nature reviews disease primers

https://doi.org/10.1038/s41572-025-00656-9

Primer

Check for updates

Androgenetic alopecia

Yingzi Liu[1,2,3], Antonella Tosti[4], Etienne C. E. Wang[5,6], Stefanie Heilmann-Heimbach[7], Crystal Aguh[8], Francisco Jimenez[9,10,11], Sung-Jan Lin[12,13,14,15,16], Ohsang Kwon[17,18,19,20] & Maksim V. Plikus[1,2,3]

Abstract

Androgenetic alopecia (AGA) is a condition of scalp hair growth characterized by progressive miniaturization of hair follicles and a reduction in the number of active follicles. In general, frontal, mid-scalp and crown hair follicles in postpubescent men and in postmenopausal women are susceptible to AGA. In rare cases, premenopausal women and prepubescent individuals are affected. In men, AGA is hypothesized to be caused by increased androgen signalling within susceptible hair follicles, altering the levels of locally produced signalling factors that sustain hair growth, whereas the molecular basis of AGA in women remains undetermined. AGA displays variability in its time of onset, severity and distribution patterns, and genome-wide association studies have uncovered more than 380 genomic loci associated with AGA, including genes involved in androgen and WNT pathways. Furthermore, epidemiological studies support substantial ancestral variation in AGA. Effective therapies for AGA include autologous transplantation of androgen-resistant occipital hair follicles, oral finasteride and topical minoxidil. Not all individuals with AGA respond to these therapies or comply with daily use of medicines, creating a need for new approaches. Emerging therapies for AGA include hair follicle-activating peptides, mRNA-containing liposomes, as well as bioengineering of new hair follicles. AGA has a negative socioemotional effect on affected individuals, and its prompt diagnosis and treatment can improve self-reported quality of life.

Sections

A full list of affiliations appears at the end of the paper. e-mail: plikus@uci.edu

Introduction

Androgenetic alopecia (AGA) is a genetic condition characterized by a visible decrease in scalp hair coverage. AGA causes miniaturization of hair follicles that produce progressively thinner and shorter hair fibres (known as vellus hair). The hair follicles stay quiescent between bouts of growth for progressively extended periods of time[1]. In an individual without AGA, the scalp skin contains ~100,000 hair follicles of which ~90% grow thick and long hair fibres (known as terminal hair) at any given time. By contrast, in advanced AGA, this percentage of terminal hair fibres drops drastically to <10%.

Although AGA does not directly lead to death or morbidity, it is a distinct physiological state commonly driven by increased levels of androgen signalling within scalp hair follicles in genetically predisposed individuals. In this regard, the molecular pathogenesis of AGA differs from that of other forms of hair loss, particularly alopecia areata — an autoimmune disease driven by breakdown of the immune privilege of the hair follicle and the ensuing immune attack on its epithelial cells[2]. Nevertheless, similar to other forms of hair loss, AGA can trigger profound negative psychological effects in affected individuals owing to social pressure to maintain 'good hair'. In addition, AGA is highly prevalent; for example, it affects ~50 million men and ~30 million women in the USA alone, and tens of millions people worldwide seek hair loss therapies[3]. This increased demand has nurtured intense research efforts into delineating the genetic, molecular and cellular bases of AGA pathogenesis, and has triggered pharmaceutical and biotechnology companies to develop novel therapeutics with better efficacy for managing AGA. Driven by these factors, our current understanding of AGA pathogenesis has greatly expanded, and numerous therapeutic strategies have entered preclinical and clinical stages of evaluation[4].

In this Primer, we describe the epidemiology, known risk factors and the current state of knowledge regarding the molecular basis of AGA pathogenesis, emphasizing the role of androgens and genetics. Next, we present common approaches to diagnosis and classification of AGA severity. We then discuss potential preventive approaches and current standard-of-care management strategies, as well as the effect of AGA on quality of life (QOL). Finally, we outline the promising preclinical research and development efforts that aim to create the next generation of efficacious AGA therapeutics.

Epidemiology

Incidence and prevalence by age

AGA affects both men and women; AGA in women is also referred to as female-pattern hair loss. The incidence of AGA varies across age, ethnicity and geography, although an accurate representation of its epidemiology is challenging owing to marked differences in study designs. Nonetheless, a general trend is that AGA has a high prevalence in postpubescent men and has a late onset in women, coinciding with the menopause[5]. A large-scale study involving 10,132 people with AGA of East Asian ancestry put its overall prevalence in men at 14.1% and in women at 5.6%[6]. Among men, AGA prevalence increased with age, rising from 2.3% among people in their twenties to 46.9% among people in their seventies, with the prevalence in intermediate decades of life of 4.0% during the thirties, 10.8% during the forties, 24.5% during the fifties and 34.3% during the sixties. By contrast, the prevalence of AGA among East Asian women was low, affecting 0.2% of women during their twenties, but increased markedly among women in their sixties (11.7%) reaching a prevalence of 24.7% at 70 years of age[6]. These age-dependent dynamics have been confirmed in independent studies[7,8]. A study in the UK found a prevalence of AGA of 6% in women <50 years of age, increasing to 38% in those aged 70 years and older[8]. Another study in Türkiye found a prevalence of AGA in women of 23.9% with an age at onset of 40.35 ± 15.25 years compared with 67.1% and 31.18 ± 11.74 years, respectively, in men[7]. Furthermore, prepubescent children can also present with AGA-like hair loss, and this pattern is often associated with a strong family history of AGA. However, the incidence and prevalence AGA in this population remains undetermined[9].

Role of ethnicity

The prevalence of AGA varies according to ancestry, although relevant comprehensive studies remain limited. Early-onset AGA (<30 years of age) is most common in men of South Asian ancestry, who also have a higher than average overall AGA prevalence of 58% during their fifties[10]. AGA occurs with lower frequencies in men of Central European descent (50% in men in their fifties)[11] and African descent[12]. East Asian men are consistently reported as less affected than men of European ancestry throughout all decades of life[6,13], whereas South Asian men display higher AGA prevalence in the vertex (the top portion of the scalp) than their European ancestry peers[12].

Studies have found similar ancestral variations in women[6,14–16]. South Asian women have been reported to have AGA onset on average 15 years earlier than white and Black women; for example, the mean age at onset was reported to be mid-thirties in South Asian women[16] and early fifties in women of white or Black ancestry. In addition, East Asian women reported lower hair loss frequencies (2–10%) by 50 years of age than women primarily of European ancestry from Australia (25%)[6,14,15]. Limited data exist on hair loss pattern distribution in women across different ancestral groups, although one cohort study noted bitemporal frontal hairline recession as the most prevalent pattern in women of European and African ancestry[16]. Moreover, Black women are highly likely to present with predominant AGA in the vertex as compared with other areas of the scalp[16]. By contrast, South Asian women are most likely to present with diffuse and widespread hair loss[16].

Risk factors for AGA

Compelling epidemiological data exist in support of systemic conditions, particularly the metabolic syndrome, as comorbidities with AGA[17,18]. Individuals with low levels of high-density lipoprotein that accompanies the metabolic syndrome have a high prevalence of AGA[18]. Furthermore, people with severe AGA were found to have 2.6 times higher odds of developing the metabolic syndrome than those with moderate AGA, whereas all people with AGA were nearly 2.5 times more likely to have low high-density lipoprotein levels than controls[18]. Although, one study noted no correlation between fasting glucose levels and the odds of developing AGA, other studies have found a relationship between AGA and insulin resistance[19,20]. Importantly, elevated glucose levels and insulin levels are associated with increased conversion of testosterone to dihydrotestosterone (DHT)[21,22]. Nevertheless, further studies are needed to establish a causal relationship between the metabolic syndrome and AGA. Furthermore, metabolic interventions have gained attention in the context of AGA treatment and prevention. High-fibre diets, such as the Mediterranean diet, confer a protective effect against AGA development[23], whereas high-fat, high-glycaemic Western diets are associated with an increased risk of AGA[24]. In East Asian men with historically low AGA prevalence, frequent consumption of sweetened beverages has been identified as a potential risk factor for the development of AGA[25]. The use of GLP1

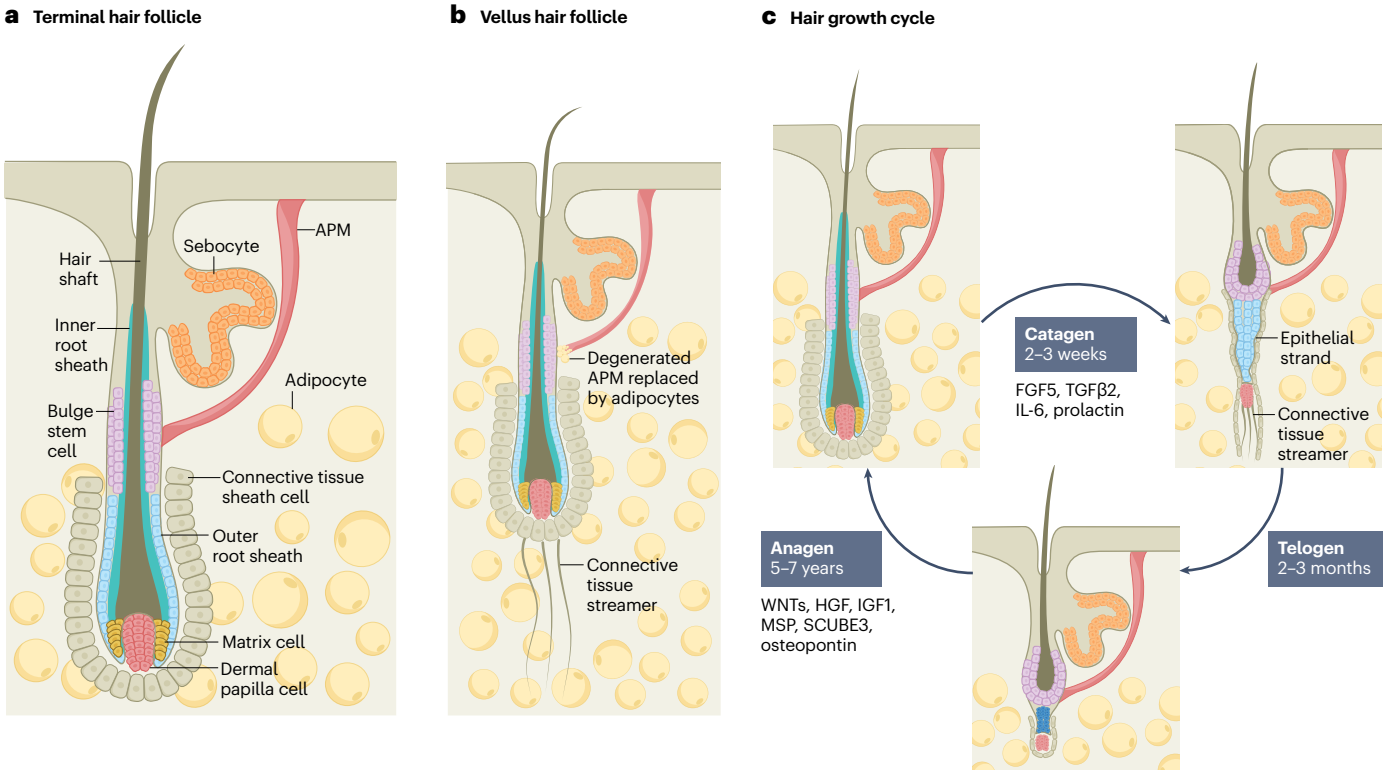


Fig. 1 | Hair follicle miniaturization and hair growth cycle. In androgenetic alopecia, large, terminal scalp hair follicles (panel **a**), that extend deep into the dermal adipose layer and produce thick and long hair fibres, undergo miniaturization, transforming into vellus hair follicles (panel **b**), which retract upwards into the dermis and produce thin and short hair fibres. Hair follicle miniaturization is accompanied by degeneration of the arrector pili muscle (APM) and its detachment from the hair follicle with the resulting space being filled by adipocytes. The hair growth cycle (panel **c**) consists of three consecutive phases: anagen, catagen and telogen. During anagen, bulge stem cells proliferate, generating several types of epithelial hair progenitors, including matrix cells, which are located in the lowermost portion of a growing hair follicle, adjacent to the dermal papilla. Hair fibre is produced as the result of differentiation by postmitotic progeny of matrix cells. Under physiological conditions, the anagen phase in a typical adult human scalp hair follicle lasts ~5–7 years. Upon transition to catagen phase, a large proportion of follicular epithelial cells undergo apoptosis, leading to regression of the lower hair follicle and formation of an epithelial strand, followed by dermal papilla and a connective tissue streamer. The catagen phase lasts 2–3 weeks, and is followed by the telogen phase, a period of relative quiescence, that lasts 2–3 months.

receptor agonists (GLP1RA) to treat metabolic diseases has sparked a lot of interest in their effect on AGA. Some studies have suggested that GLP1RA may precipitate transient hair shedding (also known as telogen effluvium)[26], whereas a case report noted significant improvement in AGA following tirzepatide monotherapy[27].

