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

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Eyebrow

Chest
Individual Follicles

Groups of 3 Primary Follicles (Mejere’s Trios)
Follicular Units

- Arrector pili
- Vellus hair
- Sebaceous gland
- Terminal hair
- Follicular units
- Terminal hair
- Sebaceous gland
- Arrector pili

[Image of follicular units with labeled structures]
The missing link in embryogenesis
Differential sensitivity of epidermal cell subpopulations to β-catenin-induced ectopic hair follicle formation

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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.
Primary and secondary hair follicles

- best studied in sheep.
- \(1^\circ\) hair develops day 70 → trio pattern with a central \(1^\circ\) & 2 x lateral \(1^\circ\)
- \(2^\circ\) follicles closely associated with the primary follicles form by day 85
- \(2^\circ\) derived follicles, branches of the \(2^\circ\) 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 become less organized with phylogenetic advancement
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.

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
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
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.
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
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
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 biopsy
- Anatomical evaluation of the isthmus
- 3D models
Normal Hair
a) Medial view

b) Lateral view
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
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.
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
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
The fine structure of the elastic tendons in the human *arrector pili* muscle

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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 (×800).
The ‘follicular trochanter’: an epithelial compartment of the human hair follicle bulge region in need of further characterization
S. Tiede, J.E. Kloeppep, D.A. Whiting and R. Paus

British Journal of Dermatology
Normal Hair:
Follicle (Blue), APM (Red), Epidermis (Black)
Phalloidin

Human Phalloidin + wga
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
Side effects

– 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