



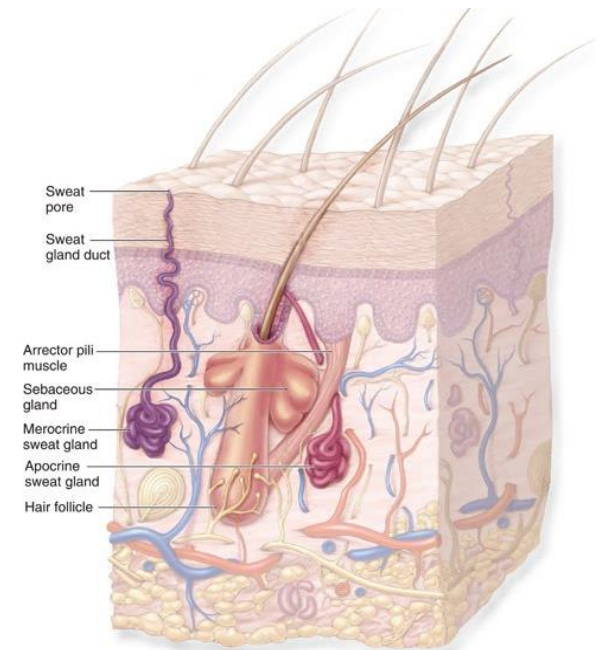
Epworth
Dermatology

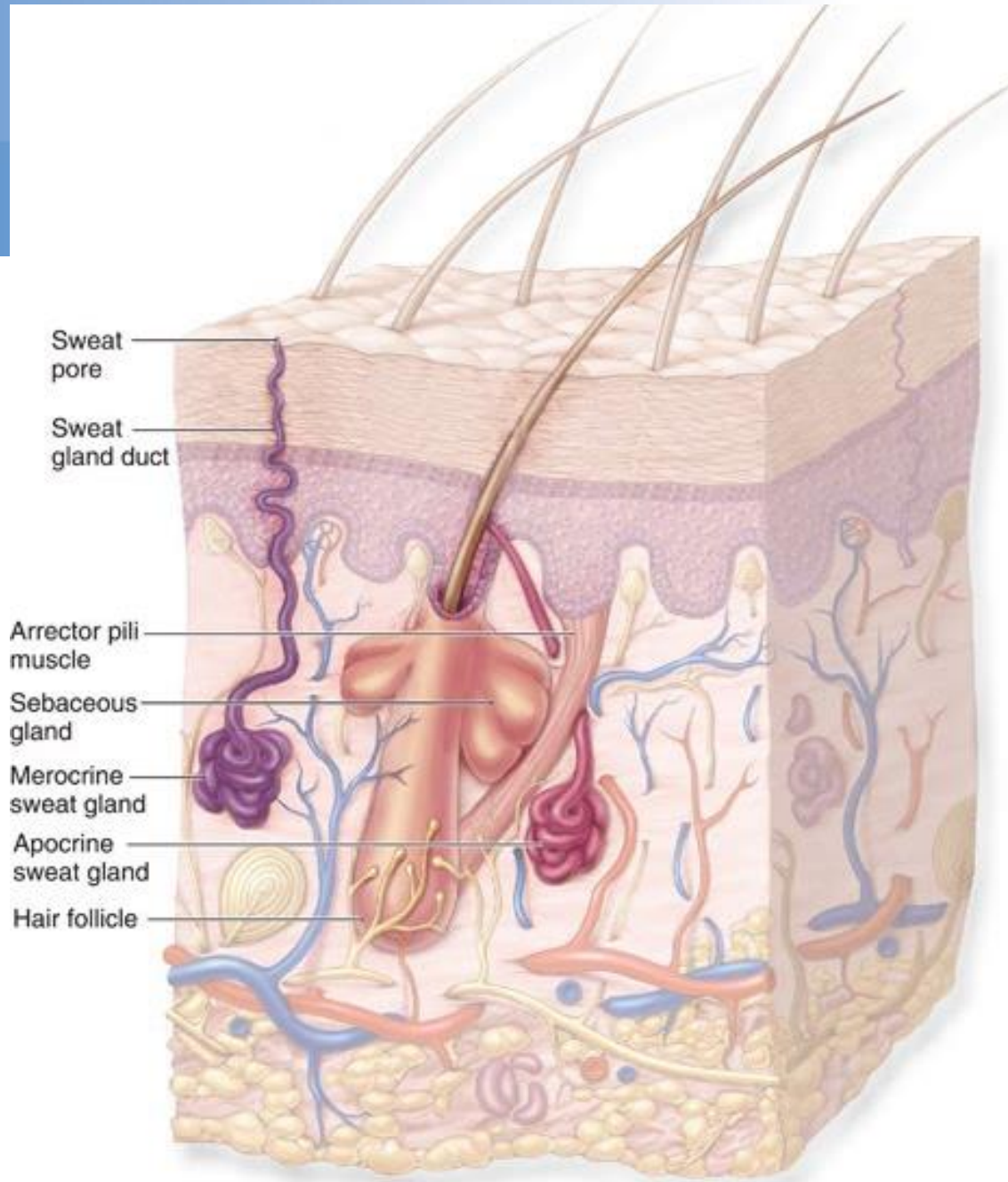


Epworth
HealthCare

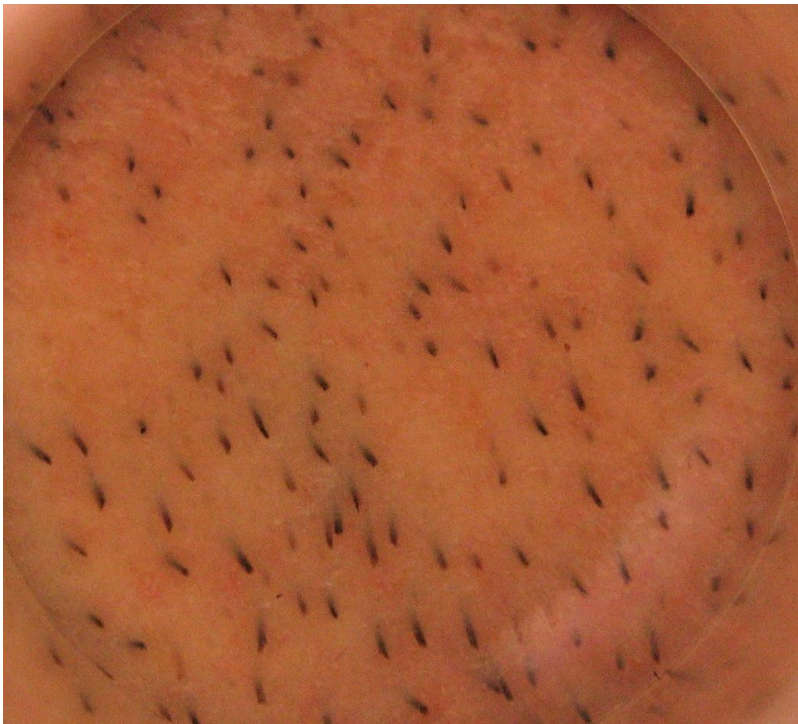
Androgenetic Alopecia: New insights into the role of the Arrector Pili Muscle