Studies have not established a definitive association between alcohol consumption and AGA[28,29]. However, smoking more than ten cigarettes per day[30] and the use of anabolic steroids and exogenous testosterone have been shown to accelerate AGA[31]. Systemic conditions, including inflammatory scalp diseases, anaemia, thyroid dysfunction and any underlying triggers of telogen effluvium may worsen AGA[32,33], and so does excessive sun exposure, as it increases the risk of cutaneous neoplasms[34].

Mechanisms/pathophysiology

The mechanism of AGA is complex and yet to be fully understood. However, AGA pathophysiology critically involves an interplay between the genetic makeup of affected individuals and androgens, which detrimentally affect hair growth-promoting signalling factor levels by hair follicle cells.

Hair follicle

The hair follicle is the target tissue of AGA pathogenesis. During active growth, terminal scalp hair follicles are shaped as elongated cylinders, extending from the epidermis into the dermal adipose layer[35] (Fig. 1). The upper segment of the hair follicle, situated between the hair-associated sebaceous gland and the arrector pili muscle, contains a self-renewing population of epithelial stem cells, known as bulge cells[36,37]. At the base of the hair follicle (that is, the bulb), fast-dividing epithelial matrix cells give rise to differentiating daughter cells, which assemble into a hardened hair fibre that grows above the skin surface and a surrounding inner root sheath that remains below skin level. In association with matrix cells are melanocytes that produce pigment[38] and dermal papilla fibroblasts that serve as the pivotal signalling centre, regulating numerous characteristics of a growing hair fibre, including its length and pigmentation[35,39].

In AGA, terminal hair follicles undergo miniaturization toward a diminutive vellus state, markedly reducing their length[40–42] and dermal papilla volume[43] (Fig. 1). Dermal papilla fibroblasts express numerous genes associated with androgen signalling and are regarded as critical pathogenic cells in AGA. Furthermore, single-cell chromatin

analysis supports this notion, revealing that many AGA-associated genomic traits link to open chromatin regions that are specific to dermal papilla fibroblasts[44]. As AGA progresses, morphological changes extend beyond the hair follicles. In particular, arrector pili muscle disconnects from its attachment site on the bulge and the resulting space becomes filled with dermal adipocytes[45,46]. Experiments in mice suggest that arrector pili muscle serves as the signalling centre for epithelial stem cells[47], although the role of muscle disengagement from the bulge in AGA pathogenesis remains undetermined.

The hair growth cycle

All hair follicles grow in recurrent cycles, consisting of consecutive phases of anagen (when follicles are actively making hair fibre), catagen (when follicles undergo involution) and telogen (when follicles rest, awaiting a new cycle)[48] (Fig. 1). In a typical adult, terminal scalp hair follicles spend ~5–7 years in continuous anagen phase, which supports the production of a characteristically long hair fibre. Upon transition to catagen, a large portion of follicular epithelial cells, including matrix cells, undergo death by apoptosis. As the apoptotic wave propagates through the hair follicle, its epithelial cylinder below the bulge collapses into a strand that then retracts upward, followed by the dermal papilla fibroblasts and connective tissue streamer, a tail-shaped extracellular matrix structure[48–50]. Although dermal papilla fibroblasts are largely spared from apoptosis, they resorb their extracellular matrix and compact closely with one another. Catagen phase in scalp hair follicles lasts ~2–3 weeks, which is followed by telogen phase that typically lasts 2–3 months[39]. At the onset of a new anagen phase, previously quiescent stem cells proliferate, generating new epithelial cells that then re-form the active portion of a growing hair follicle, including new epithelial matrix of the bulb.

The hair growth cycle is intricately regulated by numerous signalling factors. Although most molecular insights come from murine studies[51], some of the findings have been validated in humans. For example, similar to long-haired strains of mice, humans carrying loss-of-function variant of *FGF5* grow excessively long body hair and eyelashes[52]. This growth arises from prolonged anagen phase and suggests a physiological role for FGF5 in timely anagen-to-catagen transition. In addition, evidence in mice demonstrates that WNT signalling is essential during the onset and progression of anagen phase. Similarly, the level of WNT ligands increases during the telogen-to-anagen transition in human hair follicles[53], whereas a loss-of-function variant of *WNT10A* has been associated with short anagen syndrome (a condition in which hair does not grow beyond a short length owing to an unusually short anagen phase)[54]. This finding suggests an essential role for WNT signalling in initiating and sustaining a long-lasting anagen phase[54,55]. The TGFβ ligand SCUBE3 is cyclically expressed by dermal papilla fibroblasts at the onset of anagen phase in mice, and when microinjected into the skin, it triggers precocious stem cell activation as evidenced by faster regrowth of new hair than physiological growth[56]. Dermal papilla-specific SCUBE3 expression and its anagen-inducing effect are conserved in humans, as revealed by protein microinjection studies in human-on-mouse occipital hair follicle xenografts[56]. In benign lesions known as hairy naevi, the human melanocytes overexpress the CD44-binding signalling factor, osteopontin, which is physiologically expressed by dermal papilla fibroblasts[57]. When naevi occur in non-scalp skin, naturally vellus hair follicles enclosed within them become terminal, frequently enter anagen phase and produce long scalp-like hair fibres[58]. Osteopontin microinjections or its genetic overexpression in mice also potently activate stem cells as evidenced by hair regrowth faster than physiological growth[58]. Other growth factors with validated roles in human hair follicle biology include anagen-promoting IGF1 (ref. 59), HGF[60], MSP[61], FGF7 (ref. 62), catagen-promoting TGFβ2 (ref. 63), IL-6 (ref. 64) and prolactin[65]. The above examples, although not exhaustive, underscore substantial conservation of the core gene regulatory network of the hair growth cycle between mice and humans.

Androgens

Androgen signalling has a central role in AGA pathogenesis[66]. Unlike its core molecular function, the prominent signalling effect of androgens on the hair growth cycle is distinct to humans[67] and other primates, such as the stump-tailed macaque[68]. Testosterone and DHT are two principal androgens associated with AGA in men[69]. DHT is produced locally in the skin from testosterone by 5α-reductase enzyme, which has two isoforms, type I and II[70,71] (Fig. 2). Owing to its greater potency and stability, DHT is considered as the primary pathogenetic androgen in AGA[72]. Indeed, men with genetic variants that lead to deficiency in 5α-reductase type II have normal testosterone levels, but do not develop AGA[73]. In addition, PCR analysis of microdissected hair follicles showed that mRNA for 5α-reductase type I is expressed throughout the hair follicle, but mRNA for 5α-reductase type II is predominantly localized to the dermal papilla[74,75] — an expression pattern supported by single-cell RNA sequencing studies[76,77]. Moreover, higher levels and activity of 5α-reductase types I and II were reported in frontal scalp hair follicles than in occipital scalp hair follicles in people with AGA[78–81].

DHT exerts its effects through androgen receptor, which is expressed by dermal papilla fibroblasts in androgen-sensitive individuals. However, dermal papilla fibroblasts do not express the androgen receptor in androgen-resistant scalp skin regions[82–84], a difference that may arise from increased DNA methylation in *AR* in these skin regions[85]. Furthermore, the expression of androgen receptor is greatly increased in frontal dermal papilla fibroblasts of individuals with AGA[84], which may be a consequence of the positive feedback loop[86]. High expression of the DHT-producing 5α-reductase type II and DHT-binding androgen receptor by frontal dermal papilla fibroblasts in people with AGA supports their central role in the miniaturization of hair follicles. However, the precise downstream mechanism remains incompletely understood. Androgen-affected dermal papilla fibroblasts undergo premature senescence[87–89], which may irreversibly deplete their population. Moreover, the activation of androgen receptor in dermal papilla fibroblasts suppresses WNT ligands and IGF1, but promotes IL-6 (refs. 64,90,91) and TGFβ1 (ref. 84) — paracrine changes that probably detrimentally affect the proliferation of epithelial hair follicle cells.

Unlike in men, androgen signalling is not clearly implicated in AGA pathogenesis in women[92]. However, women with hyperandrogenic disorders, such as polycystic ovary syndrome, often develop early-onset AGA[93]. In addition, an AGA-like clinical presentation also occurs in women with complete androgen insensitivity syndrome[94]. Clinical data show that 5α-reductase inhibitors are less efficacious in women with AGA than in men at approved doses for AGA[95–98]. The possibility of androgen-independent pathogenesis is supported by AGA-like clinical presentation in individuals with hypogonadism and in prepubescent children[9].

Inflammation

Conventionally, AGA is classified as a non-inflammatory condition, and individuals taking immunosuppressive medicines, such as steroids, for unrelated conditions do not become protected against AGA.

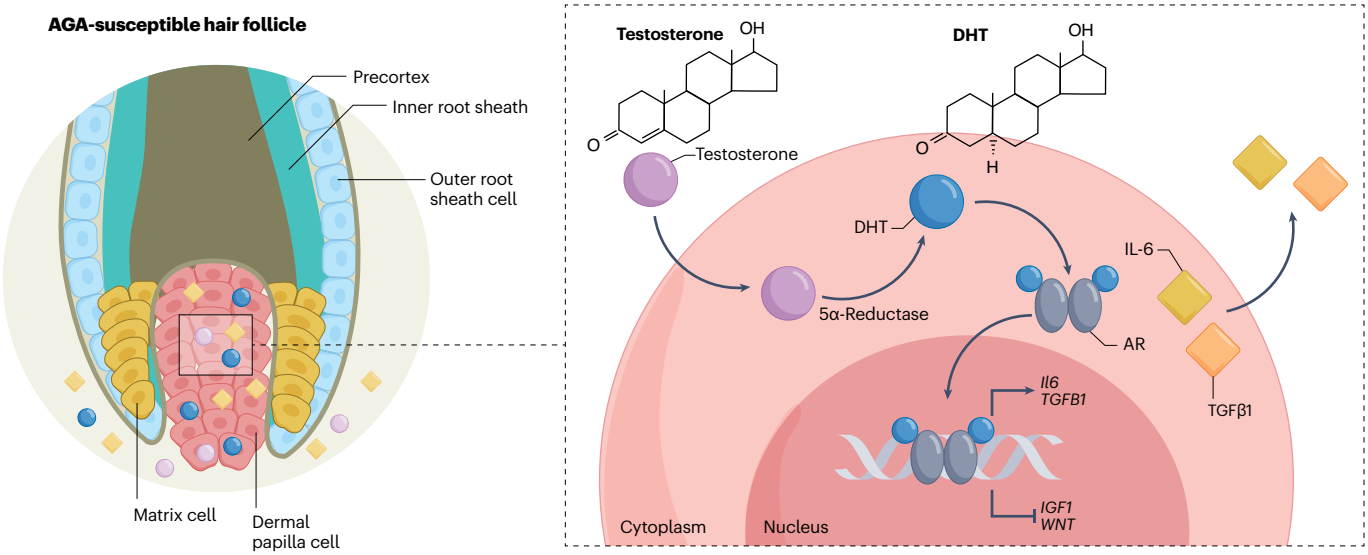


Fig. 2 | Pathogenesis of AGA. Androgen signalling in androgenetic alopecia (AGA)-susceptible scalp hair follicle. In dermal papilla fibroblasts, testosterone is metabolized to dihydrotestosterone (DHT) by 5α-reductase enzyme. DHT binds to androgen receptor (AR) in the cytoplasm, forming a DHT–AR complex, which translocates to the nucleus and regulates downstream gene transcription, such as suppression of WNT ligands and IGF1, and upregulation of IL-6 and TGFβ1. These effectors, in turn, reduce proliferation of hair follicle epithelial cells.

However, histological evidence supports immune cell infiltrates surrounding miniaturizing hair follicles in men with AGA[99–101]. Moreover, transcriptomic studies reveal upregulation of proinflammatory factors in balding scalp skin compared with occipital scalp skin[102,103]. Specifically, proinflammatory prostaglandin D_2 and its synthase are considerably overexpressed in AGA-affected scalp, particularly in mast cells, and in vitro treatment of occipital hair follicles in anagen phase with prostaglandin D_2 inhibits their growth[104]. Future research is needed to determine which specific proinflammatory pathways are involved and at what stages of AGA pathogenesis do they contribute to hair follicle miniaturization and/or secondary histopathological changes in the balding scalp.

