7. **DIFFERENCES BETWEEN ETHNIC GROUPS**

The use of horizontal sections has allowed the study of variations in size, number and density of hair follicles in different ethnic groups

25.9 5.5

21.5 5.0

16.1 3.6

40 2.2
35.5 5.5

25.0 5.0

AVERAGE TOTAL HAIRS IN A 4 mm PUNCH BIOPSY

Sperling, LC. Hair Density in African Americans. Arch Dermatol. 1999;135:656-658

Whiting DA. Diagnostic and predictive value of horizontal sections of scalp biopsy specimens in malepattern androgenetic alopecia. J Am Acad Dermatol 1993; 28:755-763

THE EVALUATION OF ALOPECIA BY HORIZONTAL AND VERTICAL SECTIONS

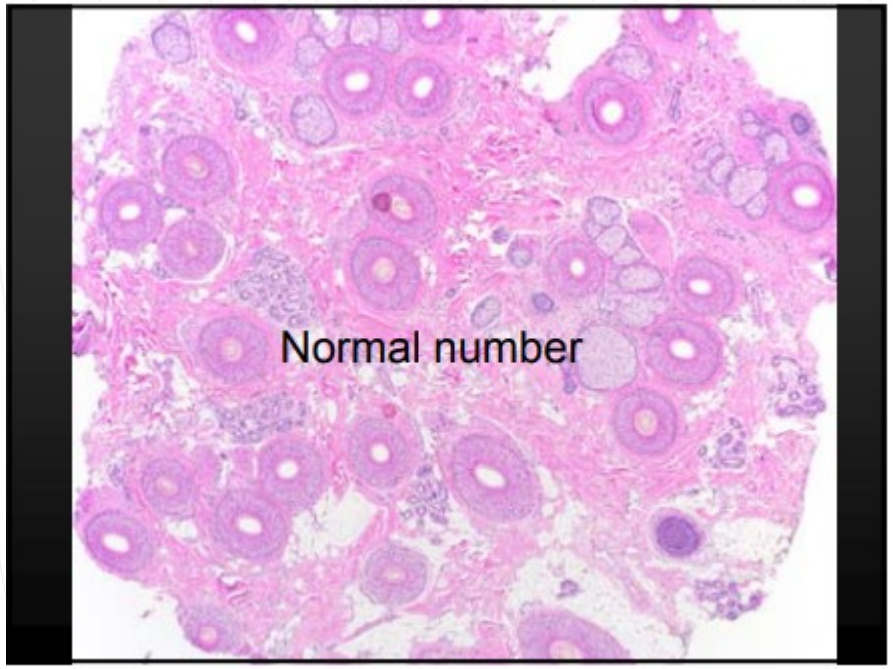
TABLE 1. Comparison of Hair Density of Taiwanese, Koreans, Iranians, American Caucasians, and African Americans

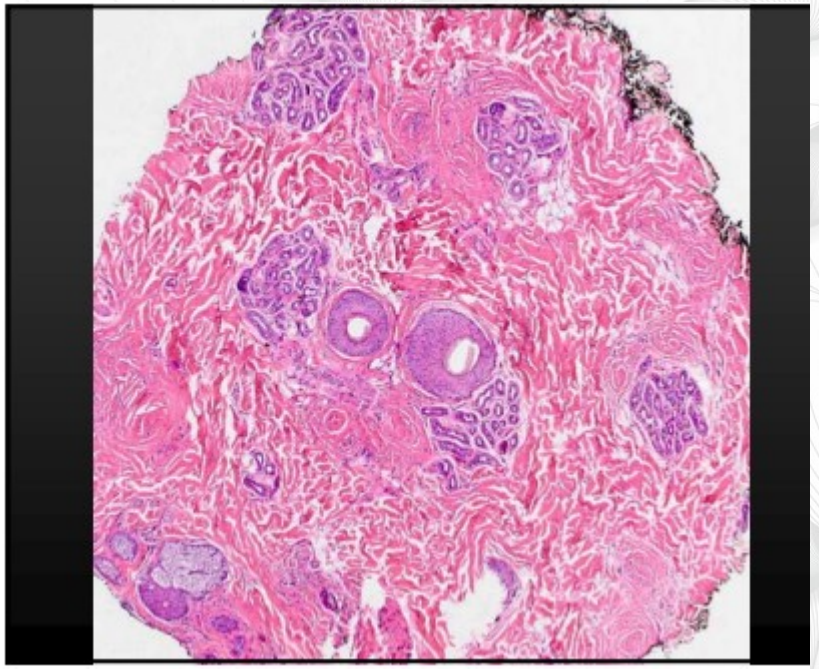
Characteristic	*Asia*			*America*		
Race	*Taiwanese, n = 31*	*Korean, n = 35*	*Iranian, n = 30*	*Caucasian, n = 22*	*African American, n = 22*	
Author	*Present study*	*Lee et al*[5]	*Aslani*[8]	*Whiting*[2]	*Sperling*[3]	p-*Value**
Age, mean ± SD	37.0 ± 15.3	33.1 ± 10.0	35.5 ± 14.7	43 ± 3.5	31.7 ± 8.5	.04
Number of terminal hairs, mean ± SD	20.5 ± 4.6	14.9 ± 3.2	34 ± 6.4	35 ± 2.1	18.4 ± 5.0	<.001
Number of vellus hairs, mean ± SD	0.8 ± 1.0	1.1 ± 1.3	2.4 ± 1.2	5 ± 0.6	3.0 ± 2.1	<.001
Number of total hairs, mean ± SD	21.3 ± 4.8	16.1 ± 3.6	36.3 ± 7.2	40 ± 2.2	21.5 ± 5.0	<.001
Number of follicular units, mean ± SD	9.4 ± 1.9	7.8 ± 1.7	ND	14 ± 0.5	ND	<.001
Anagen: telogen ratio,%	91.6:8.4	93.6:6.4	93.7:6.3	93.5:6.5	93.9:6.1	.47
Terminal: vellus ratio	25.3:1	13.5:1	17.4:1	7:1	6.1:1	<.001
Density of hair follicles/mm^2	1.69 ± 0.4	1.2 ± 0.3	2.89 ± 0.6	3.1 ± 0.8	1.65 ± 0.4	<.001
Density of follicular units/mm^2	0.75 ± 0.2	0.62 ± 0.1	ND	1.11 ± 0.04	ND	<.001

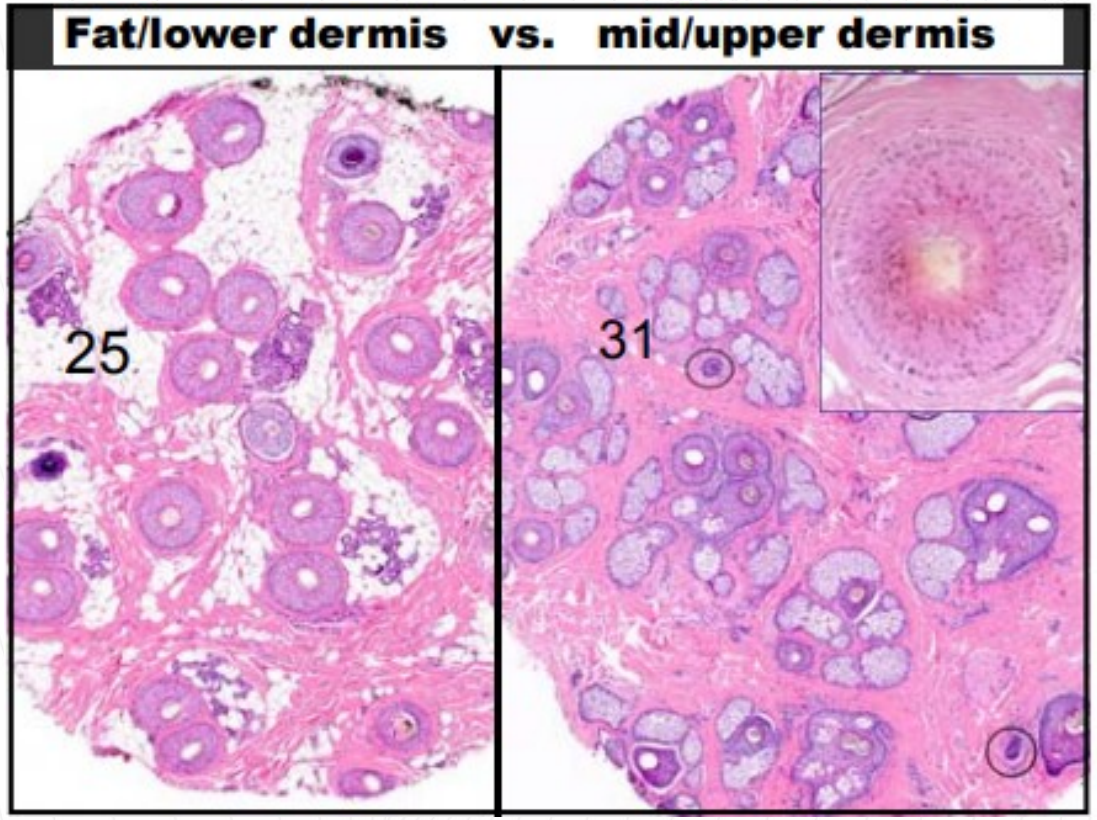
*Analysis of variance.
SD, standard deviation; ND, no data.

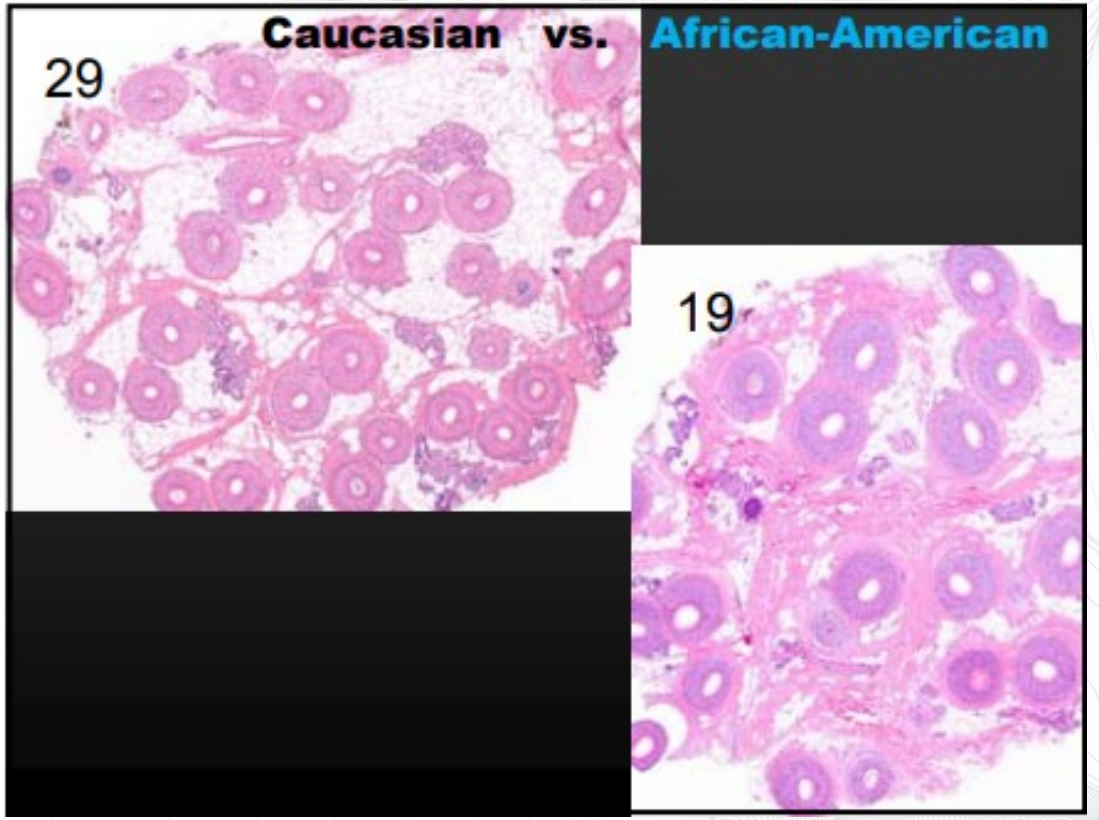
Ko J.H., Huang Y.H., Kuo T.T. Hair counts from normal scalp biopsy in Taiwan. Dermatol Surg. 2012. 38;

SUMMARY






Fat/lower dermis vs. mid/upper dermis
25
31


Caucasian vs. African-American
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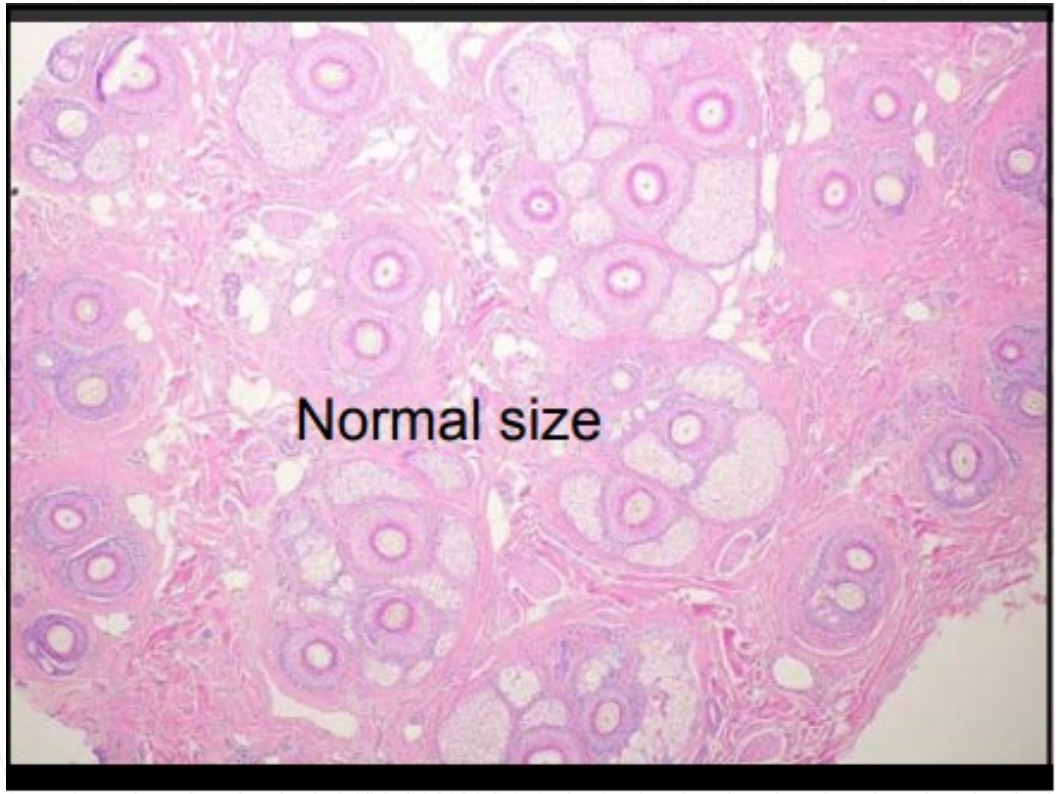
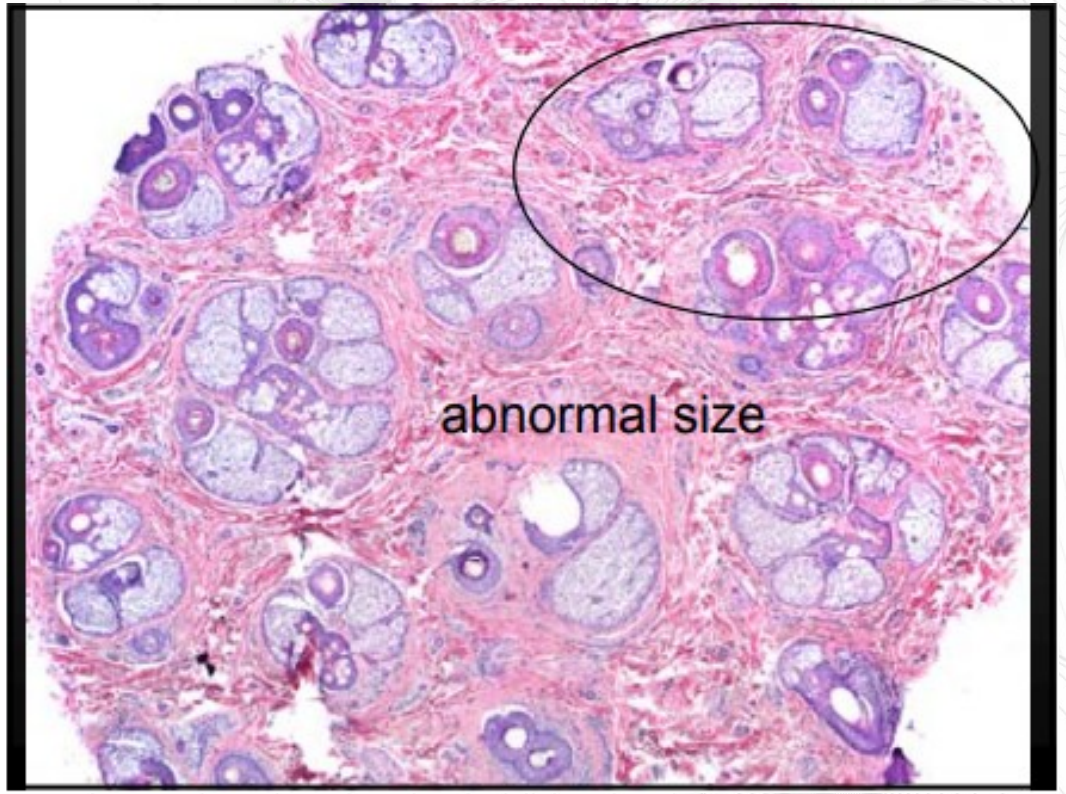
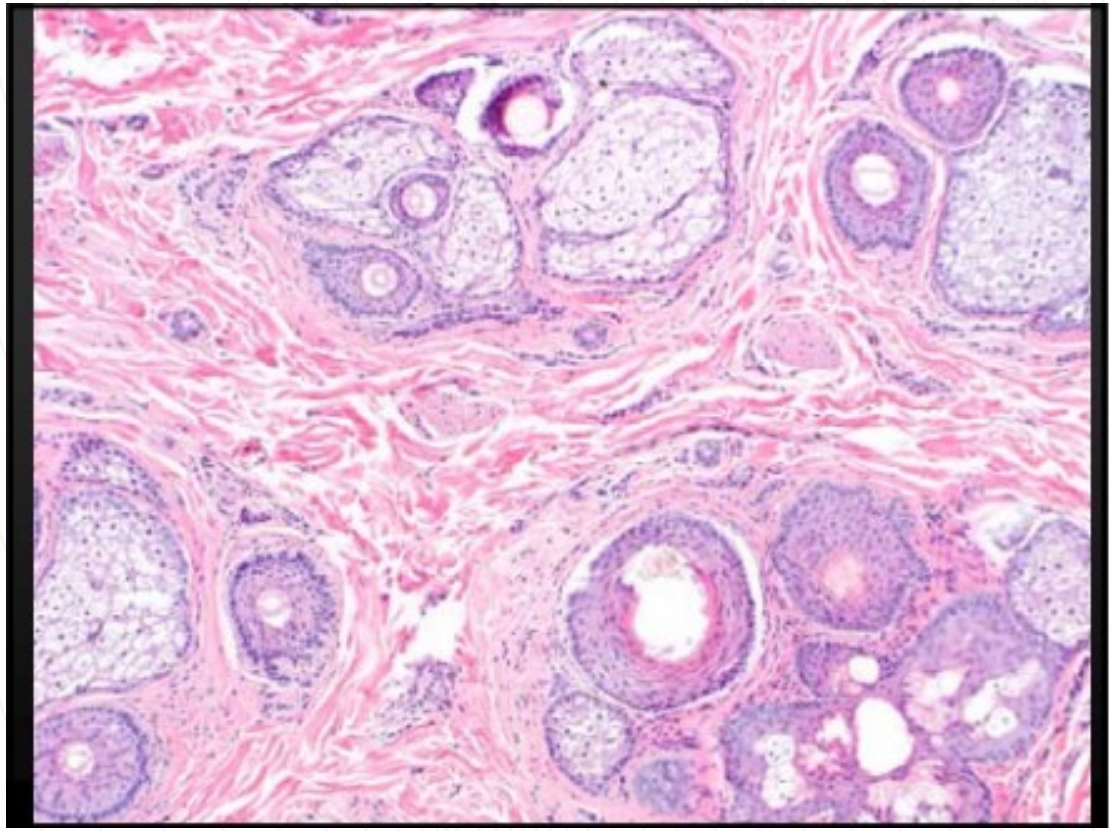
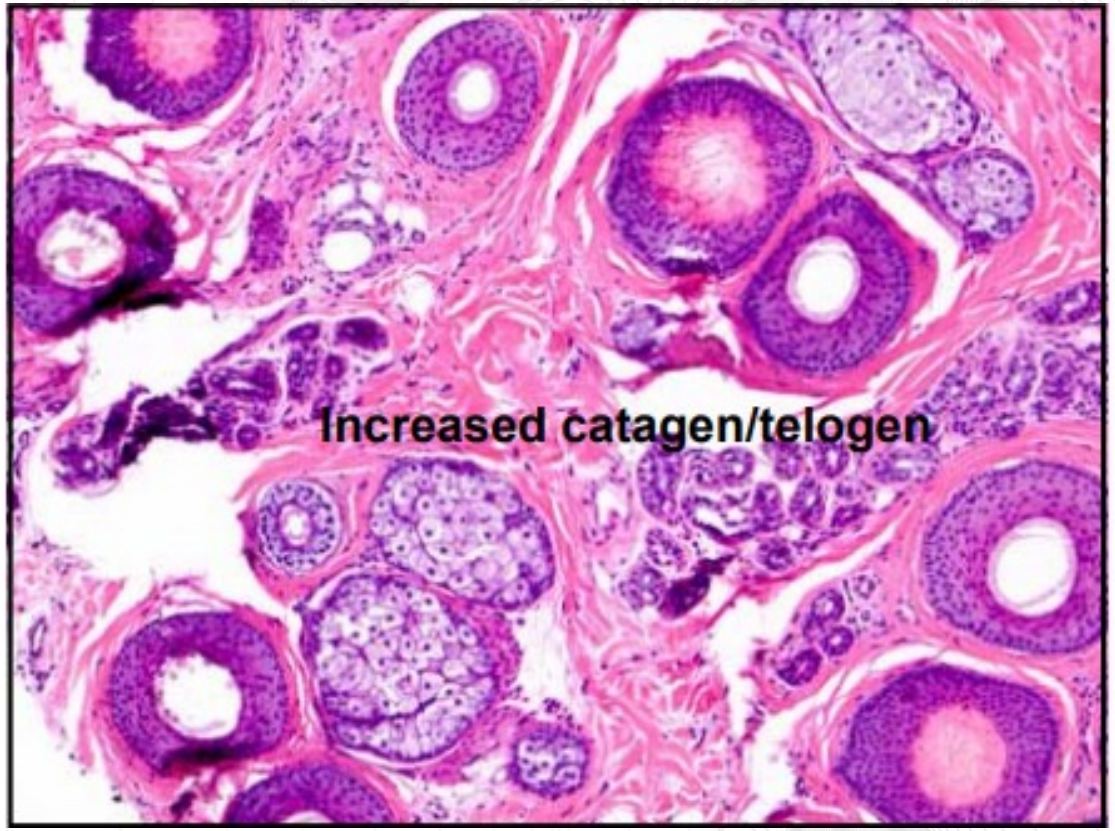
19





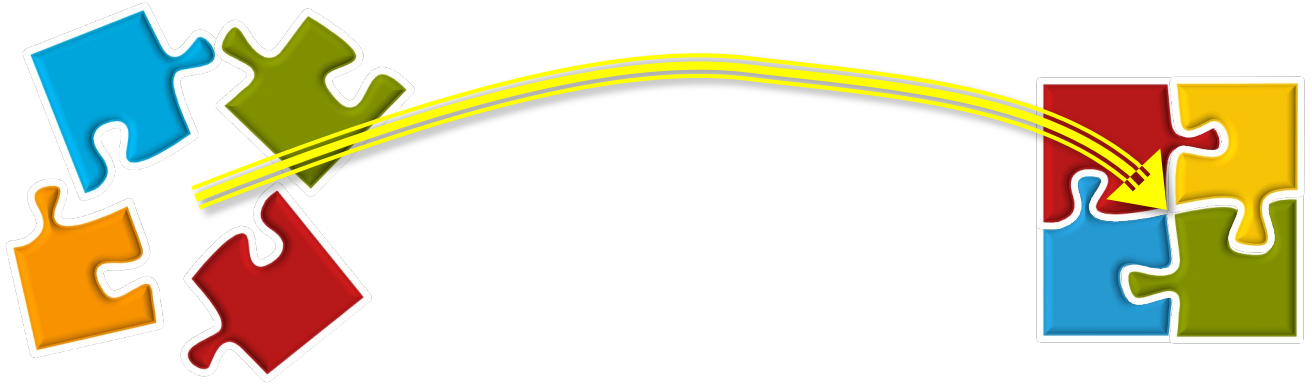




SUMMARY

Hair biopsy interpretation can be easier to interpret when you :