Rodney Sinclair
MBBS, MD, FACD





Beard



Forearm



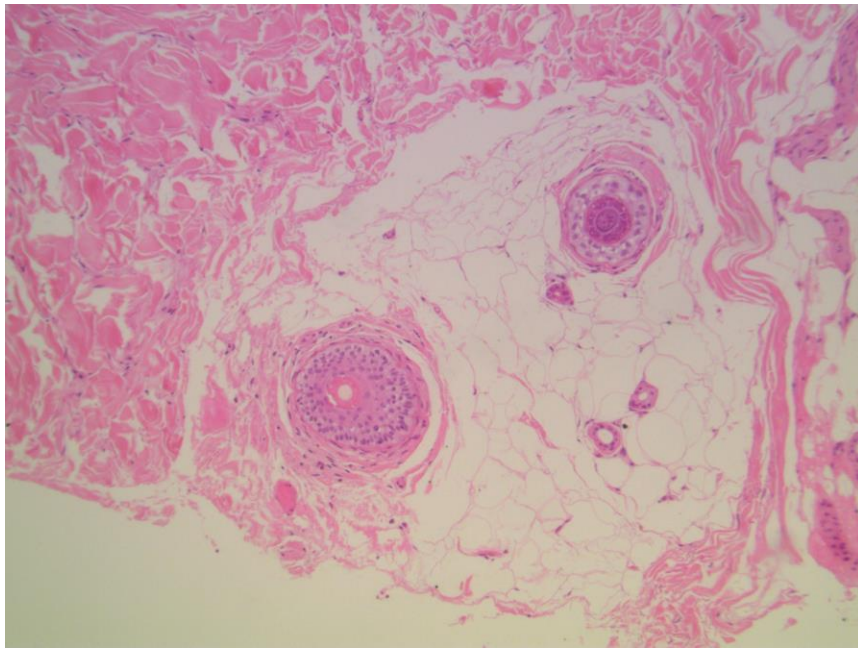
Eyebrow



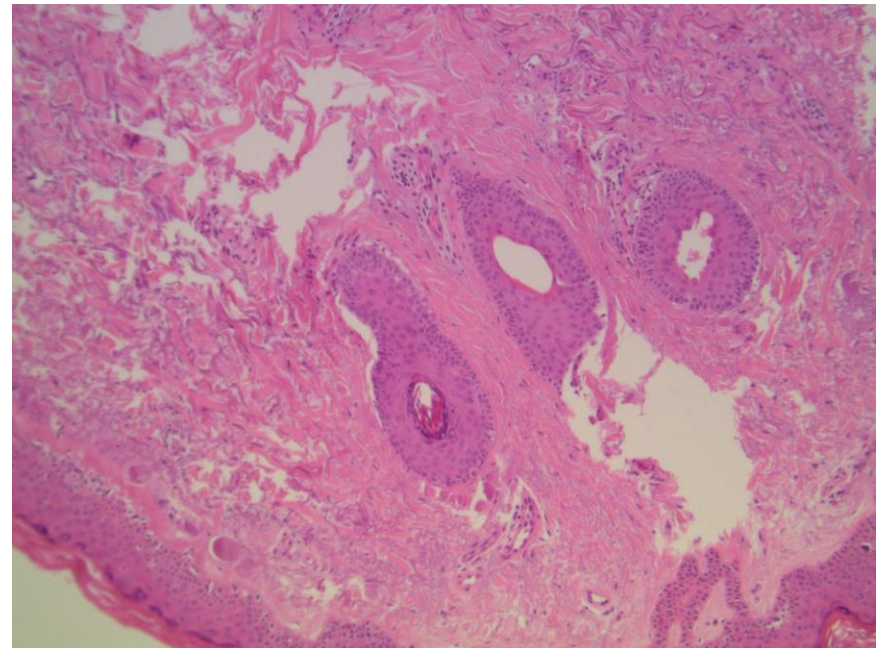
Chest

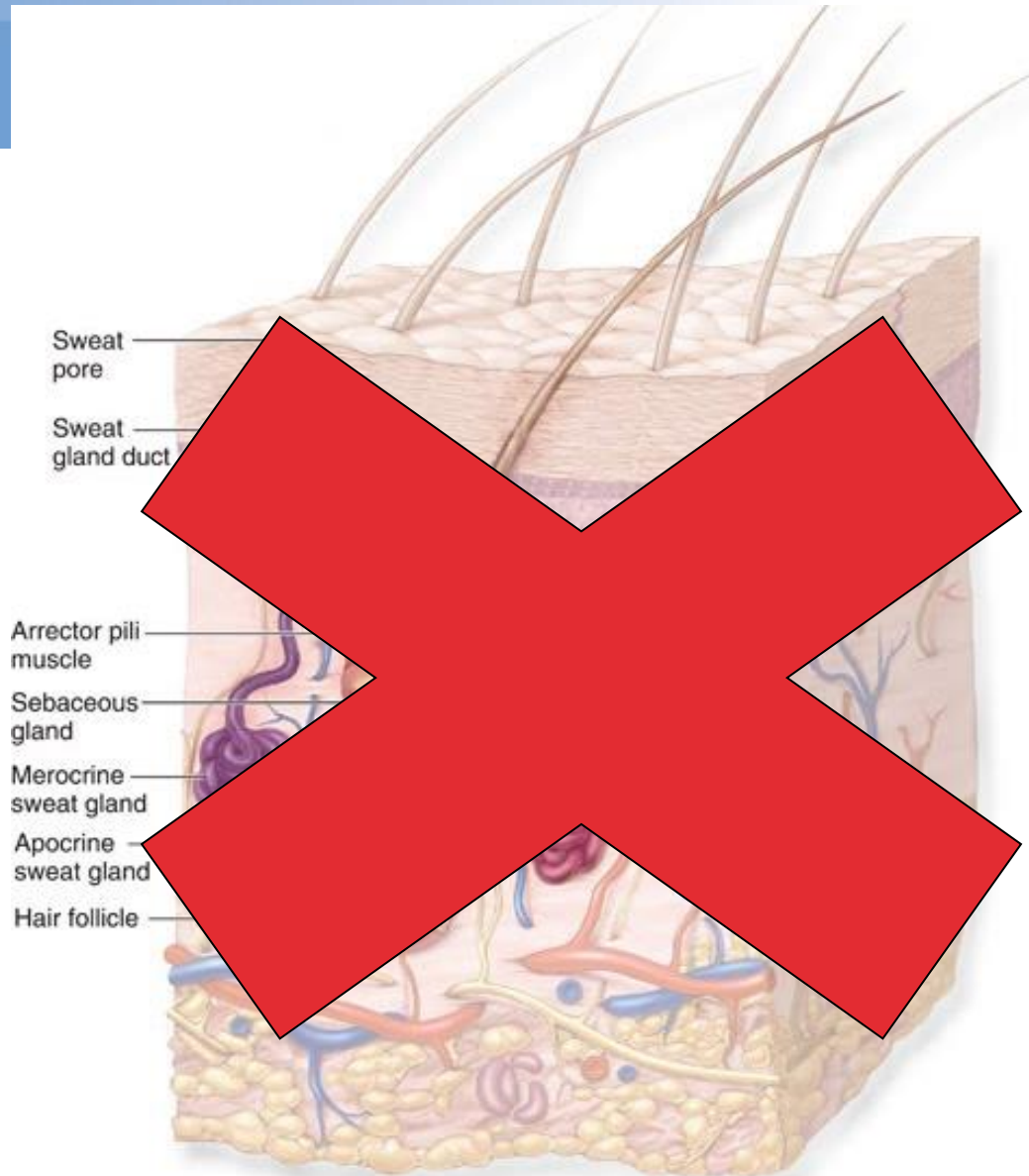


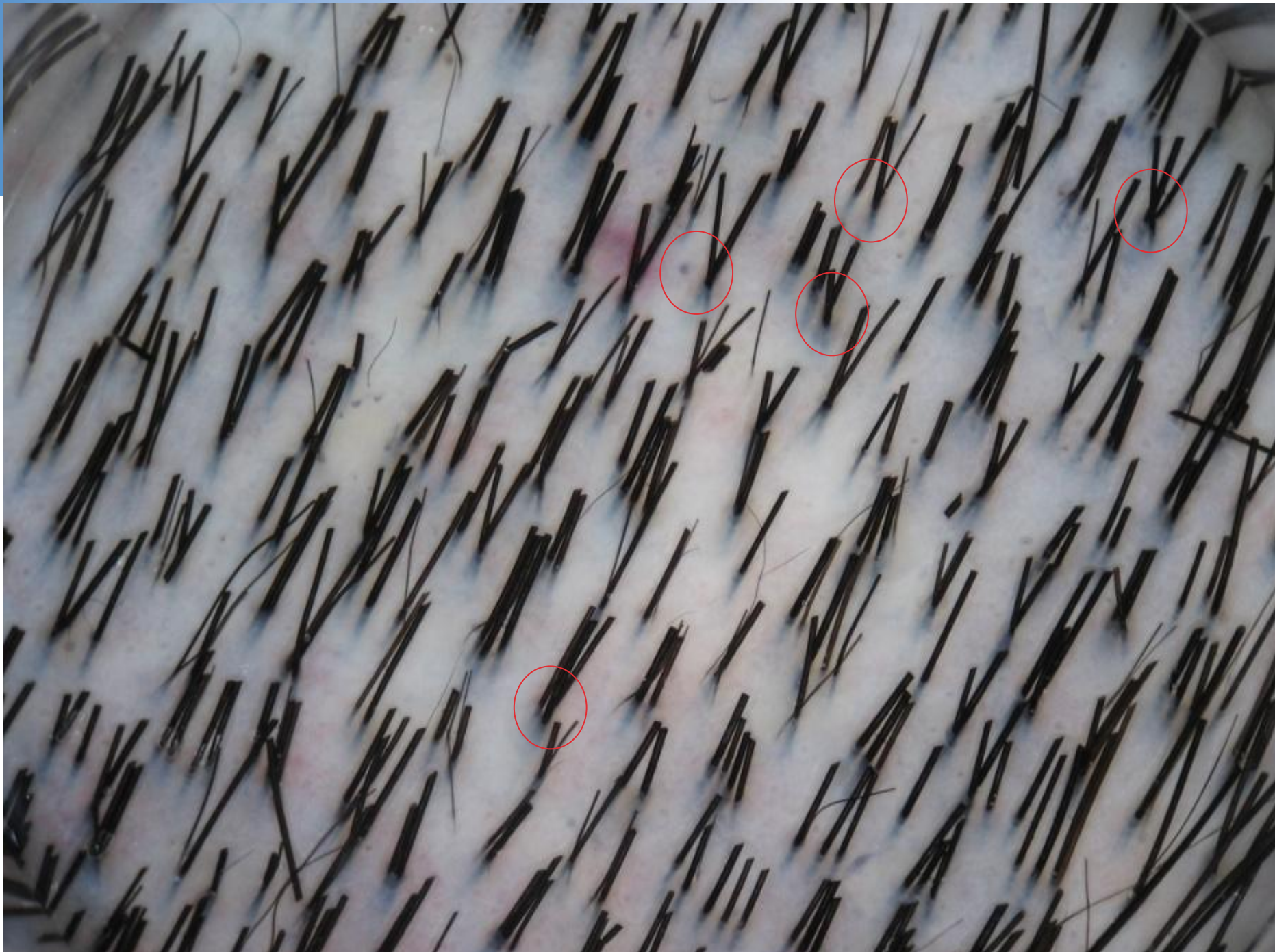
Individual Follicles



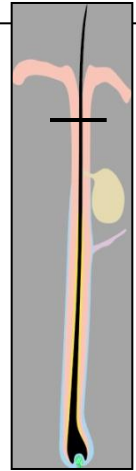
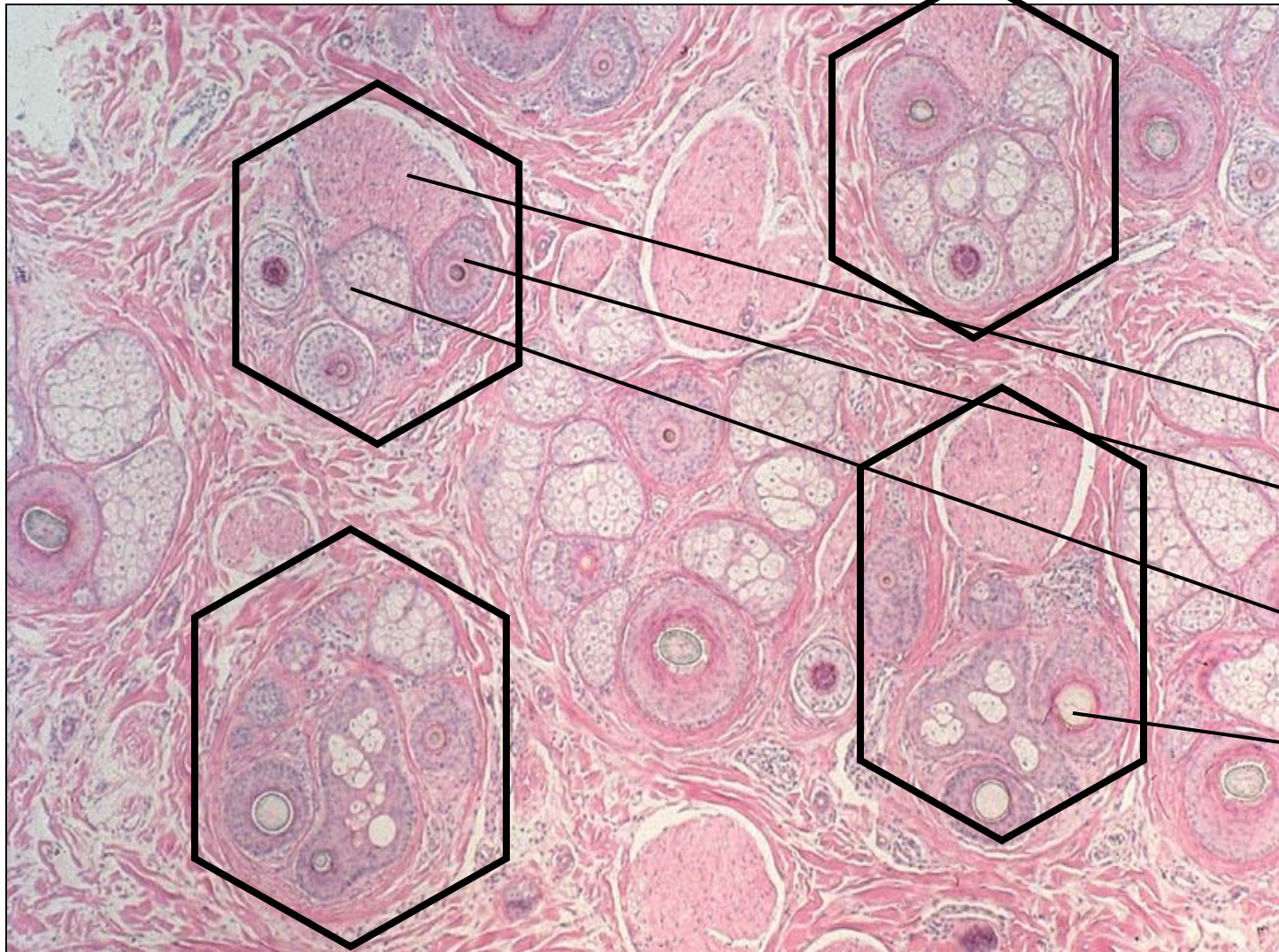
Groups of 3 Primary Follicles (Mejere's Trios)







Follicular Units



Arrector pili

Vellus hair

Sebaceous gland

Terminal hair

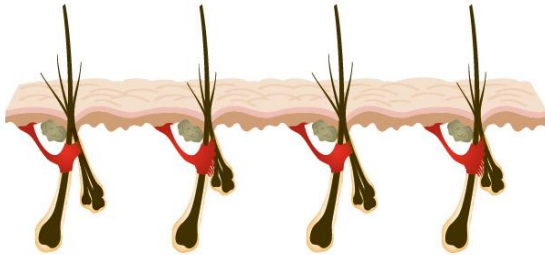
6 week old baby

3 year old child

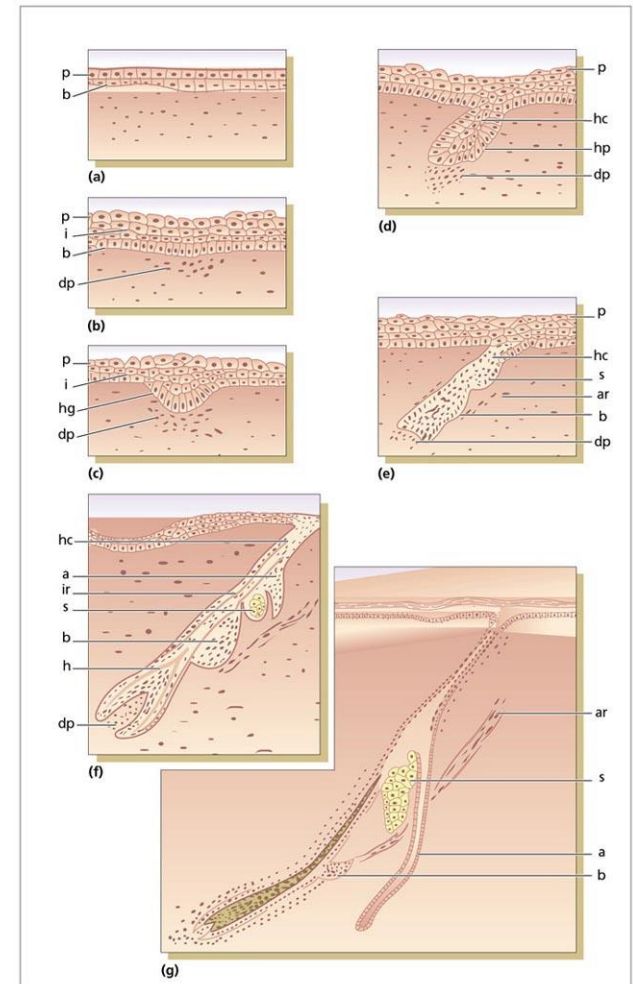
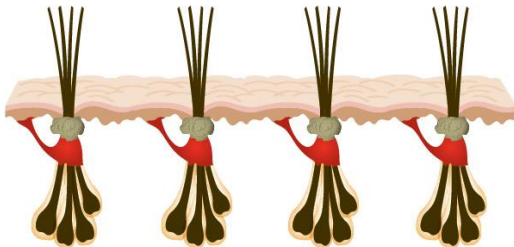


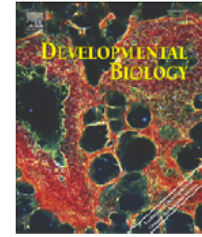
The missing link in embryogenesis

3



1





Differential sensitivity of epidermal cell subpopulations to β -catenin-induced ectopic hair follicle formation

Christopher M. Baker^a, Annemieke Verstuyf^b, Kim B. Jensen^c, Fiona M. Watt^{a,c,*}

^a CRUK Cambridge Research Institute, Li Ka Shing Centre, Robinson Way, Cambridge CB2 0RE, UK

^b Laboratory of Experimental Medicine and Endocrinology, KULeuven, Herestraat 49 bus 902, 3000 Leuven, Belgium

^c Wellcome Trust Centre for Stem Cell Research, Tennis Court Road, Cambridge CB2 1QR, UK

a subpopulation of cells at the base of the sebaceous gland readily formed ectopic follicles, resulting in complete and reversible conversion of sebaceous glands into hair follicles. Combined activation of β -catenin and the vitamin D receptor enhanced differentiation of sebaceous gland-derived hair follicles and stimulated ectopic follicle formation

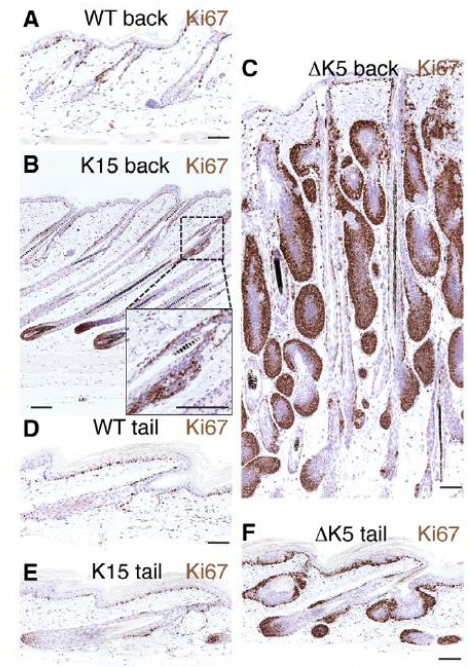
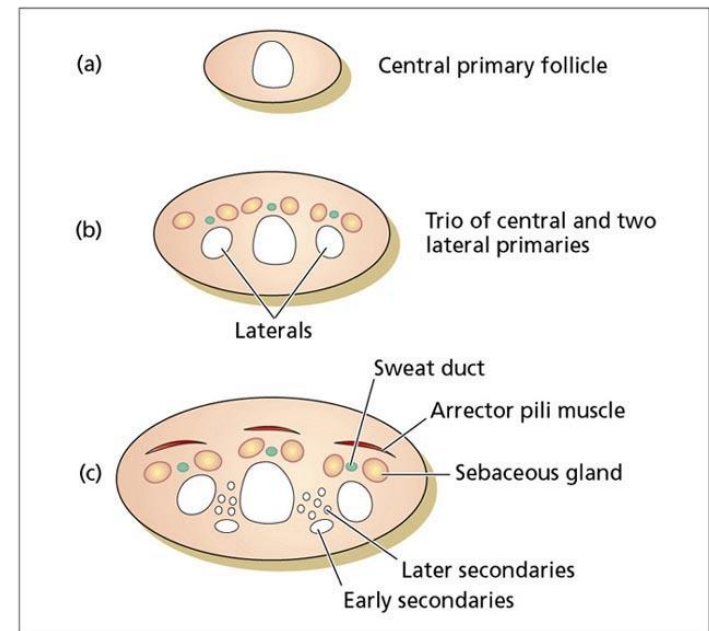


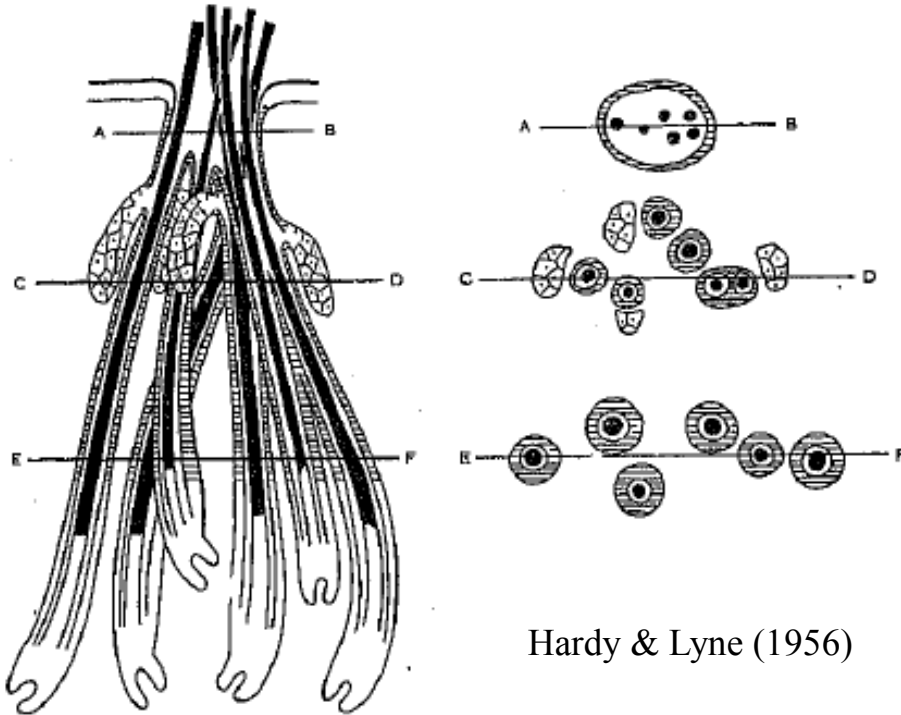
Fig. 6. Activation of β -catenin stimulates proliferation in transgene positive epidermal cells. Immunohistochemical labeling with anti-Ki67 (brown) of back and tail skin from wild type (WT) (A, D), K15 Δ N β -cateninER (K15) (B, E) and Δ K5 Δ N β -cateninER (Δ K5) (C, F) transgenic mice following treatment with 4OHT for 21 days. Scale bars: 50 μ m.