Genetics

The hereditary nature of AGA is well documented, especially in men[105]. Although early studies suggested a Mendelian inheritance pattern[106], subsequent research has confirmed a polygenic model of AGA[107,108]. Nonetheless, the relevance of genetic factors in AGA in women requires further research[109]. The proportion of variance in AGA caused by genetic factors in twin studies is $h^2_{twins} = 0.79–0.81$, whereas in pedigree-based studies, it is $h^2_{pedigree} = 0.62$ (refs. 110–112). Numerous genome-wide association studies (GWAS) have identified an association between variants in >380 genomic loci with the development of AGA[55,110,113–119]. These loci explain ~39% of the phenotypic variance in male AGA[110] and implicate numerous specific genes (Box 1). First, the most prominent association was observed in variants of *AR* and *SRD5A2* (encoding 5α-reductase type II). In addition, other genes involved are known hair growth cycle regulators, such as *WNT10A*, *FGF5* and *EDA2R*. Further associations were observed in genes implicated in WNT signalling pathway including *DKK2*, *FZD10* and *FAM53B*, and genes involved in the androgen pathway such as *TOP1*, *FAM9B*, *HDAC4* and *HDAC9* (refs. 55,113,120). Finally, variants in transcriptional factors such as *EBF1*, *TWIST1* and *TWIST2*, are associated with AGA. Bioinformatic analyses also suggest a role for oestrogen and melatonin signalling, and genes involved in epidermis development, apoptosis, adipogenesis and immunological processes[113,121,122]. Collectively, GWAS underscore the high relevance of locally acting and hormonal signals involved in normal hair growth, and suggest a potential contribution of immune function in AGA pathogenesis[113]. Importantly, these findings also show the pleiotropic nature of AGA and the shared molecular basis with immune-related phenotypes, as well as cardiovascular and neurodegenerative diseases[110,113]. In contrast to common risk variants, the contribution of rare variants on a population level seems negligible[110,123]. However, rare variants might still contribute to individual risks. Indeed, exome analysis on 72,469 men from the UK Biobank cohort identified *HEPH*, *CEPT1* and *EIF3F* as novel risk variants for AGA, and revealed association between genes of relevance, such as *WNT10A*, *HOXC13* and *LPAR6*, to rare monogenic hair disorders and AGA[123].

Although most AGA-associated genetic data to date originate from studies on European populations, epidemiological research on AGA underscores substantial ancestral variations[6,124]. Limited available data from GWAS in non-European populations reveal additional risk loci, including at 10q23.3 near *GRID1* in the Latin American population[125] and several suggestive associations in African and East Asian populations[126,127]. Furthermore, shared genetic determinants between European and East Asian populations were observed at 9q21.31 and 20p11 (refs. 127,128), and at the X-chromosomal *AR–EDA2R* locus between Latin American and European populations. No replication was achieved for *AR–EDA2R* locus in East Asian populations, either owing to implicated variants showing low frequency or being even monomorphic in these ancestries[127,128]. Additional studies in ancestrally diverse cohorts are required to expand the genetic basis of AGA and, ultimately, to enable individualized hair loss risk prediction and management.

Risk of skin cancer

Patients with AGA have an increased risk of melanoma and non-melanoma scalp skin cancers, including basal cell carcinoma and

Box 1 | Selected genes with androgenetic alopecia risk loci

Genome-wide association studies have identified >380 risk loci commonly associated with androgenetic alopecia. Selected genes linked to those risk loci are listed, categorized based on their primary role in androgen signalling, hair growth cycling and transcriptional regulation.

Androgen signalling
- *AR*
- *SRD5A2*
- *TOP1*
- *FAM9B*
- *HDAC4*
- *PRKD1*

Hair cycling
- *WNT10A*
- *FGF5*
- *EDA2R*
- *DKK2*
- *FZD10*
- *FAM53B*
- *RSPO2*
- *WNT3*
- *WNT6*
- *LGR4*
- *TCHH*

Transcription factors
- *EBF1*
- *TWIST1*
- *TWIST2*
- *TBX15*
- *RUNX3*
- *RUNX1*
- *IRF4*
- *PAX3*
- *SOX13*
- *PRRX1*
- *ZHX3*
- *TCF12*

squamous cell carcinoma[129–131]. Elevated cancer risk is attributed to the denuding effect of hair loss on scalp skin, resulting in its increased exposure to solar ultraviolet light[129,130]. Additionally, pleiotropic single nucleotide polymorphisms in genes involved in pigmentation have been implicated in the association between AGA and the risk of non-melanoma skin cancers[129]. Careful screening for skin cancers should be considered during full-body examinations in patients with AGA.

Diagnosis, screening and prevention

Clinical features

In men, AGA progressively affects androgen-sensitive scalp regions, such as frontal, mid-scalp and crown skin, and generally spares androgen-resistant parietal and occipital skin (Fig. 3). Typically, men with AGA present with bitemporal frontal hairline recession, vertex thinning, or a combination of both, with the predominant clinical course following the Hamilton–Norwood scale[132,133] (Fig. 3). In contrast, women with AGA commonly present with hair loss on the crown but not the frontal-temporal hairline, as defined by the Ludwig scale[92,134] (Fig. 3). Early AGA in women can be compared to a Christmas tree with widening of the central parting, which is more pronounced anteriorly[135] (Fig. 4). Advanced AGA in women may present with diffuse thinning across the entire upper scalp, and may extend to the parietal and occipital skin[136]. However, AGA in men tends to progress to complete baldness of the upper scalp; total baldness in any scalp region is uncommon in women.

The Hamilton–Norwood scale and the Ludwig scale classify clinical severity of hair loss in the majority of men and women with AGA, respectively[137]. However, outliers exist that may hamper classification. Some men may exhibit preservation of the frontal hairline, resembling the Ludwig scheme[138], or rarely may experience recession of the occipital hairline, a presentation known as retrograde AGA[139]. Development of kinked hair texture (that is, hair with abnormal twists and bends), particularly in the frontal scalp and sideburns is a potential early manifestation of AGA in men[140,141]. Bitemporal recession in women following the Hamilton–Norwood scheme may also occur, and it is more common after menopause and may indicate hyperandrogenism[142]. To overcome the clinical overlap between the Hamilton–Norwood and the Ludwig types of AGA, the basic and specific (BASP) classification was introduced as the universal system for classifying AGA in men and women[143] (Fig. 3). Rarely, focal areas of complete baldness, resembling scarring alopecia, may also occur in postmenopausal women. However, laboratory testing typically reveals hair follicle miniaturization rather than true scarring[144].

Quantitative assessment

Although pattern formation is the hallmark feature of AGA and becomes increasingly apparent with time, its early stages in men and relatively diffuse characteristics in women necessitate objective testing based on quantitative approaches (Fig. 3). Trichoscopy is a non-invasive imaging method used for assessing people presenting with excessive hair shedding. On trichoscopy, AGA is characterized by increased variation in scalp hair diameter owing to progressive hair follicle miniaturization (Fig. 4). High-magnification trichoscopy can be used to quantify this change, and variation exceeding 20% establishes the diagnosis[145]. On imaging, vellus hairs appear short, <0.03 mm in diameter, hypopigmented and sometimes, coiled. Openings of miniaturized hair follicles on the skin surface may present as pigmented dots, which are either empty or contain vellus hairs. A threshold of >10% or more than seven vellus hairs in the frontal scalp under 40× magnification is diagnostic for AGA in women and early-stage AGA in men[146].

Trichoscopy is a valuable quantitative tool for the diagnosis of early-stage AGA. However, if it is inconclusive, additional tests can be performed. The pull test is another non-invasive quantitative approach that involves grasping and gently tugging on 50–100 hair strands at once and then counting pulled hairs. The results are confirmative of AGA when six or more hairs are pulled in the androgen-sensitive scalp, which indicates a shortened and partially synchronized hair growth cycle, a characteristic feature of AGA. The pluck test has greater accuracy than the pull test, as it measures anagen to telogen ratio of plucked hairs[147]. Positive results of the pull test or pluck test across the entire scalp may, instead, indicate telogen effluvium, necessitating further evaluation, including measurements of blood iron, ferritin and vitamin D, and thyroid-stimulating hormone levels[32]. Laboratory tests measuring total blood testosterone and sex hormone-binding globulin are particularly important in people presenting with acne, seborrhoea or hirsutism, as these may be clinical signs of an underlying endocrine disorder[148]. Further, in young women with AGA, ovarian ultrasonography is recommended to screen for polycystic ovary syndrome[149]. In most people with hair loss, non-invasive methods and blood tests provide sufficient diagnostic accuracy, rendering additional invasive tests unnecessary. However, in challenging instances, histopathology on 4 mm scalp skin biopsies may facilitate diagnosis. Horizontal tissue sections enable precise hair counting, whereas vertical sections aid in assessing scalp inflammation.

Differential diagnosis

Several conditions can mimic AGA, particularly in their early stages. Although its distinct pattern makes AGA diagnosis in men

straightforward, diagnosing AGA in women is often challenging, owing to its diffuse pattern and the high prevalence of other forms of alopecia (Fig. 3), necessitating thorough medical history and clinical assessment[150]. Three major types of scarring alopecia can occur in scalp areas of women affected by AGA[151]. The most prominent type is central centrifugal cicatricial alopecia (CCCA), a chronic, progressive scarring alopecia predominantly affecting women of African descent (Fig. 5). CCCA typically manifests as hair loss at the vertex with slow centrifugal expansion. In its early stages, CCCA may resemble AGA, but on trichoscopy it displays characteristic white or grey halos surrounding hair follicle openings[152]. In advanced CCCA, affected skin appears shiny owing to extensive hair follicle destruction, and it can be definitively diagnosed on biopsy, which reveals fibrosis and inflammation[153]. The next major type is frontal fibrosing alopecia (FFA), a common scarring alopecia that often accompanies AGA, particularly in postmenopausal women. FFA is characterized by progressive frontal–temporal hairline recession and partial or total eyebrow loss (Fig. 5). Additionally, hair loss on arms and legs is also frequently observed. Early FFA can be overlooked in people with concomitant AGA unless the hairline is specifically examined by trichoscopy, revealing the absence of vellus hairs[154]. The third type is fibrosing alopecia in a pattern distribution (FAPD). Histopathologically, FAPD shares features of both AGA and lichen planopilaris, a chronic scalp skin inflammatory condition[155] (Fig. 5). People with FAPD often report scalp itching or dysaesthesia (feeling of discomfort upon skin touch), resulting in frequent misdiagnosis as AGA associated with seborrhoeic dermatitis[156]. Importantly, FAPD is an absolute contraindication for hair transplantation owing to its scarring nature[157]. In all types of scarring alopecia, destruction of hair follicles and associated sebaceous glands results in the loss of visible follicular openings on the skin surface, giving it a 'slick' appearance. Signs of inflammation can help differentiate scaring alopecia from AGA, unless AGA is associated with conditions such as seborrhoeic dermatitis or psoriasis.

AGA should also be differentiated from non-scarring hair loss conditions, which commonly include endocrine therapy-induced alopecia and persistent chemotherapy-induced alopecia (PCIA). Endocrine therapy-induced alopecia presents as patterned alopecia in women undergoing adjuvant endocrine therapy for hormone receptor-positive breast cancer[158]. Endocrine therapy-induced alopecia closely resembles AGA and can be effectively treated with minoxidil, that is typically used to manage patients with AGA[158,159]. A history of treatment with aromatase inhibitors or selective oestrogen receptor modulators in the previous 24 months supports the differential diagnosis. PCIA is defined by incomplete hair regrowth within 6 months of chemotherapy completion and manifests as diffuse hair loss (Fig. 5). Androgen-sensitive scalp is often severely affected, prompting misdiagnosis as AGA. Yet, unlike AGA, chemotherapy-induced alopecia often involves loss of pubic, axillary, eyebrow and eyelash hair, and histopathology reveals a marked reduction in terminal hair follicles without perifollicular inflammation or scarring[160].

Other hair loss disorders include telogen effluvium and loose anagen syndrome. These conditions can be differentiated from AGA by the reduction in hair density and positive hair pull test beyond androgen-sensitive scalp areas[161]. Microscopic examination of pulled hair fibres shows only telogen-shaped hairs in telogen effluvium, but a mix of telogen-shaped and anagen-shaped hairs in loose anagen syndrome[162]. Additionally, self-inflicted hair loss, called trichotillomania, and traction alopecia may also resemble early AGA, but show a negative hair pull test and differing trichoscopy[150]. In addition to scalp hair, evaluation of facial and body hair density and distribution, as well as nails, can aid in differential diagnosis. Absence of eyebrows, eyelashes or body hair may suggest diffuse autoimmune alopecia areata[2]. Nail abnormalities are uncharacteristic of AGA, but may accompany alopecia areata, lichen planus or certain nutritional deficiencies[163].

Prevention

Patients at most risk of developing AGA include those with a strong family history of hair loss on either the maternal or the paternal side, or those experiencing visible hair thinning at a young age (that is, <30 years of age)[164]. In such cases, preventative treatment with early use of topical minoxidil (see below) is a relatively safe method to stave off the progression of AGA. Although not recommended by current guidelines, the preventative use of oral finasteride (see below) is increasing. Currently, no evidence exists for the preventive use of dietary or lifestyle changes for AGA, and studies with greater power are required in this area.

Management

The goals of AGA treatment range from slowing down further hair loss to stimulating new hair growth, to provide individuals with cosmetically satisfactory scalp hair density. Current FDA-approved medicines for AGA include topical minoxidil and oral finasteride for men, and low-strength topical minoxidil for women (Table 1). With both drugs, which are administered daily, clinically meaningful improvements in hair growth can take up to 6 months to achieve owing to latency in the reversal of hair follicle miniaturization (Fig. 6).