- **Know how the biopsy was taken and why.**
- **Correctly choose the type of section (vertical, horizontal, both?) to perform in the lab.**
- **Have in depth knowledge of healthy hair follicle anatomy, hair cycle, changes in terminal follicles and vellus hair.**
- **And finally, integrate all the information and make a diagnosis.**



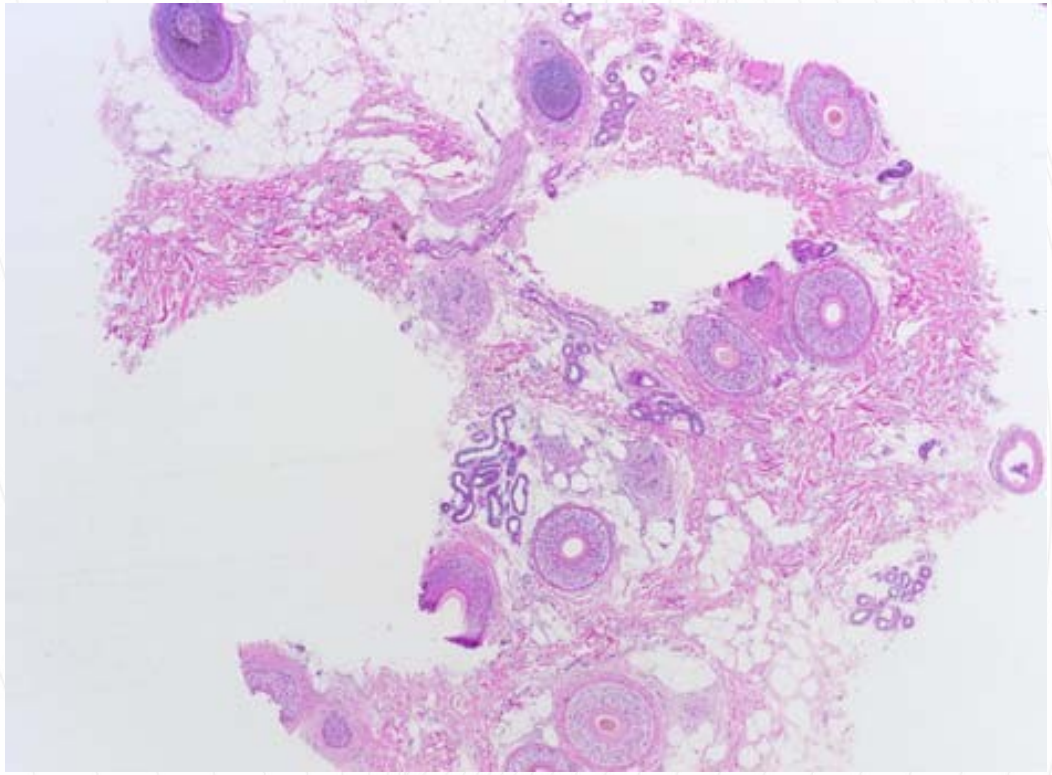
Clinical Cases

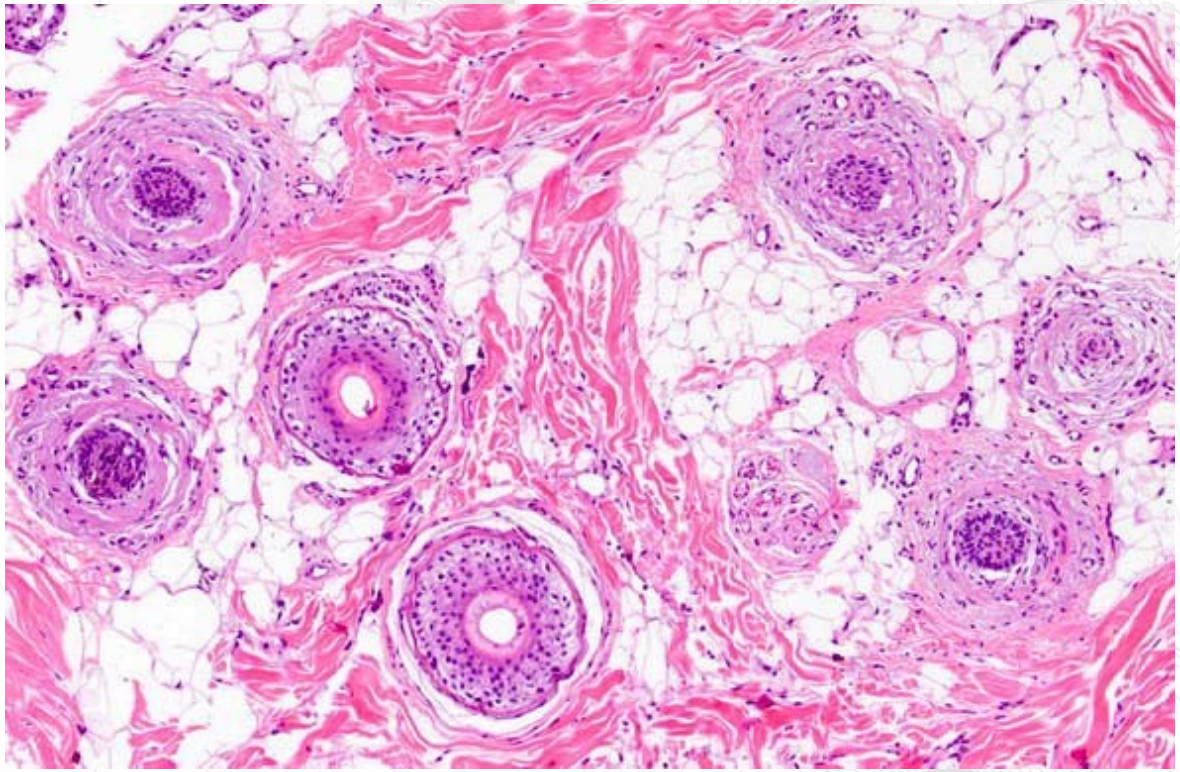
Case 1

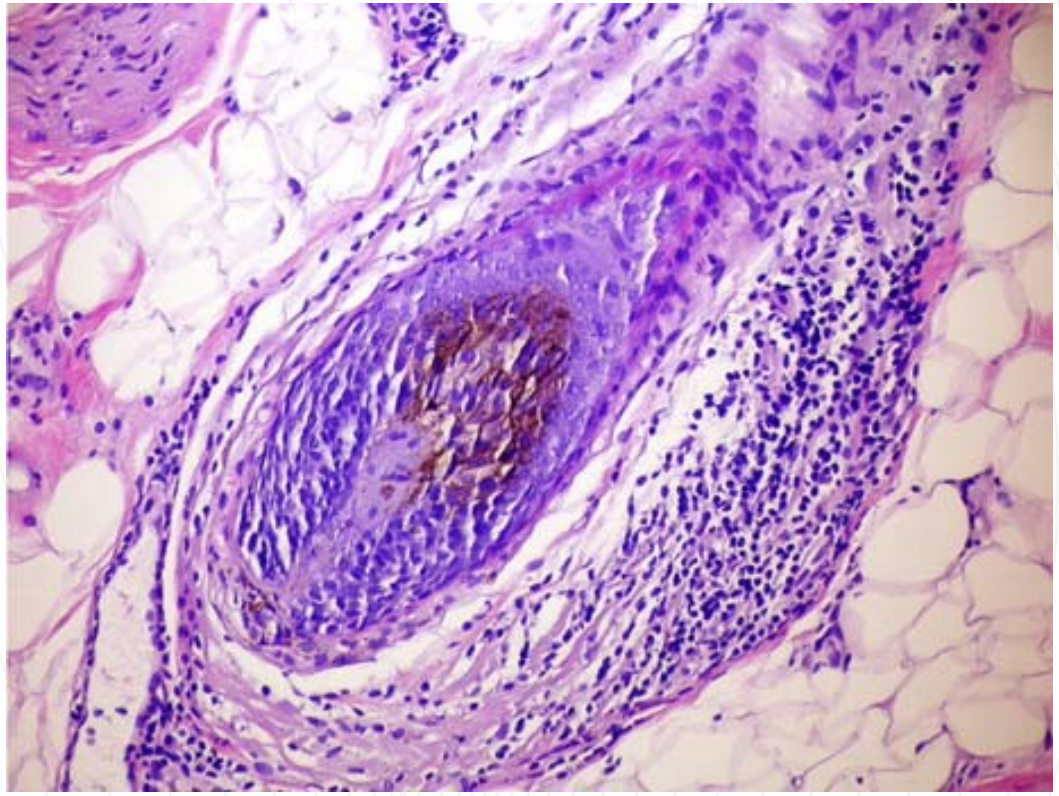
35-year-old woman complaining of patchy hair loss and scalp pruritus.

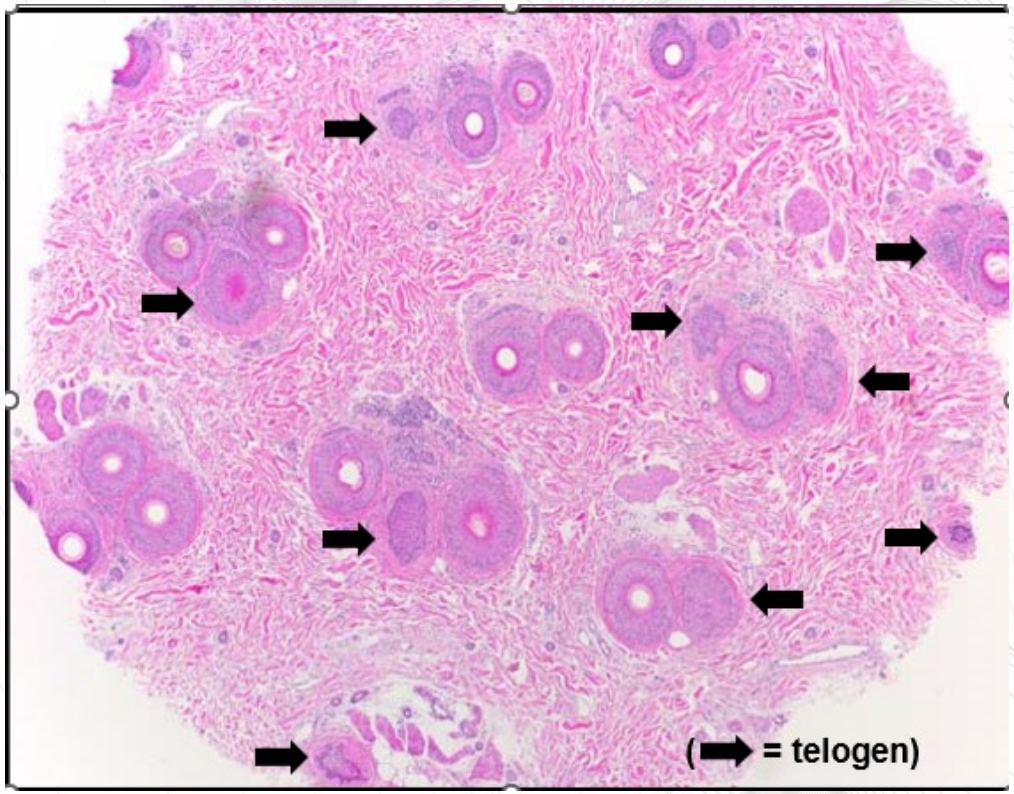
Clinical differential diagnosis

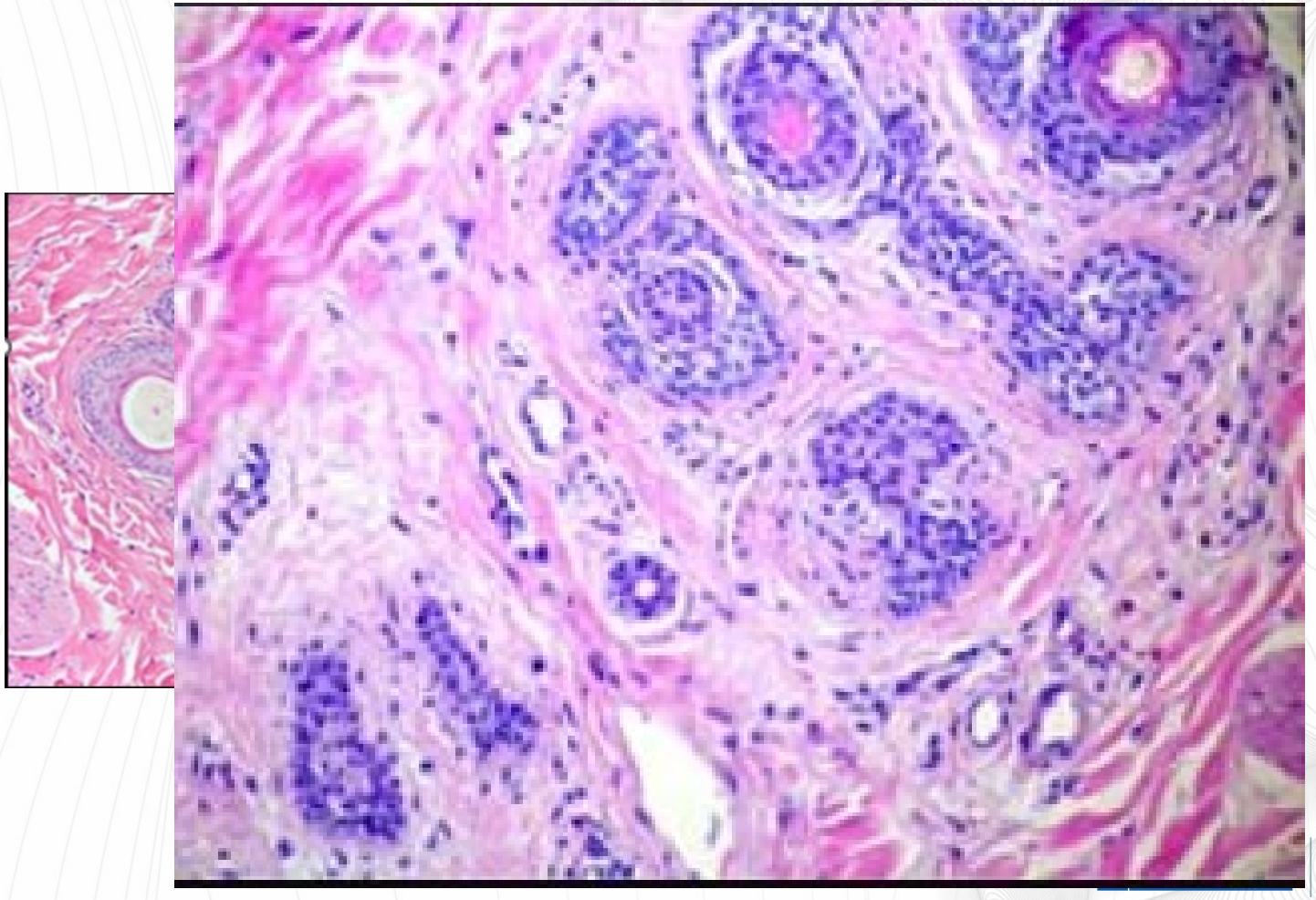
1. Tinea capitis.
2. Chronic cutaneous lupus erythematosus
3. Seborrhoeic dermatitis
4. Syphilitic alopecia
5. Psoriasis plus alopecia areata
6. Psoriatic alopecia





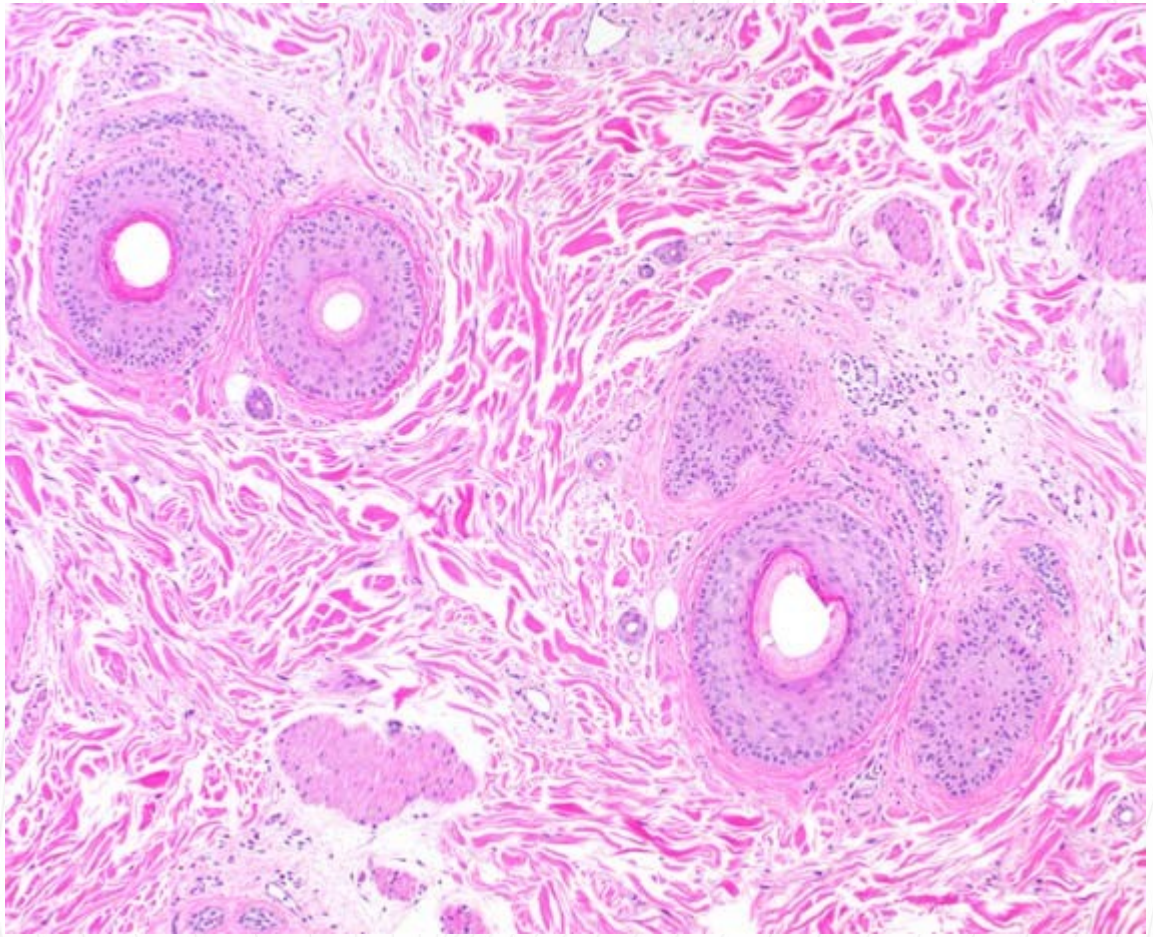




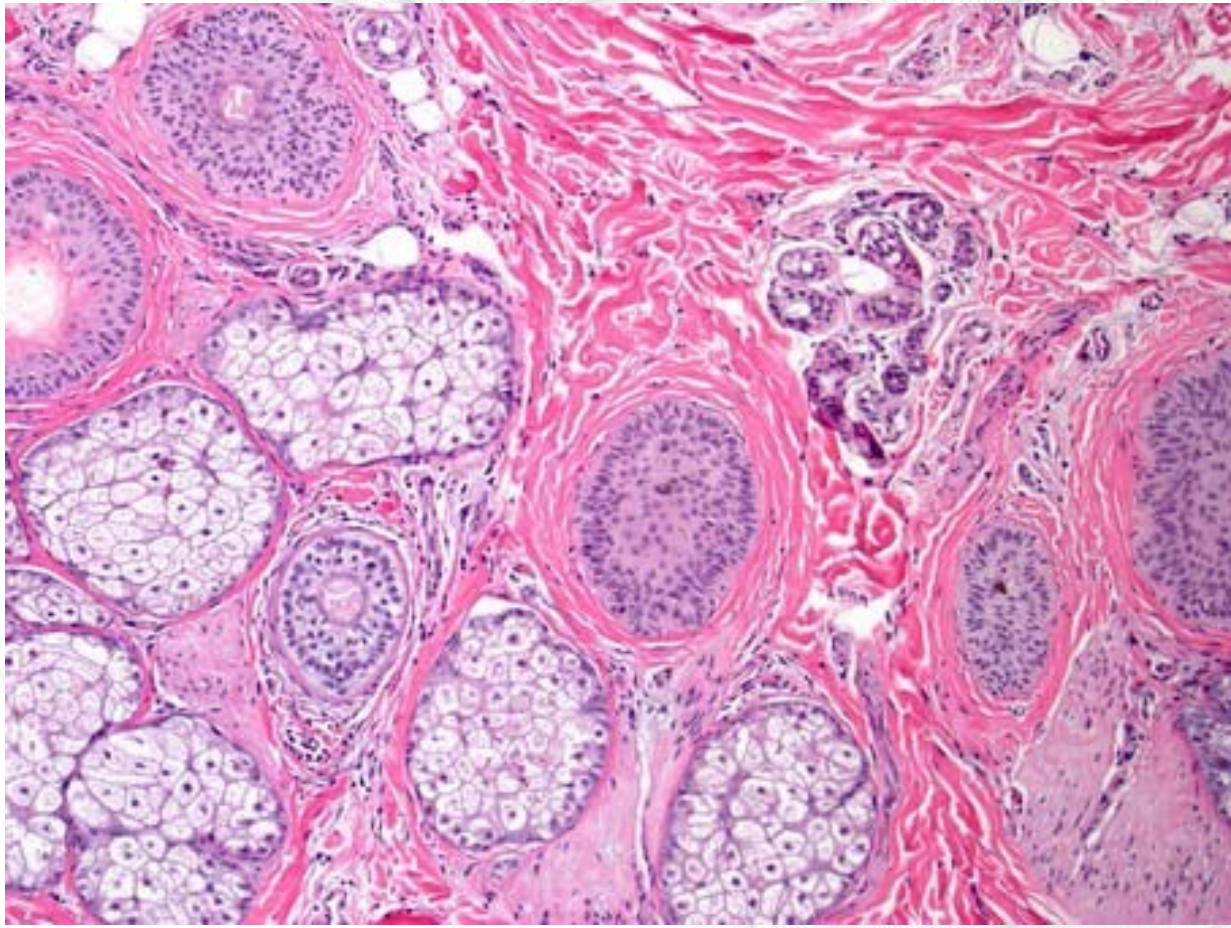


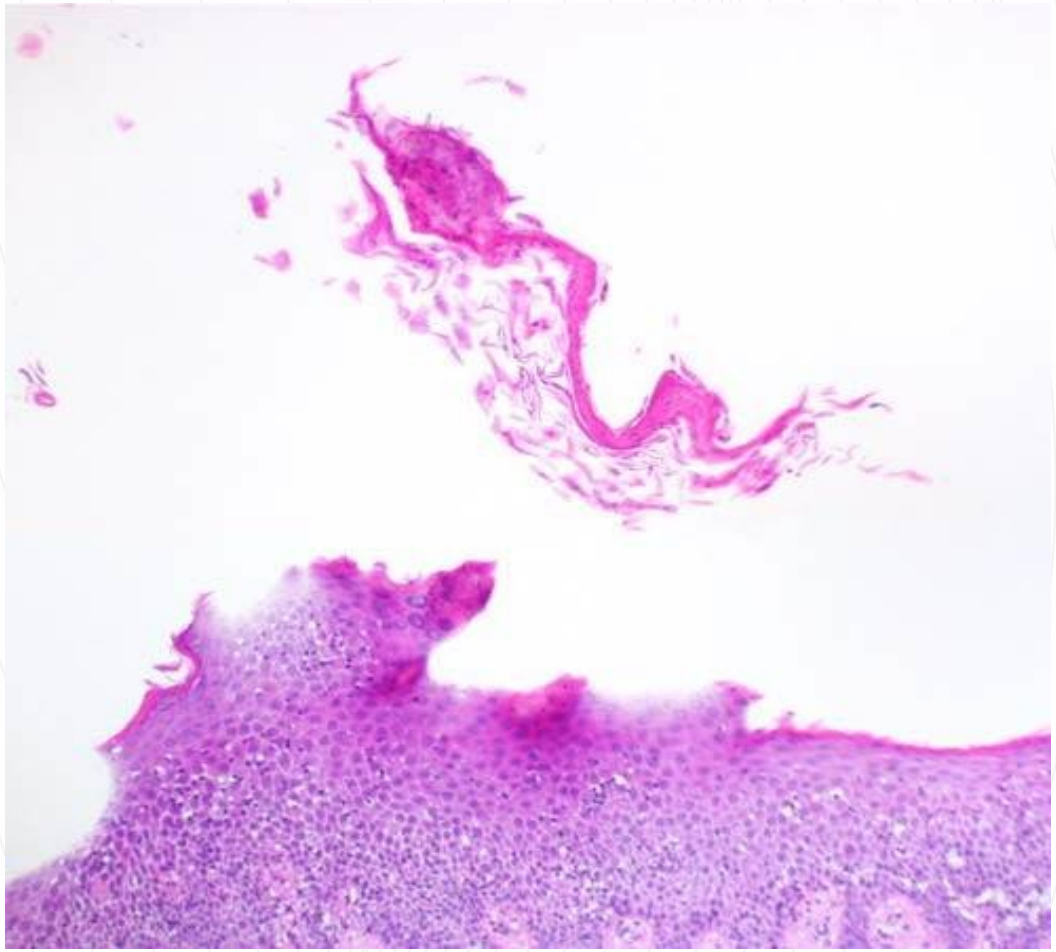
For comparison:

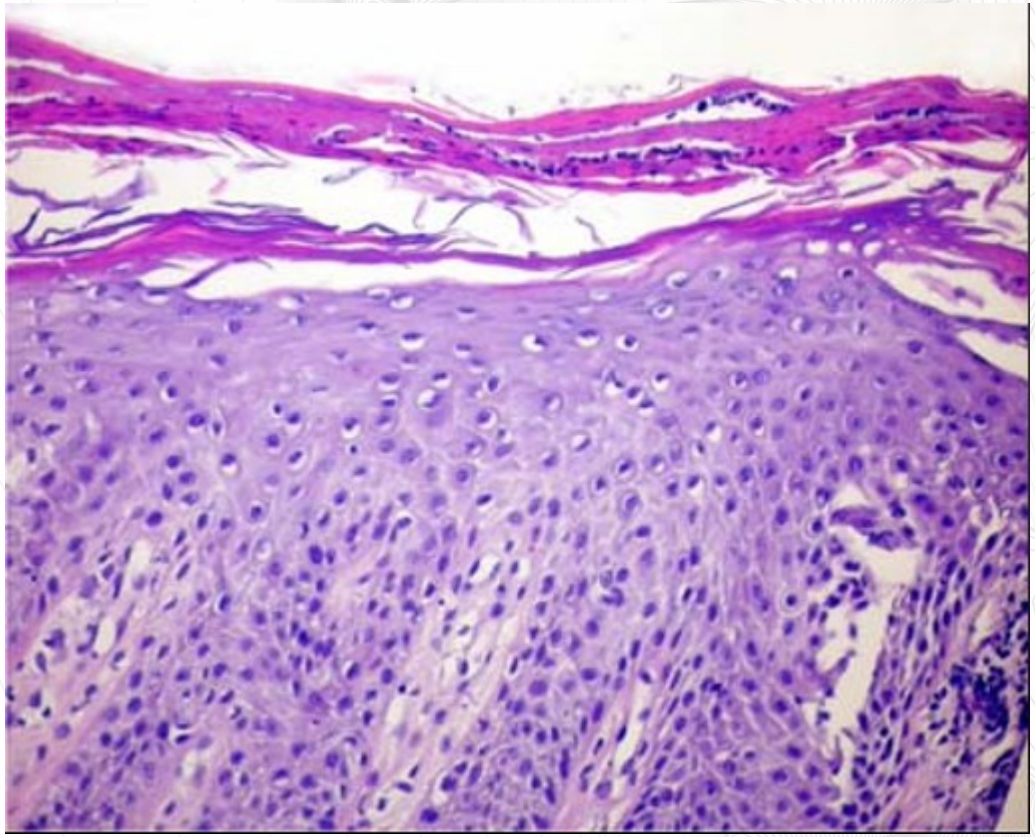
Case 1



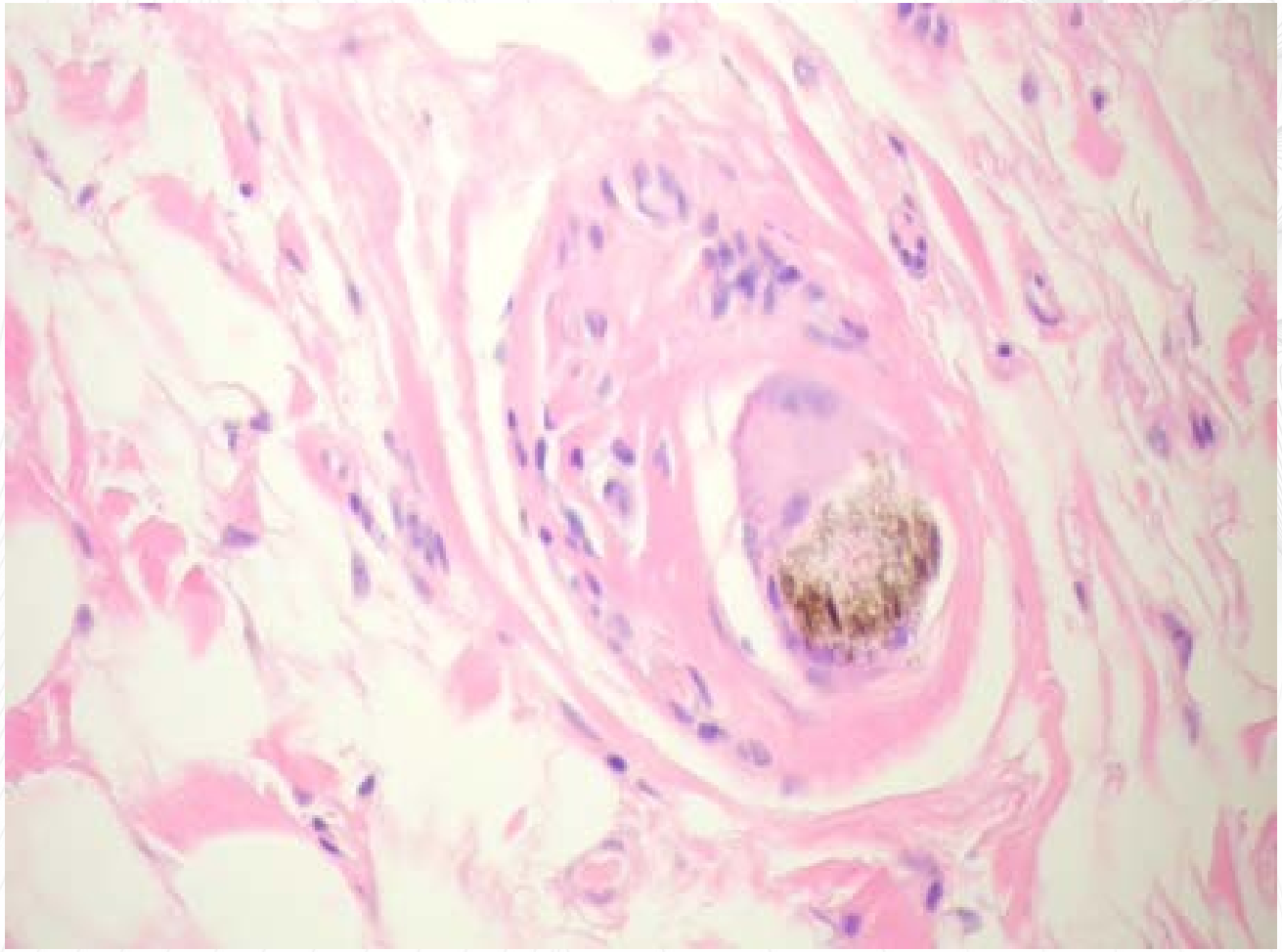
Alopecia areata







Follicular destruction



Histologic findings in summary

1. Normal or nearly normal number of hairs
2. Increased catagen/telogen
3. Follicular miniaturisation
4. Dramatic sebaceous gland atrophy
5. +/- epidermal changes of psoriasis
6. +/- peribulbar lymphocytes.
7. +/-focal follicular destruction.

Diagnosis?

Final diagnosis

Psoriatic alopecia

Note

Psoriatic alopecia is a historic mimic of alopecia areata, but with sebaceous gland atrophy.

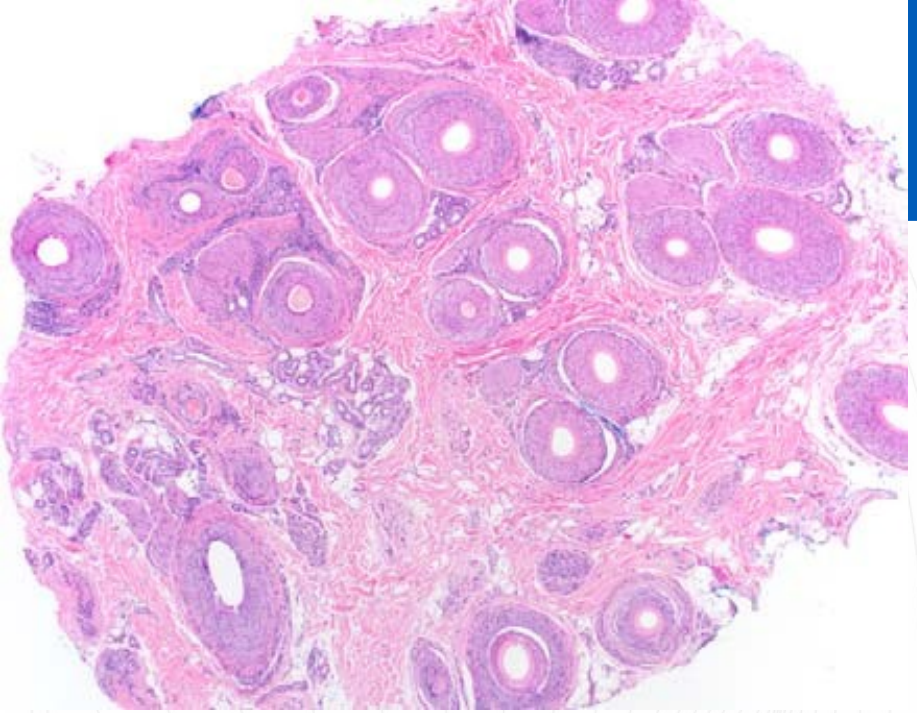
Case 2

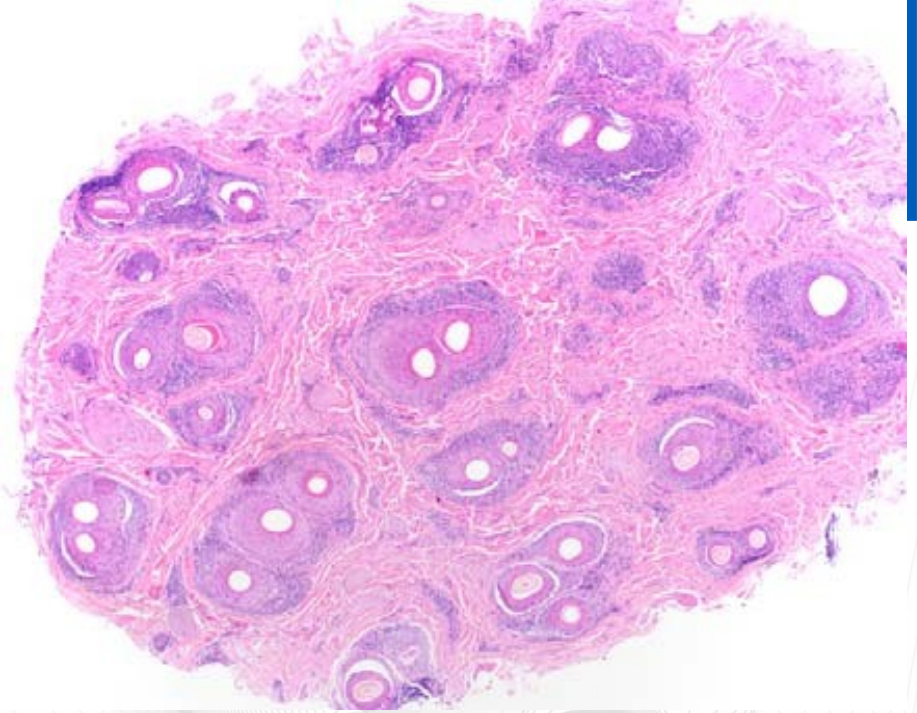
A 4 mm punch biopsy specimen was taken from an inflamed bald spot on the scalp of a healthy 45-year-old woman.

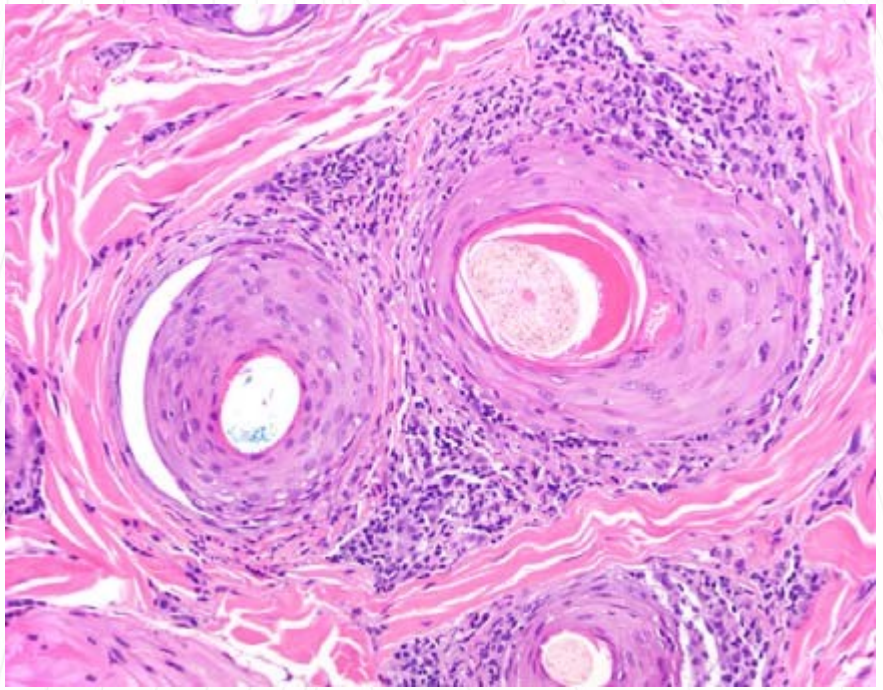

01/29/2014 10:07

Differential diagnosis

1. Lichen planopilaris
2. Mycosis fungoides
3. Central centrifugal scarring alopecia
4. Folliculitis decalvans
5. Chronic cutaneous lupus erythematosus (DLE)







Summary of histological findings

1. Total number of hairs decreased
2. Size of hairs normal
3. Catagen/telogen normal or increased
4. Inflammation is prominent: Vacuolar interface alteration and dense perifollicular inflammation
5. Epidermal changes not present

Diagnosis?

Diagnosis

Lichen planopilaris

Lichen planopilaris- Clinical

1. Typical lesions of lichen planopilaris (LPP) present with atrophic, ill-defined patches of scarring alopecia with decreased follicular orifices.
2. The margins of the alopecia, where the process is still active, will show perifollicular erythema with follicular scale
3. Cutaneous lesions of lichen planus may be present in up to 28% of cases
4. Frontal fibrosing alopecia, the changes of LPP appear not only to be localized to the scalp, but also to involve the eyebrows and the peripheral body hair.

LPP

LPP

Active margin of the alopecia with perifollicular erythema and follicular scale

Lichen planopilaris- Histology

Histopathologically, the features of LPP and its variants are similar, irrespective of clinical presentation.

In early lesions there is

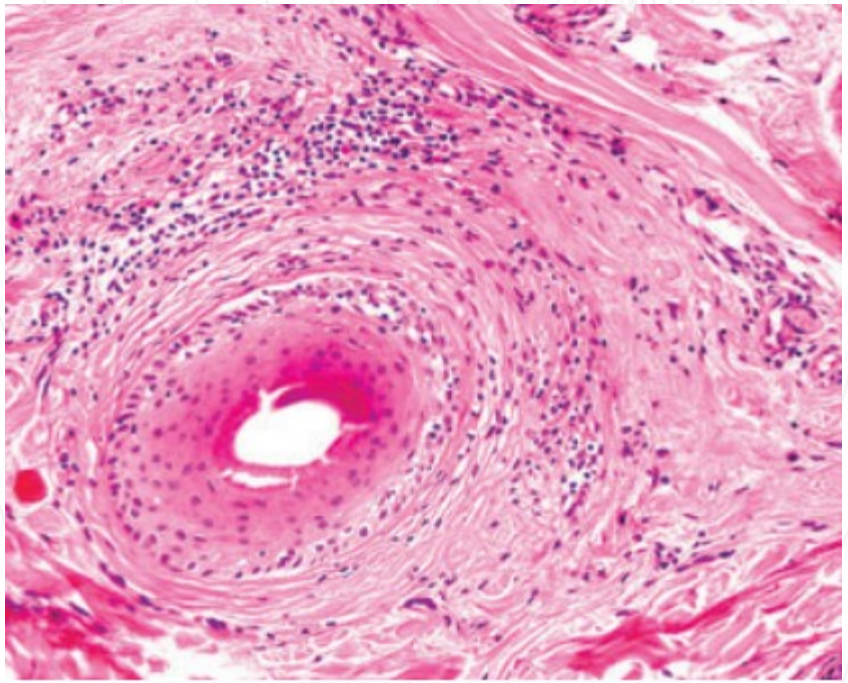
1. Vacuolar interface change
2. Moderately dense perifollicular lichenoid lymphocytic cell infiltrate at the level of the infundibulum and isthmus.
3. Occasionally, the interfollicular epidermis may have an associated lichenoid infiltrate.

In advanced lesions,

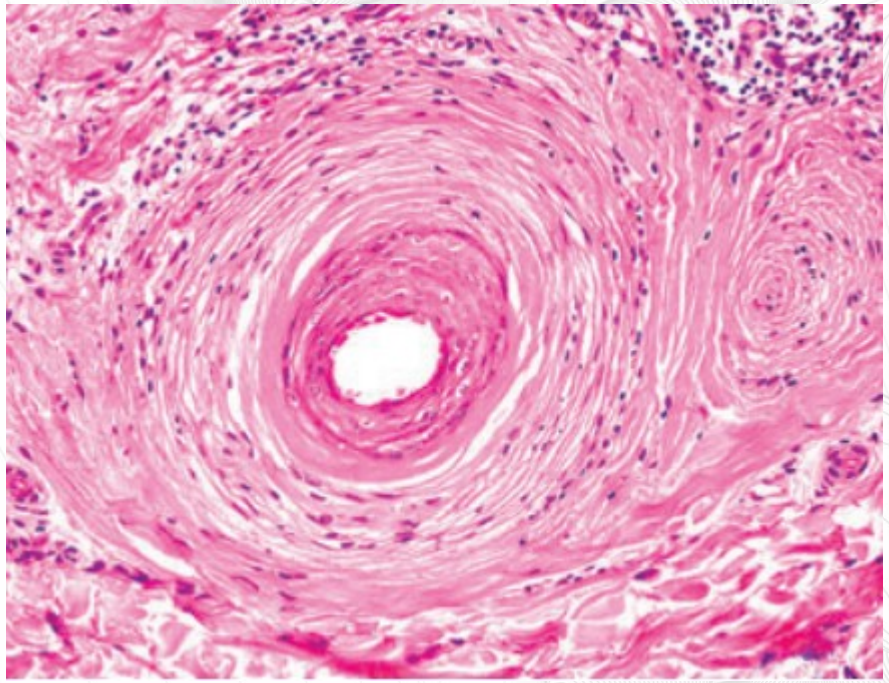
4. Concentric lamellar perifollicular fibrosis
5. The lichenoid infiltrate ‘backs away’ from the follicle.
6. Clefting between the follicular epithelium and the stroma may be seen in longstanding lesions.

LPP

Isthmus: a hair follicle showing interface alteration, perifollicular fibrosis and a mild perifollicular lymphoid cell infiltrate.



Another hair follicle with a more advanced perifollicular concentric fibrosis, and with a lymphoid cell infiltrate that ‘backs away’ from the hair follicle.



Lichen planopilaris- Histology

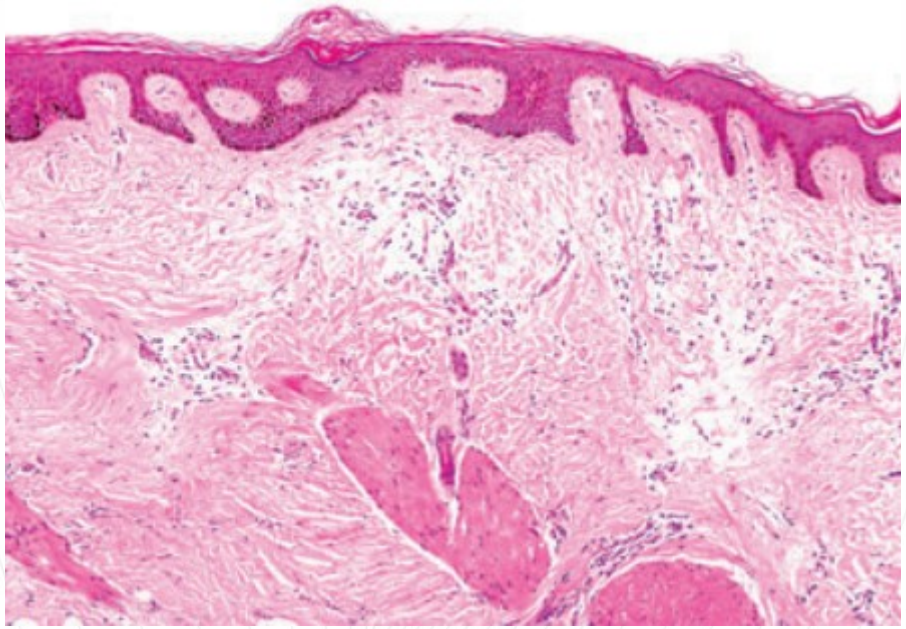
End-stage LPP will show loss of elastic fibres in a superficial dermal wedge-shaped scar ..... which is better demarcated with the Verhoeff–van Gieson elastic stain

Direct immunofluorescence highlights the presence of colloid bodies in the peri-infundibular/isthmic area staining with IgM (less frequently with IgG, IgA and C3).

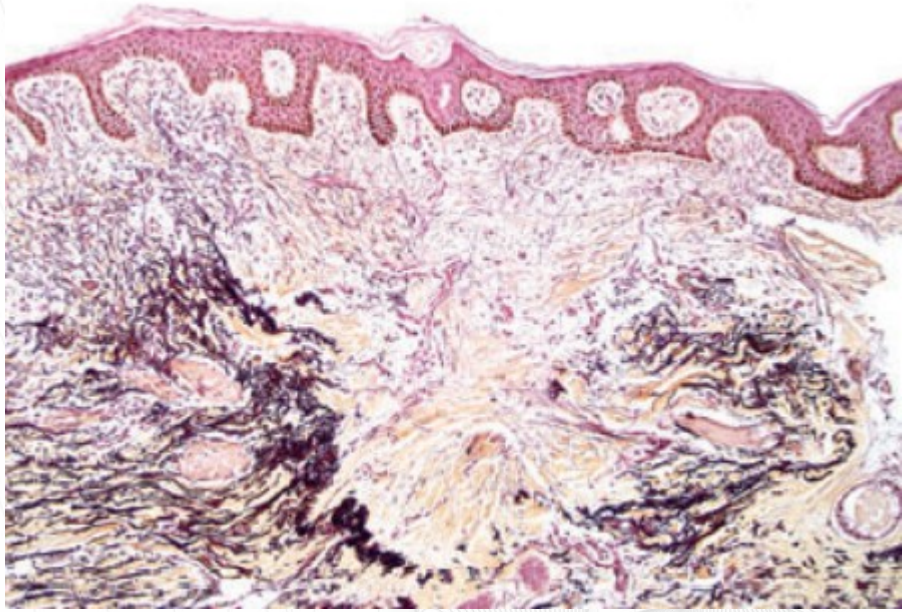
There is a 'shaggy' or linear band of fibrinogen deposition along the basement membrane zone of affected follicles, while the interfollicular epidermis is negative for immunoreactants.