Primary and secondary hair follicles

- best studied in sheep.
- 1° hair develops day 70 → trio pattern with a central 1° & 2 x lateral 1°
- 2° follicles closely associated with the primary follicles form by day 85
- 2° derived follicles, branches of the 2° follicles appear by day 105 → form bulk of fleece

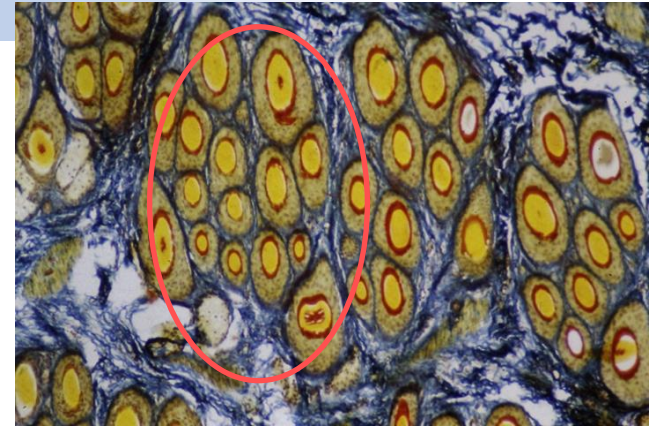


Compound Follicles

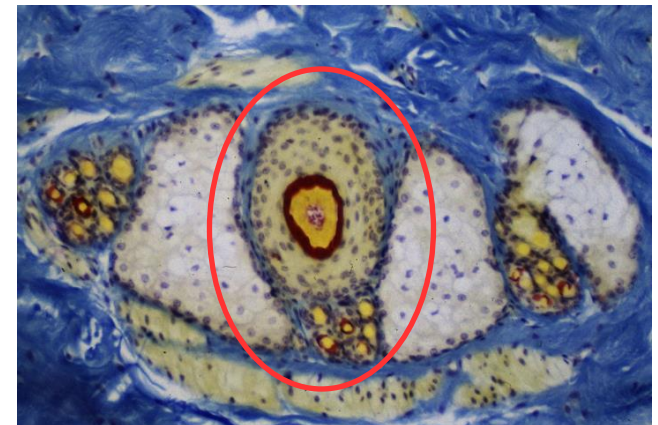


Hardy & Lyne (1956)

Secondary follicle bundle
in Merino sheep



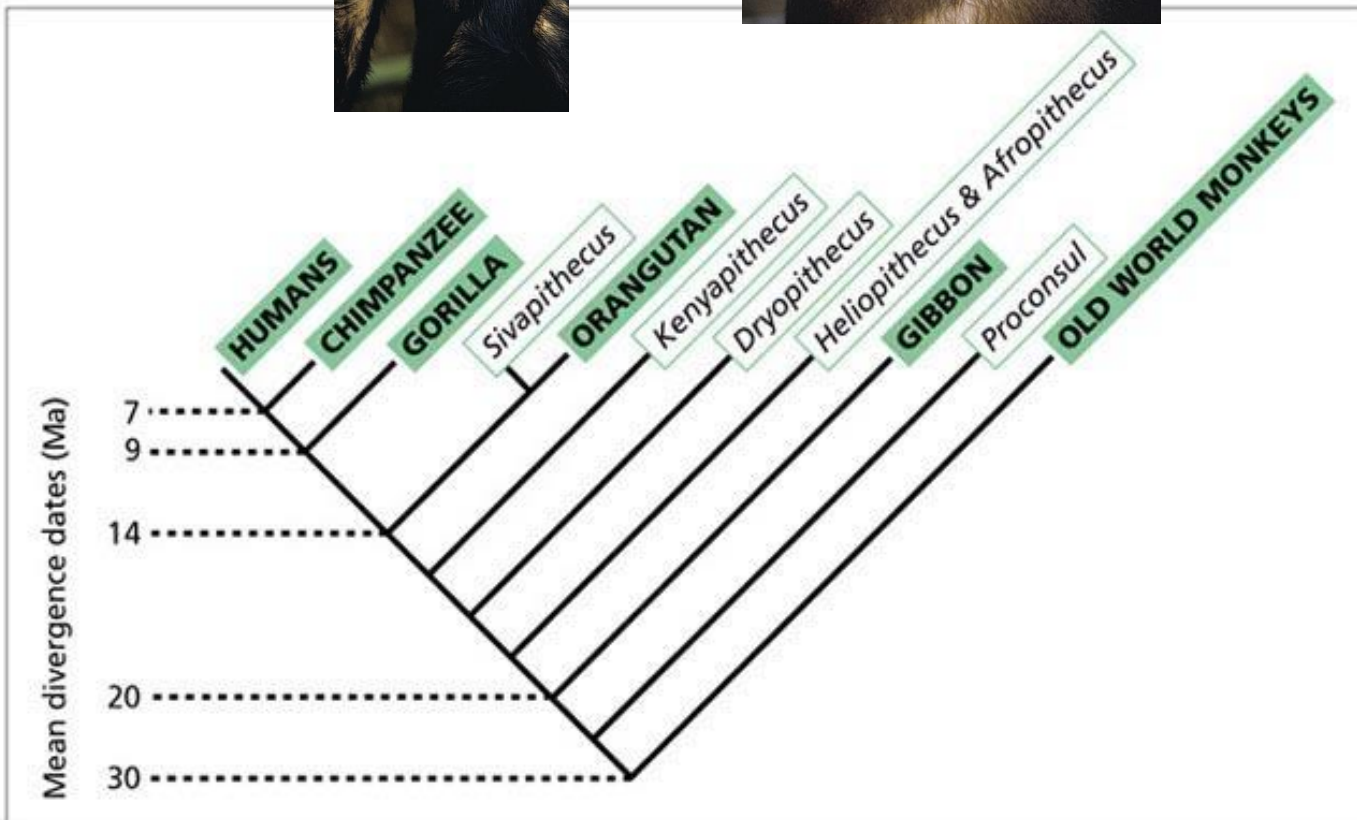
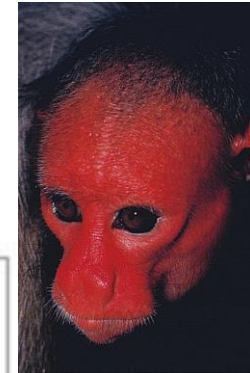
Goat



Ferret

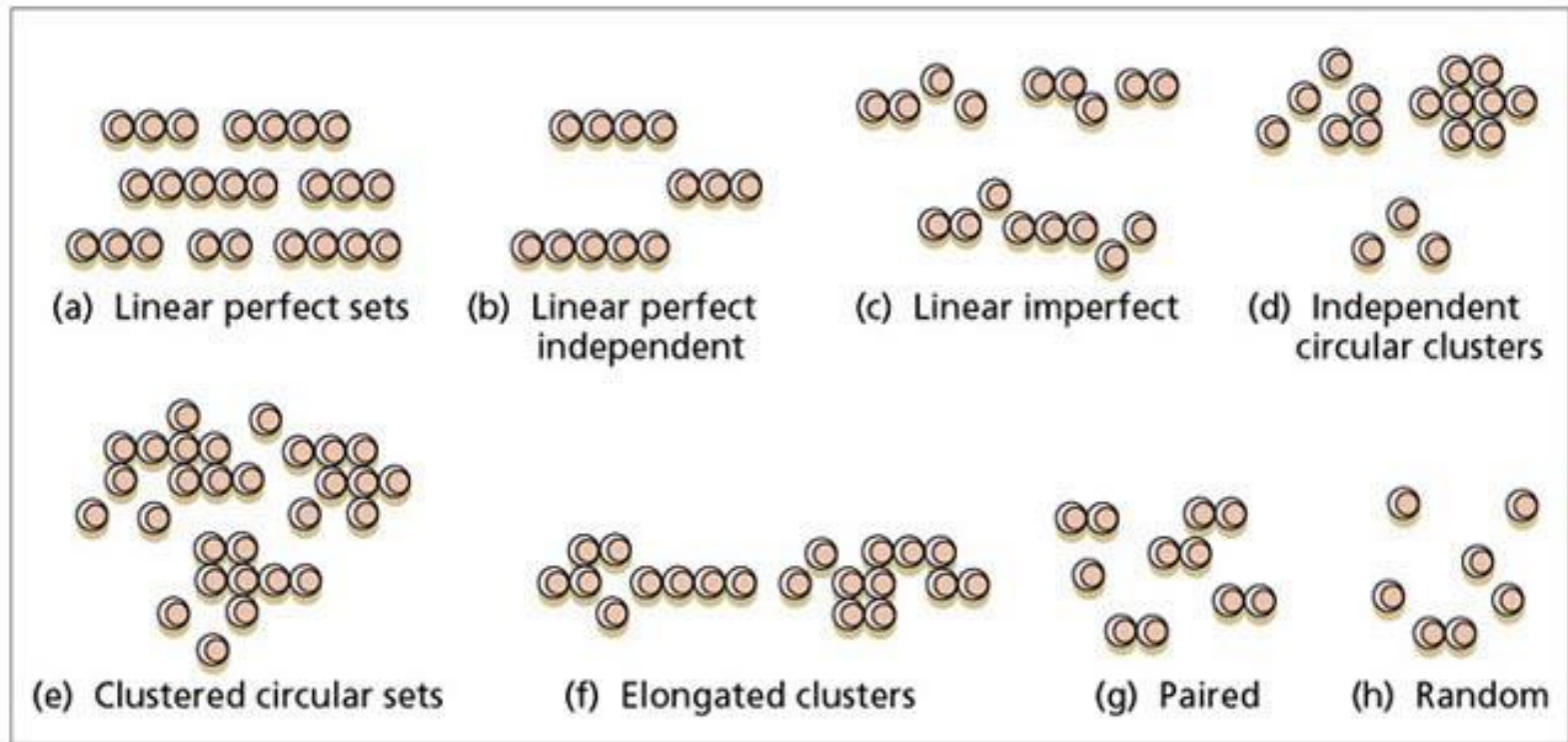
Hair Groupings in Primates

Perkins 1969



Hair Groupings in Primates

Perkins 1969



Hair groupings become less organized with phylogenetic advancement

Primary and secondary hair follicles



Under surface of the epidermis of a 6-month fetus, showing many developing groups of hair follicles. Each group consists of a primary follicle (P) flanked by secondary follicles (arrows). The humps (E) between the follicles are primordial eccrine sweat glands.

Montagna W, Kligman AM, Carlisle KS. Atlas of Normal Human Skin. Berlin: Springer-Verlag, 1992; 314–15.

Common Clinical Scenario

35 year old woman presents with increased hair shedding, a reduction in the thickness of her pony tail by a third but apparently normal hair density over mid frontal scalp.

Scalp biopsy shows androgenetic alopecia with a terminal to vellus hair ratio of 2:1



Diffuse Thinning precedes Baldness in women

Yazdabadi A, Magee J, Harrison S, Sinclair R.

The Ludwig pattern of androgenetic alopecia is due to a hierarchy of androgen sensitivity within follicular units that leads to selective miniaturization and a reduction in the number of terminal hairs per follicular unit.

Br J Dermatol. 2008



Stage 1

Stage 2

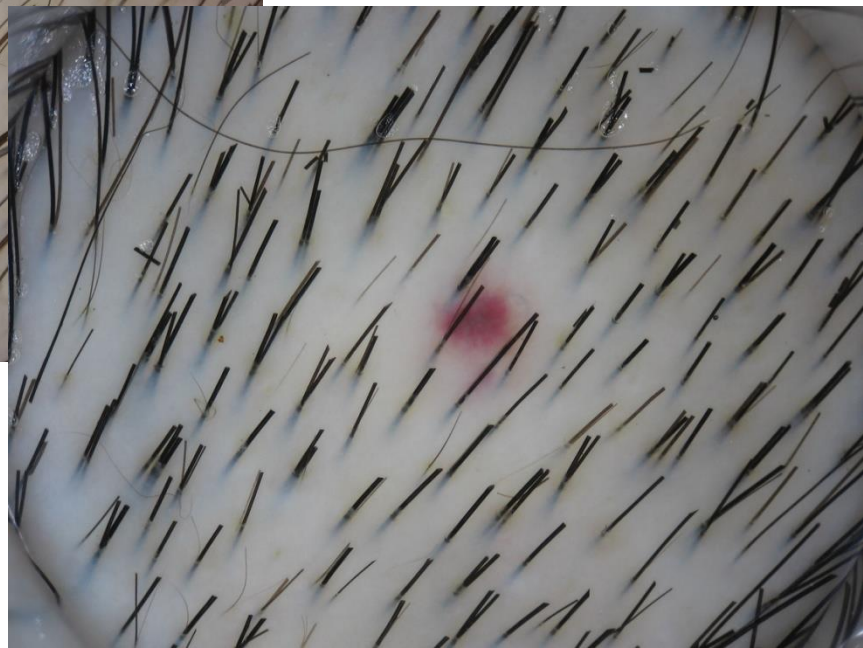
Stage 3

Stage 4

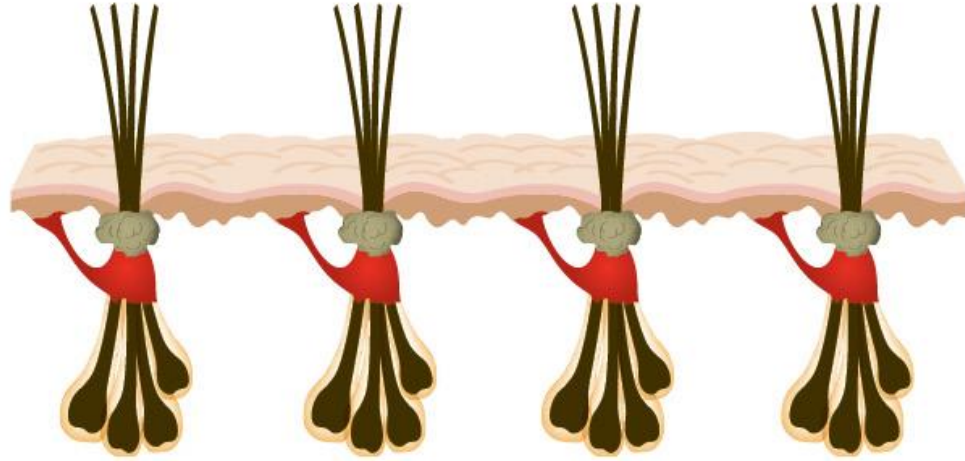
Stage 5



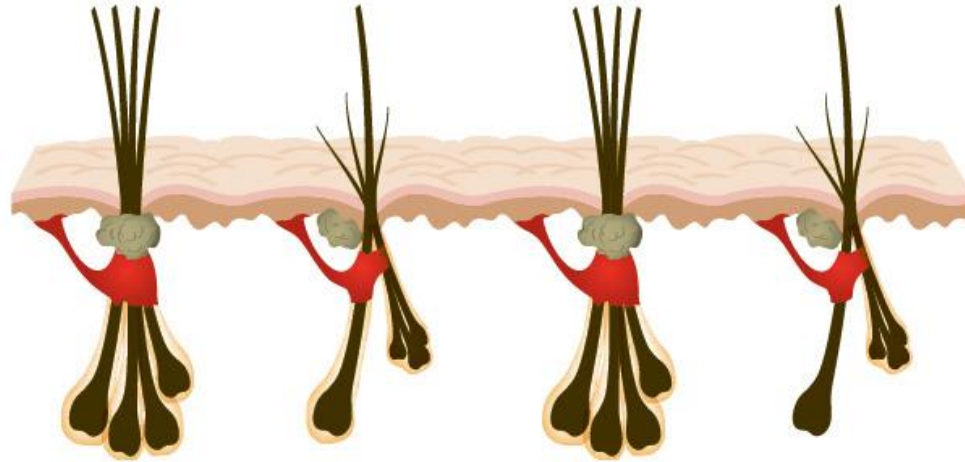
Diffuse hair loss in women is due to a reduction in the number of hairs per follicular unit rather than uniform miniaturization of entire follicular units



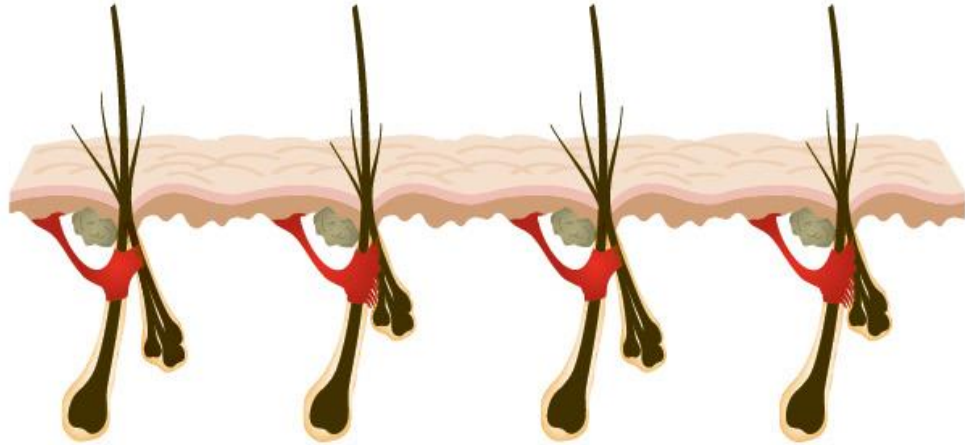
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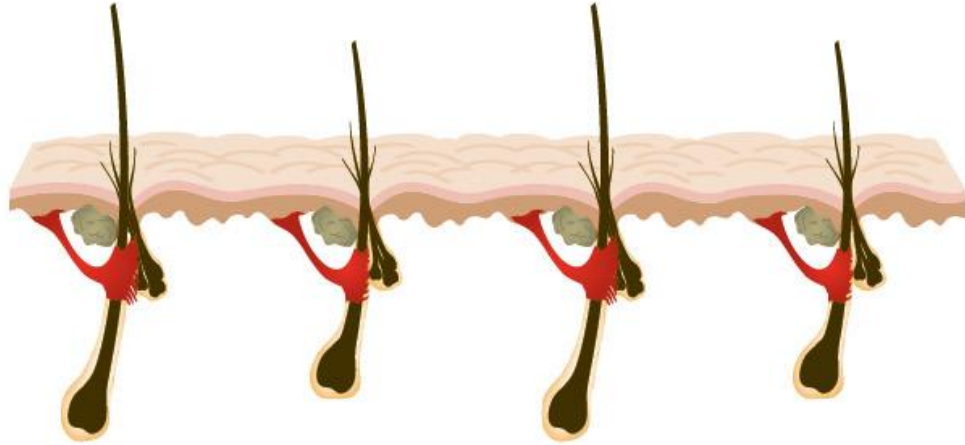
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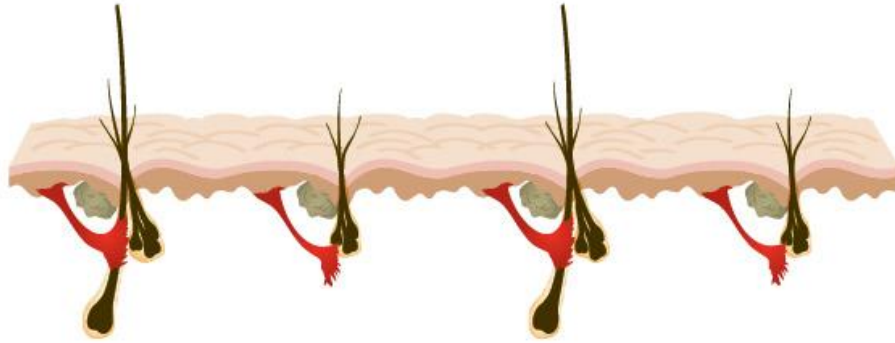
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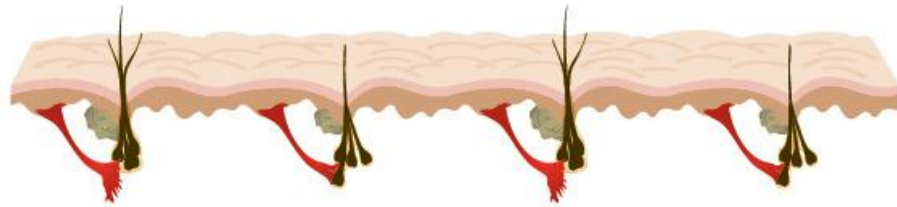
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6