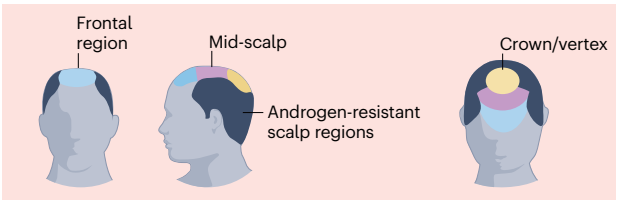
Minoxidil

Minoxidil is a vasodilator, initially developed for hypertension. However, in trials of oral minoxidil, female participants reported undesirable hypertrichosis (excessive hair growth), and a notable minority of patients experienced life-threatening pericardial effusion, limiting its use[165]. Thereafter, its topical formulation was found to promote scalp hair growth[166], and in 1988, the FDA approved the use of topical minoxidil for the treatment of AGA. In hair follicles, minoxidil becomes converted to minoxidil sulfate by SULT1A1 (ref. 167). The precise mechanism of action of minoxidil remains unknown, although it probably involves the opening of ATP-dependent potassium channels on dermal papilla fibroblasts, including ABCC8 and ABCC9 (refs. 168,169), thereby altering their membrane potential with as-yet undetermined downstream effects. Mutations in *ABCC9* lead to constitutive activation of the ATP-sensitive potassium channel and cause Cantu syndrome, which is characterized by congenital hypertrichosis[170]. This association provides a potential mechanistic link to the mode of action of minoxidil. Naturally varying expression levels of SULT1A1 by hair follicle cells are believed to underpin clinically observed variability in the responsiveness of topical minoxidil[171]. Currently, off-label use of low-dose oral minoxidil has gained popularity for the treatment of AGA[172], as low doses are not associated with blood pressure anomalies in most people. Moreover, oral minoxidil is preferred by some people for being more affordable and user-friendly than topical formulations, and its safety has also been documented[172].

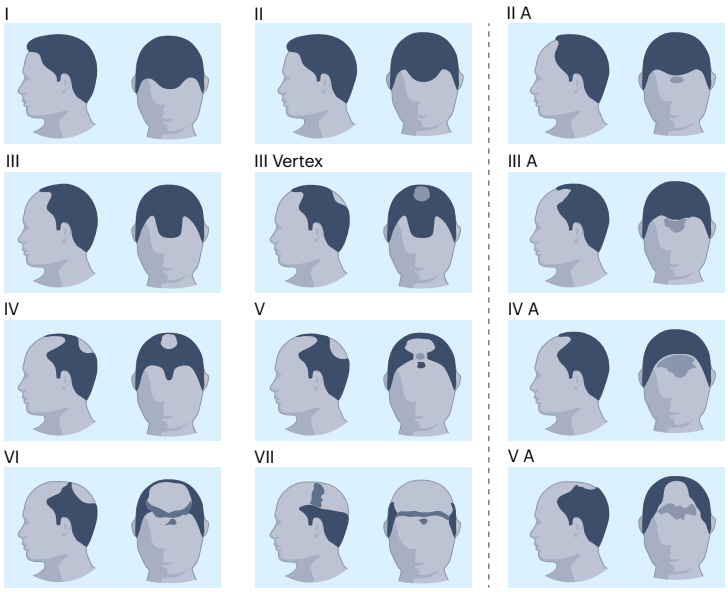
5α-Reductase inhibitors

5α-Reductase inhibitors, including finasteride, were originally developed to treat benign prostate hyperplasia, as patients with 5α-reductase type II deficiency have reduced serum DHT levels and an under-developed prostate[173]. These individuals also seem to be

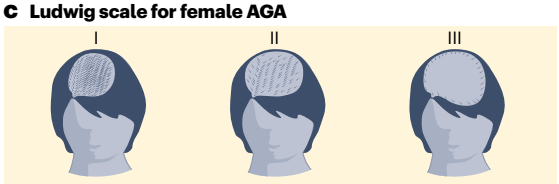
a Scalp regions



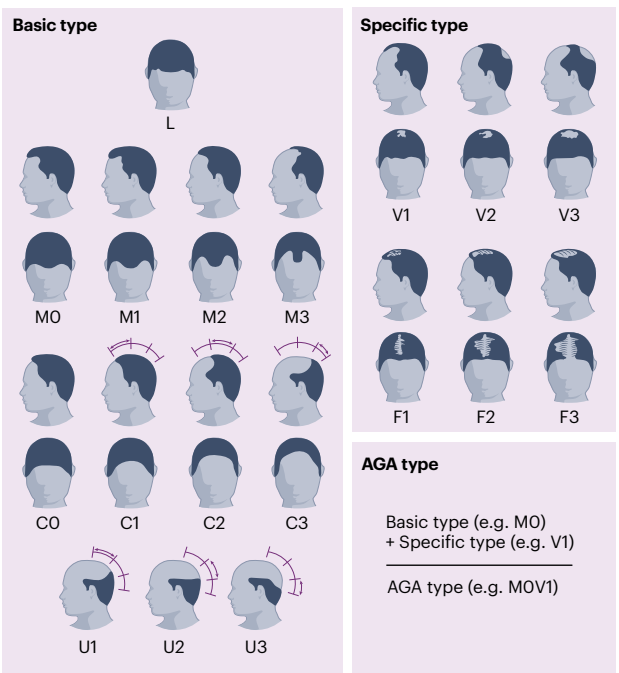
b Hamilton–Norwood scale for male AGA



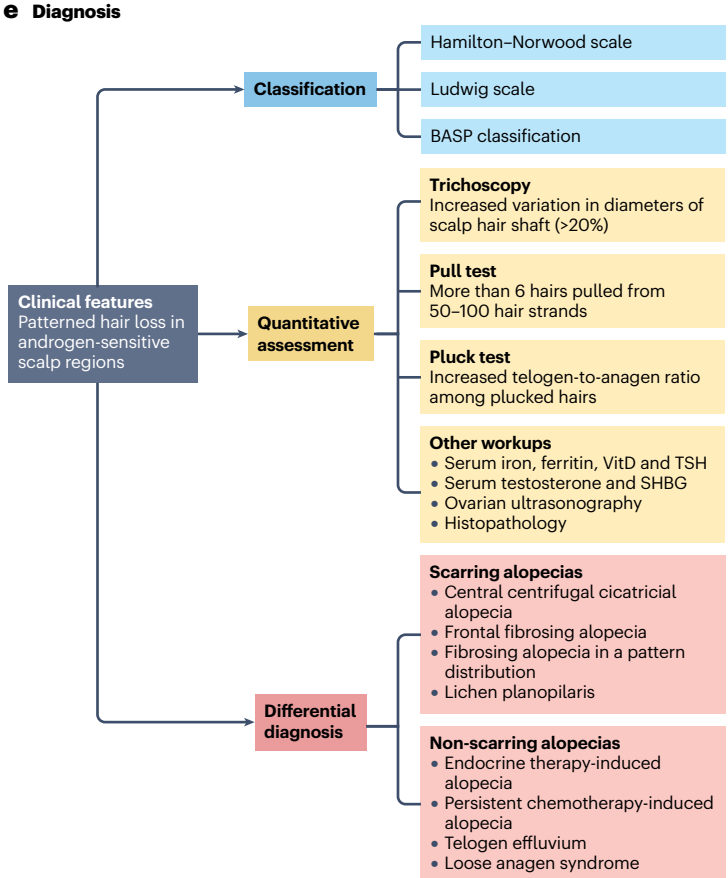
c Ludwig scale for female AGA



d BASP classification



e Diagnosis



resistant to hair loss. Subsequently, oral finasteride was approved by the FDA for the treatment of AGA in men[174]. Numerous long-term studies support the safety and efficacy of finasteride use in men with AGA, as well as in benign prostate hyperplasia[175–177]. Yet, finasteride, which inhibits only 5α-reductase type II, has limited efficacy in some people. This limitation paved the way to the use of dutasteride, a dual

Fig. 3 | Scalp regions and hair loss scales in AGA. a, Regional differences in androgen-induced hair loss in men. Androgenetic alopecia (AGA) primarily affects androgen-sensitive scalp, including frontal (blue), mid-scalp (mauve) and crown–vertex (yellow) regions. AGA generally spares androgen-resistant scalp, including parietal and occipital regions (black). **b**, The Hamilton–Norwood scale for assessing severity and progression of male AGA. Stages are indicated with Roman numerals and substages with additional letters. **c**, The Ludwig scale that describes severity and progression of female-pattern hair loss. Stages are indicated with Roman numerals. **d**, The basic and specific (BASP) classification for the universal categorization of AGA across sexes. Basic and specific hair loss types are indicated as combinations of letters and numbers, and AGA types as combinations of basic and specific alphanumeric types. Letters L, M, C and U represent four basic types of hair loss: L indicates 'linear' type; M and C indicate hair loss with the hairline shaped as the letter M or the letter C, respectively; and U indicates hair loss when the hairline recedes beyond the vertex and resembles the letter U. Letters F and V represent two specific types of hair loss. **e**, Diagnostic algorithm for AGA. SHBG, sex hormone-binding globulin; TSH, thyroid-stimulating hormone; VitD, vitamin D.

inhibitor of type I and II 5α-reductase[178]. Oral dutasteride, used off-label for the treatment of AGA, has better efficacy than and similar tolerability to finasteride, although up to 6% of people experience mild and reversible erectile difficulties and a lowered libido[179]. In a meta-analysis of monotherapies for AGA in men, oral dutasteride was found to be superior to oral finasteride and low-dose oral minoxidil[180]. Since the mid-2010s, topical minoxidil has been slowly being replaced by its oral counterpart, and oral 5α-reductase inhibitors are being increasingly abandoned for their off-label topical versions. This change is in part owing to FDA warning regarding the risk of depression and suicidal ideation[181] and in part owing to the risk of developing prolonged impotence after drug cessation[182]. Driven by these factors, topical finasteride is becoming an increasingly common off-label option that is as effective as topical minoxidil in early comparative studies[183] with fewer adverse effects than oral finasteride. Intralesional dutasteride is also starting to be used off-label[184,185], although its efficacy requires additional investigation.

Although the role of androgen signalling in female AGA remains unclear, finasteride has demonstrated efficacy in treating hair loss in postmenopausal women. However, its use in this population is off-label, with limited safety data available. Additionally, finasteride is contraindicated in women who are pregnant, may become pregnant, are breastfeeding or have an oestrogen-sensitive cancer[186].

Hair transplantation

People who have experienced slowing of hair loss following optimal pharmacological therapy are prime candidates for hair transplantation to address the residual symptoms of AGA. Hair transplantation relies on the donor dominance principle, whereby hair follicles maintain their original growth characteristics after being grafted to a different body site[187]. Hair transplantation aims to redistribute hair follicles sourced from the occipital scalp across skin regions affected by AGA[188–190] (Fig. 7). Adhering to the donor dominance principle, androgen-resistant occipital hair follicles remain unaffected by AGA upon engraftment[80]. However, as the grafted hair follicles do not alter androgen sensitivity of hair follicles native to the recipient site, initial cosmetic results commonly wane over time as AGA progresses.

Suitability for hair transplantation is mainly determined by four factors[191]. First, age is an important consideration. Men in their early twenties, especially with family history of hair loss, are regarded as poor candidates. Their continuing AGA is likely to be aggressive, commonly uncovering patches of long grafted hairs. Second, donor skin characteristics are an important factor. The amount of available donor hair follicles is rate limiting, and people with low hair density, especially when presenting with diffuse AGA, are regarded as poor candidates. Third, the degree of hair loss must be considered. Individuals with mild and moderate AGA are generally well suited for hair transplantation, whereas those with advanced AGA are eligible only as long as they have a wide donor area with high hair density. Finally, people with unrealistic expectations are poor candidates for hair transplantation.

Hair transplantation is typically performed as an outpatient procedure. Surgical techniques have evolved from grafting large, 3–4 mm skin punches, which produces an undesirable doll's hair look, to follicular unit transplantation, which uses solitary hair follicles or natural groups of two to four hair follicles and produces more natural aesthetic outcomes than conventional methods[192–194]. Donor hair follicles are typically obtained via strip harvesting or follicular unit extraction, with the latter method being currently preferred[195]. Strip harvesting removes large skin regions followed by their microdissection into follicular units, whereas follicular unit extraction uses 0.8–1.0 mm punches to directly incise skin around follicular units, which are then removed with forceps[196] (Fig. 7). Strip harvesting necessitates suturing and leads to a large linear scar, whereas follicular unit extraction microwounds heal by secondary intention with minimal scarring. Although commonly the donor area is shaved prior to harvesting, newer instrumentation allows harvesting follicular units with long hair shafts, which conceals donor skin wounds and facilitates a preview of the final, long-hair appearance in the recipient area[197–199] (Fig. 7).

The number of grafts is estimated in advance according to the donor and recipient area characteristics. Hair implantation is performed using different devices, with modern versions comprising a hollow needle into which follicular units are loaded and a piston, which propels follicular units into the recipient skin. A typical transplantation procedure grafts 1,500–3,000 follicular units, which translates to 3,000–7,500 individual hair follicles[200], has graft survival rate of 85–93%, and aims to achieve a density of 30–45 follicular units per square centimetre, a target which may necessitate follow-up transplantation session. Hair follicles enter telogen phase after grafting and shed hair fibres shortly after the procedure. As transplanted hair follicles can take 2–4 months to re-enter anagen phase, it can take between 6 and 12 months to achieve cosmetically meaningful hair coverage. Hence, the follow-up transplantation session should only be considered 1 year after transplantation.