Lichen planopilaris- Histology

Superficial dermal wedge-shaped scar with loss of hair follicles and residual arrector pili muscle



Verhoeff–van Gieson elastic stain demarcates the wedge-shaped morphology of the scar with loss of elastic fibres



Note: LPP versus DLE

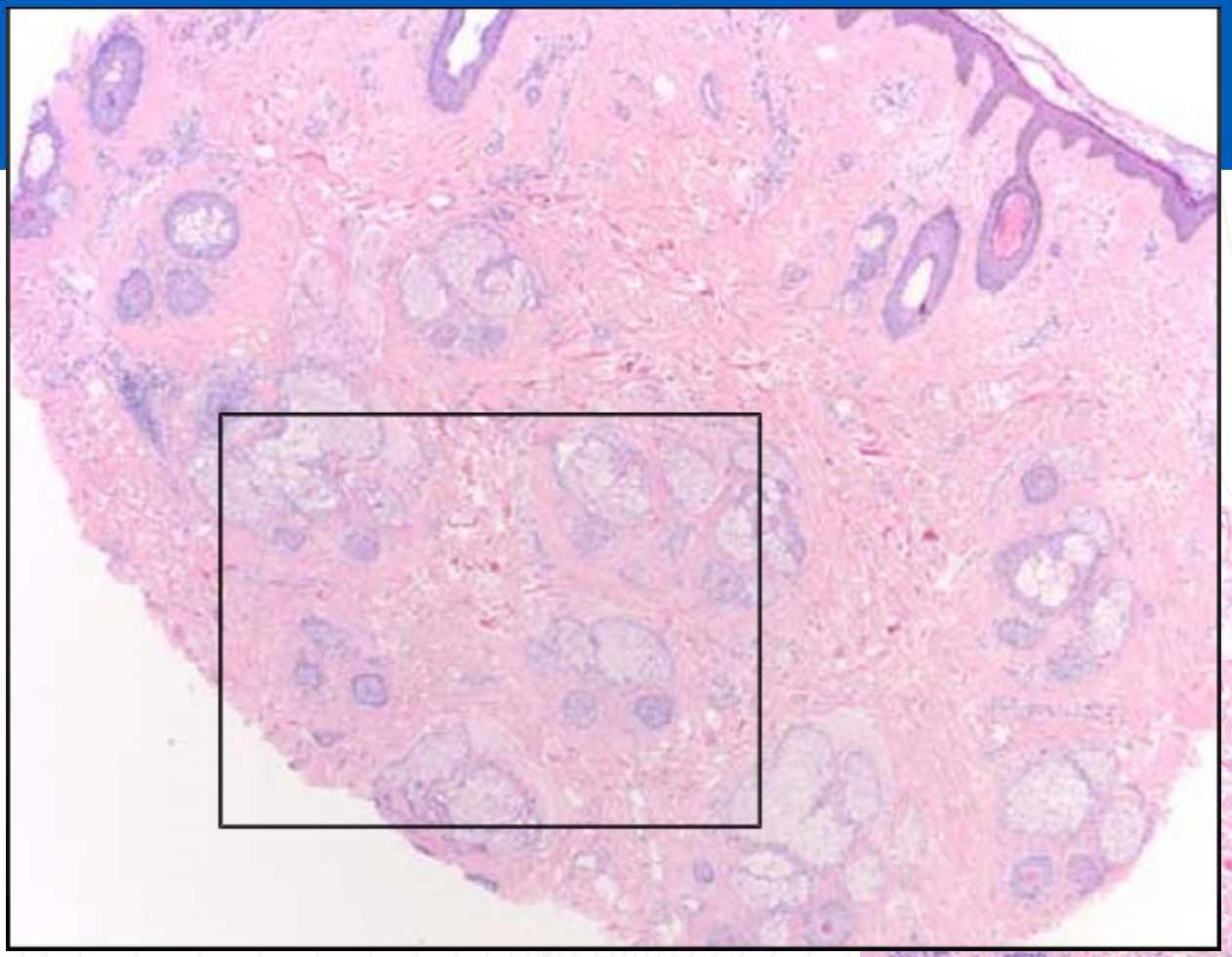
In LPP:

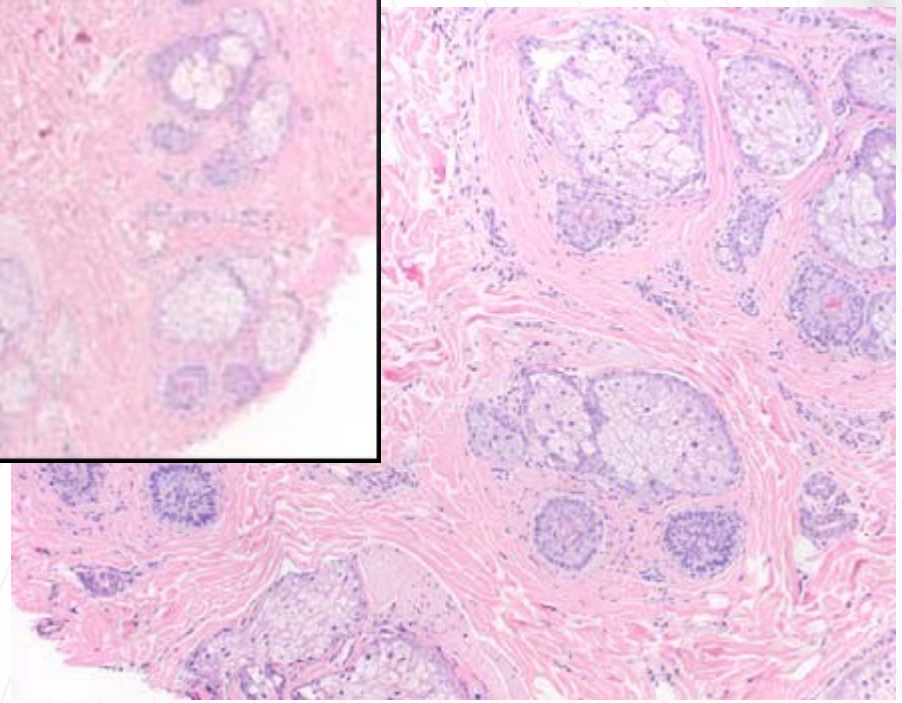
1. No increase in deep mucin
2. No peri-eccrine inflammation
3. No foci of dense, deep, non-follicular inflammation
4. No hair miniaturisation

Case 3

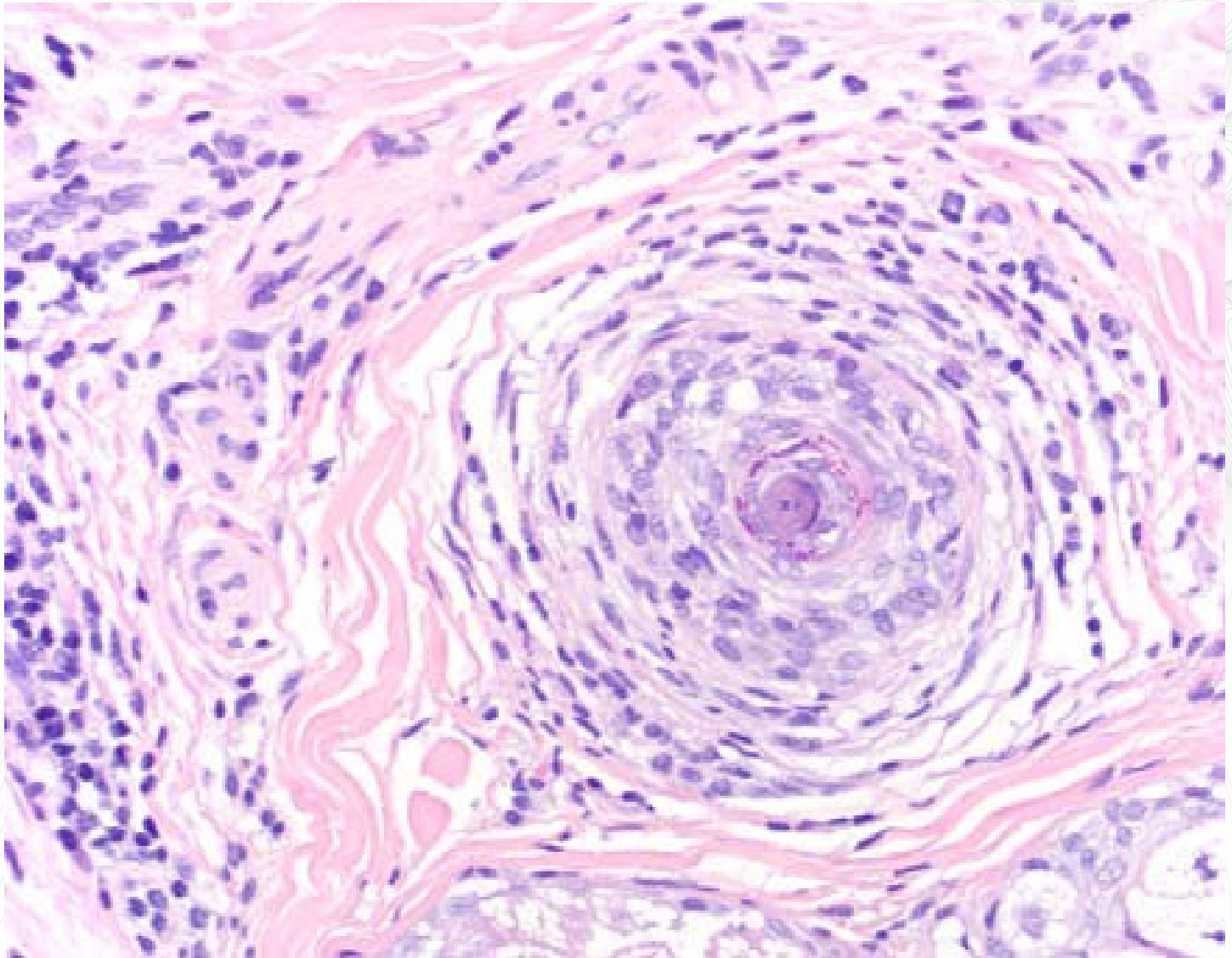
A 4 mm punch biopsy specimen was taken from an otherwise healthy woman who complains of recent hair loss.

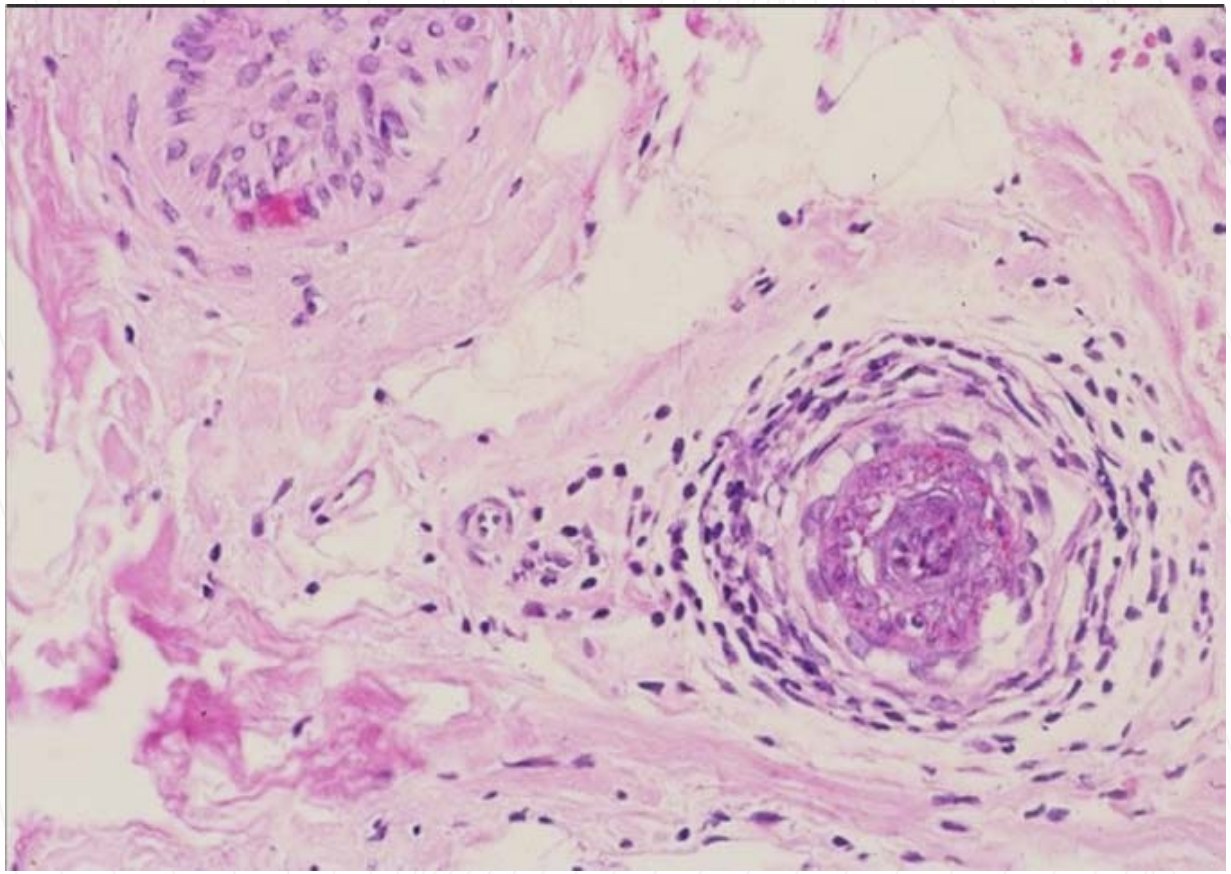
Case 3

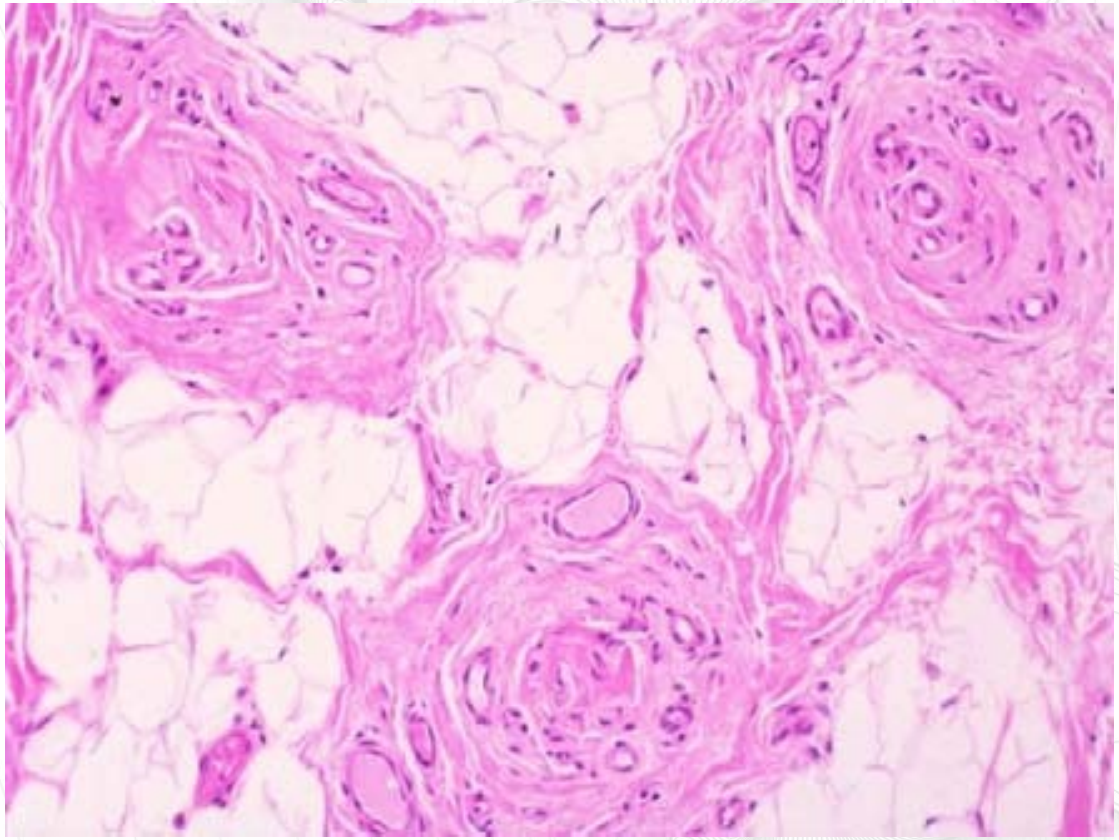




Hair bulb







Diagnosis?

Diagnosis:

Alopecia areata

Alopecia areata

Alopecia areata (AA) is thought to be an organ-specific autoimmune disorder.

It commonly occurs in association with other autoimmune diseases such as vitiligo and thyroiditis, and the lifetime risk of acquiring AA is approximately 1.7%.

It equally affects males and females at all ages, and 60% of patients before the age of 20 years.

Clinically, it is characterized by sudden onset of patches of nonscarring hair loss, with ‘exclamation-point’ hairs

Alopecia areata

It may undergo spontaneous remissions or exacerbations.

May become extensive to involve the entire scalp (alopecia totalis) and body hair (alopecia universalis).

Nail changes (pitting, thickening and ridging) may be seen in 10–66% of cases.

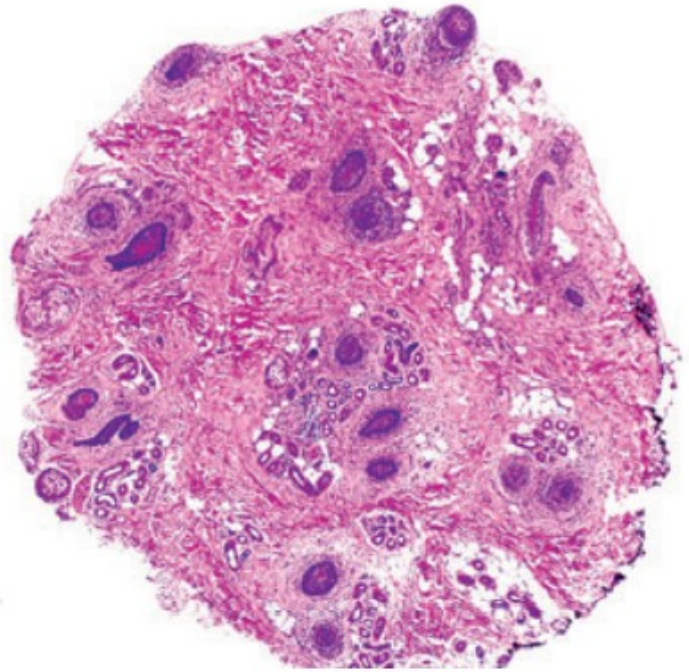
Summary of histological findings of alopecia areata

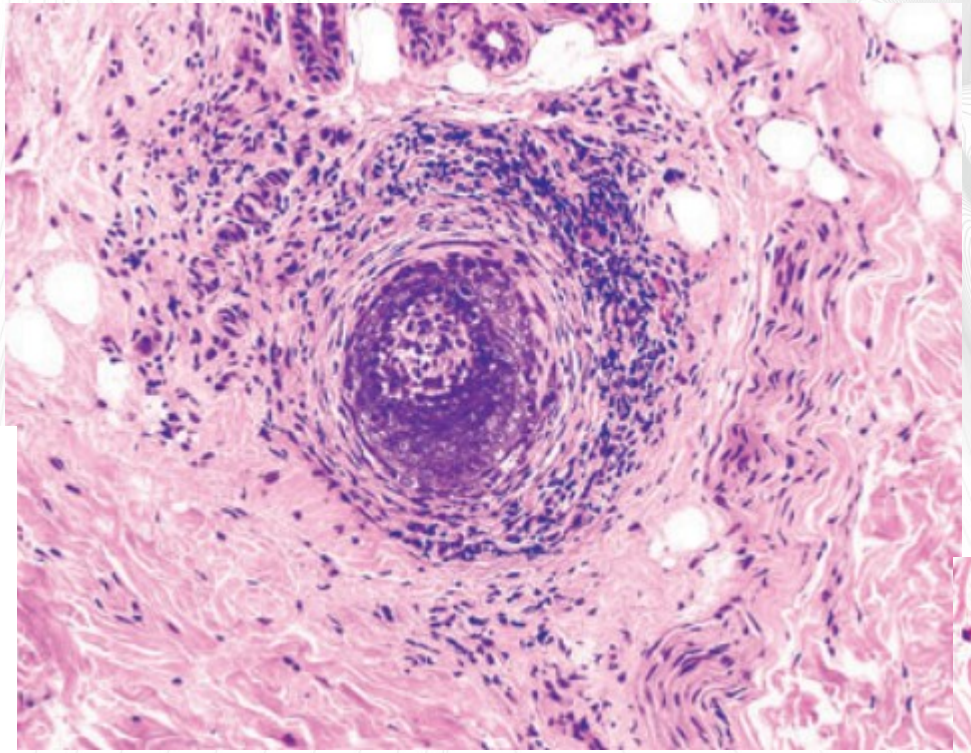
1. Normal number of hairs
2. Most hairs are in catagen/telogen
3. +/- focal, mild, bulbar inflammation

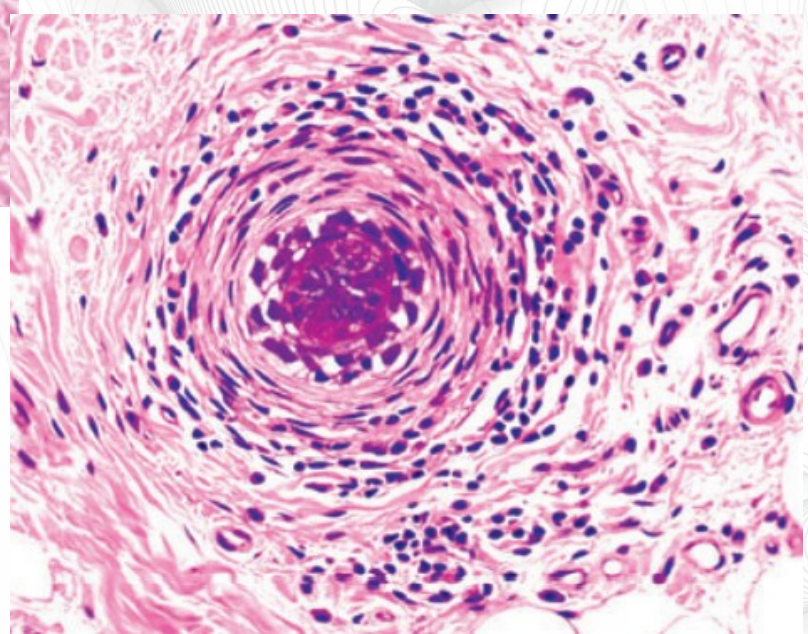
DDx: mimics of this histological picture include especially:

4. Syphilitic alopecia,
5. SLE

1. Sub-isthmic region: a hair bulb with peribulbar lymphoid cell infiltrate (‘swarm of bees’).
2. ‘Shift out of anagen’: all the hair follicles are in telogen phase.
3. Anagen-like nanogen hair follicle with no central hair shaft, and perifollicular lymphocytes.







Alopecia areata- differential diagnosis

The main differential diagnosis is with the nonscarring variant of SLE, where peribulbar lymphoid cells are seen as in AA.

Distinguishing features are the presence in the former of:

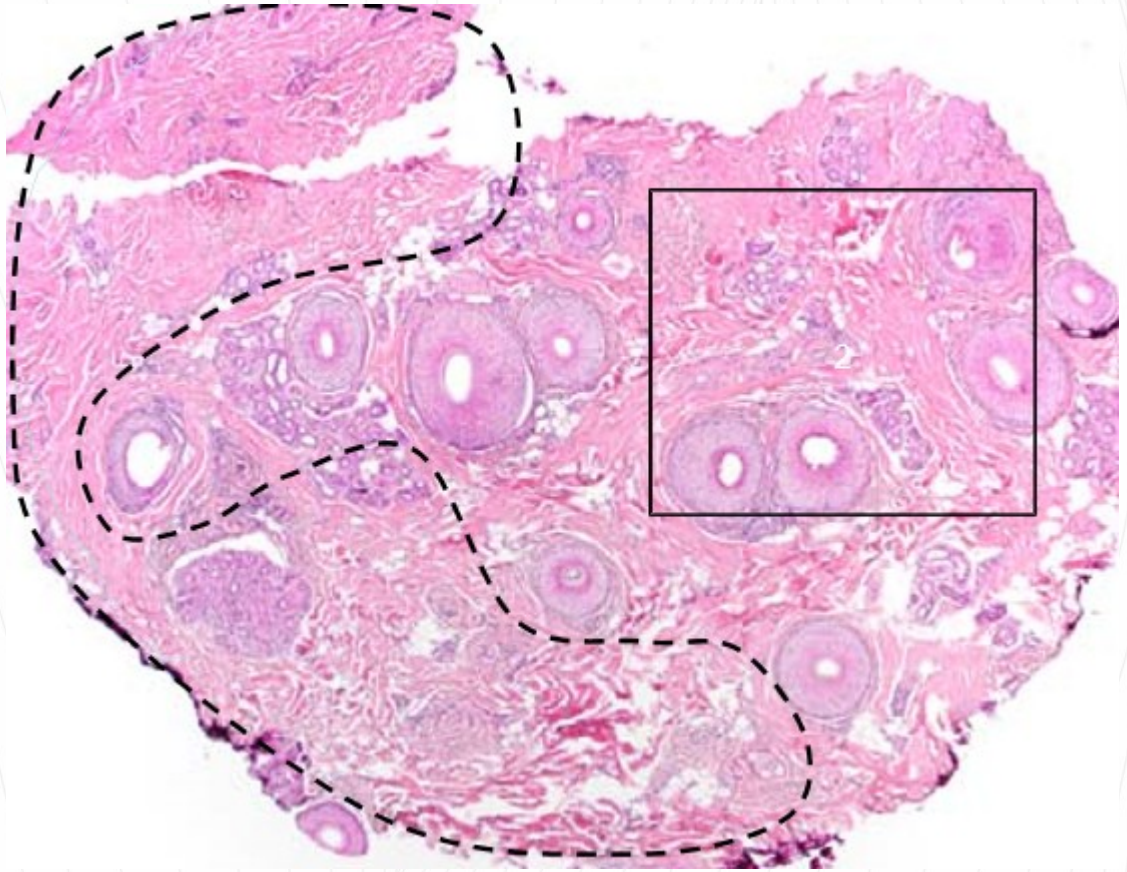
1. Perieccrine and perivascular lymphoplasmacellular cell infiltrate
2. Increased interstitial mucin, particularly if in the deep dermis.