Summary

New model for early AGA

- **Hair growth on the scalp is different to the rest of the body**
- **There is a hierarchy in follicular units with primary and secondary hairs**
- **Secondary hairs arise in utero from a stem cell population below sebaceous gland but above bulge**
- **Secondary hairs miniaturize first in AGA**
- **Reduction in the number of hairs emerging from each pore is a sign of early AGA**

Patient 102-Androcur 100mg for 10 days per month



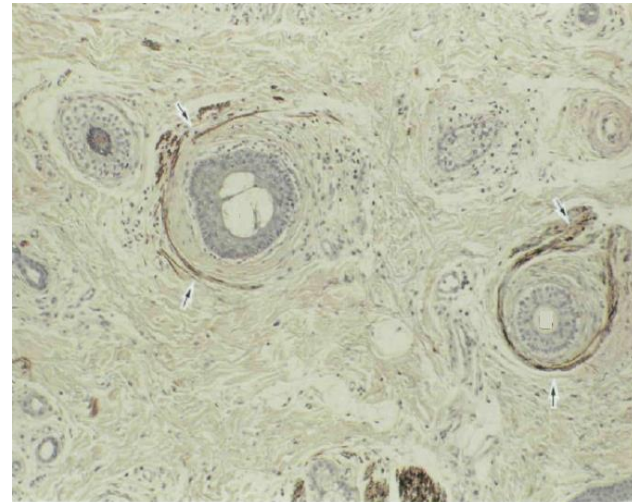
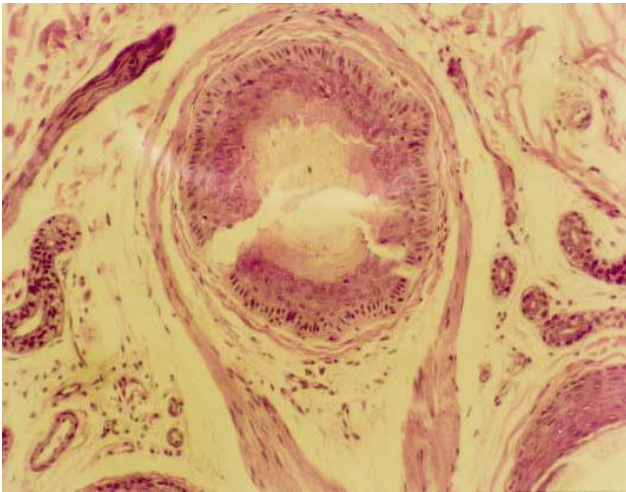
Baseline

6 months

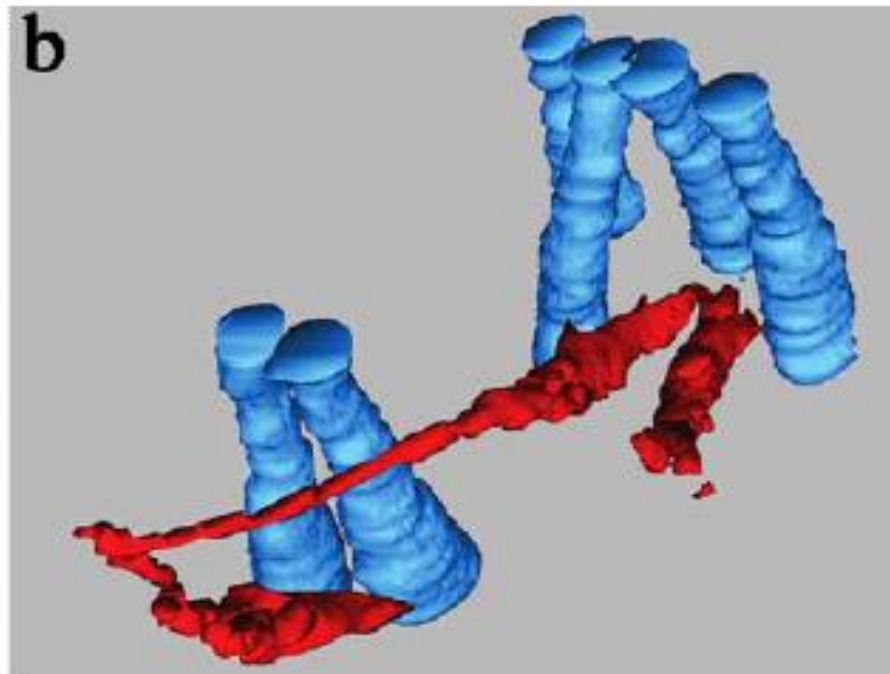
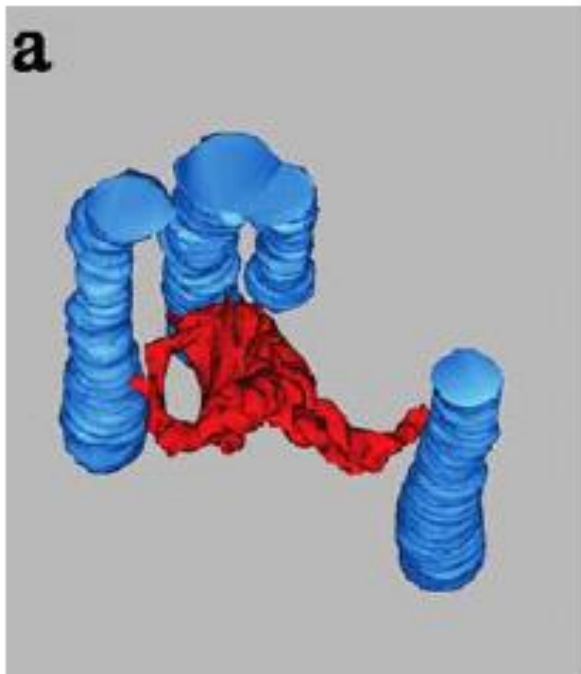
12 months

24 months

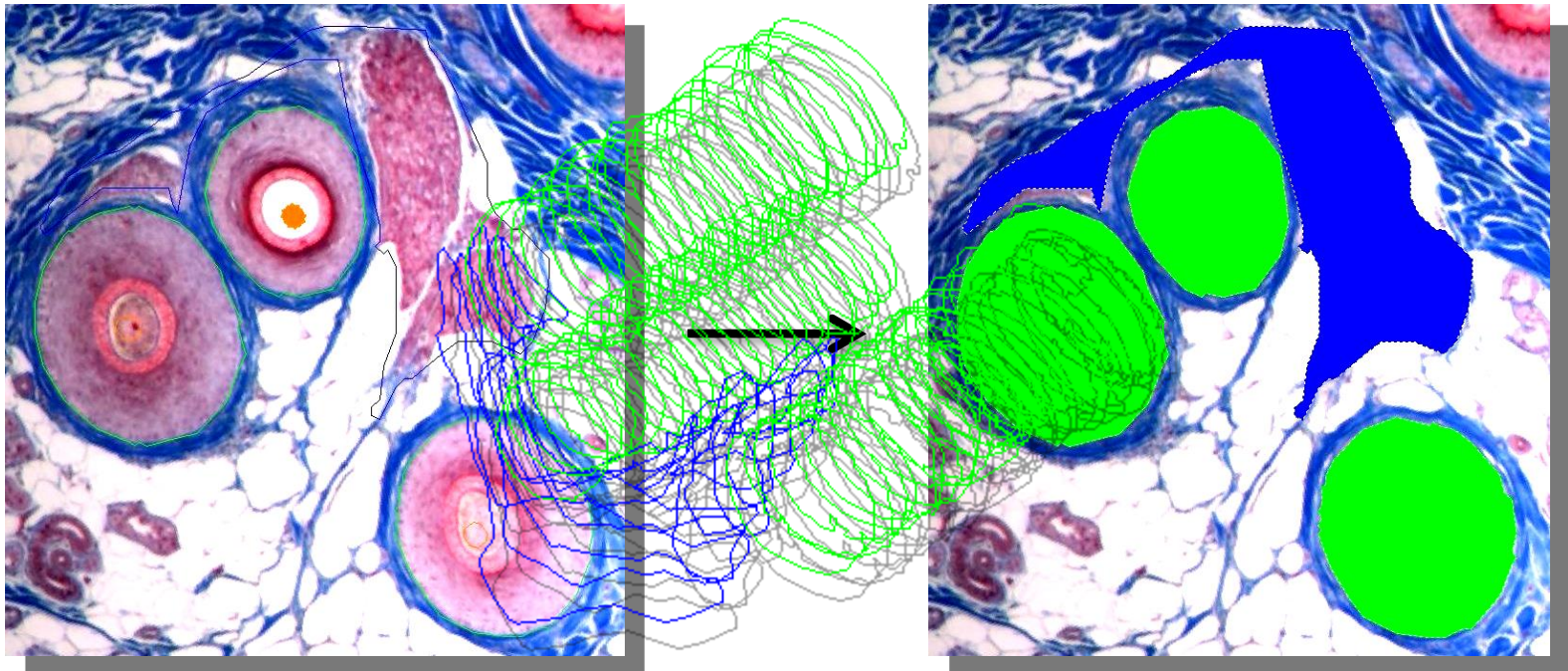
- *Arrector pili muscle surrounds human facial vellus hair follicles*



Arrector pili muscle

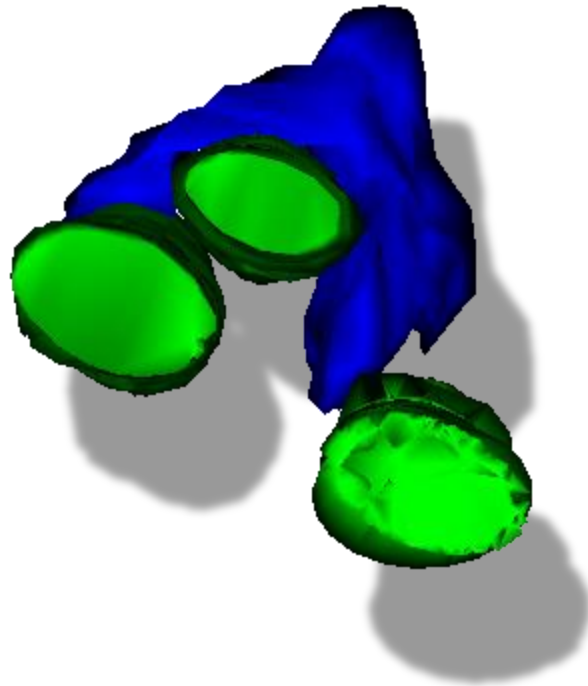


Method

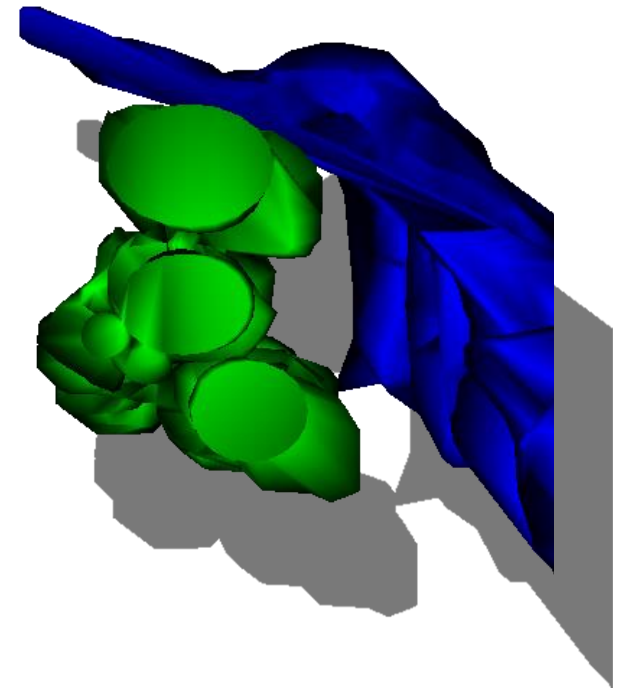
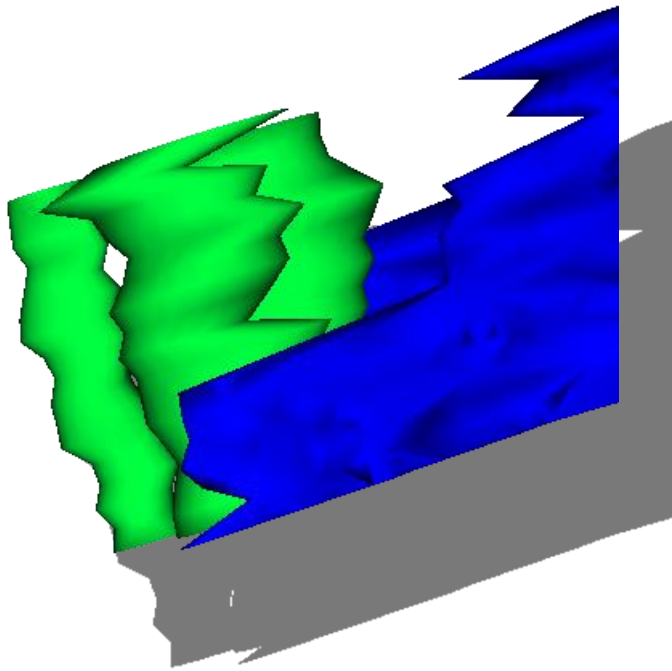