Surgical complications occur in ~5% of transplantation procedures[201], and include folliculitis, prolonged paraesthesia and telogen effluvium in the recipient area. Yet, most common complications arise from poor technique, which include donor site depletion owing to overharvesting of follicular units, unnatural looking hairline and transplanted hair misdirection[202]. Hair transplantation is a surgical procedure with a profound artistic component, in which the surgeon's skills are paramount for satisfactory results and minimal complications.

Adjunctive therapies

Many adjunctive therapies are offered for AGA, with low-level light therapy (LLLT), platelet-rich plasma (PRP) injections, and

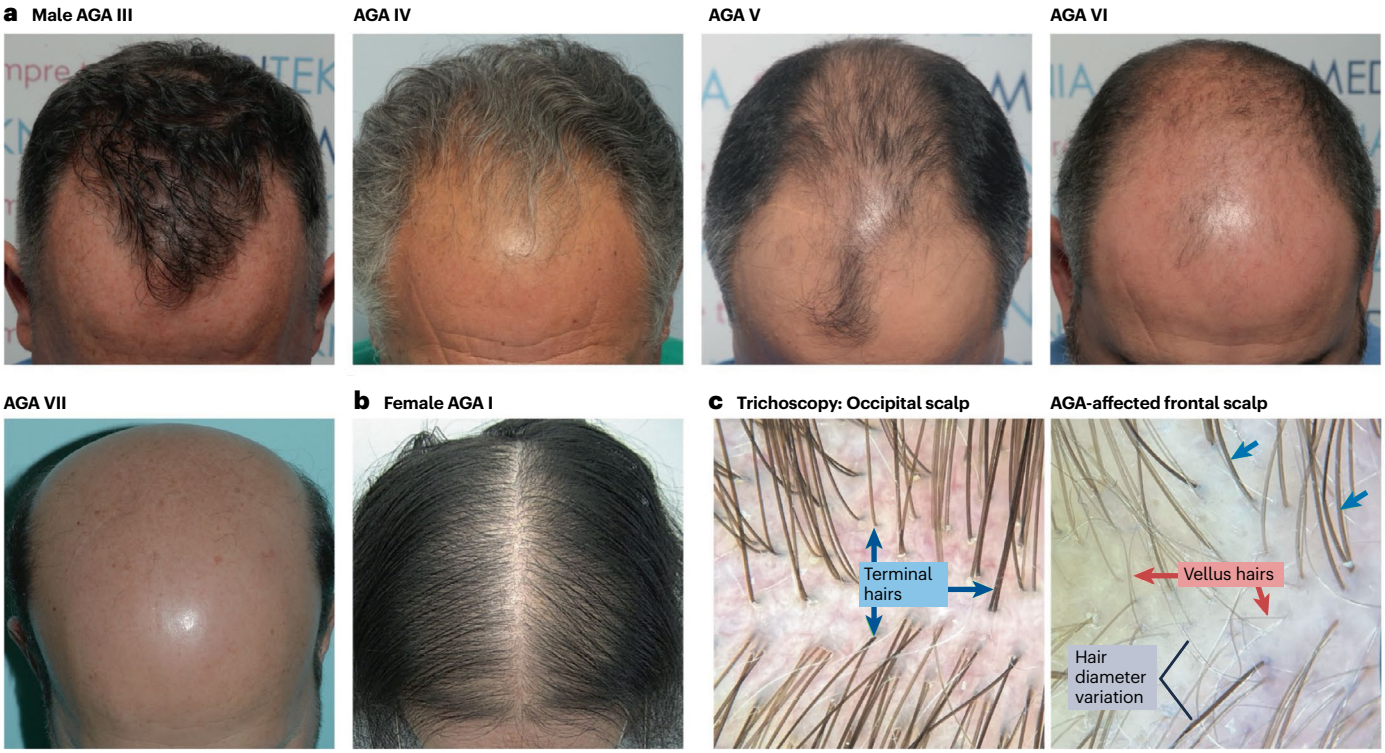


Fig. 4 | Clinical manifestations of AGA. a, Representative photographs of individuals with androgenetic alopecia (AGA), stages III through VII based on the Hamilton–Norwood scale, showing progressive hair loss in the frontal, mid-scalp and vertex regions. **b**, Representative image of an individual with female-pattern hair loss stage I based on the Ludwig scale. **c**, Representative trichoscopy photographs of the occipital (left) and frontal (right) scalp from the same person with AGA. Blue arrows indicate terminal hair fibres. Red arrows indicate vellus hair fibres in the frontal scalp that are thin, short and hypopigmented. The frontal scalp exhibits variation in hair diameter.

microtrauma-inducing procedures being the most prevalent. In patients with AGA, adjunctive therapies are typically combined with the use of finasteride and/or minoxidil, especially when the patient decides against hair transplantation. Systematic reviews have demonstrated efficacy for some of these therapies; however, most primary studies are afflicted by considerable inconsistencies in protocols and techniques[203–206]. LLLT devices are regarded as safe by the FDA, but PRP injections and microneedling are off-label treatment modalities. Limited clinical evidence and lack of standardized protocols and guidelines for these therapies have led to many unsupported claims as to their efficacy.

Low-level light therapy. LLLT, in which polarized infrared light of 600–1,600 nm wavelength is directed to the scalp, is thought to stimulate anagen phase re-entry through several complementary mechanisms[207], including by promoting epithelial cell proliferation and secretion of signalling factors, such as FGF7 (ref. 208). Although some controlled trials have shown that LLLT significantly induces hair regrowth in people with AGA[209], other reports are mixed and show substantial variation[210].

PRP injections. PRP is a common outpatient procedure, whereby autologous venous blood is centrifuged to obtain a platelet-rich fraction, which is then injected intradermally[203,211]. PRP is classified based on its composition into pure PRP, leukocyte and PRP, pure platelet-rich fibrin, and leukocyte and platelet-rich fibrin. Whether the inclusion of leukocytes provides PRP with therapeutic benefits remains debated[212]. Activation of PRP prior to its injection might not be necessary as clinical studies have shown no significant difference in efficacy between activated PRP and non-activated PRP[213]. Spontaneous degranulation of activated platelets after exposure to dermal collagen and thrombin upon injection is postulated to release various growth factors, which in scalp skin may stimulate anagen phase re-entry by AGA-affected hair follicles. Yet, PRP injections were not superior to sham injections in a split-head (in which both injections are done in the same participant, one on the left and another on the right side of the head) randomized controlled study[214], a conclusion supported by other studies on PRP using saline injections as placebo[215,216]. This suggests that microtrauma resulting from the act of injection, rather than PRP, may be a potential hair growth stimulus.

Microneedling. Microneedling, in its many forms, may be an effective adjunct treatment for AGA[217]. Both mechanical and laser devices can inflict skin microtrauma. At present, definitive evidence on the ideal protocol, modality and intensity of microtrauma for AGA is lacking[218–220]. Although the hair growth-promoting mechanism of microneedling remains undetermined, it may involve activation of cellular and molecular pathways that are part of the physiological wound healing programme[221,222], including upregulation of cytokines, such as TNF, IL-1β, and IL-6 (ref. 223). As with all adjunctive therapies that do not have FDA

approval, patients should be counselled to refrain from self-administered microneedling, which runs the risk of scarring and infection.

Emerging therapies

Emerging modalities for the management of AGA are numerous and include topical prostaglandin analogues[224,225], intradermal microinjections of botulinum toxin[226,227], synthetic peptides mimicking growth factors, exosomes derived from sources such as mesenchymal stem cells or dermal papilla fibroblasts[228], and intradermal injections of autologous mesenchymal cells, such as hair follicle-associated fibroblasts[229]. The prostaglandin analogue, latanoprost, was approved for the treatment of hypotrichosis of the eyelashes following the observation of increased eyelash growth in patients with glaucoma receiving latanoprost eye drops[224]. A pilot clinical study investigating topical 0.1% latanoprost for AGA in men demonstrated increased scalp hair density[225,230]. Furthermore, studies have evaluated the use of botulinum toxin injections for managing AGA in men, and its therapeutic benefit remains uncertain, with conflicting outcomes reported across clinical trials[226,227]. Additionally, consideration of the cost-effectiveness of incorporating botulinum toxin into AGA treatment regimens is warranted[231]. Clinical trials on autologous mesenchymal cell injections suggest that they increase hair density and hair fibre diameter in both men and women with AGA[229,232]. However, the technical complexity of this approach, which involves cell harvesting, culture, freezing and thawing, might limit its broad clinical application. Overall, implementation of these emerging modalities remains limited owing to the lack of comprehensive clinical data documenting efficacy and safety.

Quality of life

In many modern societies, a full head of hair is regarded as a conventionally desirable physical attribute. The detrimental effect of AGA on QOL rivals that of other skin diseases with obvious presentation, such

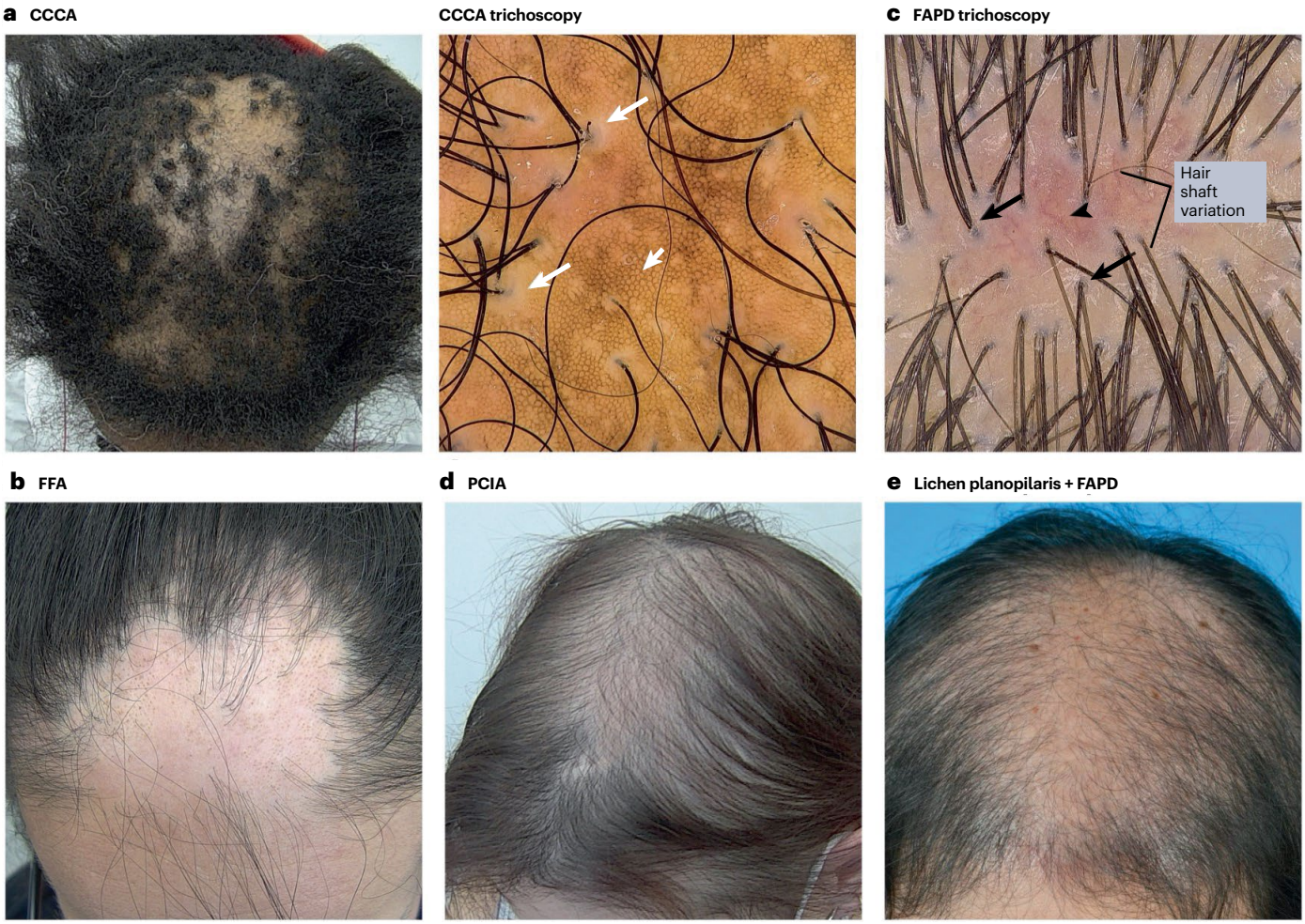


Fig. 5 | Major differential diagnosis of androgenetic alopecia. a, Representative photograph (left) of an individual with central centrifugal cicatricial alopecia (CCCA), characterized by hair loss in the vertex and mid-scalp regions with centrifugal pattern. Representative trichoscopy photograph of CCCA scalp (right) shows white halos surrounding hair follicle openings (large white arrows) and a honeycomb pigmented network (small white arrow). **b**, Representative photograph of an individual with frontal fibrosing alopecia (FFA), showing extensive hair loss in the frontal region. **c**, Representative trichoscopy photograph of a person with fibrosing alopecia in a pattern distribution (FAPD), displaying increased variation in hair diameter and scalp inflammation (black arrowhead) with peripilar casts (black arrows). **d**, Representative photograph of an individual with persistent chemotherapy-induced alopecia (PCIA), presenting as diffuse hair loss. **e**, Representative photograph of an individual with lichen planopilaris and FAPD, presenting as hair loss in the frontal and mid-scalp regions with signs of scarring and inflammation.