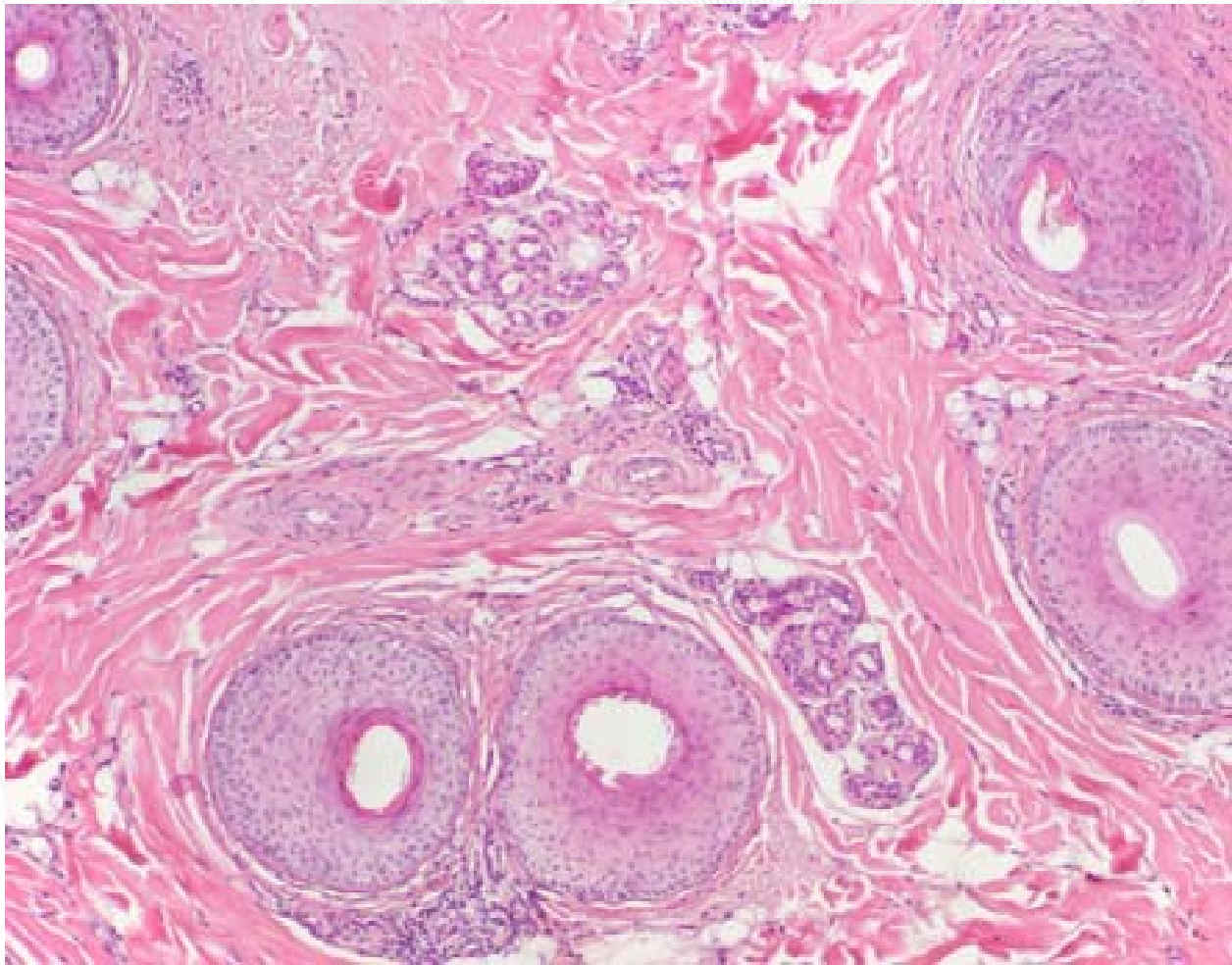
Note on alopecia areata

If we are looking for swarm of bees appearance around hair bulbs, we may miss a lot of alopecia areata

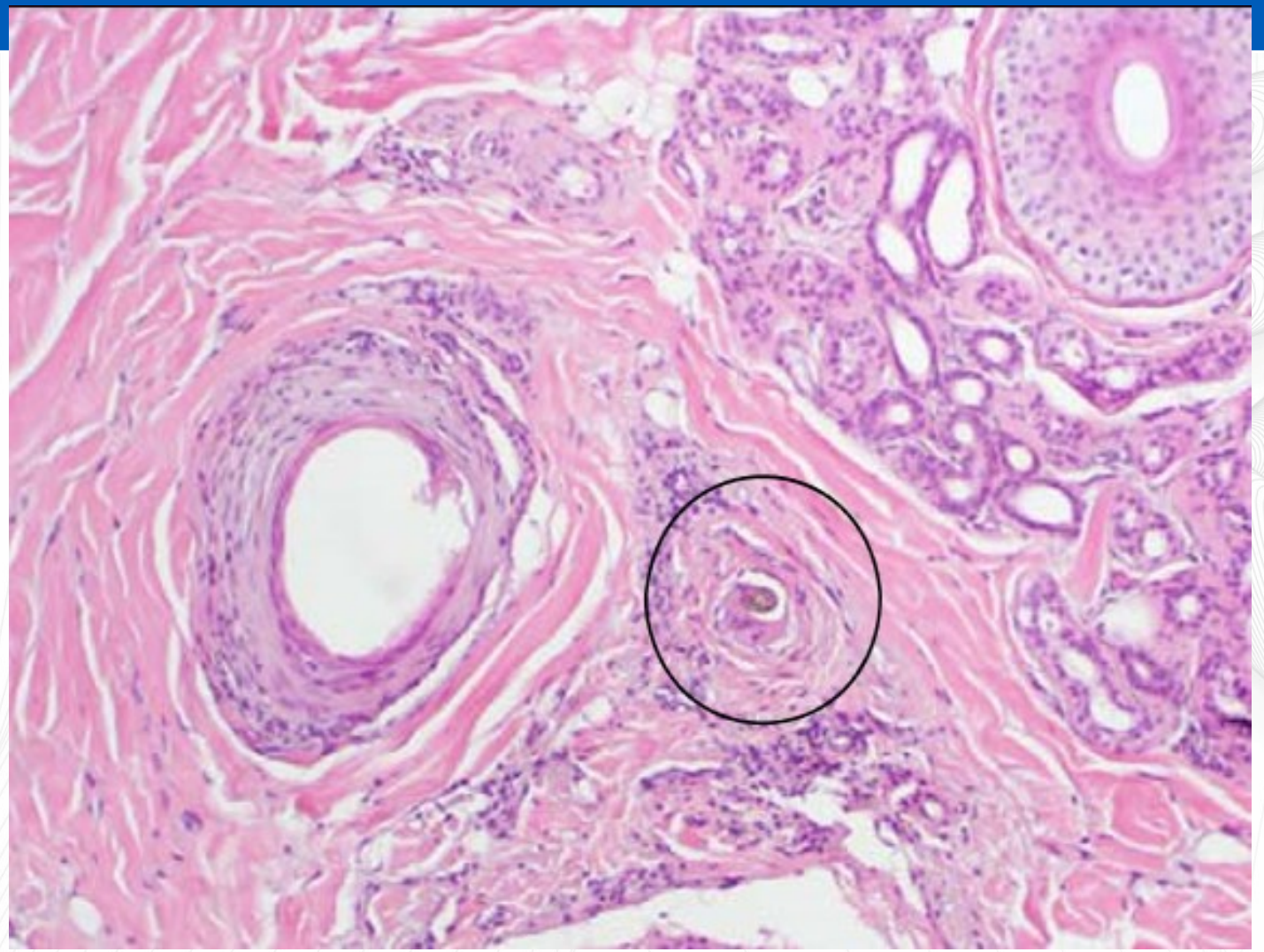
Case 4

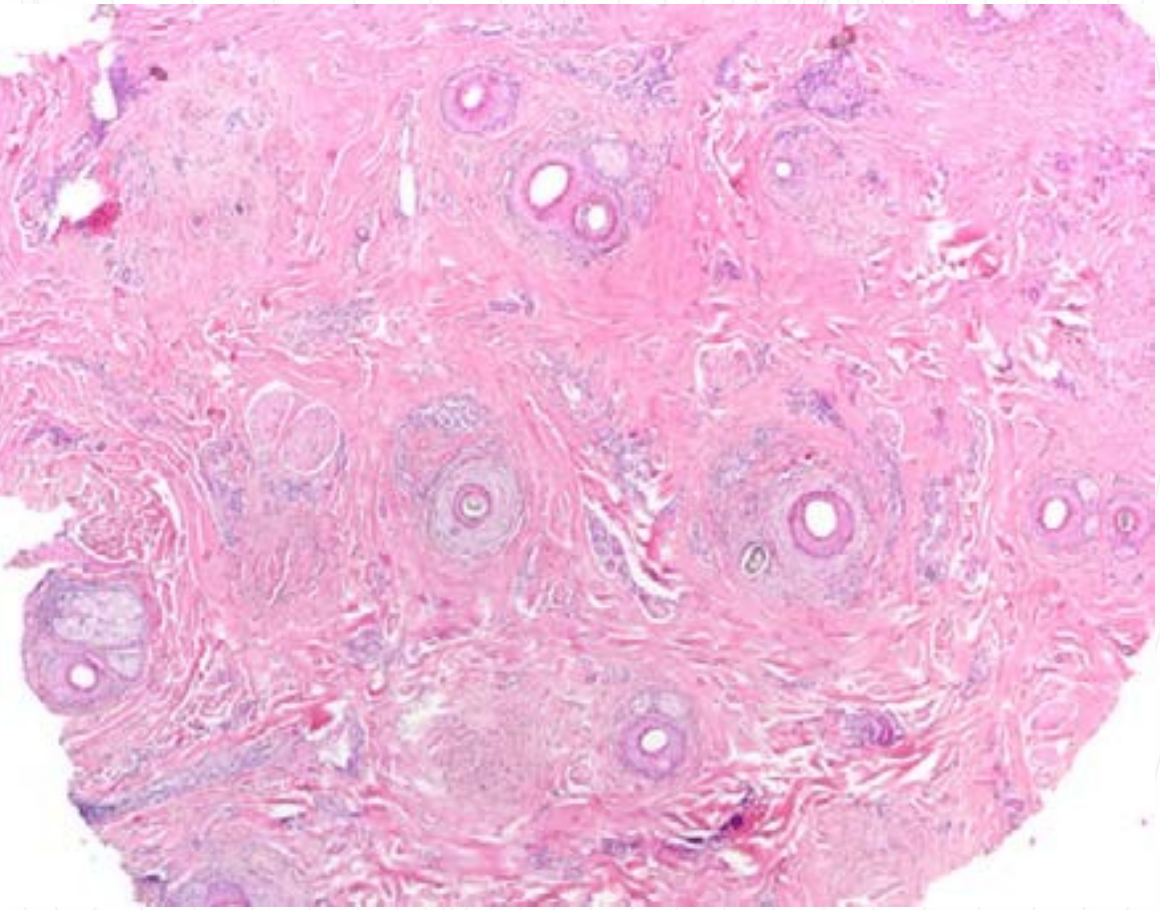
A 4 mm punch biopsy specimen was taken from the crown of the scalp of a 45-year-old African-American woman.

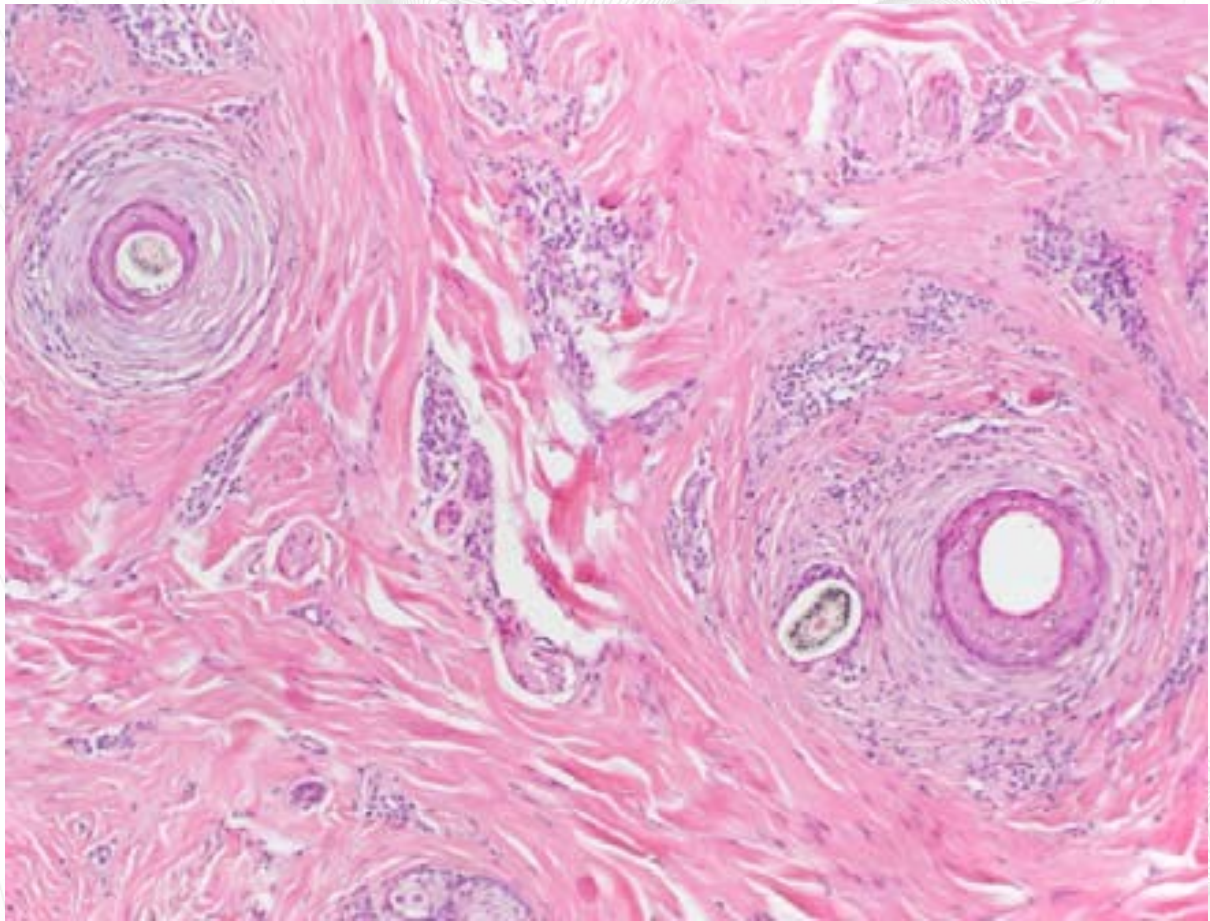


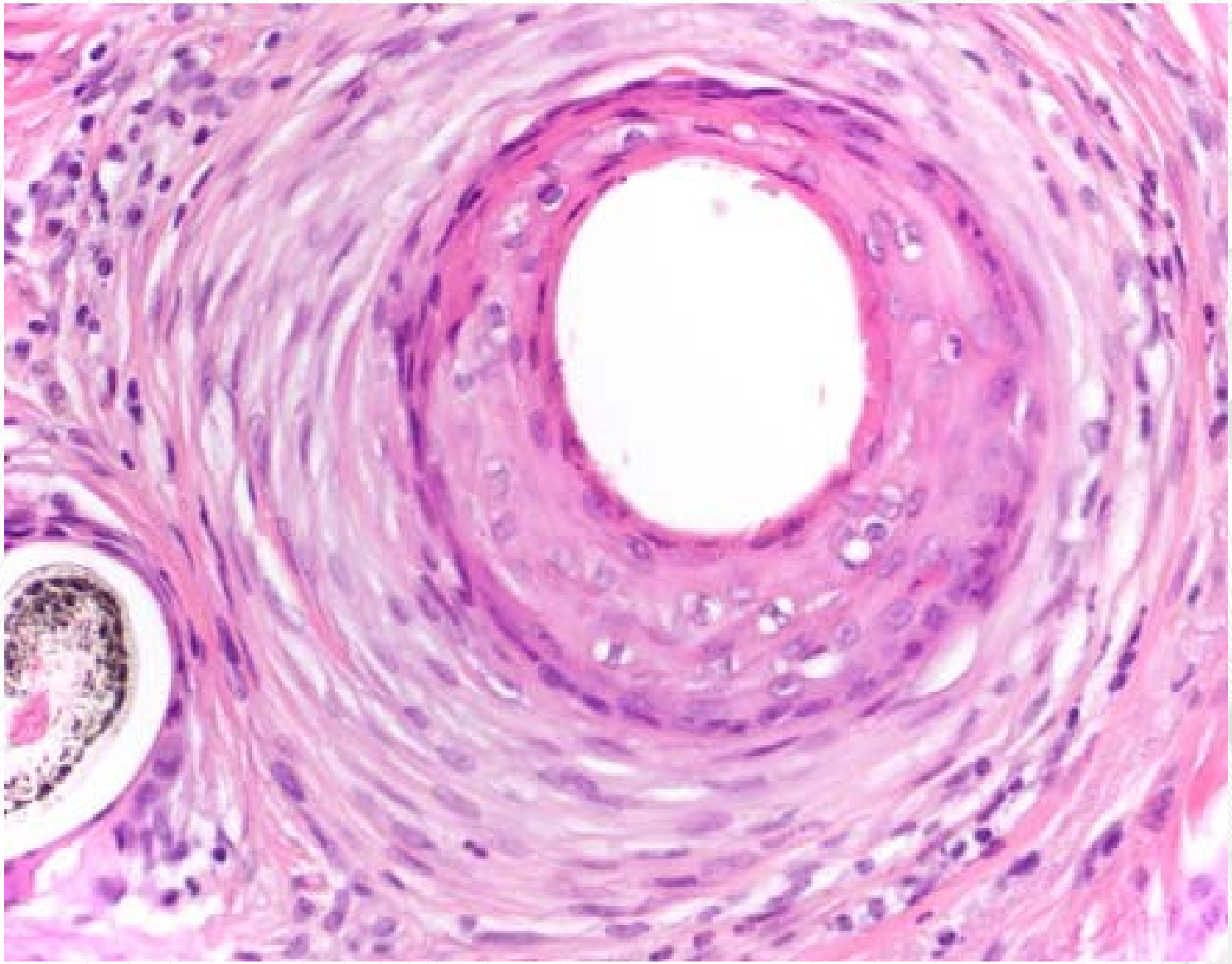


Premature desquamation of the inner root sheath (PDIRS) below the isthmus









Diagnosis?

Central centrifugal cicatricial alopecia

Central centrifugal cicatricial alopecia

Formerly known as ‘hot comb alopecia’ or ‘follicular degeneration syndrome’.

A progressive form of scarring alopecia that is most commonly seen in young to middle-aged women of African descent.

Patients often report a history of traumatic hairstyling involving a combination of hair straighteners and perms, oils, heat, chemicals and traction.

In the early stages, it may show associated features of folliculitis decalvans, with pustules, crusting and erythema with bacterial superinfection.

CCCA histology

1. Total number of hairs: Decreased
2. Size of hairs: Normal
3. Catagen/telogen: Usually normal
4. Earliest change (may appear in normal scalp) is premature desquamation of inner root sheath
5. At later stages…. Lamellar fibroplasia and perifollicular inflammation, most intense at level of isthmus
6. Then hair shafts migrate into the dermis as epithelium is destroyed by reactive inflammation.

Note

Premature desquamation of the inner root sheath can be found in other inflammatory conditions of the scalp, including LPP

However, in the latter instance, the follicles are damaged by the inflammatory cell infiltrate, and represent an ‘end-stage’ follicle.

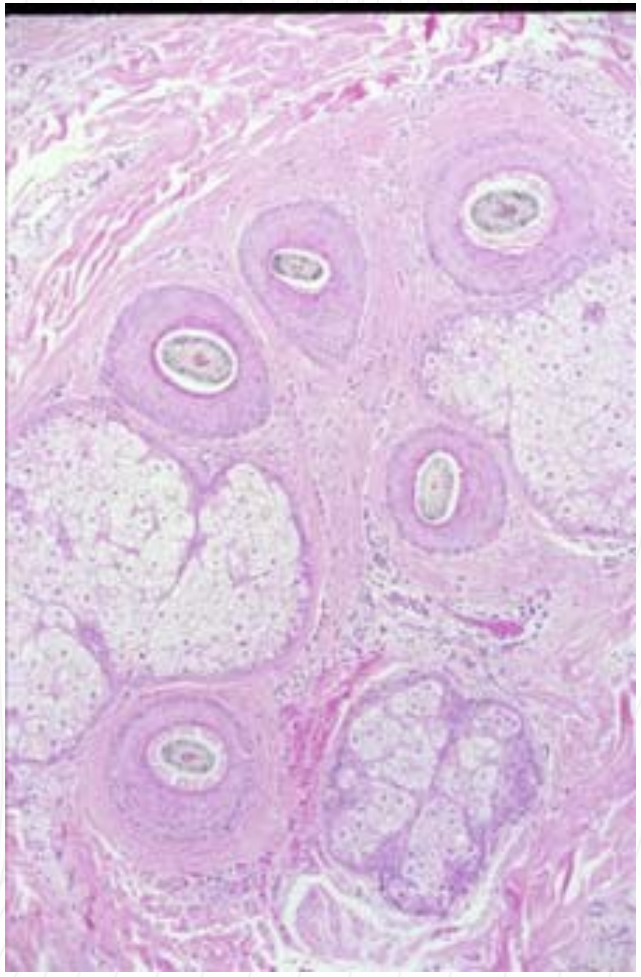
In CCCA premature desquamation of the inner root sheath may be observed also in otherwise normal, unaffected hair follicles, suggesting that it is a characteristic feature of this entity

Features that should be absent in CCCA:

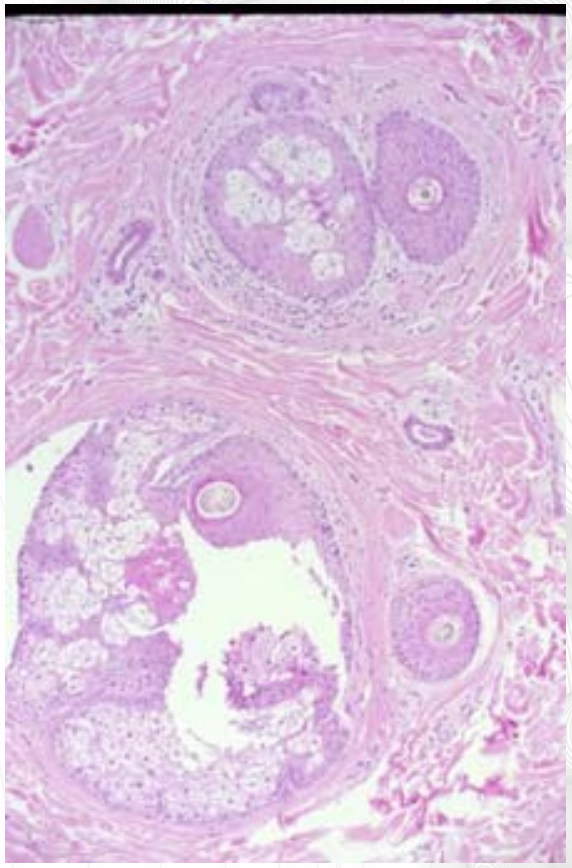
1. Clear cut vacuolar interface alteration
2. Prominent epithelial/stromal clefting
3. Prominent lymphocytic exocytosis