Diffuse Alopecia

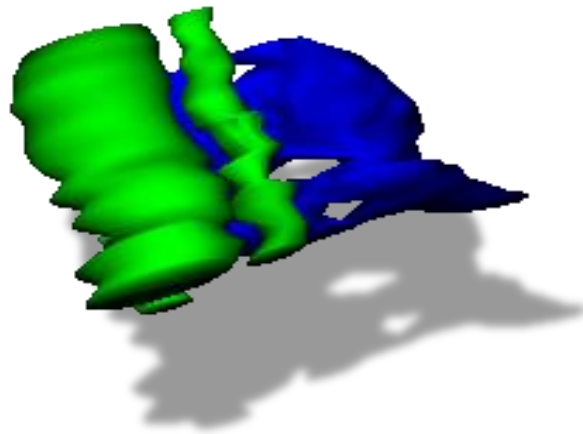


Female Pattern Hair Loss



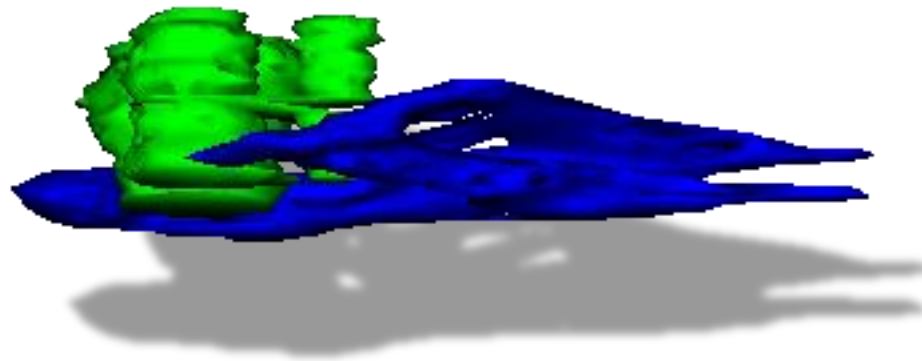


Male Pattern Hair Loss





Alopecia Areata



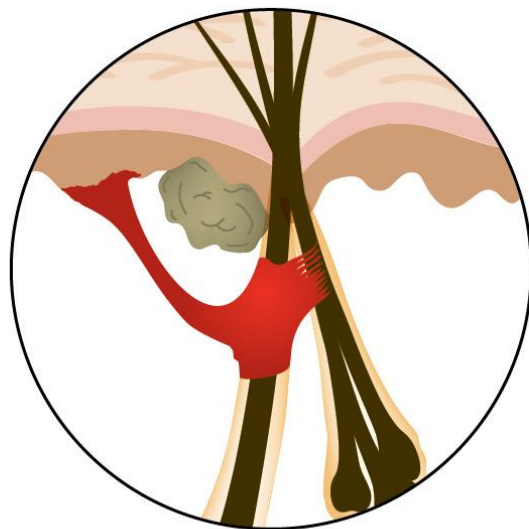


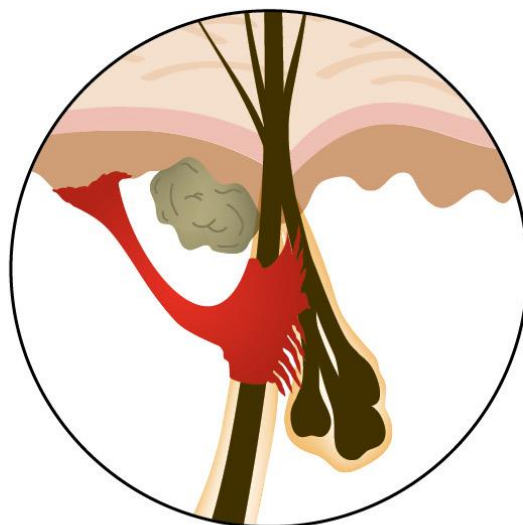
International Journal of Trichology

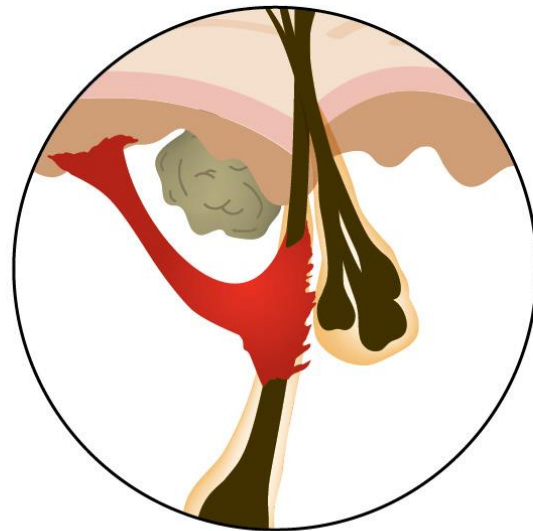
Miniaturized hairs maintain contact with the arrector pili muscle in alopecia areata but not in androgenetic alopecia: A model for reversible miniaturization and potential for hair regrowth

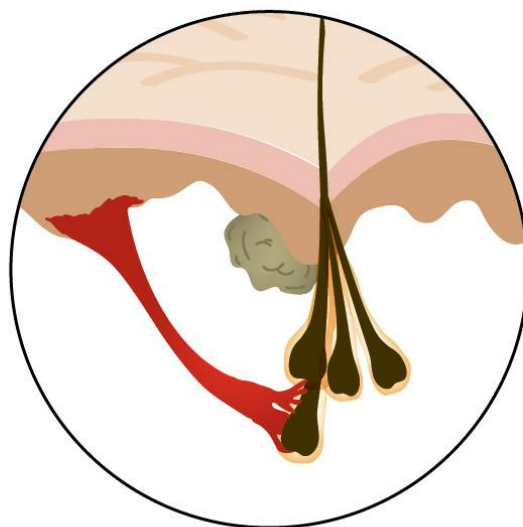
Anousha Yazdabadi¹, D Whiting², NW Rufaut¹, R Sinclair¹,
Int J Trichol 2012;4:154-157

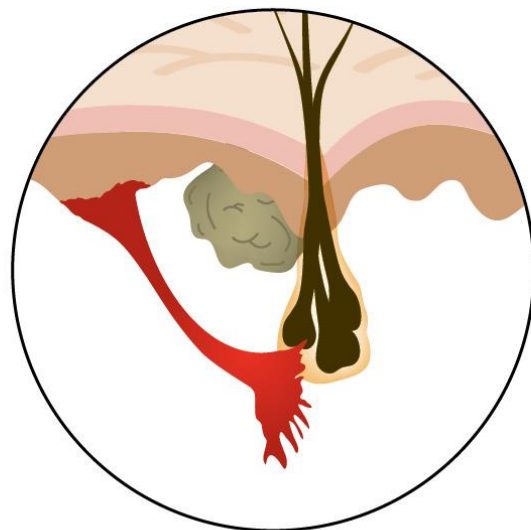


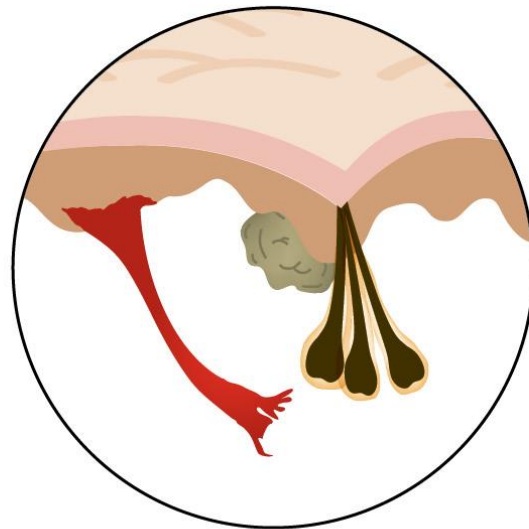


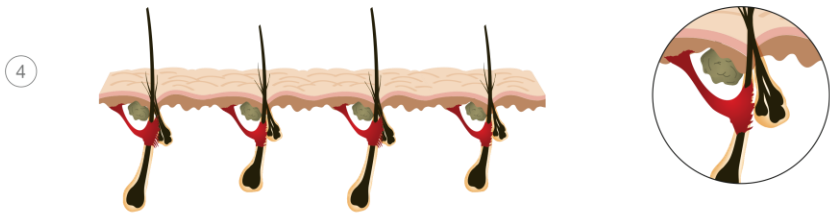
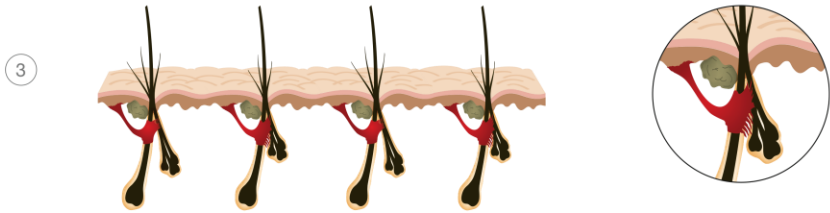
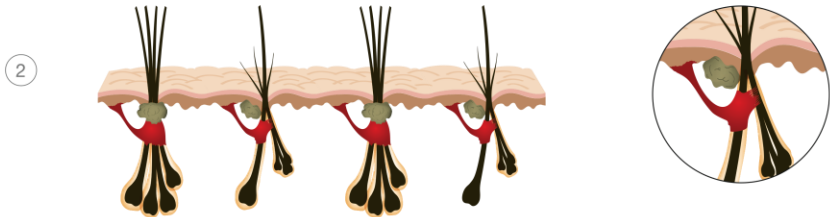
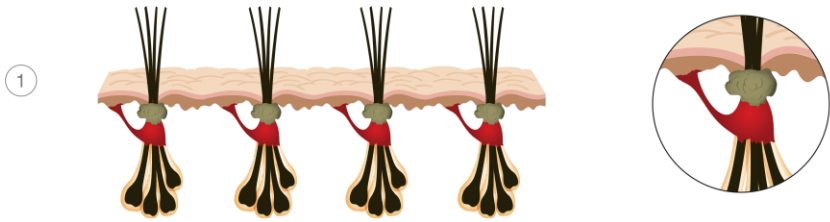




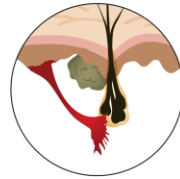
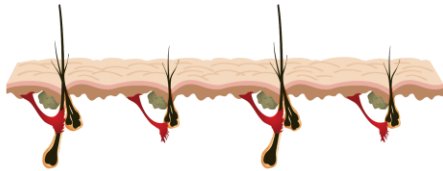




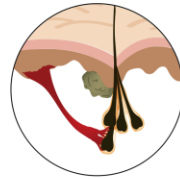




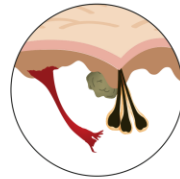
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Printed in U.S.A.

STUDIES OF COMMON BALDNESS OF THE STUMPTAILED MACAQUE

I. DISTRIBUTION OF THE HAIR FOLLICLES*

HIDEO UNO, M.D.†, FULVIO ALLEGRA, M.D.‡, KENJI ADACHI, M.D., PH.D.,
AND WILLIAM MONTAGNA, PH.D.

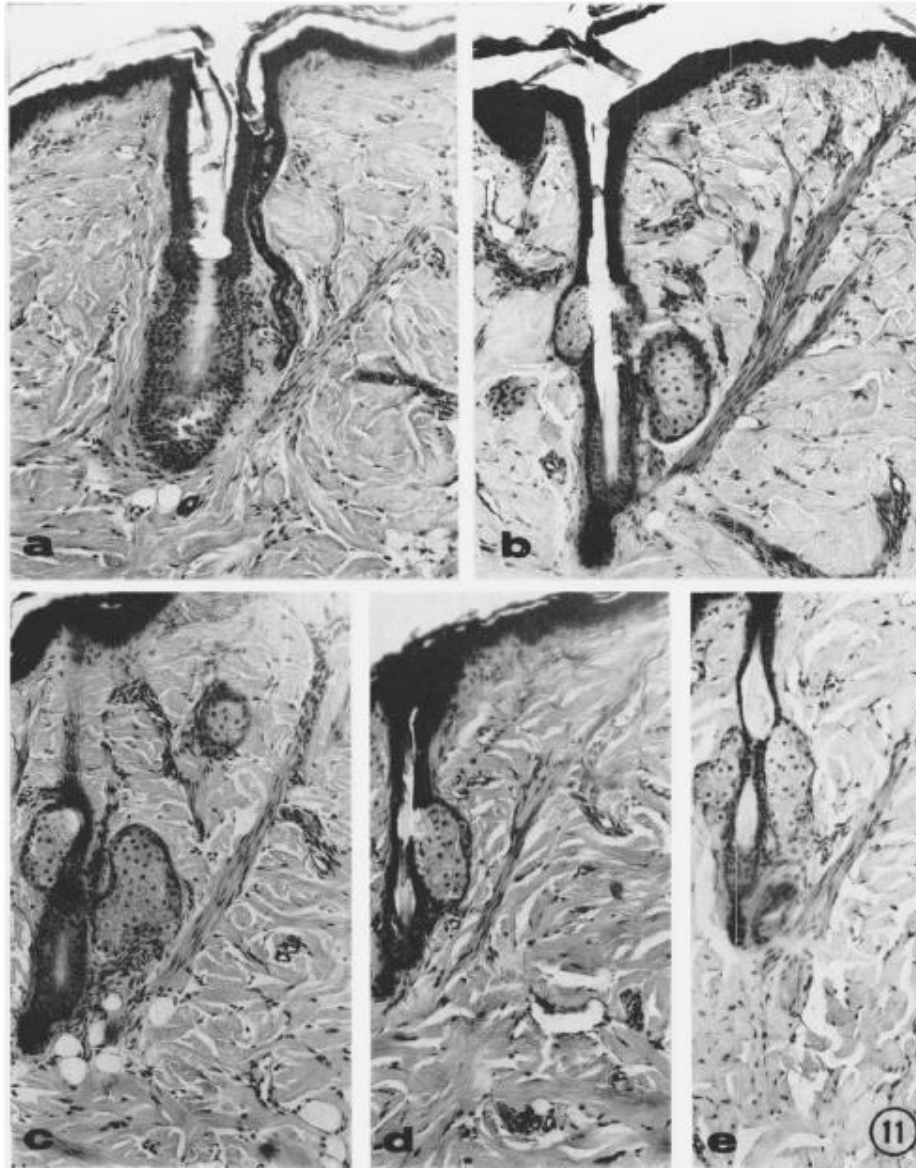
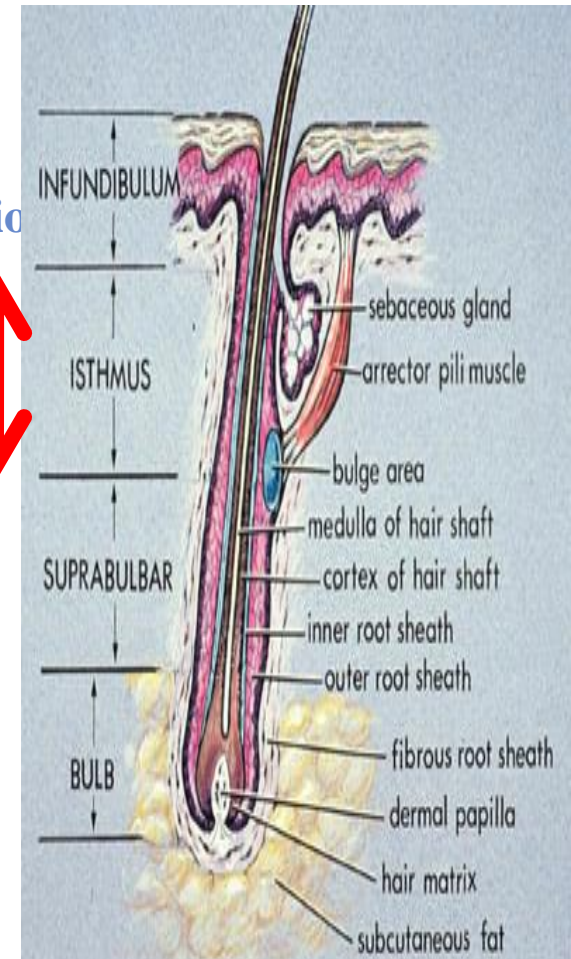


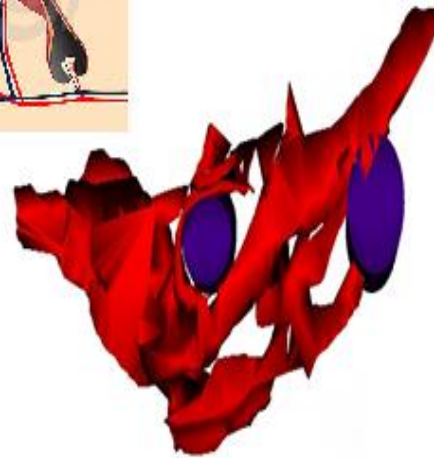
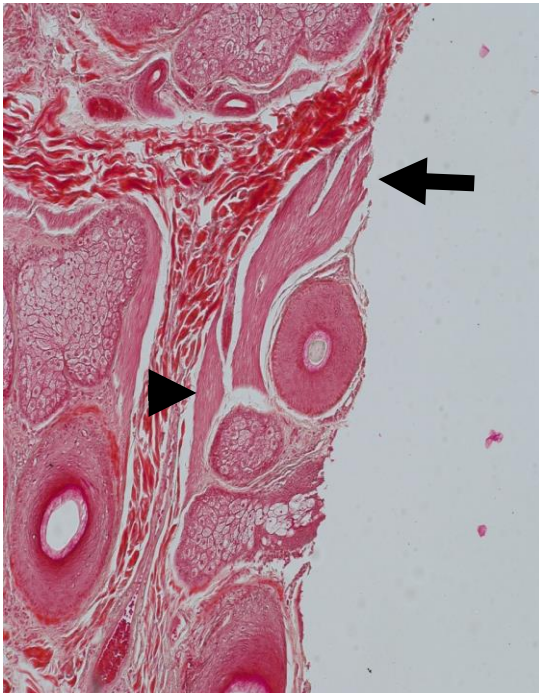
FIG. 11a, b, c, d, e. Vellus telogen hair follicles. In all of these figures the arrector pili muscle has lost its insertion to the follicle. As in Figure 10 this was ascertained by tracing each of these follicles in serial sections.