Table 1 | Profiles of selected AGA therapies

Therapy	FDA approval status	Efficacy[a]	Mechanism of action	Adverse effects	Refs.
Dutasteride	Off-label	86.89	Dual type I and II 5α-reductase inhibitor	Mild and reversible erectile difficulties and lowered libido	179
Finasteride	Approved	62.13	Type II 5α-reductase inhibitor	Decreased libido; erectile dysfunction; suicidality; psychological adverse events	253,254
5% Minoxidil	Approved	53.1	Unknown; potentially alters membrane potential by opening ATP-dependent potassium channels on dermal papilla fibroblasts	Irritation; allergic contact dermatitis; photoallergic reaction; hypertrichosis	255
2% Minoxidil	Approved	49.16			
LLLT	Cleared	51.18	Unknown; potentially stimulates anagen re-entry by telogen HFs	Dry skin; scalp irritation	256

Profiles are based on a meta-analysis study that compared the efficacy of monotherapies for androgenetic alopecia (AGA)[180]. HF, hair follicle; LLLT, low-level laser therapy. [a]Efficacy of regimens is expressed as the increase in total hair density (measured as hairs per square centimetre) at 24 weeks after treatment.

as alopecia areata or acne vulgaris[233]. Hair loss negatively impacts the affected individual's self-image and self-confidence, and alters social behaviour, causing health-related impairments in QOL. A study investigating the detrimental psychosocial effects of AGA found that hair loss can increase negative socioemotional events, such as looking older or feeling less attractive, having lower self-esteem, and decreased life satisfaction compared with the general population[221]. These adverse psychosocial effects, confirmed by many other studies, are more common in women than in men with AGA[234].

In a meta-analysis of 41 studies involving 7,995 people, the Skindex-29 score, calculated based on a self-reported questionnaire tailored to hair, showed an association between AGA and moderate impairment of QOL, especially in the emotion dimension[233,235]. Subgroup analysis of questionnaire-based Dermatology Life Quality Index scores found no statistically significant difference in QOL between men and women, although other studies have found greater psychological burden and QOL impairment in women than in men with AGA[236]. This finding is probably because, in many modern societies, hair loss is viewed as a

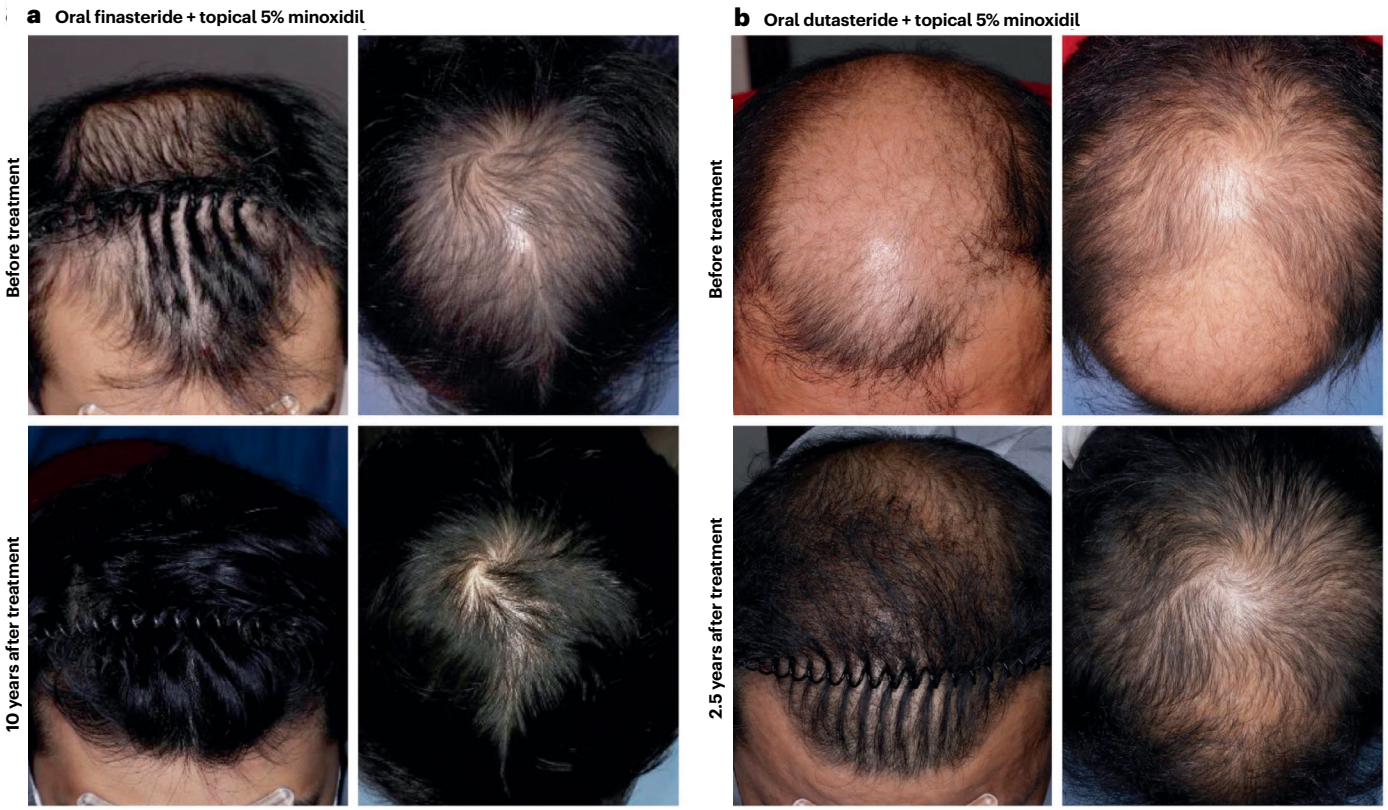


Fig. 6 | Efficacy of pharmaceutical treatments. a, Representative photographs of the scalp of a person with androgenetic alopecia (AGA) before (top) and 10 years after (bottom) treatment with a combination of oral finasteride and topical 5% minoxidil, showing prominent hair regrowth. **b**, Representative photographs of the scalp of a person with AGA before (top) and 2.5 years after (bottom) treatment with a combination of oral dutasteride and topical 5% minoxidil, showing substantial hair density improvement.

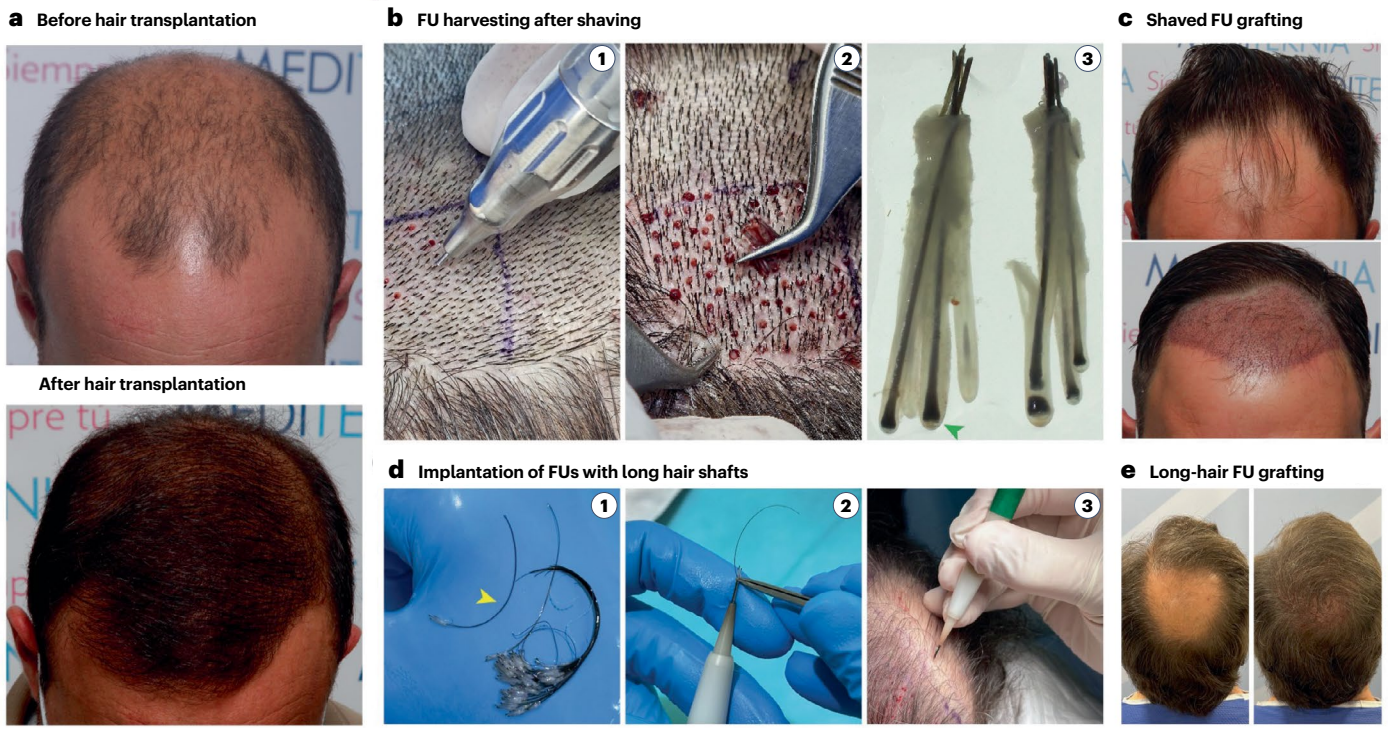


Fig. 7 | Hair transplantation. a, Representative photographs of an individual with androgenetic alopecia (AGA) stage V before (top) and 1 year after transplantation of 3,700 follicular unit (FU) grafts (bottom), showing substantial hair restoration. **b**, After hair shaving, FUs are harvested using a 0.95 mm punch attached to a motorized device (1) and extracted with forceps (2). Representative extracted FUs with intact terminal anagen hair follicles (green arrowhead) are shown (3). **c**, Appearance of the frontal scalp skin prior to (top) and 24 h after transplantation of 2,100 shaved FUs (bottom) in an individual with AGA stage IV. **d**, Hair transplantation technique using long-hair FUs. FUs are harvested from the donor area with their long hair fibres preserved (1). The yellow arrowhead indicates a single FU. FUs with long hair fibres are loaded into an implanter device (2) and then implanted into the recipient area (3). **e**, Appearance of the vertex scalp skin prior to (left) and after transplantation of long-hair FUs (right) in a person with AGA stage III vertex.

natural consequence of ageing in men but not in women. Young individuals, <30 years of age, and single persons with AGA are especially prone to psychological problems, with reduced QOL[237]. By contrast, being married or having a partner, and receiving medical treatments are associated positively with QOL[233].

Importantly, physician-rated hair loss severity has been found not to be a factor affecting QOL, whereas self-rated hair loss severity is, indicating that individual perception is more important in terms of psychological well-being than an objective assessment. Treatment of AGA, therefore, can have a profound and early positive impact on psychosocial functioning. For instance, the use of topical minoxidil has been associated with meaningful improvements in QOL[238]. Similarly, marked improvements in QOL in women with diffuse hair loss have been noted in those treated with low-dose oral minoxidil[239]. In men, QOL improvements were also noted following treatment with oral finasteride, suggesting that commencing appropriate treatment is an effective intervention for the psychosocial impact of AGA[240]. Few studies have examined the impact of hair transplantation on QOL and psychosocial functioning. Hair transplantation showed promise in improving psychological function 1 year after the procedure, enhancing self-esteem and increasing satisfaction with physical appearance in treated individuals[188,190,241]. Thus, prompt clinical evaluation and treatment referral remain critical for achieving overall treatment success and positive psychosocial well-being in individuals with AGA.

Outlook

Since the 2000s, our understanding of AGA genetics and pathogenesis has remarkably increased, with new therapeutic targets emerging from next-generation genomic sequencing and functional molecular studies on hair follicles in vivo and in vitro. The impetus to develop new therapeutics for AGA by pharmaceutical and biotechnology companies is likely to change the future landscape of hair loss management.

Future genetic research holds promise for advancing our understanding of the molecular underpinnings of AGA. Going forward, whole-genome sequencing across ancestrally diverse populations will be essential for generating a holistic view of the genetic landscape of AGA and for elucidating population-specific versus universally shared genetic risk factors of patterned hair loss. Furthermore, functional annotation of already identified risk variants remains a critical challenge. To this end, a multiomics approach that combines genomic, transcriptomic, epigenomic and proteomic data, will be key in assigning specific risk variants to specific skin domains, cell types and hair growth-associated biological events. As the volume of genomic data grows and understanding deepens, precision medicine will become achievable for AGA, with genetically informed risk predictions guiding the selection of individually tailored treatment regimens.