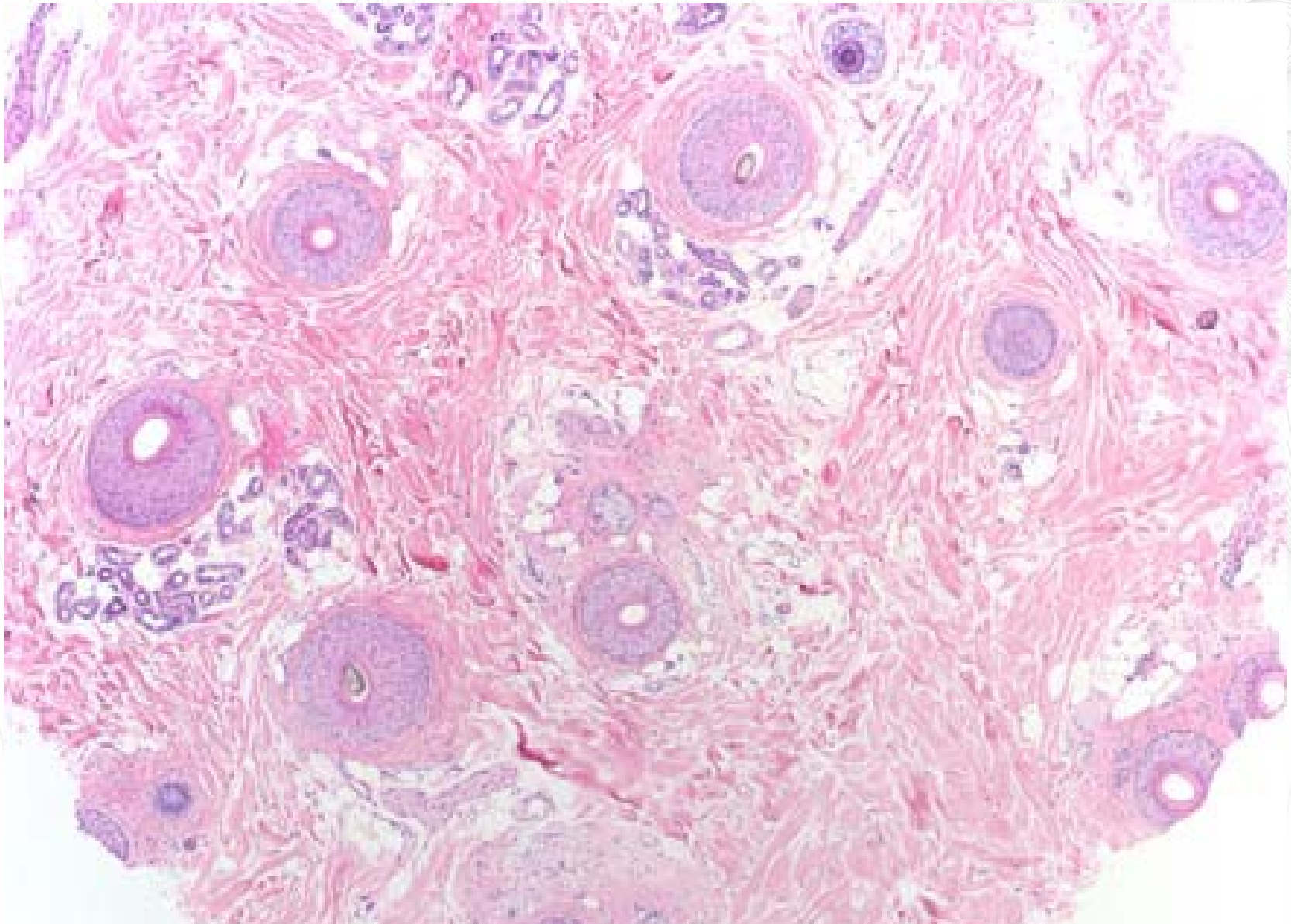
Case 5

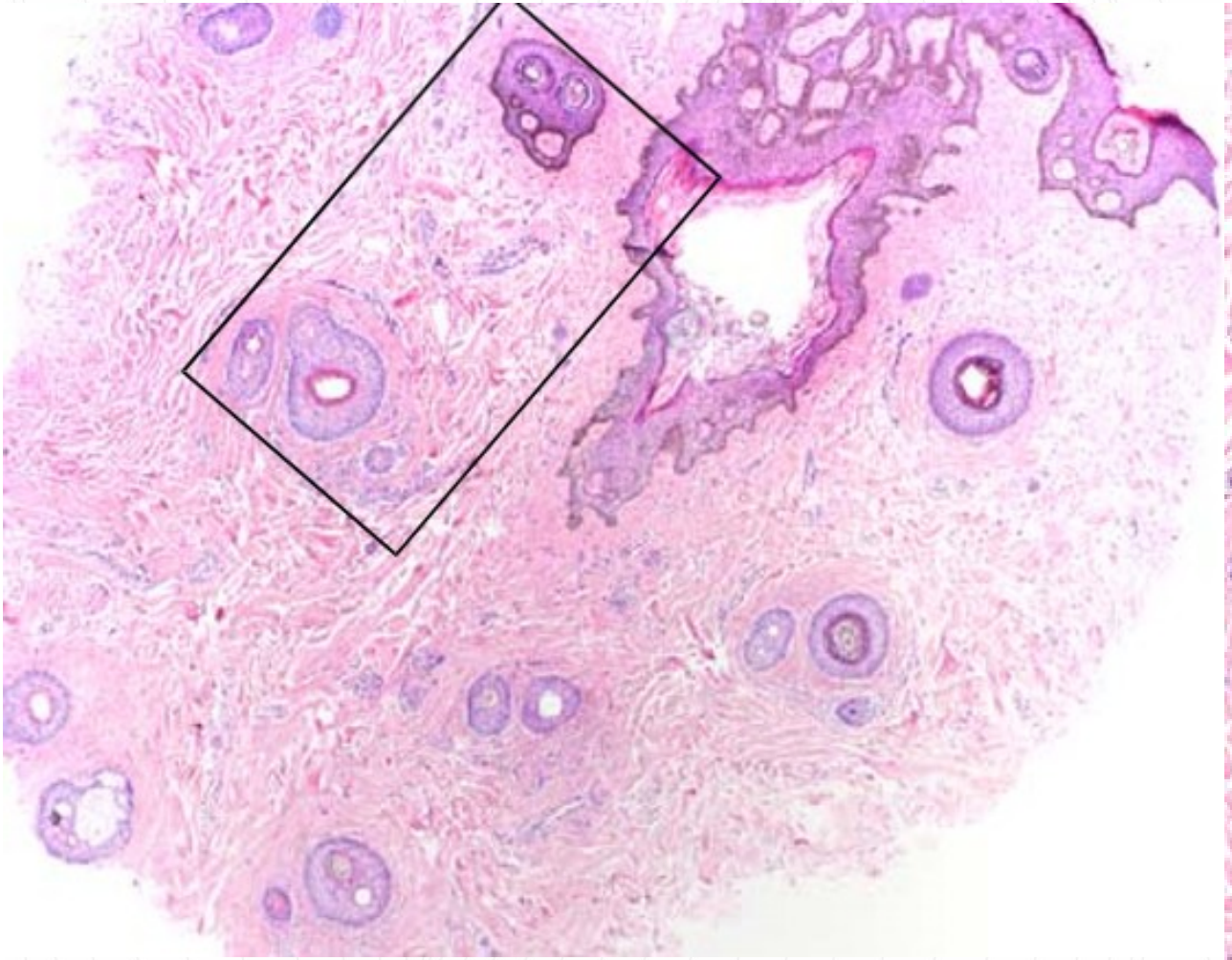
Occiput

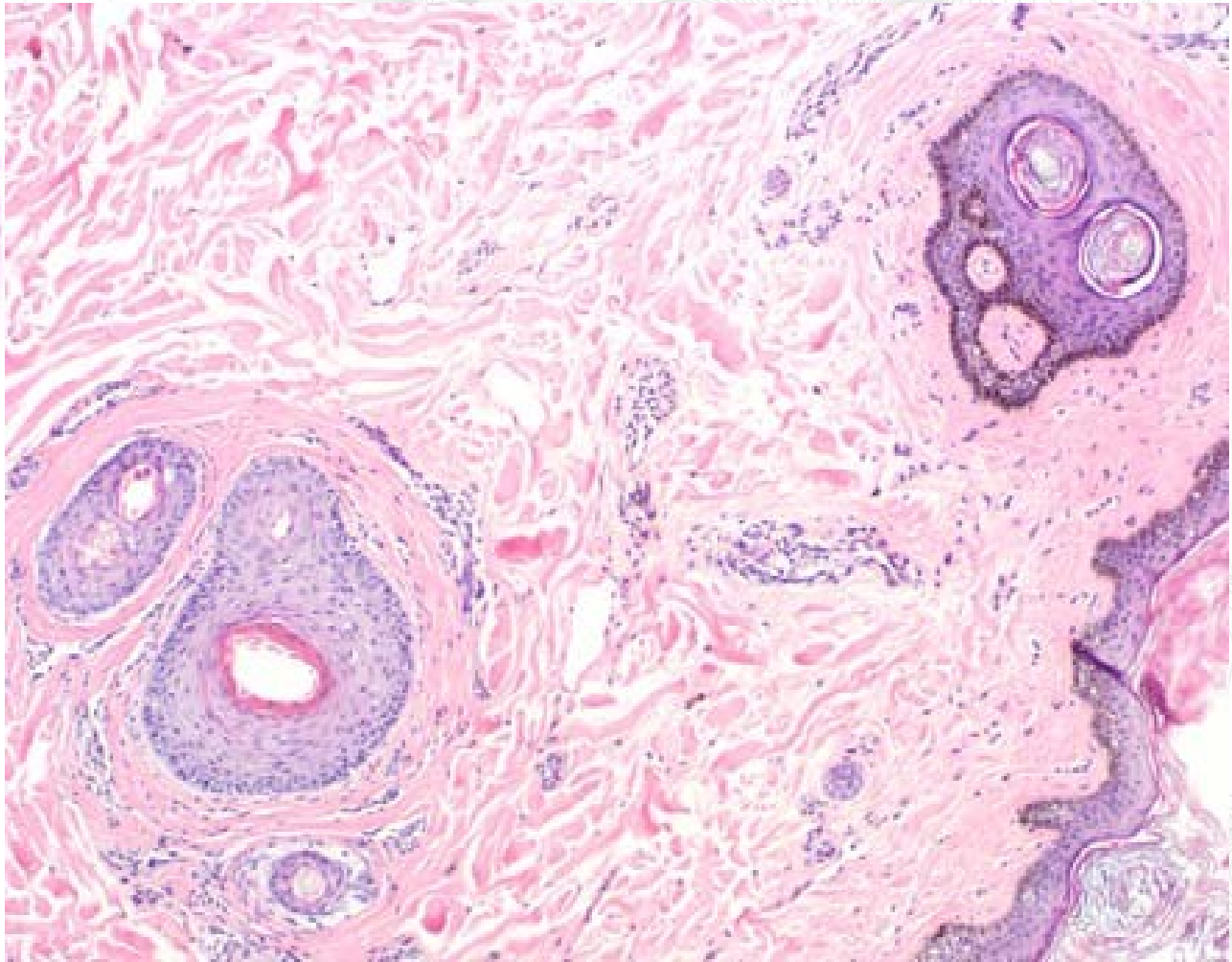


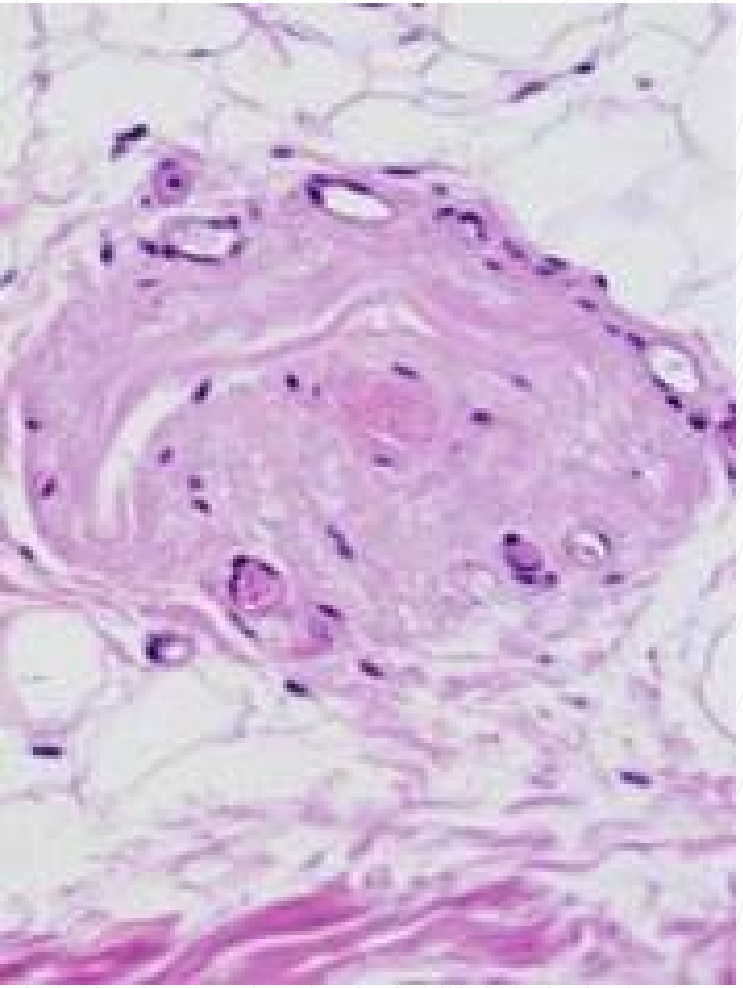
Crown

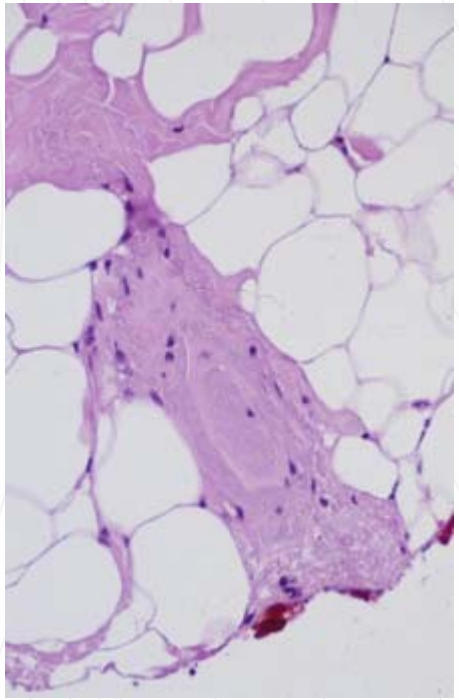


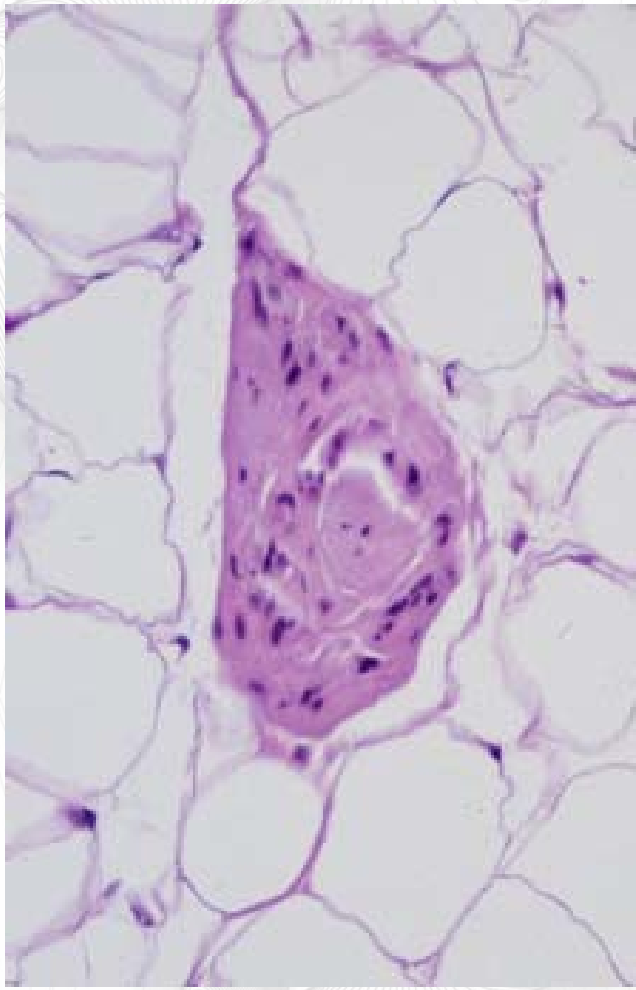












Diagnosis?

Diagnosis:

Androgenic alopecia

Androgenic alopecia

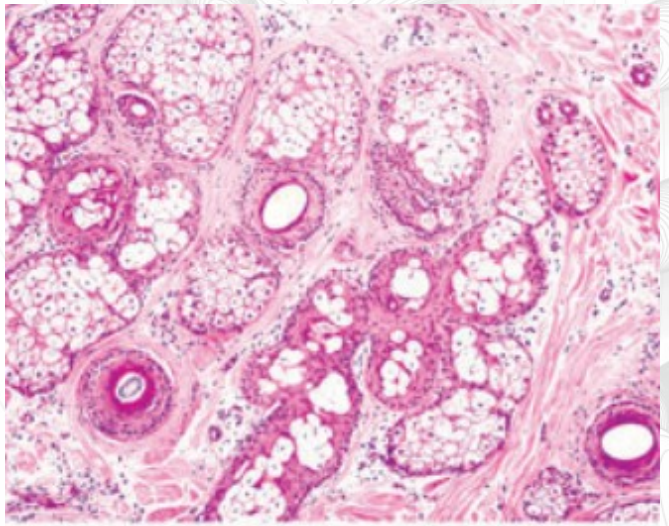
Androgenic alopecia is the most common type of hair loss. It is a disorder of dominant inheritance with variable penetrance, affecting approximately half of the population by the age of 50 years, of both sexes.

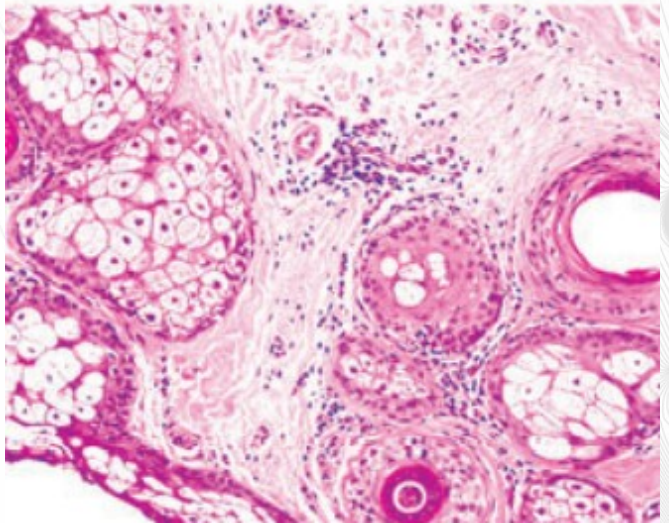
Clinically, it is a patterned alopecia, in that it is characterized by bitemporal recession and vertex balding in men, and in women (female pattern hair loss) by diffuse hair thinning of the crown with an intact frontal hairline.

Hair ‘thinning’ at the vertex.

Isthmus: hair follicle miniaturization with variation in hair follicle size. And…

Mild perifollicular lymphoid cell infiltrate.

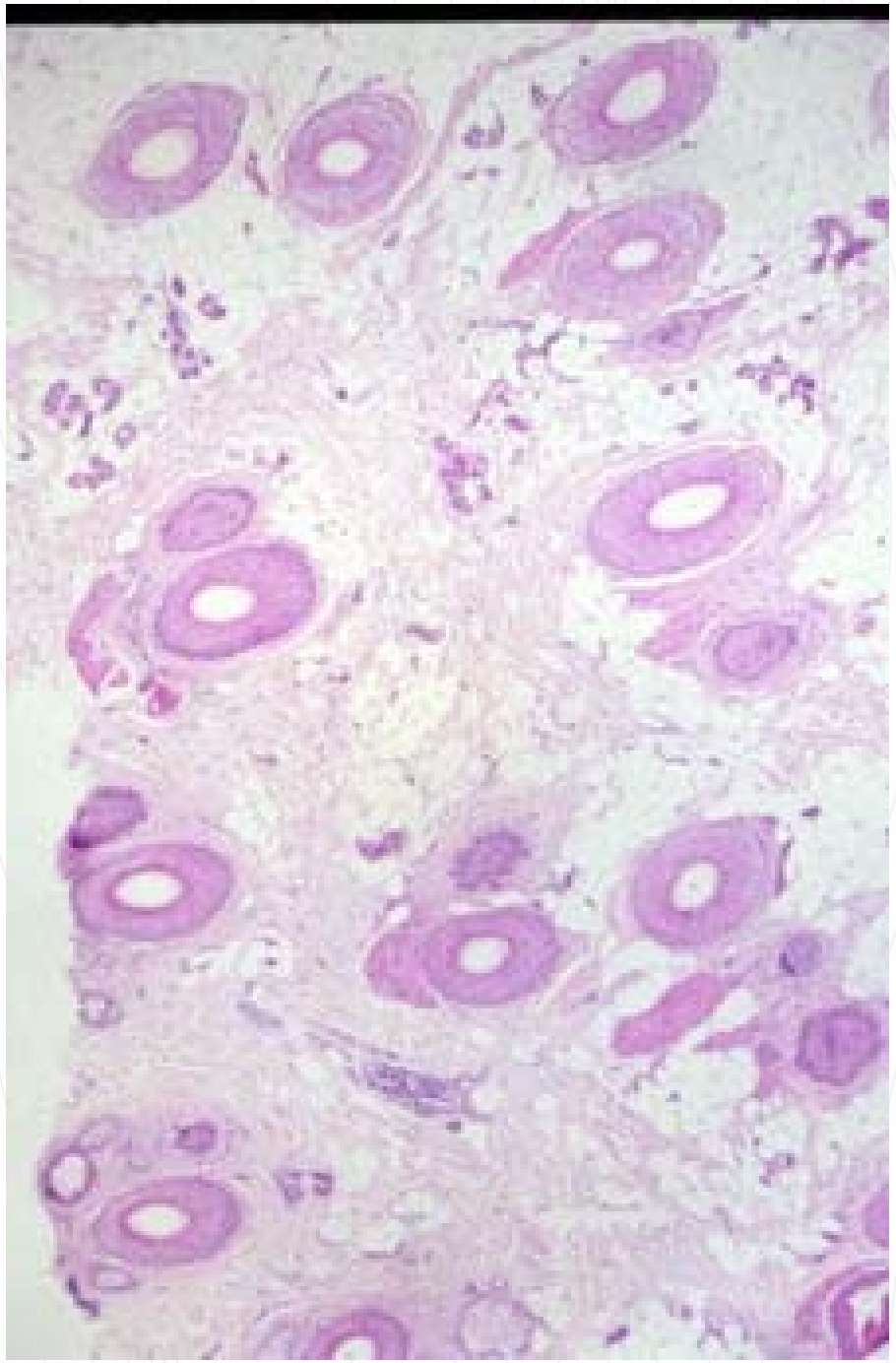


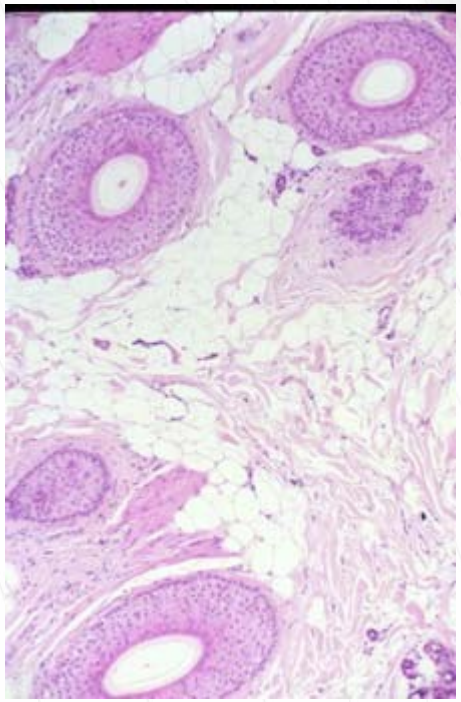


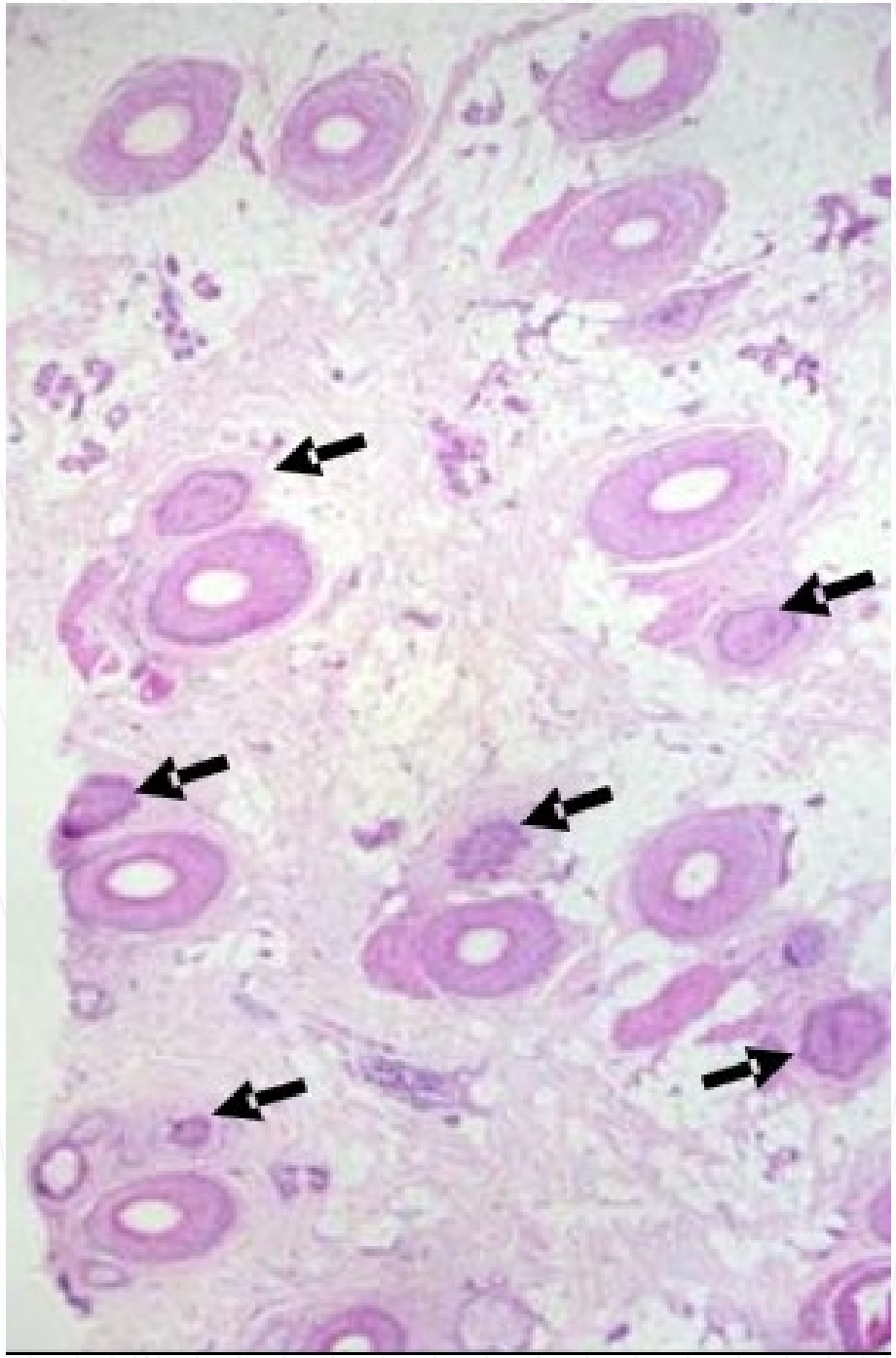
Histological summary of androgenic alopecia