Methods & Material

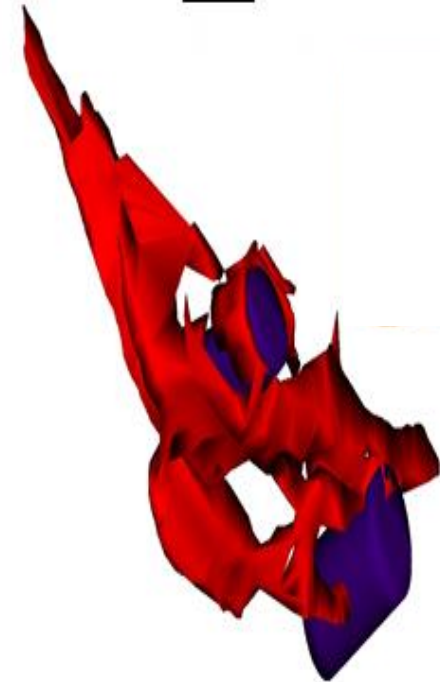
- 8 AGA , 6 TE archival blocks and one normal new bio
- Anatomical evaluation of the isthmus
- 3D models



Normal Hair

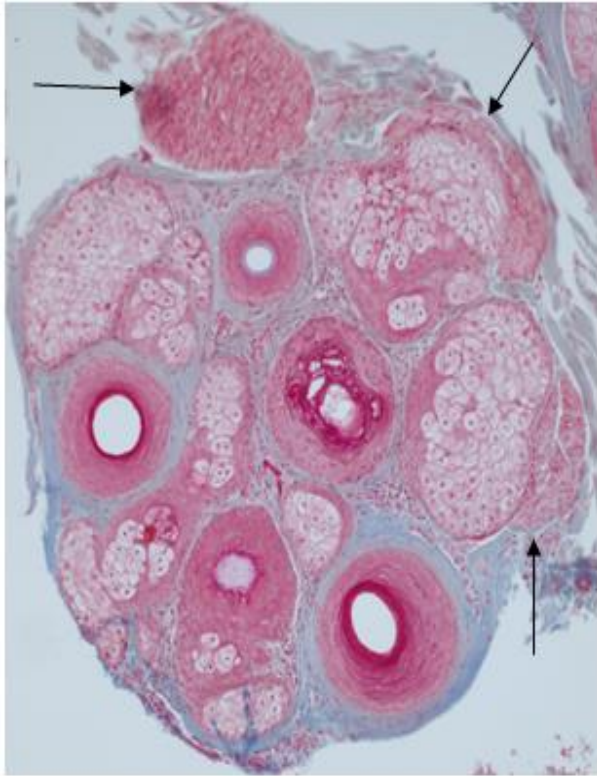


(a)



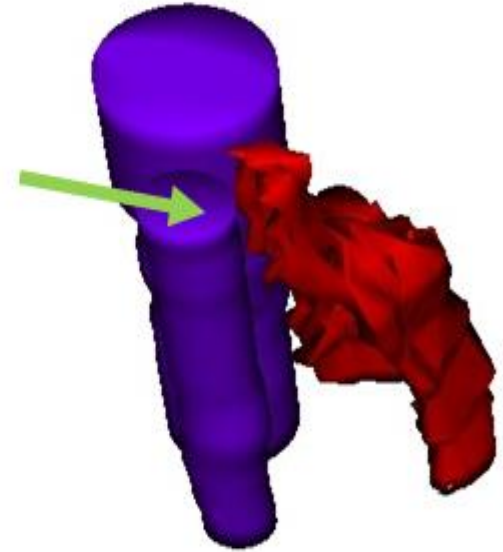
(b)

TE



(a)

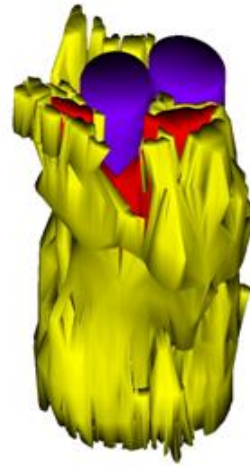
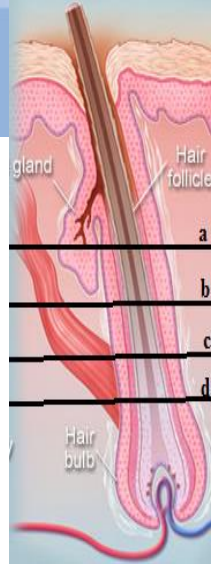
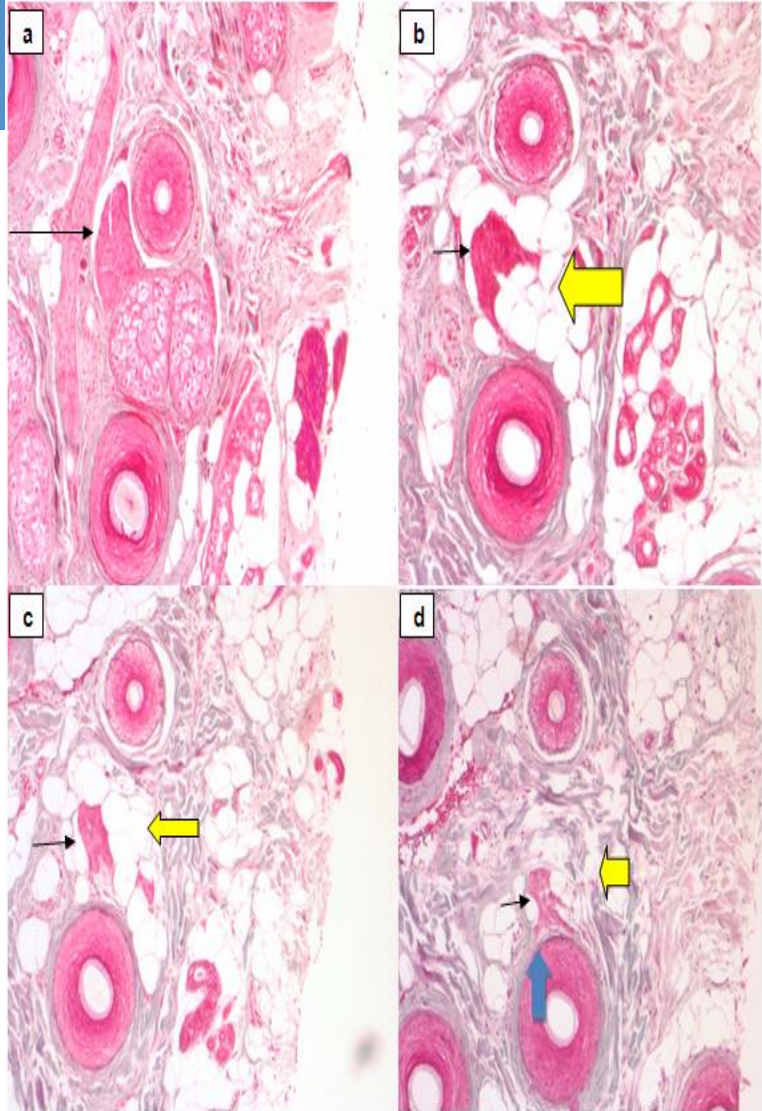
a) Medial
view



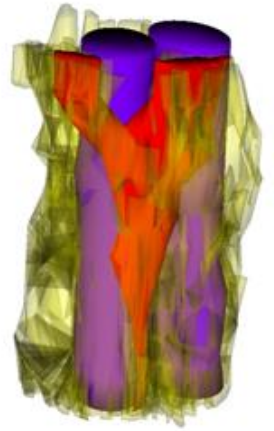
(b)

b) Lateral
view

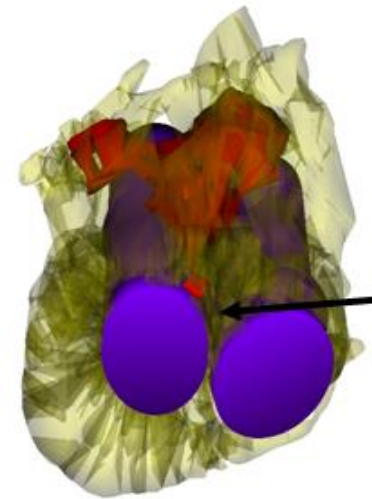
AGA



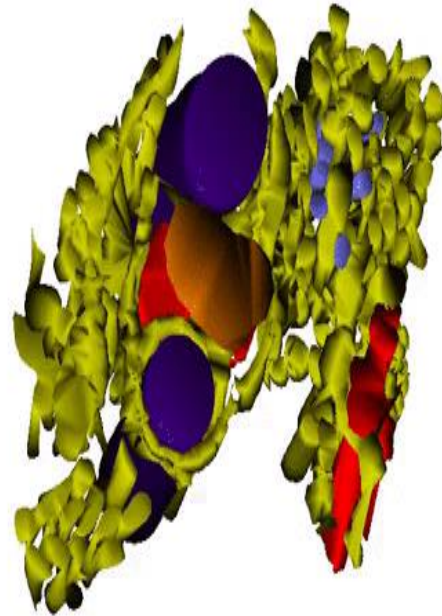
(a)



(b)



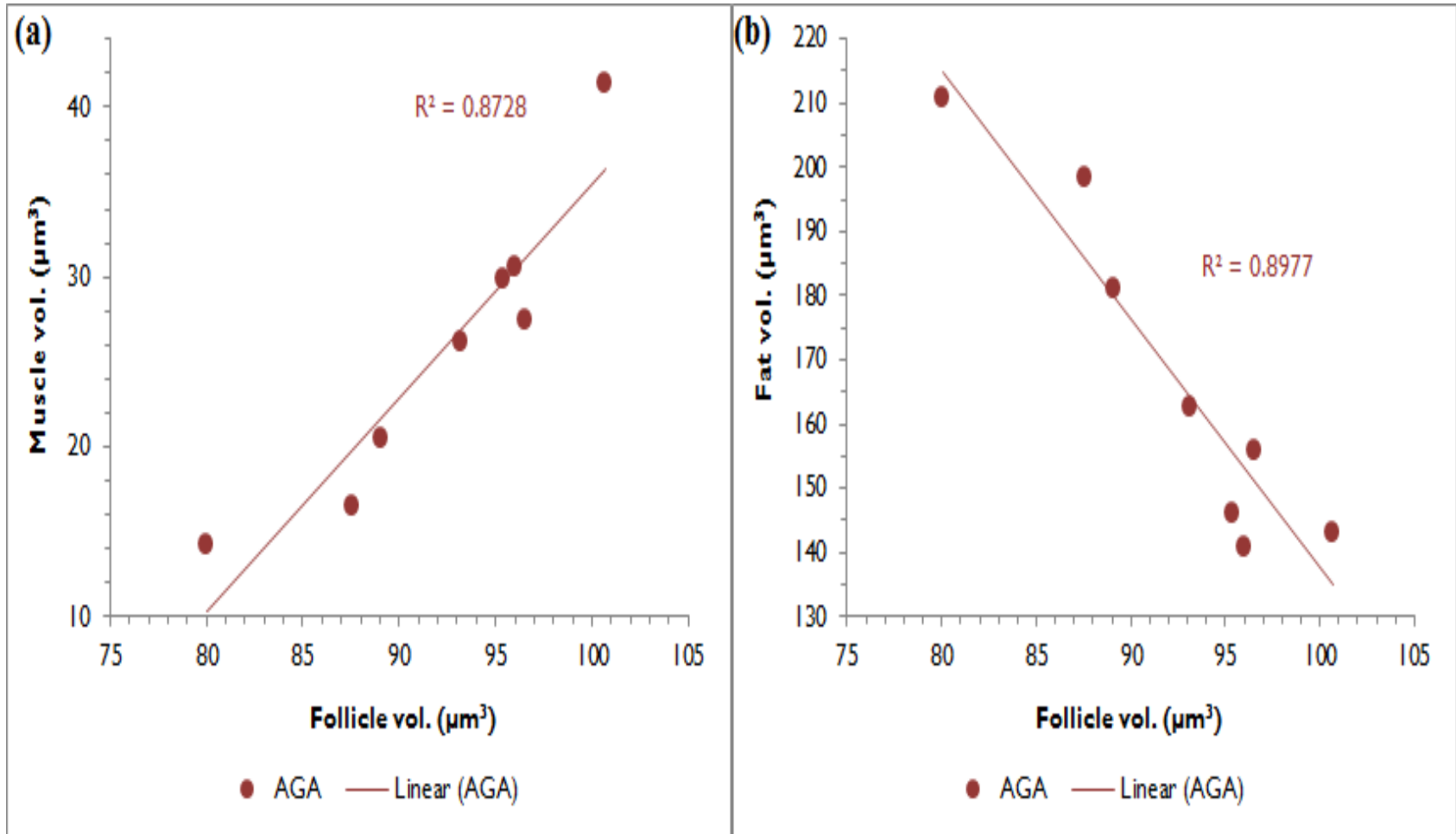
(c)



AGA:

Fat (Yellow), Terminal hair (Purple), Vellus hair (Blue),
Sebaceous gland (Brown) , APM (Red)

An increase in fat volume results directly in muscle loss





Clinical and laboratory investigations

Destruction of the arrector pili muscle and fat infiltration in androgenic alopecia

N. Torkamani, N.W. Rufaut, L. Jones and R. Sinclair

***DOI: [10.1111/bjd.12921](https://doi.org/10.1111/bjd.12921)**

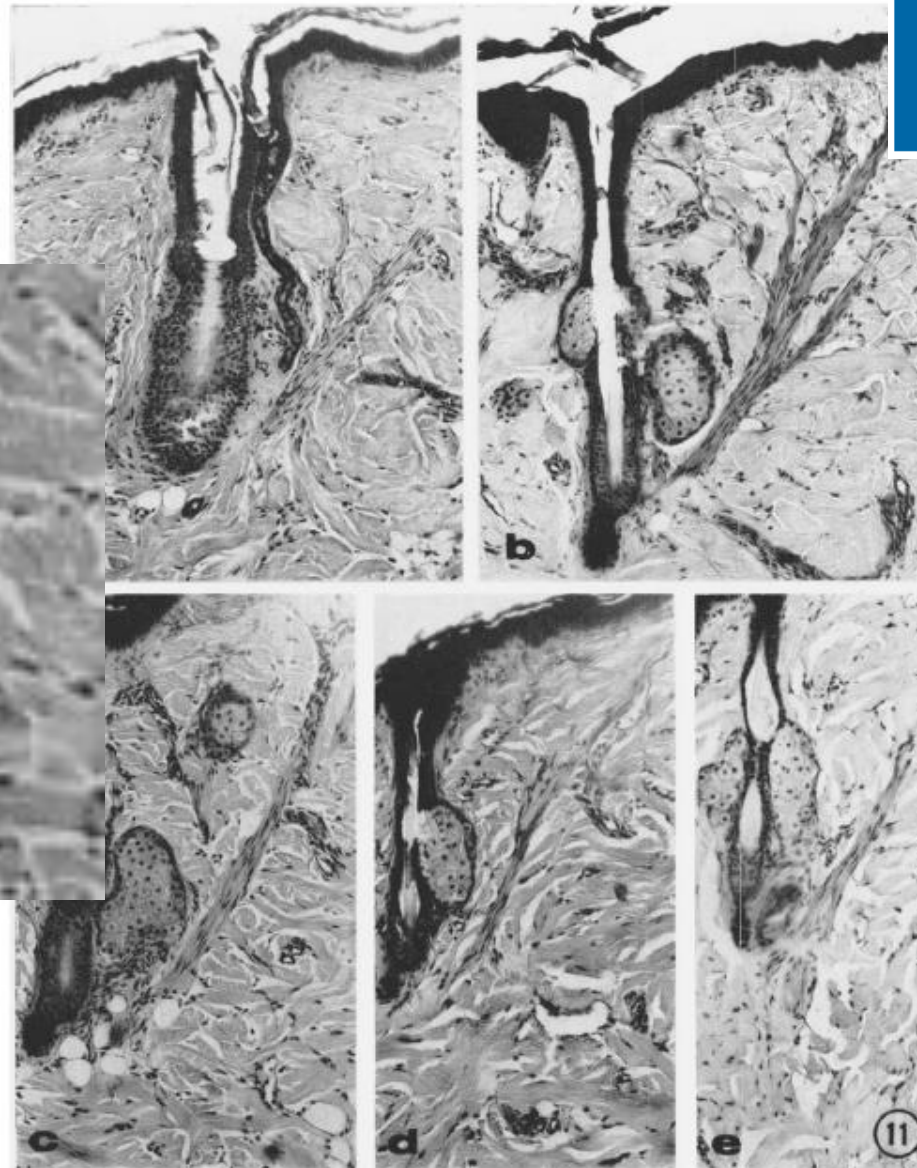


FIG. 11a, b, c, d, e. Vellus telogen hair follicles. In all of these figures the arrector pili muscle has lost its insertion to the follicle. As in Figure 10 this was ascertained by tracing each of these follicles in serial sections.