Further investigation of cellular and signalling mechanisms of hair follicle miniaturization is crucial. Specifically, future work is needed to determine what hair growth-altering modifications are driven by

Glossary

Cantu syndrome
Rare genetic disorder characterized by hypertrichosis, among other abnormalities.

Hamilton–Norwood scale
Scale for classifying clinical severity of AGA in men.

Loose anagen syndrome
A type of hair loss caused by weakly anchored anagen hairs that shed easily.

Ludwig scale
Scale for classifying clinical severity of AGA in women.

Retrograde AGA
AGA pattern that starts at the nape of the neck and propagates upwards towards the crown.

Scarring alopecia
A type of hair loss caused by the permanent destruction of hair follicles.

Traction alopecia
Hair loss caused by prolonged and excessive pulling on hair, such as from tight hair styles.

Trichotillomania
Hair loss associated with frequent irresistible urges to pull out hair.

androgens in dermal papilla fibroblasts. This includes an androgen receptor-dependent premature cellular senescence programme[87,88], as well as androgen receptor-dependent gene regulatory network changes, particularly its negatively affected signalling growth factor genes. Future strategies for selectively depleting senescent dermal papilla fibroblasts[242] or selectively augmenting otherwise depleted dermal papilla-specific growth factors[56,58] may emerge as effective strategies for preventing and reversing hair follicle miniaturization.

Future epidemiological studies should focus on understanding the relationship between androgen-dependent hair loss and scarring alopecia. In Japanese populations and in Black women, studies have shown analogous spatial co-distribution of scarring alopecia and AGA[16,243]. Rather than being two separate hair loss conditions, CCCA might possibly be a fibrosed variant of AGA, developing in individuals predisposed to inflammatory dysregulation[244]. If this is indeed the case, future research should determine factors influencing the progression of AGA towards scarring. In addition, the association between the metabolic syndrome and the impact of various modifying factors on AGA must be better understood. As we better understand the role of metabolic dysfunction on skin biology and in particular, on hair growth, we may consider instituting lifestyle changes and medical remedies aimed at improving overall health as part of the therapeutic approach to treating hair loss.

Regarding the management of AGA, substantial changes are anticipated. First, approved treatments are repurposed into different modes of administration[4], enabling customization of treatments. Second, novel delivery methods for existing drugs, such as intralesional injections of dutasteride[184] or application of minoxidil-laden microneedles[245], are being actively explored. In this regard, larger studies on the safety and efficacy of these delivery modalities are required for future regulatory approval. Third, the current popular adjunctive treatments for AGA require greater clinical scrutiny and in-depth investigation of their mechanisms of action. Specifically, microtrauma-based treatment modalities, microneedling, ablative and non-ablative lasers are being used globally for AGA, but protocols vary greatly, and reported results are operator-dependent[246]. Additional experimental and translational work is required to uncover specific hair growth-promoting molecular pathways stimulated by skin microtrauma and to develop protocols optimized for stimulating these pathways. Furthermore, newly identified paracrine signalling activators of human hair growth, such as osteopontin[58] or SCUBE3 (ref. 56), might be the next generation of microinjectable AGA therapeutics, in the form of either recombinant peptides or peptide-encoding mRNAs formulated within lipid nanoparticles. Next, bioengineering of hair-bearing human skin equivalents will eventually offer an alternative treatment for different forms of hair loss, including AGA and scarring alopecia. Although new human hair follicles can be produced in embryonic stem cell-derived organoids[247] or via cell seeding into micropatterned extracellular matrix constructs[248–251], considerable future progress is necessary to assure that bioengineered hair follicles competently grow cyclically and produce desirable hair fibre morphologies in terms of their length, texture and pigmentation[252]. Lastly, as we enter the age of artificial intelligence, new treatments for AGA may also arise from employing computational tools to model the complexity of the human hair growth cycle and to perform predictive mathematical simulations on AGA pathogenesis. Conceivably, such in silico approaches could screen and rank therapeutic candidates, so that only the most promising ones can advance to functional validation.

Published online: 09 October 2025

References

1. Otberg, N., Finner, A. M. & Shapiro, J. Androgenetic alopecia. *Endocrinol. Metab. Clin. North. Am.* **36**, 379–398 (2007).
2. Pratt, C. H., King, L. E. Jr., Messenger, A. G., Christiano, A. M. & Sundberg, J. P. Alopecia areata. *Nat. Rev. Dis. Primers* **3**, 17011 (2017).
3. Peyravian, N., Deo, S., Daunert, S. & Jimenez, J. J. The inflammatory aspect of male and female pattern hair loss. *J. Inflamm. Res.* **13**, 879–881 (2020).
4. McElwee, K. J. & Sundberg, J. P. Innovative strategies for the discovery of new drugs against androgenetic alopecia. *Expert. Opin. Drug. Discov.* **20**, 517–536 (2025).
5. Chaikittisilpa, S. et al. Prevalence of female pattern hair loss in postmenopausal women: a cross-sectional study. *Menopause* **29**, 415–420 (2022).
6. Paik, J. H., Yoon, J. B., Sim, W. Y., Kim, B. S. & Kim, N. I. The prevalence and types of androgenetic alopecia in Korean men and women. *Br. J. Dermatol.* **145**, 95–99 (2001). **A large-scale study establishing AGA prevalence across age groups in both men and women.**
7. Salman, K. E., Altunay, I. K., Kucukunal, N. A. & Cerman, A. A. Frequency, severity and related factors of androgenetic alopecia in dermatology outpatient clinic: hospital-based cross-sectional study in Turkey. *An. Bras. Dermatol.* **92**, 35–40 (2017).
8. Birch, M. P., Messenger, J. F. & Messenger, A. G. Hair density, hair diameter and the prevalence of female pattern hair loss. *Br. J. Dermatol.* **144**, 297–304 (2001).
9. Griggs, J., Burroway, B. & Tosti, A. Pediatric androgenetic alopecia: a review. *J. Am. Acad. Dermatol.* **85**, 1267–1273 (2021).
10. Krupa Shankar, D., Chakravarthi, M. & Shilpakar, R. Male androgenetic alopecia: population-based study in 1,005 subjects. *Int. J. Trichology* **1**, 131–133 (2009).
11. DeMuro-Mercon, C., Rhodes, T., Girman, C. J. & Vatten, L. Male-pattern hair loss in Norwegian men: a community-based study. *Dermatology* **200**, 219–222 (2000).
12. Yildirim, A. M., Yousaf, A., Fang, W. & Kolodney, M. S. A cross-sectional study of male balding patterns in people of color. *J. Am. Acad. Dermatol.* **87**, 1203–1205 (2022).
13. Pathomvanich, D., Pongratananukul, S., Thienthaworn, P. & Manoshai, S. A random study of Asian male androgenetic alopecia in Bangkok, Thailand. *Dermatol. Surg.* **28**, 804–807 (2002).
14. Su, L. H., Chen, L. S. & Chen, H. H. Factors associated with female pattern hair loss and its prevalence in Taiwanese women: a community-based survey. *J. Am. Acad. Dermatol.* **69**, e69–e77 (2013).
15. Gan, D. C. & Sinclair, R. D. Prevalence of male and female pattern hair loss in Maryborough. *J. Investig. Dermatol. Symp. Proc.* **10**, 184–189 (2005).
16. Gadre, A., Sun, Y. & Aguh, C. Unique presentations of female pattern hair loss evident in Asian and black women. *Clin. Exp. Dermatol.* **49**, 1717–1719 (2024).
17. Lie, C., Liew, C. F. & Oon, H. H. Alopecia and the metabolic syndrome. *Clin. Dermatol.* **36**, 54–61 (2018).
18. Su, L. H. & Chen, T. H. Association of androgenetic alopecia with metabolic syndrome in men: a community-based survey. *Br. J. Dermatol.* **163**, 371–377 (2010).
19. Acibucu, F., Kayatas, M. & Candan, F. The association of insulin resistance and metabolic syndrome in early androgenetic alopecia. *Singap. Med. J.* **51**, 931–936 (2010).
20. Bakry, O. A., Shoeib, M. A., El Shafiee, M. K. & Hassan, A. Androgenetic alopecia, metabolic syndrome, and insulin resistance: is there any association? A case-control study. *Indian. Dermatol. Online J.* **5**, 276–281 (2014).