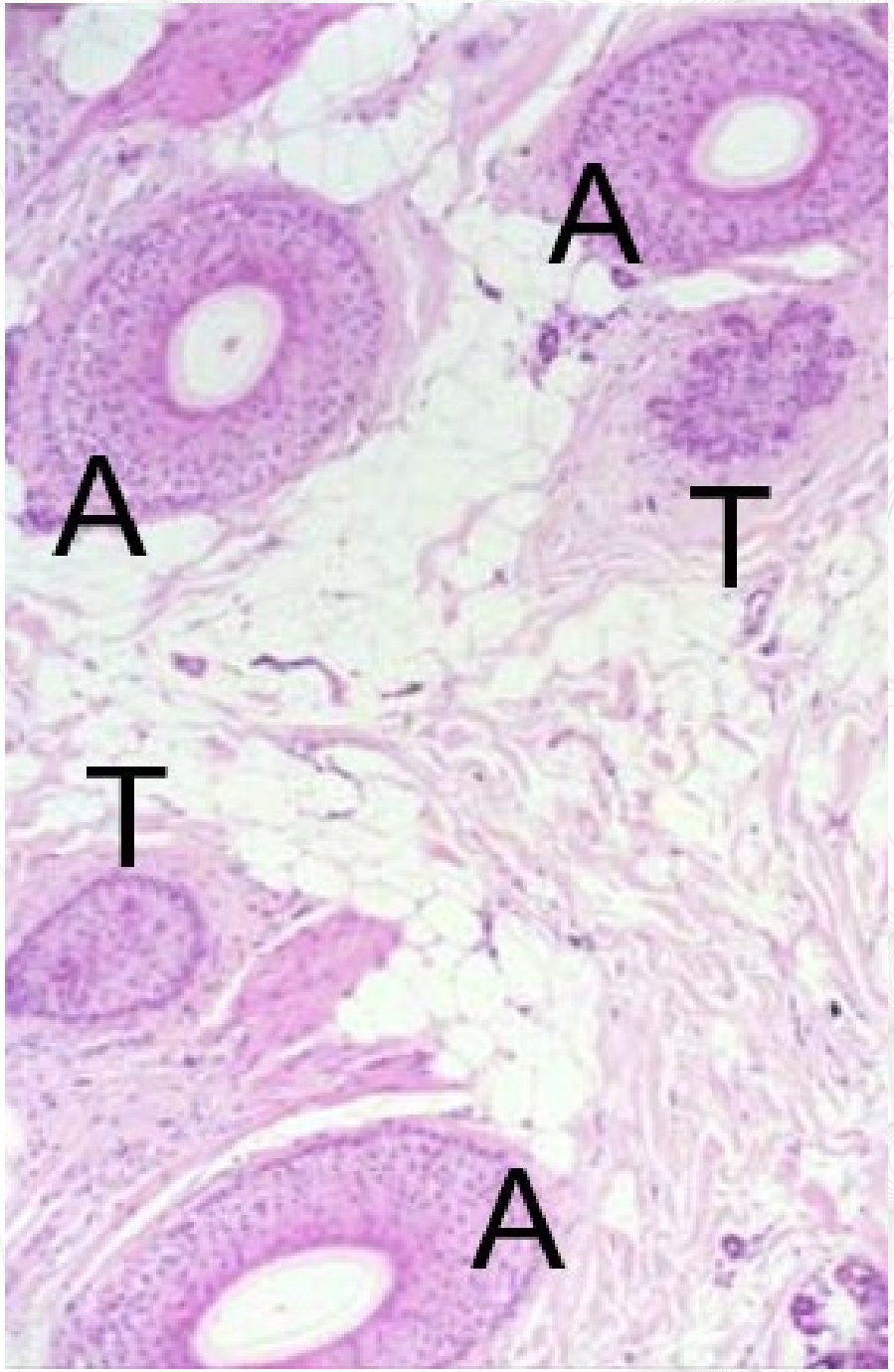
1. Normal total number of hairs
2. Decreased terminal : Villous ratio (less than 4:1) (vs7:1)
3. Many fibrous streamers below miniaturised/villous hairs
4. Often the telogen count is increased
5. No significant inflammation
6. Uninvolved scalp appears normal

Case 6





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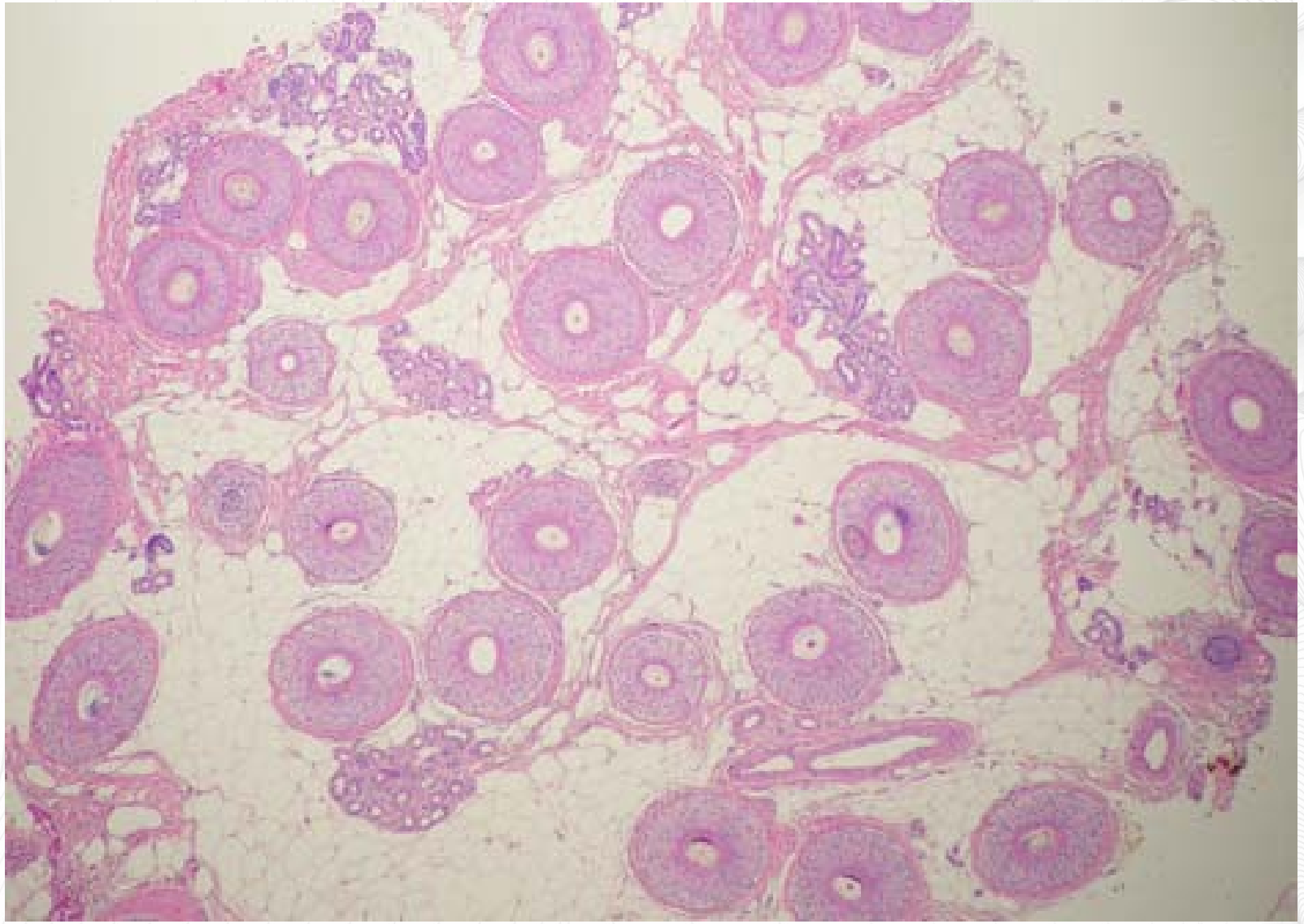
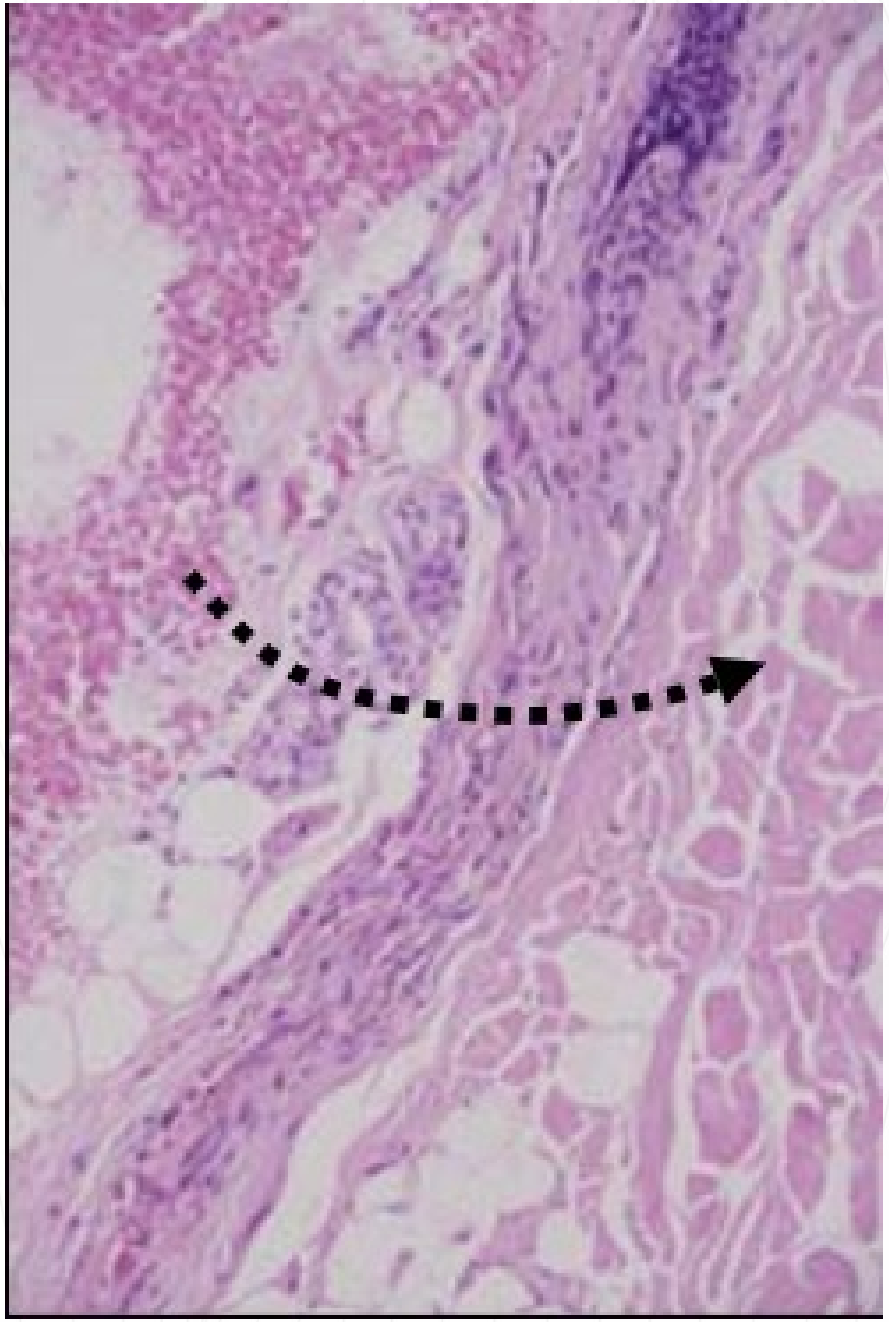
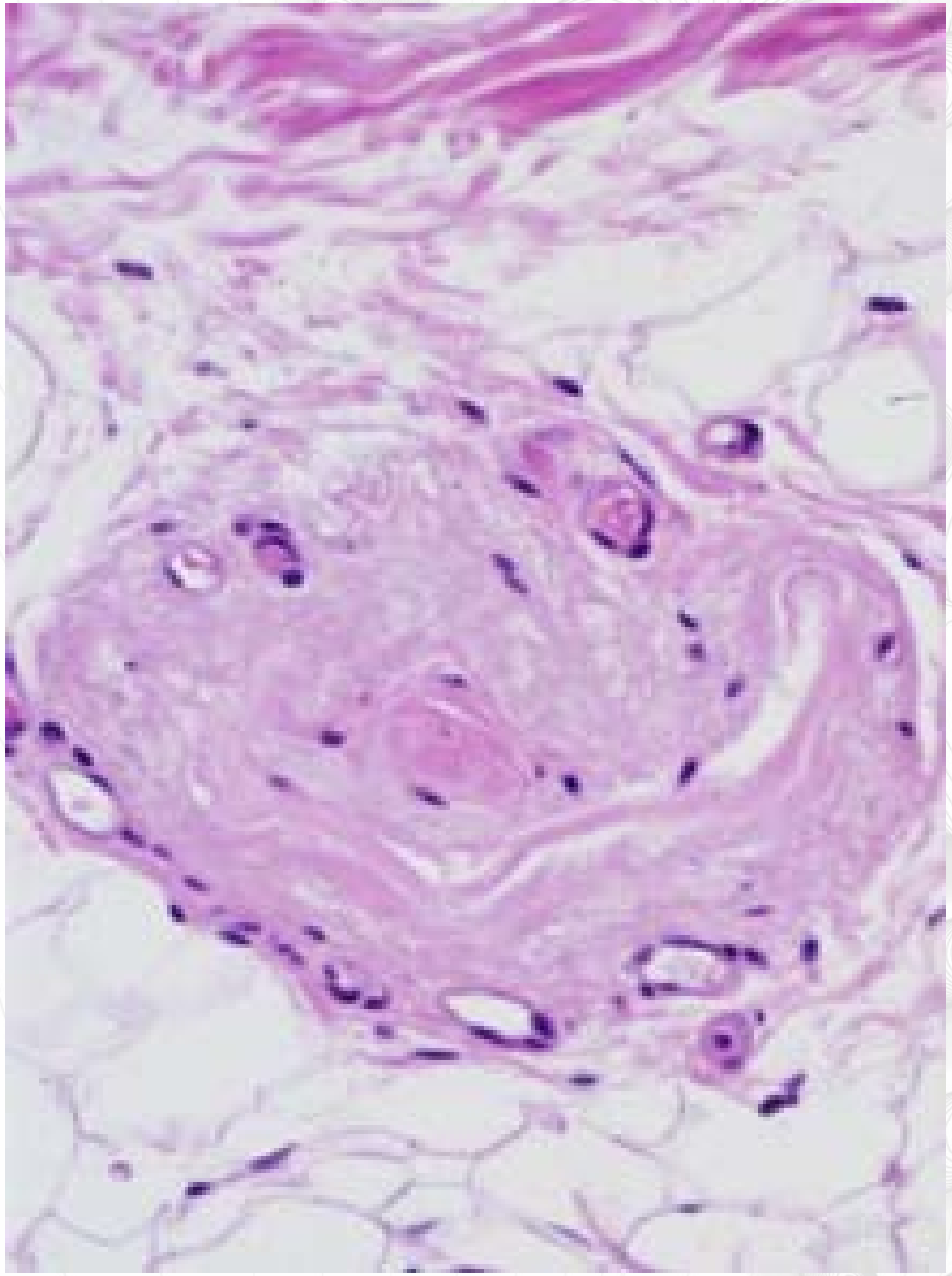
For comparison, normal hair







Diagnosis?

Diagnosis:

Telogen effluvium

Telogen effluvium

A diffuse form of alopecia, in which the hair shedding may be acute or chronic.

Clinically, acute telogen effluvium can occur in both sexes and be triggered by numerous precipitating factors (major surgery, injury, severe illness, childbirth, crash diet and numerous medications);

There is no obvious trigger factor in chronic telogen effluvium.

- This latter entity is characterized by diffuse scalp hair thinning in middle-aged women, and has a prolonged and fluctuating course.

It may be confused with female pattern hair loss, but is distinguished from it by the lack of hair follicle miniaturization. However, overlap cases have been reported.

Histological features of telogen effluvium

Acute

Normal number of hair follicles with no miniaturization, and resembles normal scalp.

Chronic

In chronic telogen effluvium there is also a normal number of hair follicles, but with an increased number (20–30%) of telogen hairs (normal scalp 5–10% telogen hairs), and some evidence of miniaturization if it is superimposed on an evolving androgenic alopecia.

Histological features of telogen effluvium

1. Total number and size of hairs is normal.
2. Marked increase in percentage of terminal telogen hairs (more than 20% but less than 60%)
3. Presence of fibrous streamers indicating Conversion to telogen hairs
4. No significant inflammation.

DDx with female pattern hair loss

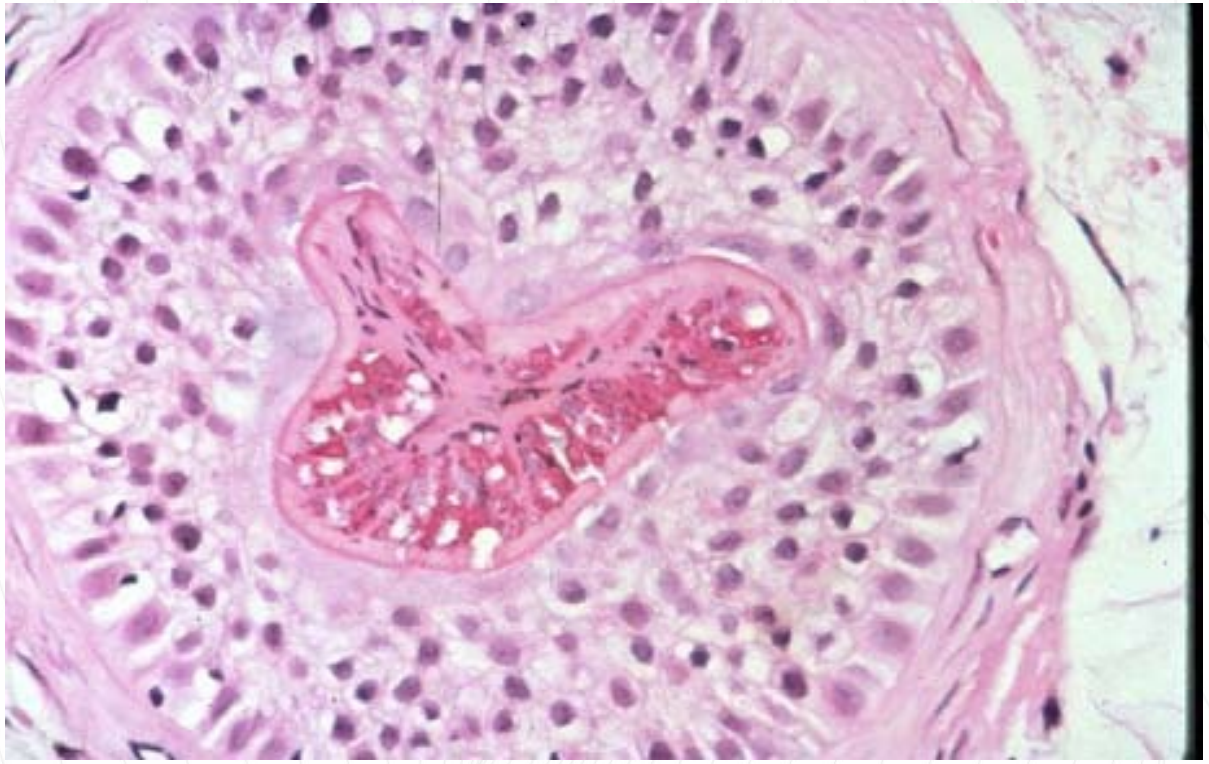
The standard cut-off points for the differential diagnosis between chronic telogen effluvium and female pattern hair loss are T:V = >8:1 for chronic telogen effluvium, and T:V = < 4:1 for female pattern hair loss.

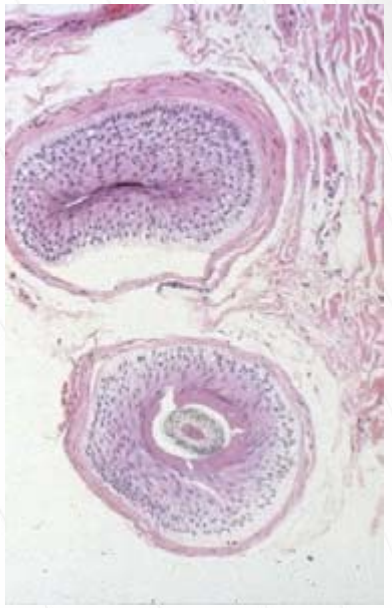
However, this difference does not include the presence of intermediate hair follicles, which would suggest early evolving female pattern hair loss.