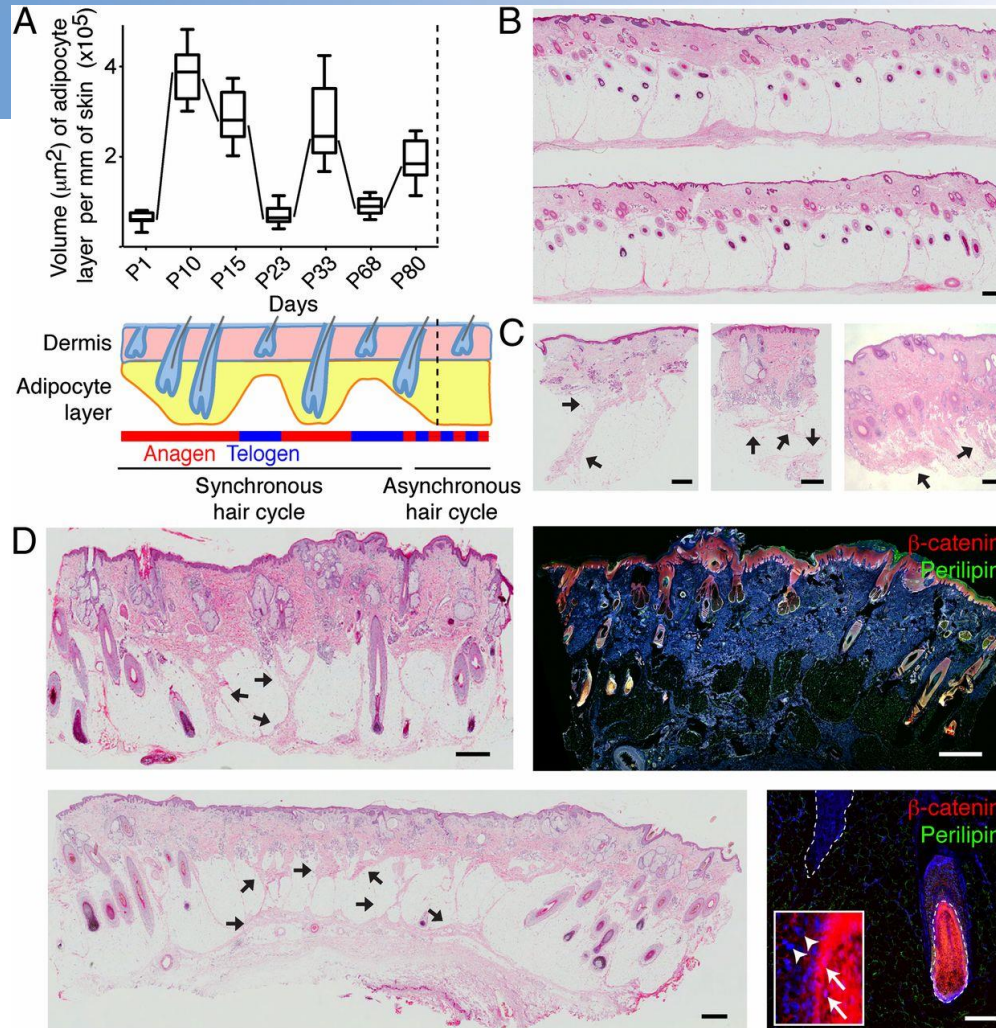
Summary

New model for early AGA

- Hair follicle miniaturization is reversible in alopecia areata but not AGA
- Miniaturized hairs maintain contact with the APM in AA, but lose contact in AGA
- Loss of contact between the bulge and APM might explain irreversible miniaturization
- Fat infiltration is seen in AGA and may explain the loss of contact between the bulge and APM



Relationship between hair follicle growth and the thickness of the dermal adipocyte layer.



Donati G et al. PNAS 2014;111:E1501-E1509

Epidermal Wnt/ β -catenin signaling regulates adipocyte differentiation via secretion of adipogenic factors

Giacomo Donati^{a,b}, Valentina Proserpio^{c,1}, Beate Maria Lichtenberger^{a,1}, Ken Natsuga^{b,d}, Rodney Sinclair^e, Hironobu Fujiwara^{b,f,2,3}, and Fiona M. Watt^{a,2,3}

Activation of Wnt signalling stimulates hair follicles to enter anagen and can reprogram inter-follicular epidermis to form ectopic hairs follicles

Epidermal activation of Wnt/ β catenin signalling stimulates adipocyte differentiation in vivo

Epidermal inhibition of Wnt/ β catenin signalling decreases adipocyte differentiation in vivo





British Journal of Dermatology (1975) **93**, 631.

The fine structure of the elastic tendons in the human *arrector pili* muscle

F. GUERRA RODRIGO,* G. COTTA-PEREIRA AND
J. F. DAVID-FERREIRA

Laboratory of Cell Biology, Gulbenkian Institute of Science, Oeiras, Portugal; Department of Dermatology, Faculty of Medicine, Lisbon, Portugal; Departments of Histology and Embryology, State University of Guanabara and Federal University of Rio de Janeiro, Guanabara, Brazil

Accepted for publication 14 March 1975

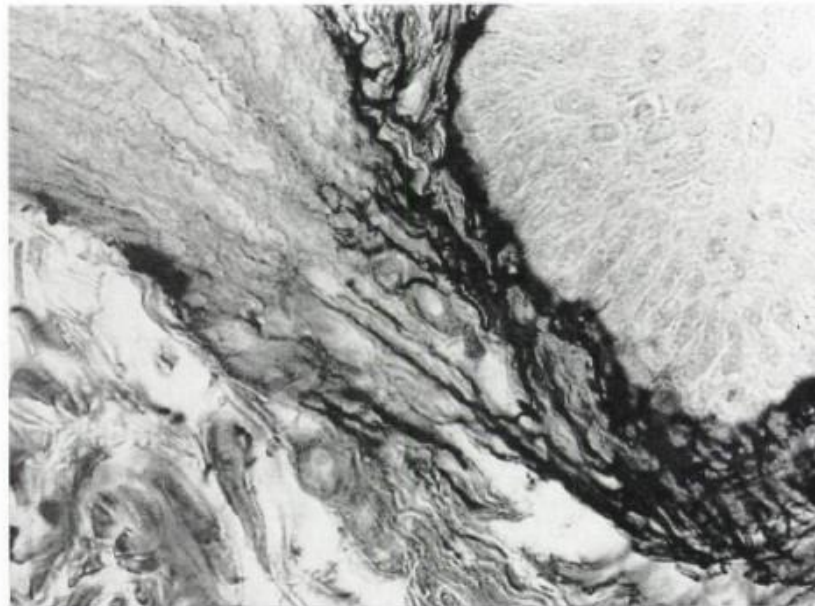
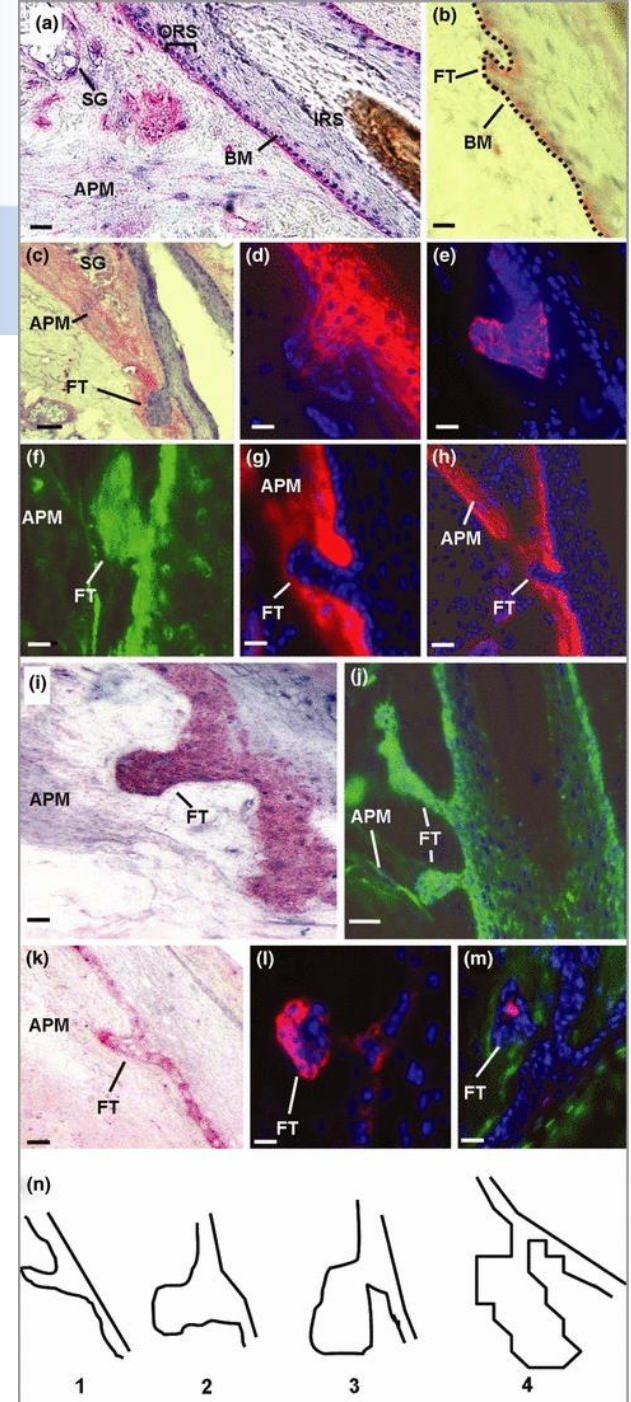


FIGURE 1. Hair insertion of the *arrector pili* muscle. Note the elastic tendons binding the extremity of the muscle to the bulge of the follicle. Weigert's resorcin fuchsin after peracetic acid oxidation ($\times 800$).

The 'follicular trochanter': an epithelial compartment of the human hair follicle bulge region in need of further characterization

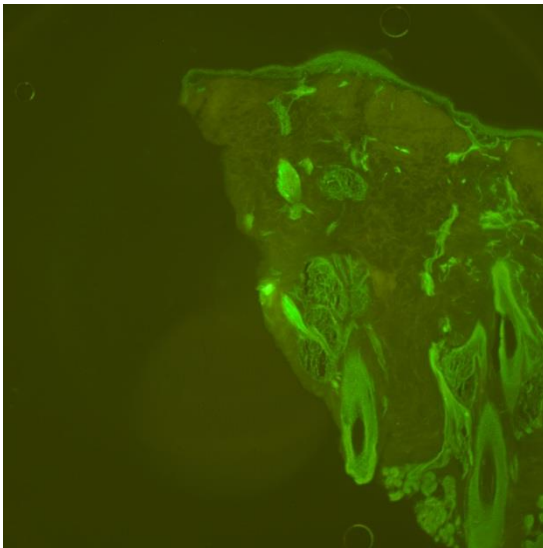
S. Tiede, J.E. Kloepper, D.A. Whiting and R. Paus

British Journal of Dermatology
Volume 157, Issue 5, pages 1013–1016, November 2007

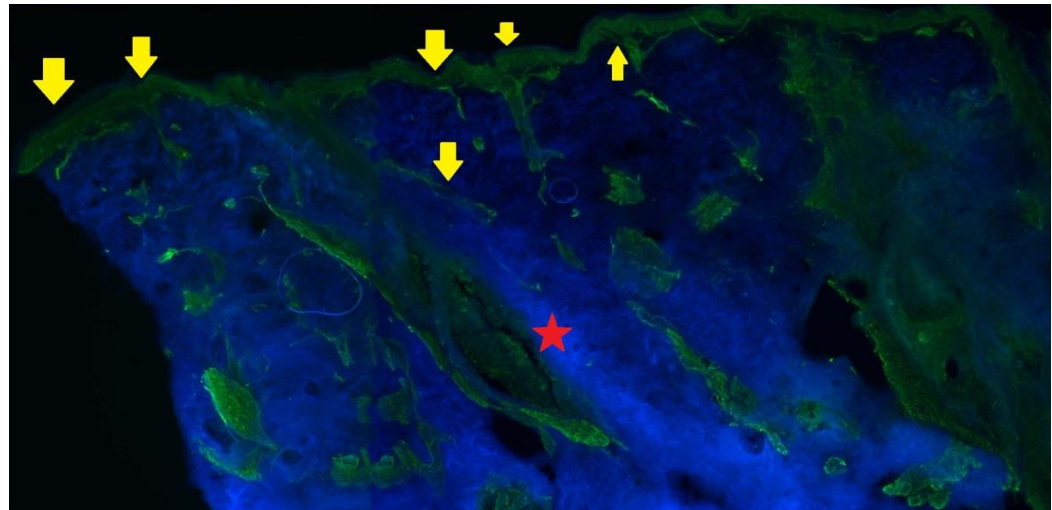




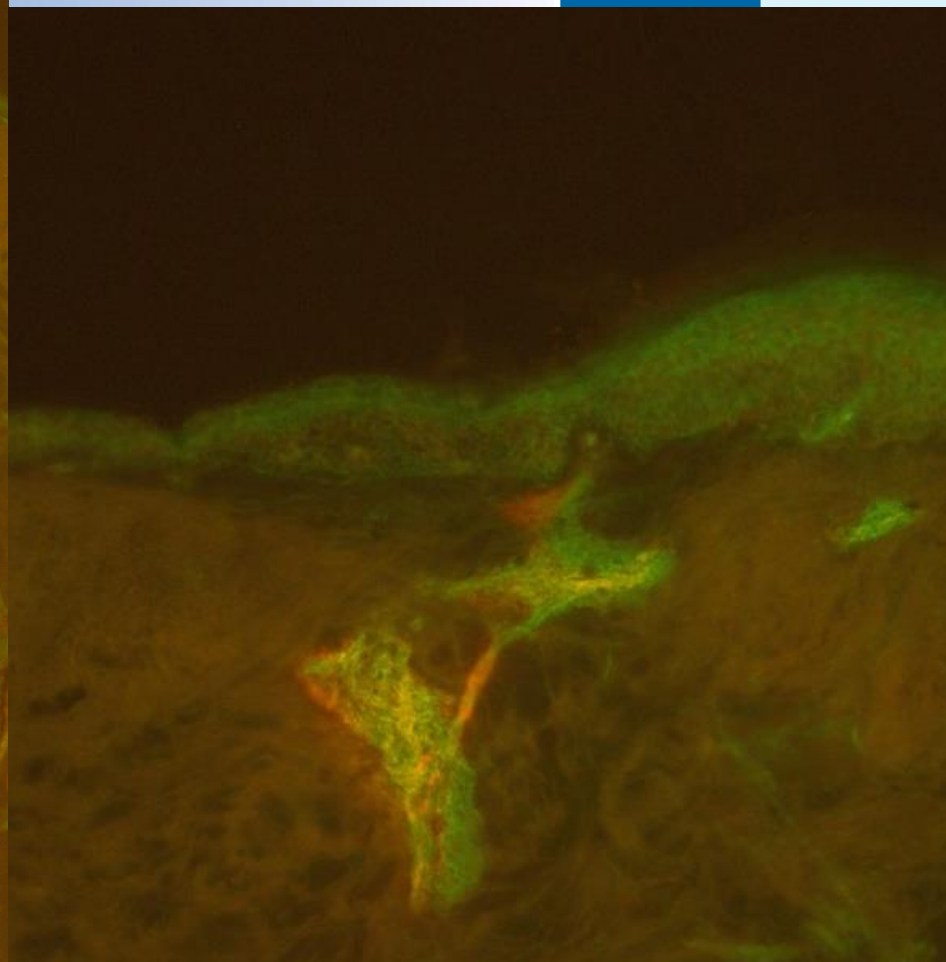
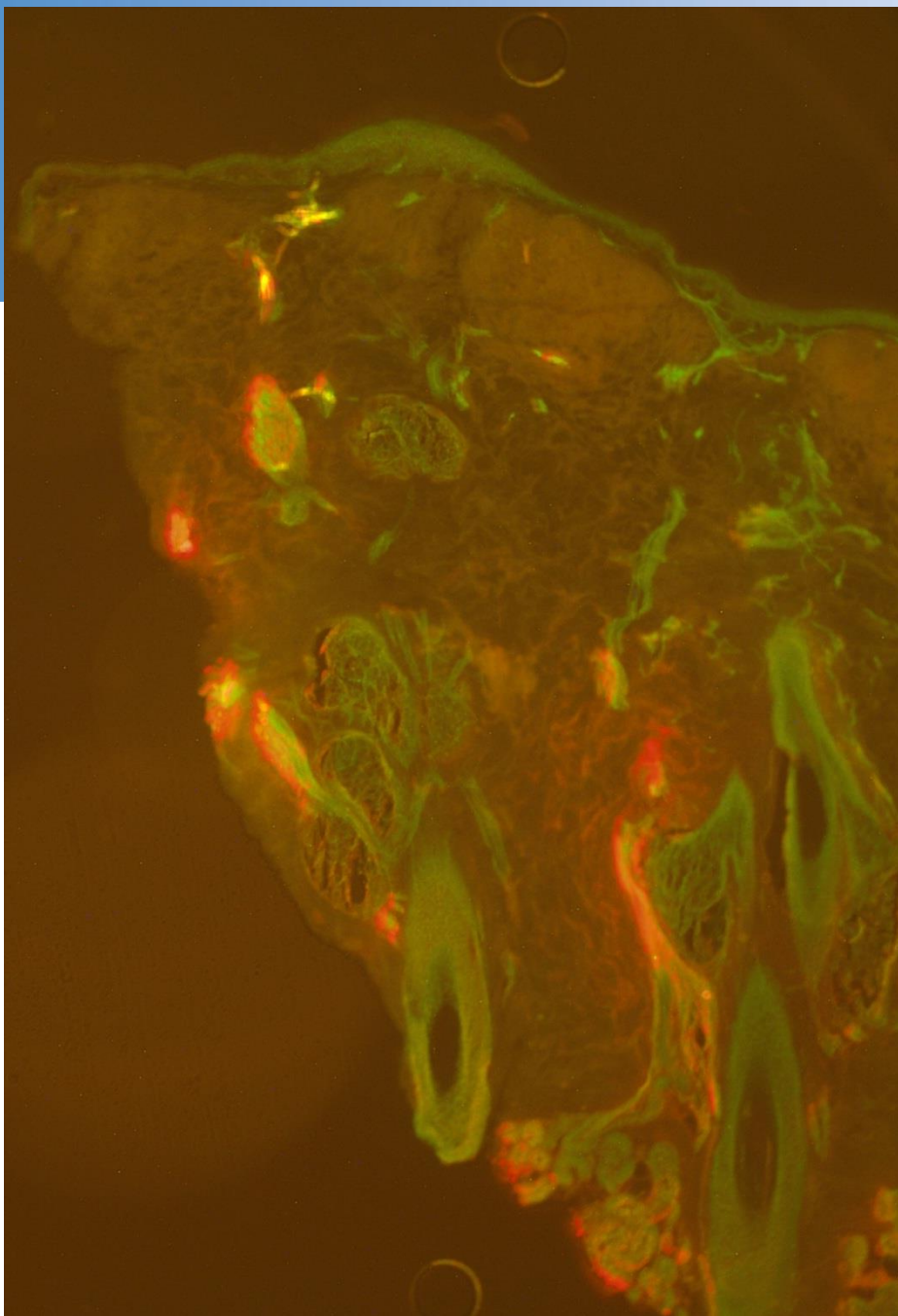
Normal Hair:
Follicle (Blue), APM (Red), Epidermis (Black)



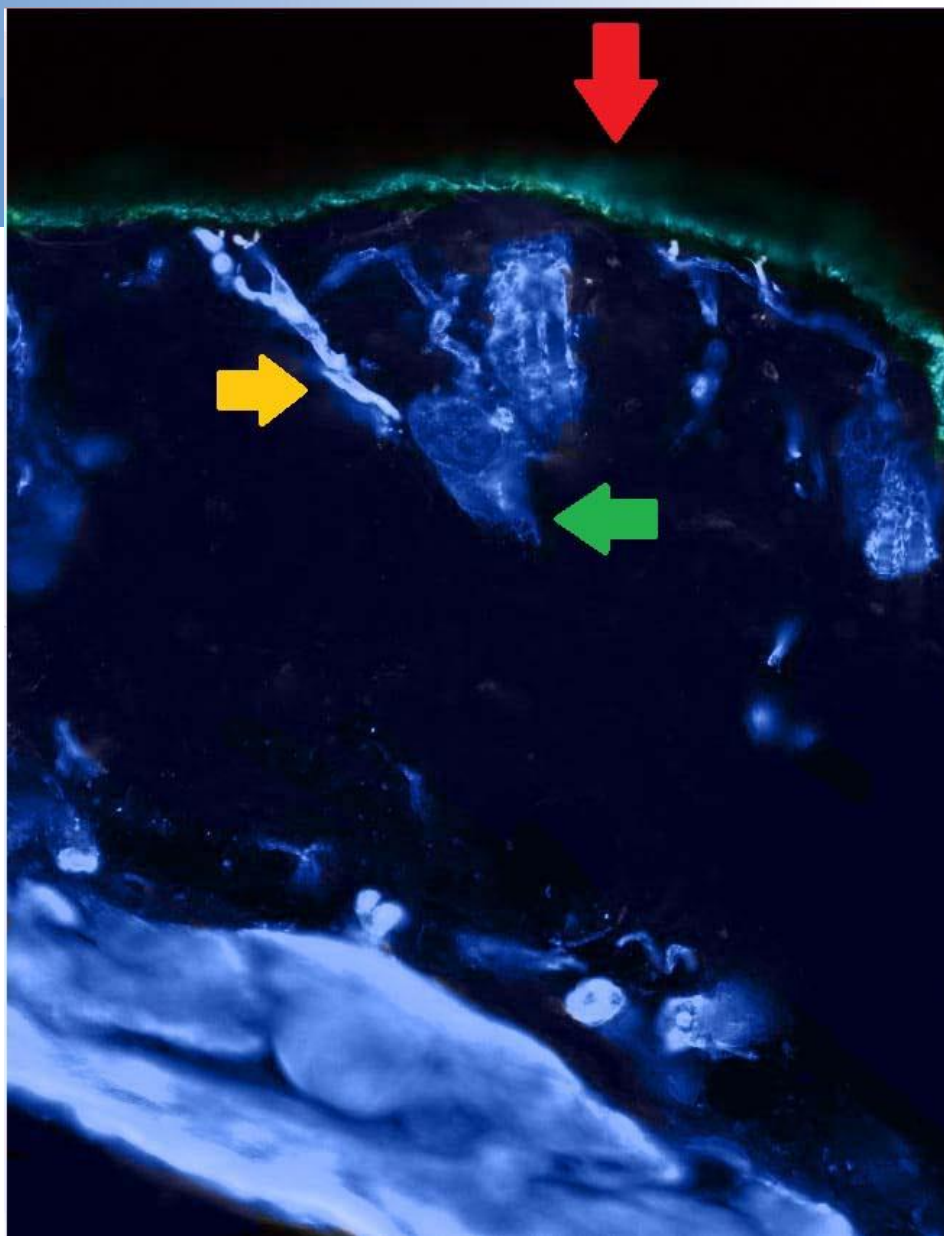
Phalloidin

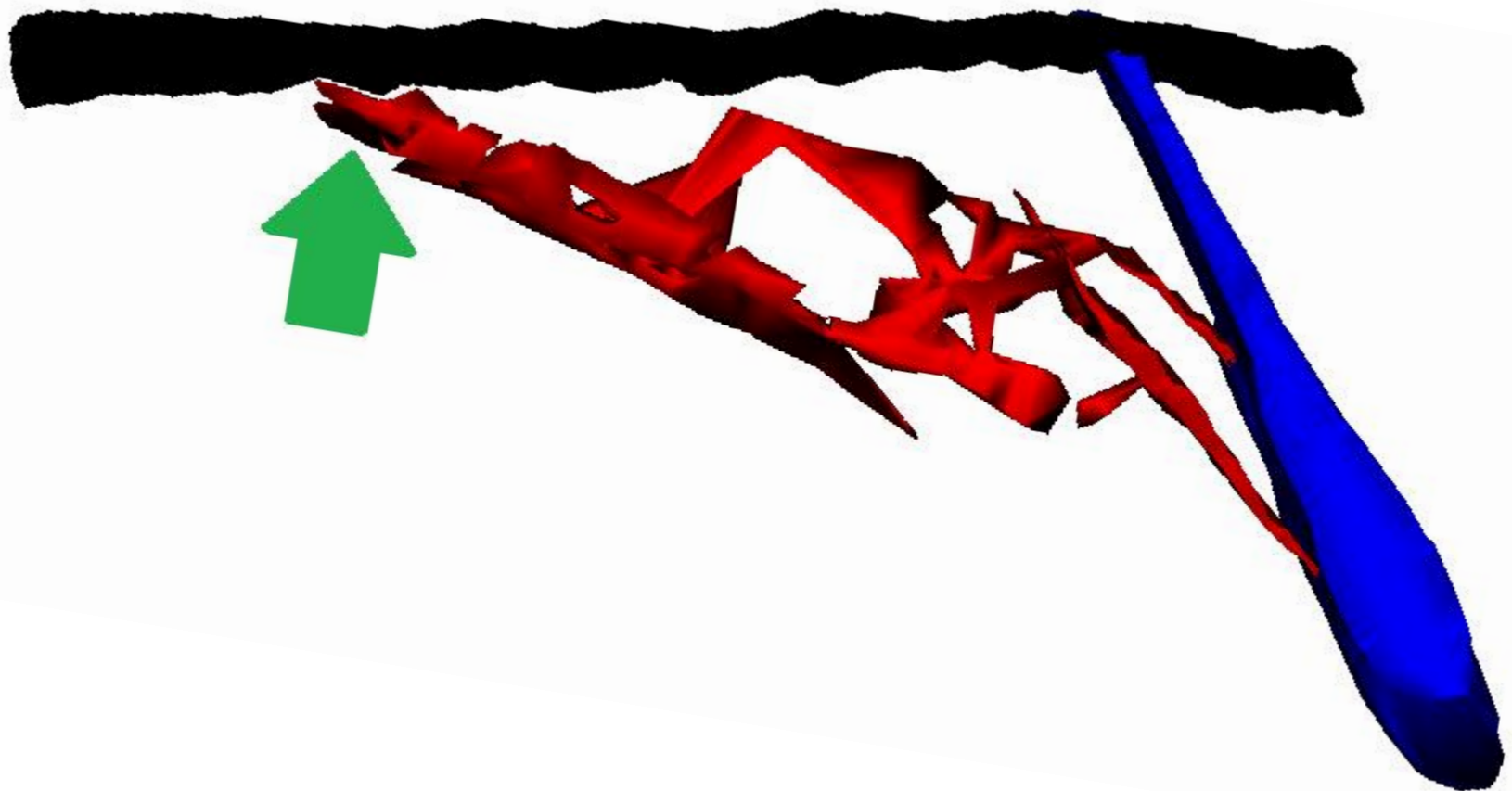


Human Phalloidin + wga



Merged fol







Bonney wrench

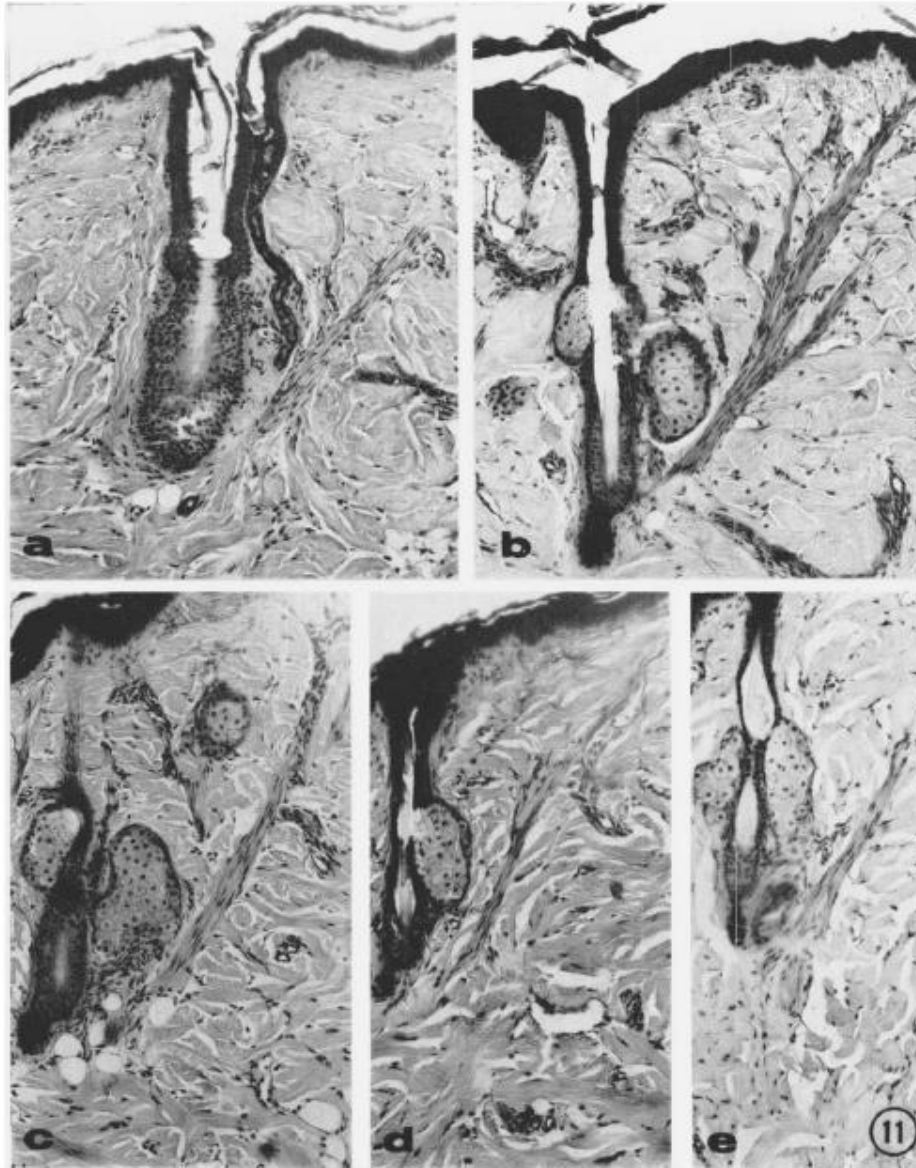
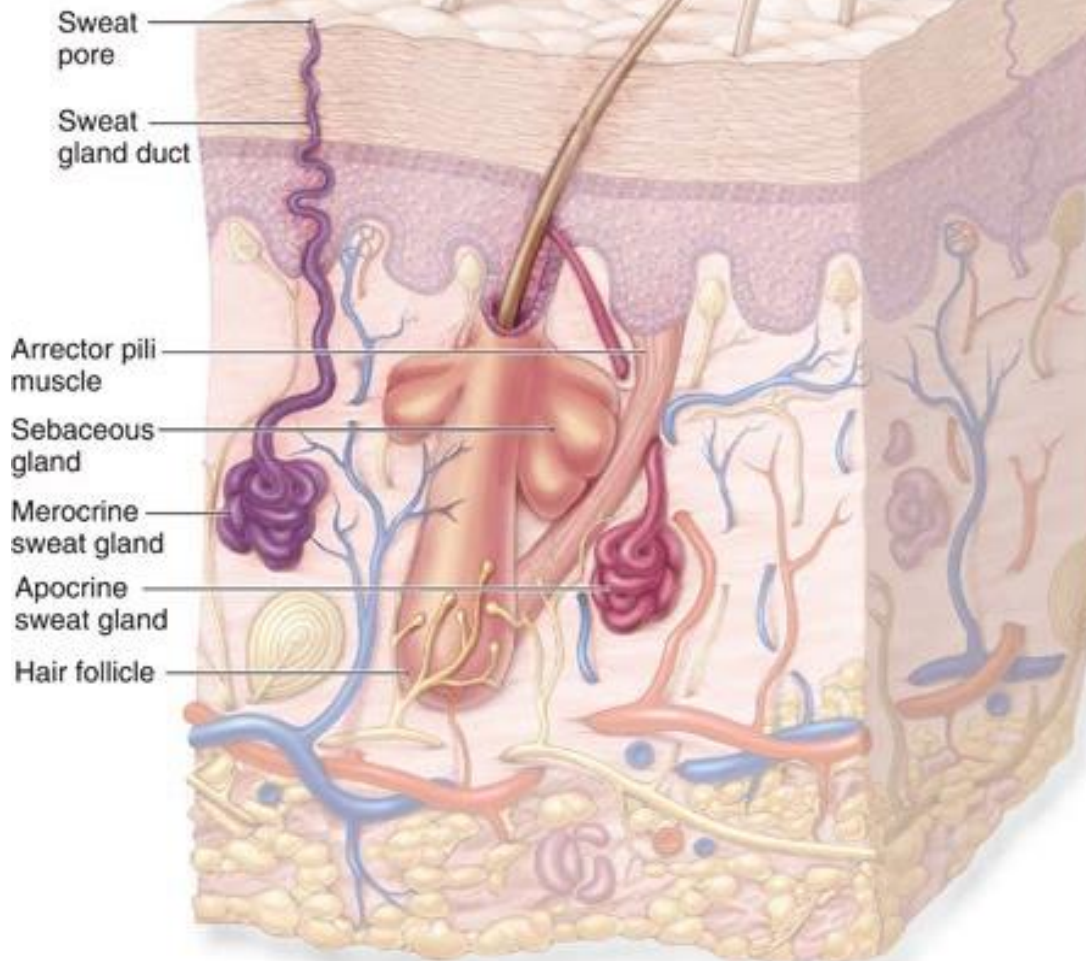


FIG. 11a, b, c, d, e. Vellus telogen hair follicles. In all of these figures the arrector pili muscle has lost its insertion to the follicle. As in Figure 10 this was ascertained by tracing each of these follicles in serial sections.





- Oral Minoxidil at doses of 1mg daily appears well tolerated from the cardiovascular point of view
- Concomitant use of spironolactone minimises the development of peripheral oedema and weight gain and probably has a synergistic effect
- Hypertrichosis may occur in up to 30% of patients but is generally mild, well tolerated and responds to dose reduction



- Not observed at dose of 1 mg/d minoxidil
- Fluid retention not seen in any man
- No postural dizziness or palpitations
- No patient discontinued treatment





Summary



- **Low dose oral minoxidil appears promising as a hair growth promoter**
- **Patients should be counselled re initial transient shedding reflecting postulated mechanism of action for the drug**
- **Allows dose reduction of finasteride with fewer adverse sexual side effects**