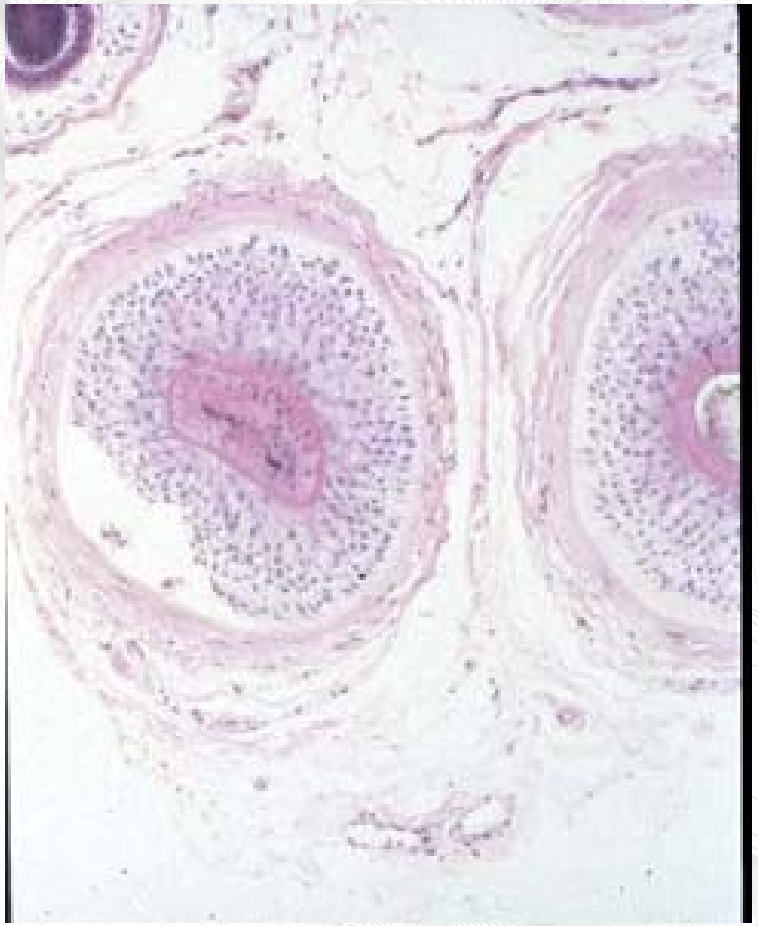
Case 7

Incomplete or distorted hair anatomy

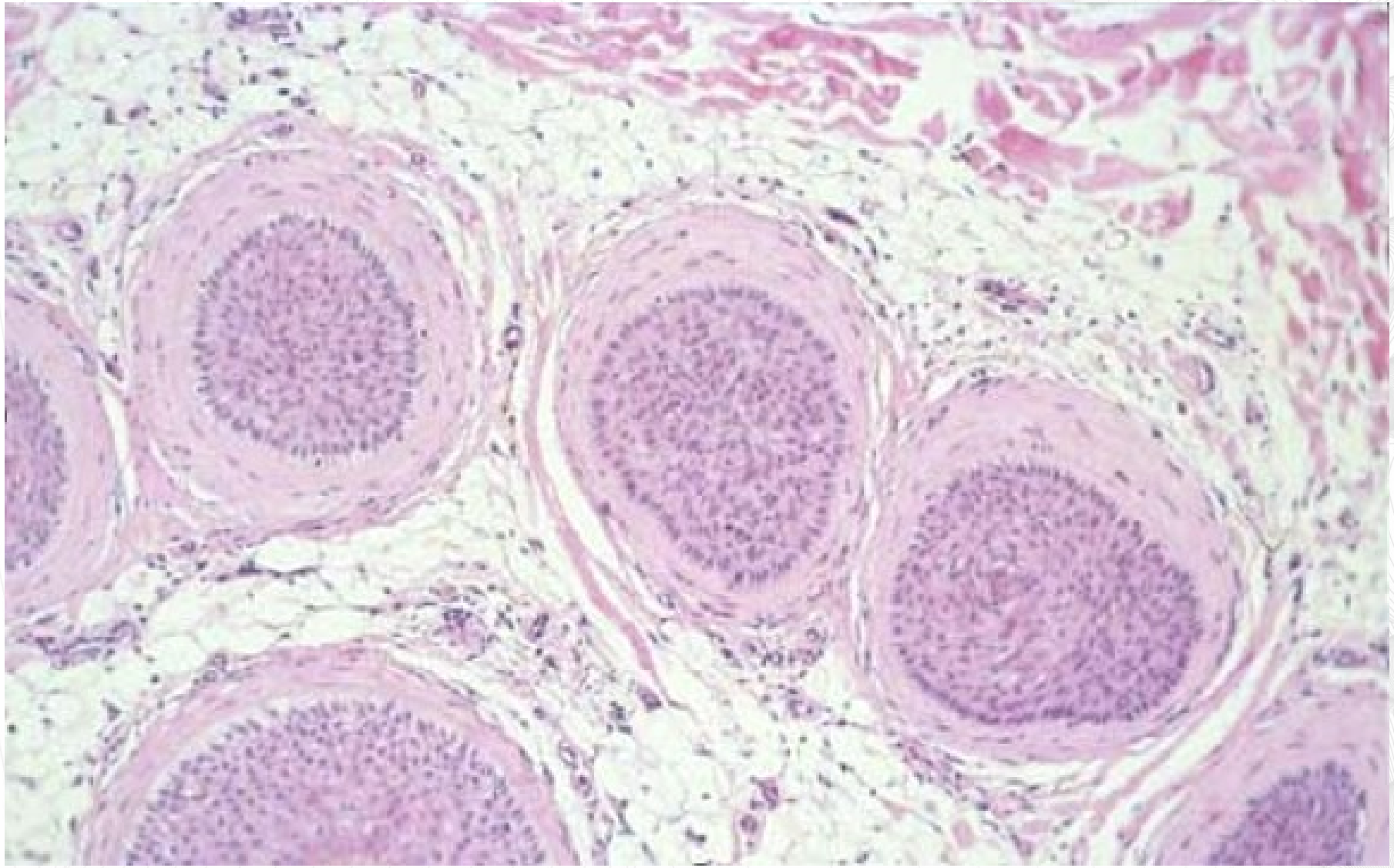
Distorted anatomy





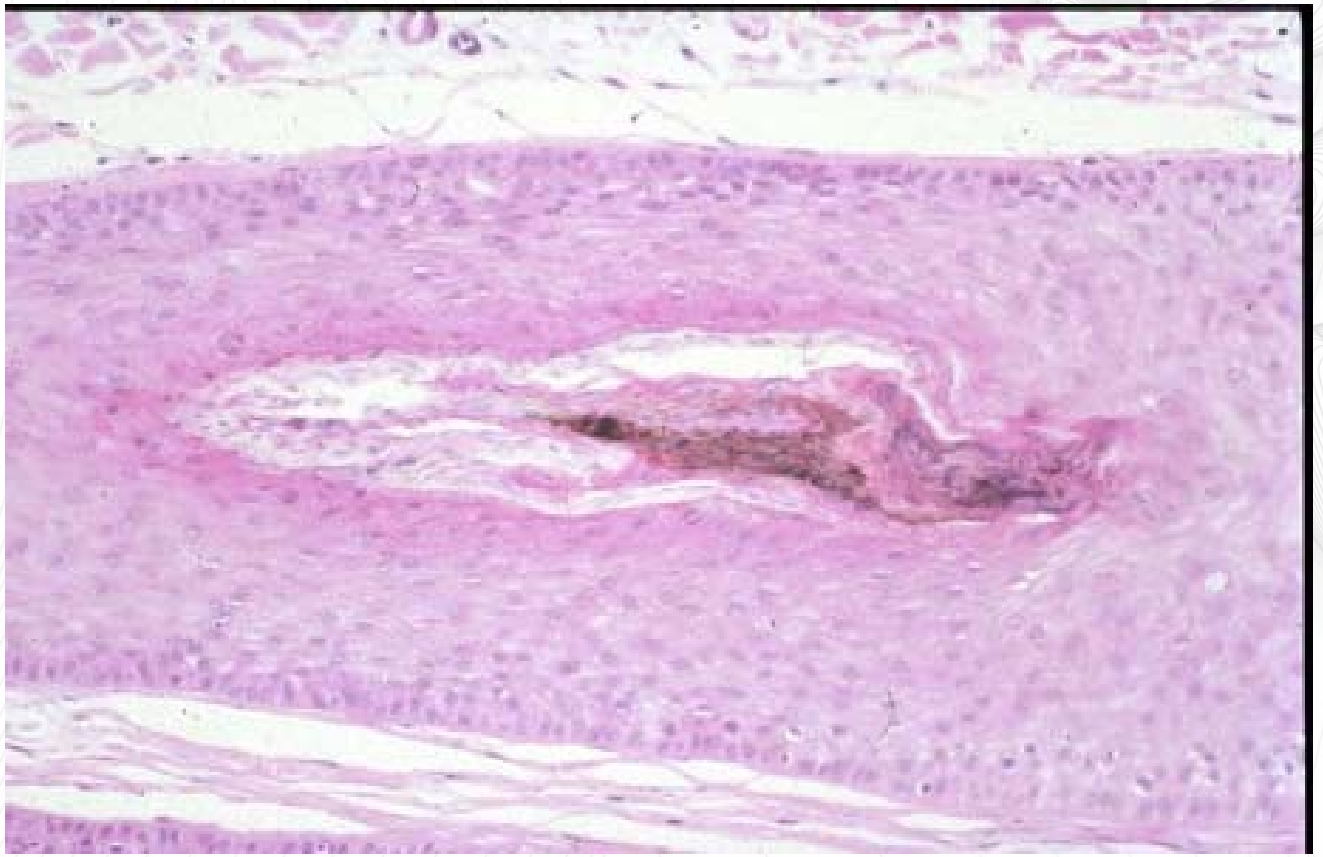


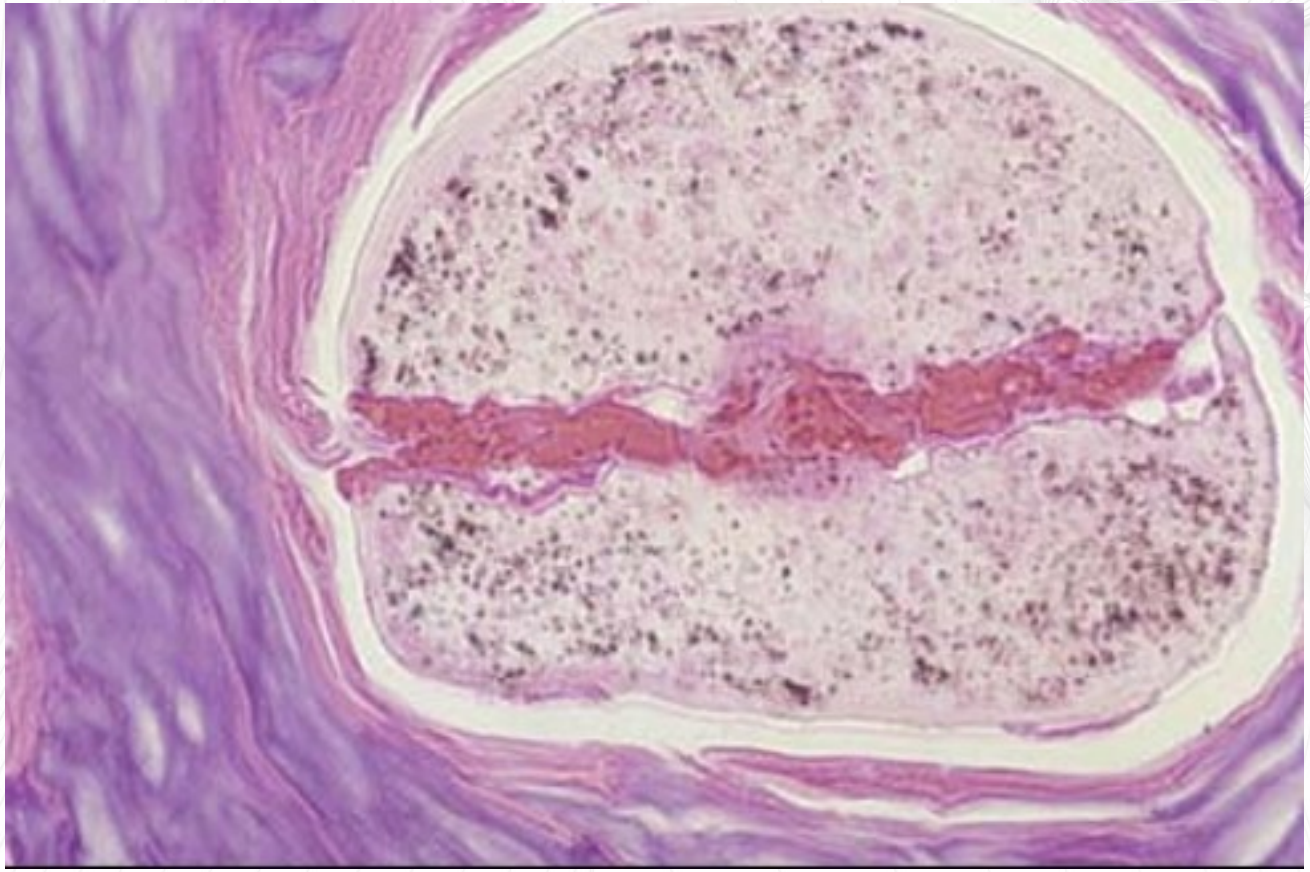
Increased catagen and/or telogen hairs



Pigment casts

Trichomalacia





Diagnosis?

Diagnosis:

Trichotillomania

Trichotillomania

Trichotillomania is characterized by the compulsive intentional pulling or twisting of the hair.

This hair loss disorder may reflect a background of emotional instability, and often occurs in children.

A biopsy is an important tool to provide the clinician objective support for the diagnosis, as often both the child and parents deny hair-pulling as a cause of the hair loss.

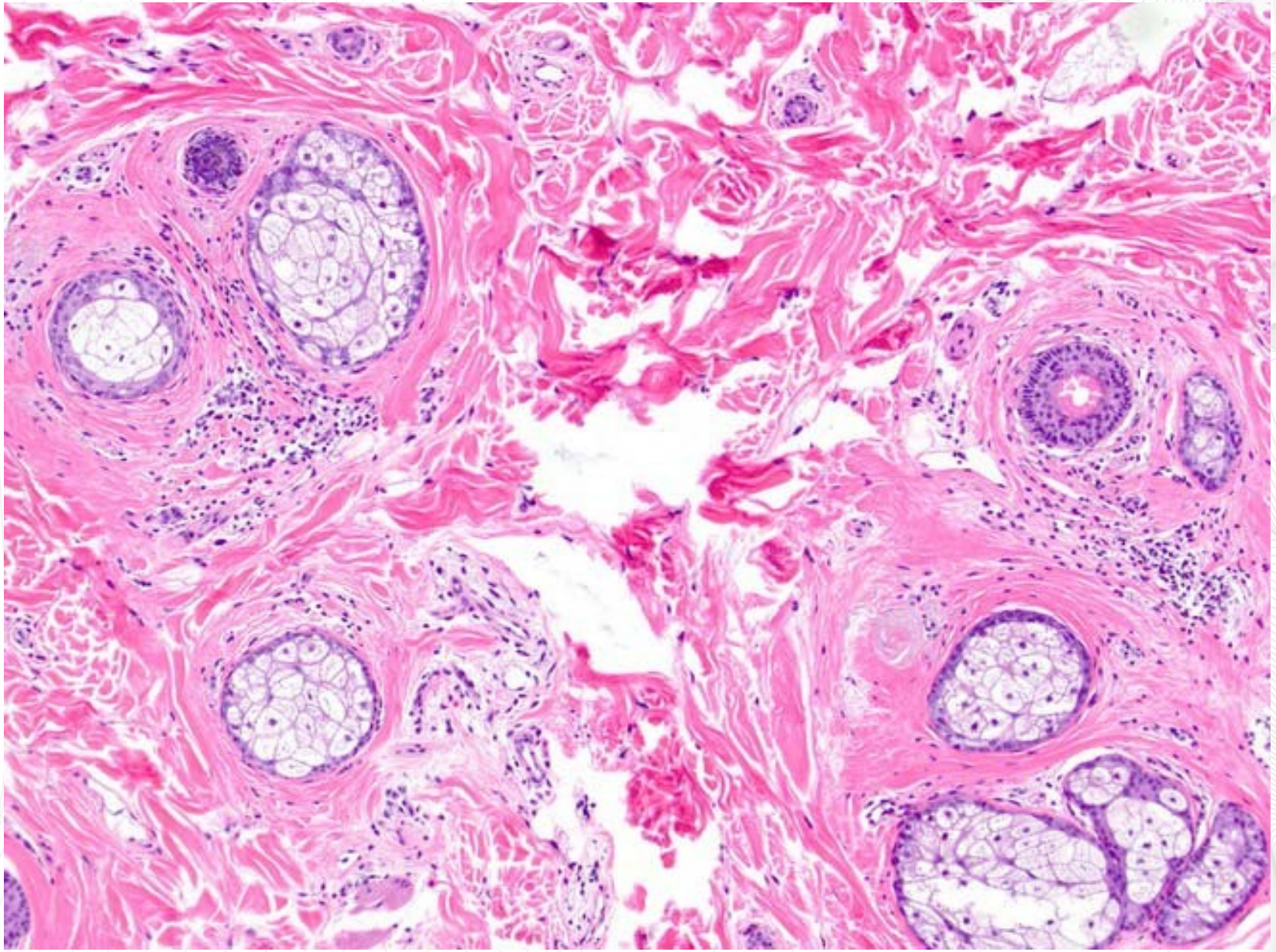
Clinically, the patients present with diffuse or bizarre-shaped patches of hair loss.

The hair shafts have various lengths, due to different points of fracture of the hair shafts or to the hair being pulled at different times.

Histological summary of Trichotillomania

1. Non-inflammatory non-scarring alopecia
2. Incomplete or distorted hair anatomy
3. Increased numbers of catagen/telogen hairs
4. Number of hair follicles is normal
5. Tricomalacia and hamburger bun sign
6. Pigment casts
7. Perifollicular and intrafollicular haemorrhage

Case 8



Diagnosis?

Diagnosis

Traction alopecia

Traction alopecia

Traction alopecia, like trichotillomania, is a noninflammatory, non-scarring alopecia

Secondary to mechanical damage, which is usually hairstyle related, and is seen in women of African descent.

Clinically, the hair loss is often seen at the margins of the scalp, involving the frontal, temporal and parietal regions.

In early traction alopecia the hair loss is temporary, provided that the damaging noxa is suspended, whereas in late ‘burnt out’ alopecia, where the excessive traction persists, the hair loss is permanent.

Histopathologically, the features observed in early traction alopecia are similar to those seen in trichotillomania.

Whereas in late traction alopecia there is marked loss of the terminal follicles with preservation of the vellus hairs and sebaceous glands.

- The follicular units at the isthmus are replaced by fibrous tissue, consistent with a scarring process, and thus permanent alopecia.

Traction alopecia (end-stage)

1. Follicular dropout (replacement of terminal follicles by connective tissue)
    1. Without loss of associated sebaceous glands.
2. No significant inflammation

Histopathology of primary scarring (cicatricial) alopecia

Scarring (cicatricial) alopecia represents a complex group of hair disorders all characterized by having as a common final pathway the destruction of the hair follicle unit.

Biphasic scarring alopecias comprise another subset of permanent alopecias; in these cases, early non-scarring hair loss is followed by permanent follicle drop-out. This situation occurs in longstanding :

1. Androgenic alopecia,
2. AA
3. Traction alopecia.

Histopathologically, primary scarring (cicatricial) alopecia is characterized by the presence of fibrous tissue replacing the hair follicles. This corresponds clinically to loss of hair follicle ostia.

Chronic cutaneous (discoid) lupus erythematosus (DLE)

Clinically characterized by:

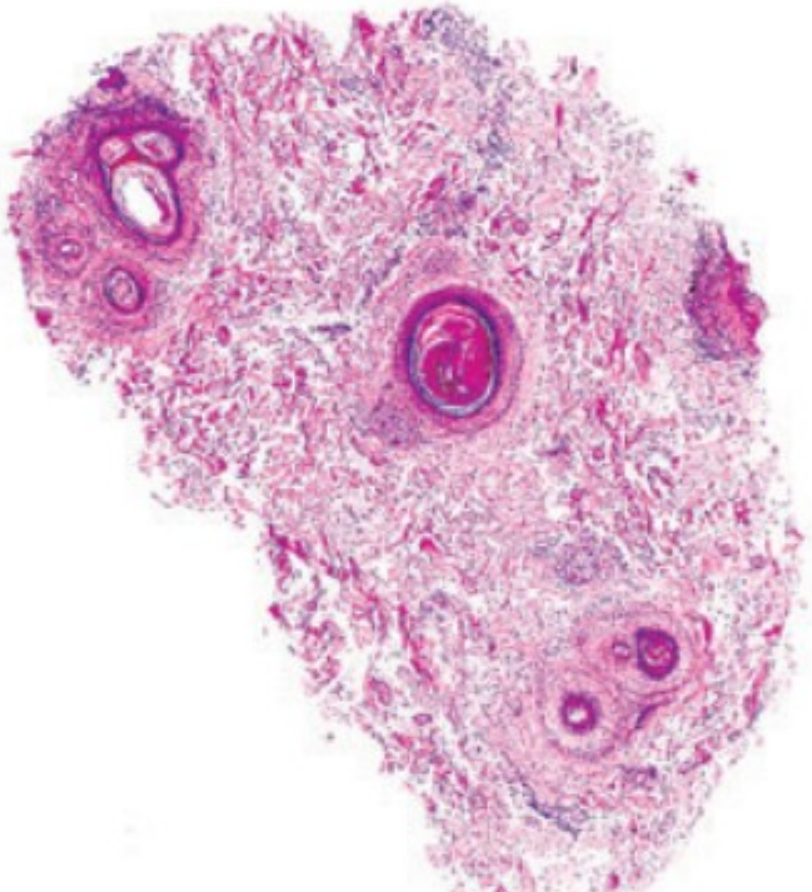
1. Ill-defined patches of alopecia,
2. Decreased follicular orifices
3. Scale
4. Erythema,
5. Follicular plugging
6. Depigmentation
7. Atrophy

Chronic cutaneous (discoid) lupus erythematosus

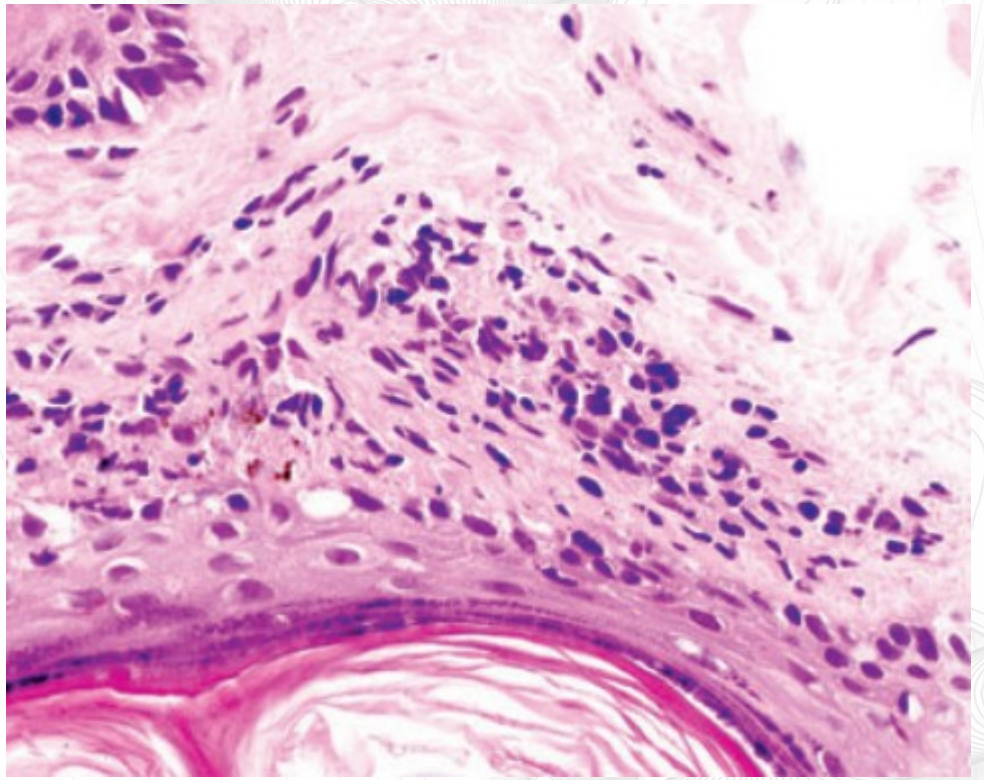
Histopathological features include:

1. Follicular hyperkeratosis
2. Vacuolar-interface folliculitis at the level of the infundibulum
3. The interfollicular epidermis may at times also be involved,
4. Perivascular and periappendageal superficial and deep lymphoid cell infiltrate with plasma cells.
5. Late stages are characterized by concentric lamellar perifollicular fibroplasia and by basement membrane zone thickening that is highlighted by PAS
6. Suprabasilar dyskeratosis, pigmentary incontinence and dermal mucin may also be seen.
7. On vertical sections the Verhoeff–van Gieson elastic stain shows loss of the elastic fibres throughout the dermis.
8. Direct immunofluorescence will confirm the diagnosis with granular deposits of IgG and C3 along the epidermal and follicular basement membrane zone

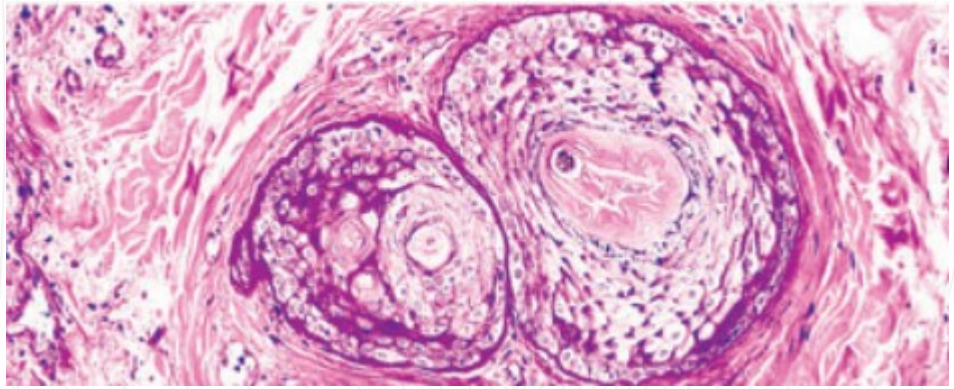
Reduced hair follicles with follicular hyperkeratosis.



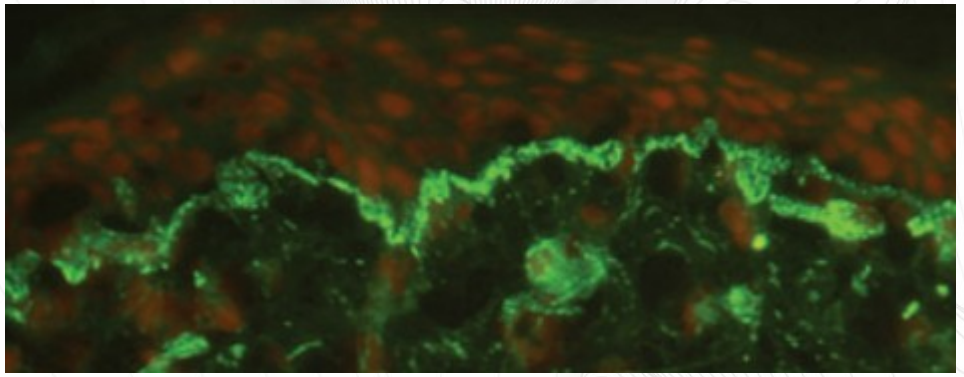
Vacuolar-interface change of the follicular epithelium



Periodic acid–Schiff highlights the perifollicular basement membrane zone thickening.



Granular deposits of IgG along the basement membrane zone



Pseudopelade of brocq

Pseudopelade of Brocq is an idiopathic and slowly progressive form of cicatricial alopecia, clinically presenting with multiple small alopecic patches on the vertex and parietal areas, in a pattern that has been defined as ‘footprints in the snow’.

While the clinical presentation is characteristic, the histopathology simply shows features of end-stage scarring alopecia. Thus, it is still debated whether this is an entity per se, or instead represents the end stage of other scarring alopecias, such as chronic cutaneous lupus erythematosus or LPP.

The histopathology shows all features of end-stage scarring alopecia, with concentric perifollicular lamellar fibrosis, loss of sebaceous glands, loss of follicular units with follicular scars and a minimal residual inflammatory cell infiltrate.

Any Questions?

Thank you