21. Sadgrove, N. J. The 'bald' phenotype (androgenetic alopecia) is caused by the high glycaemic, high cholesterol and low mineral 'western diet'. *Trends Food Sci. Technol.* **116**, 1170–1178 (2021).
22. Nabaie, L. et al. Androgenic alopecia and insulin resistance: are they really related? *Clin. Exp. Dermatol.* **34**, 694–697 (2009).
23. Fortes, C., Mastroeni, S., Mannooranparampil, T., Abeni, D. & Panebianco, A. Mediterranean diet: fresh herbs and fresh vegetables decrease the risk of androgenetic alopecia in males. *Arch. Dermatol. Res.* **310**, 71–76 (2018).
24. Peng, L., Liu, Y., Wu, W., Zhou, Y. & Huang, X. Unhealthy diet and lifestyle factors linked to female androgenetic alopecia: a community-based study from Jidong study, China. *BMC Public. Health* **25**, 606 (2025).
25. Shi, X. et al. The association between sugar-sweetened beverages and male pattern hair loss in young men. *Nutrients* **15**, 214 (2023).
26. Burke, O., Sa, B., Cespedes, D. A., Sechi, A. & Tosti, A. Glucagon-like peptide-1 receptor agonist medications and hair loss: a retrospective cohort study. *J. Am. Acad. Dermatol.* **92**, 1141–1143 (2025).
27. Gordon, E. R., Musleh, S. & Bordone, L. A. Treatment of insulin resistance with tirzepatide leading to improvement of hair loss. *JAAD Case Rep.* **50**, 123–125 (2024).
28. Fortes, C., Mastroeni, S., Mannooranparampil, T. J. & Ribuffo, M. The combination of overweight and smoking increases the severity of androgenetic alopecia. *Int. J. Dermatol.* **56**, 862–867 (2017).
29. Severi, G. et al. Androgenetic alopecia in men aged 40–69 years: prevalence and risk factors. *Br. J. Dermatol.* **149**, 1207–1213 (2003).
30. Gupta, A. K., Bamimore, M. A. & Talukder, M. A meta-analysis study on the association between smoking and male pattern hair loss. *J. Cosmet. Dermatol.* **23**, 1446–1451 (2024).
31. Tran, B. N. et al. Androgenic steroids in over-the-counter dietary supplements: analysis for association with adverse health effects. *Steroids* **193**, 109199 (2023).
32. Durusu Turkoglu, I. N., Turkoglu, A. K., Soylu, S., Gencer, G. & Duman, R. A comprehensive investigation of biochemical status in patients with telogen effluvium: analysis of Hb, ferritin, vitamin B12, vitamin D, thyroid function tests, zinc, copper, biotin, and selenium levels. *J. Cosmet. Dermatol.* **23**, 4277–4284 (2024).
33. Bin Dayel, S. et al. Is thyroid dysfunction a common cause of telogen effluvium?: A retrospective study. *Medicine* **103**, e36803 (2024).
34. Trueb, R. M. Is androgenetic alopecia a photoaggravated dermatosis? *Dermatology* **207**, 343–348 (2003).
35. Schneider, M. R., Schmidt-Ullrich, R. & Paus, R. The hair follicle as a dynamic miniorgan. *Curr. Biol.* **19**, R132–R142 (2009).
36. Cotsarelis, G., Sun, T. T. & Lavker, R. M. Label-retaining cells reside in the bulge area of pilosebaceous unit: implications for follicular stem cells, hair cycle, and skin carcinogenesis. *Cell* **61**, 1329–1337 (1990).
37. Ohyama, M. et al. Characterization and isolation of stem cell-enriched human hair follicle bulge cells. *J. Clin. Invest.* **116**, 249–260 (2006).
38. Casalou, C., Mayatra, J. M. & Tobin, D. J. Beyond the epidermal-melanin-unit: the human scalp anagen hair bulb is home to multiple melanocyte subpopulations of variable melanogenic capacity. *Int. J. Mol. Sci.* **24**, 12809 (2023).
39. Paus, R. & Cotsarelis, G. The biology of hair follicles. *N. Engl. J. Med.* **341**, 491–497 (1999).
40. Lattanand, A. & Johnson, W. C. Male pattern alopecia a histopathologic and histochemical study. *J. Cutan. Pathol.* **2**, 58–70 (1975).
41. Sinclair, R. et al. Morphological approach to hair disorders. *J. Investig. Dermatol. Symp. Proc.* **8**, 56–64 (2003).
42. Whiting, D. A. Possible mechanisms of miniaturization during androgenetic alopecia or pattern hair loss. *J. Am. Acad. Dermatol.* **45**, S81–S86 (2001).
43. Van Scott, E. J. & Ekel, T. M. Geometric relationships between the matrix of the hair bulb and its dermal papilla in normal and alopecic scalp. *J. Invest. Dermatol.* **31**, 281–287 (1958).
44. Ober-Reynolds, B. et al. Integrated single-cell chromatin and transcriptomic analyses of human scalp identify gene-regulatory programs and critical cell types for hair and skin diseases. *Nat. Genet.* **55**, 1288–1300 (2023).
45. Torkamani, N., Rufaut, N. W., Jones, L. & Sinclair, R. Destruction of the arrector pili muscle and fat infiltration in androgenic alopecia. *Br. J. Dermatol.* **170**, 1291–1298 (2014).
46. Yazdabadi, A., Whiting, D., Rufaut, N. & Sinclair, R. 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. *Int. J. Trichology* **4**, 154–157 (2012).
47. Shwartz, Y. et al. Cell types promoting goosebumps form a niche to regulate hair follicle stem cells. *Cell* **182**, 578–593.e19 (2020).
48. Oh, J. W. et al. A guide to studying human hair follicle cycling in vivo. *J. Invest. Dermatol.* **136**, 34–44 (2016).
This paper is a detailed atlas of human hair follicles in the scalp skin across different hair growth stages.
49. Montagna, W. & Chase, H. B. Histology and cytochemistry of human skin. X. X-irradiation of the scalp. *Am. J. Anat.* **99**, 415–445 (1956).
50. Kligman, A. M. The human hair cycle. *J. Invest. Dermatol.* **33**, 307–316 (1959).
51. Zhang, B. & Chen, T. Local and systemic mechanisms that control the hair follicle stem cell niche. *Nat. Rev. Mol. Cell Biol.* **25**, 87–100 (2024).
52. Higgins, C. A. et al. FGF5 is a crucial regulator of hair length in humans. *Proc. Natl Acad. Sci. USA* **111**, 10648–10653 (2014).
53. Hawkshaw, N. J., Hardman, J. A., Alam, M., Jimenez, F. & Paus, R. Deciphering the molecular morphology of the human hair cycle: Wnt signalling during the telogen–anagen transformation. *Br. J. Dermatol.* **182**, 1184–1193 (2020).
54. Cesarato, N. et al. Short anagen hair syndrome: association with mono- and biallelic variants in WNT10A and a genetic overlap with male pattern hair loss. *Br. J. Dermatol.* **189**, 741–749 (2023).
55. Heilmann, S. et al. Androgenetic alopecia: identification of four genetic risk loci and evidence for the contribution of WNT signaling to its etiology. *J. Invest. Dermatol.* **133**, 1489–1496 (2013).
56. Liu, Y. et al. Hedgehog signaling reprograms hair follicle niche fibroblasts to a hyper-activated state. *Dev. Cell* **57**, 1758–1775.e7 (2022).
57. Yu, D. W. et al. Osteopontin gene is expressed in the dermal papilla of pelage follicles in a hair-cycle-dependent manner. *J. Invest. Dermatol.* **117**, 1554–1558 (2001).
58. Wang, X. et al. Signalling by senescent melanocytes hyperactivates hair growth. *Nature* **618**, 808–817 (2023).
59. Philpott, M. P., Sanders, D. A. & Kealey, T. Effects of insulin and insulin-like growth factors on cultured human hair follicles: IGF-I at physiologic concentrations is an important regulator of hair follicle growth in vitro. *J. Invest. Dermatol.* **102**, 857–861 (1994).
60. Nicu, C. et al. Dermal adipose tissue secretes HGF to promote human hair growth and pigmentation. *J. Invest. Dermatol.* **141**, 1633–1645.e13 (2021).
61. McElwee, K. J., Huth, A., Kissling, S. & Hoffmann, R. Macrophage-stimulating protein promotes hair growth ex vivo and induces anagen from telogen stage hair follicles in vivo. *J. Invest. Dermatol.* **123**, 34–40 (2004).
62. Iino, M. et al. Adenosine stimulates fibroblast growth factor-7 gene expression via adenosine A2b receptor signaling in dermal papilla cells. *J. Invest. Dermatol.* **127**, 1318–1325 (2007).
63. Soma, T., Tsuji, Y. & Hibino, T. Involvement of transforming growth factor-β2 in catagen induction during the human hair cycle. *J. Invest. Dermatol.* **118**, 993–997 (2002).
64. Kwack, M. H., Ahn, J. S., Kim, M. K., Kim, J. C. & Sung, Y. K. Dihydrotestosterone-inducible IL-6 inhibits elongation of human hair shafts by suppressing matrix cell proliferation and promotes regression of hair follicles in mice. *J. Invest. Dermatol.* **132**, 43–49 (2012).
65. Foitzik, K. et al. Human scalp hair follicles are both a target and a source of prolactin, which serves as an autocrine and/or paracrine promoter of apoptosis-driven hair follicle regression. *Am. J. Pathol.* **168**, 748–756 (2006).
66. Hamilton, J. B. Effect of castration in adolescent and young adult males upon further changes in the proportions of bare and hairy scalp. *J. Clin. Endocrinol. Metab.* **20**, 1309–1318 (1960).
67. Deplewski, D. & Rosenfield, R. L. Role of hormones in pilosebaceous unit development. *Endocr. Rev.* **21**, 363–392 (2000).
68. Sundberg, J. P., King, L. E. & Bascom, C. Animal models for male pattern (androgenetic) alopecia. *Eur. J. Dermatol.* **11**, 321–325 (2001).
69. Banka, N., Bunagan, M. J. & Shapiro, J. Pattern hair loss in men: diagnosis and medical treatment. *Dermatol. Clin.* **31**, 129–140 (2013).
70. Ceruti, J. M., Leiros, G. J. & Balana, M. E. Androgens and androgen receptor action in skin and hair follicles. *Mol. Cell Endocrinol.* **465**, 122–133 (2018).
71. Hoffmann, R., Rot, A., Niiyama, S. & Billich, A. Steroid sulfatase in the human hair follicle concentrates in the dermal papilla. *J. Invest. Dermatol.* **117**, 1342–1348 (2001).
72. Hoffmann, R. Hormonal interaction and hair growth [French]. *Ann. Dermatol. Venereol.* **129**, 787–792 (2002).
73. Imperato-McGinley, J., Guerrero, L., Gautier, T. & Peterson, R. E. Steroid 5α-reductase deficiency in man: an inherited form of male pseudohermaphroditism. *Science* **186**, 1213–1215 (1974).
74. Eicheler, W., Happle, R. & Hoffmann, R. 5α-Reductase activity in the human hair follicle concentrates in the dermal papilla. *Arch. Dermatol. Res.* **290**, 126–132 (1998).
This is a foundational study establishing the activity of 5α-reductase, a target enzyme for finasteride, in the dermal papilla fibroblasts of human hair follicles.
75. Asada, Y. et al. 5α-Reductase type 2 is constitutively expressed in the dermal papilla and connective tissue sheath of the hair follicle in vivo but not during culture in vitro. *J. Clin. Endocrinol. Metab.* **86**, 2875–2880 (2001).
76. Redmond, L. C., Limbu, S., Farjo, B., Messenger, A. G. & Higgins, C. A. Male pattern hair loss: can developmental origins explain the pattern? *Exp. Dermatol.* **32**, 1174–1181 (2023).
77. Shim, J. et al. Comparative spatial transcriptomic and single-cell analyses of human nail units and hair follicles show transcriptional similarities between the onychodermis and follicular dermal papilla. *J. Invest. Dermatol.* **142**, 3146–3157.e12 (2022).
78. Ha, S. J., Kim, J. S., Myung, J. W., Lee, H. J. & Kim, J. W. Analysis of genetic polymorphisms of steroid 5α-reductase type 1 and 2 genes in Korean men with androgenetic alopecia. *J. Dermatol. Sci.* **31**, 135–141 (2003).
79. Sawaya, M. E. Steroid chemistry and hormone controls during the hair follicle cycle. *Ann. N. Y. Acad. Sci.* **642**, 376–383 (1991).
80. Sawaya, M. E. & Price, V. H. Different levels of 5α-reductase type I and II, aromatase, and androgen receptor in hair follicles of women and men with androgenetic alopecia. *J. Invest. Dermatol.* **109**, 296–300 (1997).
81. Ellis, J. A., Stebbing, M. & Harrap, S. B. Genetic analysis of male pattern baldness and the 5α-reductase genes. *J. Invest. Dermatol.* **110**, 849–853 (1998).
82. Itami, S., Sonoda, T., Kurata, S. & Takayasu, S. Mechanism of action of androgen in hair follicles. *J. Dermatol. Sci.* **7** (Suppl), S98–S103 (1994).
83. Randall, V. A., Thornton, M. J., Hamada, K. & Messenger, A. G. Mechanism of androgen action in cultured dermal papilla cells derived from human hair follicles with varying responses to androgens in vivo. *J. Invest. Dermatol.* **98**, 86S-91S (1992).
84. Deng, Z. et al. Androgen receptor-mediated paracrine signaling induces regression of blood vessels in the dermal papilla in androgenetic alopecia. *J. Invest. Dermatol.* **142**, 2088–2099.e9 (2022).

85. Cobb, J. E. et al. Evidence of increased DNA methylation of the androgen receptor gene in occipital hair follicles from men with androgenetic alopecia. *Br. J. Dermatol.* **165**, 210–213 (2011).
86. Fu, D. et al. Dihydrotestosterone-induced hair regrowth inhibition by activating androgen receptor in C57BL6 mice simulates androgenetic alopecia. *Biomed. Pharmacother.* **137**, 111247 (2021).
87. Upton, J. H. et al. Oxidative stress-associated senescence in dermal papilla cells of men with androgenetic alopecia. *J. Invest. Dermatol.* **135**, 1244–1252 (2015).
88. Huang, W. Y. et al. Stress-induced premature senescence of dermal papilla cells compromises hair follicle epithelial-mesenchymal interaction. *J. Dermatol. Sci.* **86**, 114–122 (2017).
89. Bahta, A. W., Farjo, N., Farjo, B. & Philpott, M. P. Premature senescence of balding dermal papilla cells in vitro is associated with $p16^{INK4a}$ expression. *J. Invest. Dermatol.* **128**, 1088–1094 (2008).
90. Leiros, G. J., Attorresi, A. I. & Balana, M. E. Hair follicle stem cell differentiation is inhibited through cross-talk between Wnt/β-catenin and androgen signalling in dermal papilla cells from patients with androgenetic alopecia. *Br. J. Dermatol.* **166**, 1035–1042 (2012).
91. Li, K. et al. The AR/miR-221/IGF-1 pathway mediates the pathogenesis of androgenetic alopecia. *Int. J. Biol. Sci.* **19**, 3307–3323 (2023).
92. Starace, M., Orlando, G., Alessandrini, A. & Piraccini, B. M. Female androgenetic alopecia: an update on diagnosis and management. *Am. J. Clin. Dermatol.* **21**, 69–84 (2020).
93. Futterweit, W., Dunaif, A., Yeh, H. C. & Kingsley, P. The prevalence of hyperandrogenism in 109 consecutive female patients with diffuse alopecia. *J. Am. Acad. Dermatol.* **19**, 831–836 (1988).
94. Cousen, P. & Messenger, A. Female pattern hair loss in complete androgen insensitivity syndrome. *Br. J. Dermatol.* **162**, 1135–1137 (2010).
95. Sanchez, P., Serrano-Falcon, C., Torres, J. M., Serrano, S. & Ortega, E. 5α-Reductase isozymes and aromatase mRNA levels in plucked hair from young women with female pattern hair loss. *Arch. Dermatol. Res.* **310**, 77–83 (2018).
96. Redler, S. et al. Selected variants of the steroid-5-α-reductase isoforms SRD5A1 and SRD5A2 and the sex steroid hormone receptors ESR1, ESR2 and PGR: no association with female pattern hair loss identified. *Exp. Dermatol.* **21**, 390–393 (2012).
97. van Zuuren, E. J. & Fedorowicz, Z. Interventions for female pattern hair loss. *JAMA Dermatol.* **153**, 329–330 (2017).
98. Starace, M. V. R. et al. The comparative effects of monotherapy with topical minoxidil, oral finasteride, and topical finasteride in postmenopausal women with pattern hair loss: a retrospective cohort study. *Skin. Appendage Disord.* **10**, 293–300 (2024).
99. Heymann, W. R. The inflammatory component of androgenetic alopecia. *J. Am. Acad. Dermatol.* **86**, 301–302 (2022).
100. Plante, J., Valdebran, M., Forcucci, J., Lucas, O. & Elston, D. Perifollicular inflammation and follicular spongiosis in androgenetic alopecia. *J. Am. Acad. Dermatol.* **86**, 437–438 (2022).
101. Whiting, D. A. Diagnostic and predictive value of horizontal sections of scalp biopsy specimens in male pattern androgenetic alopecia. *J. Am. Acad. Dermatol.* **28**, 755–763 (1993).
102. Michel, L. et al. Study of gene expression alteration in male androgenetic alopecia: evidence of predominant molecular signalling pathways. *Br. J. Dermatol.* **177**, 1322–1336 (2017).
103. Miao, Y. et al. Identification of functional patterns of androgenetic alopecia using transcriptome profiling in distinct locations of hair follicles. *J. Invest. Dermatol.* **138**, 972–975 (2018).
104. Garza, L. A. et al. Prostaglandin D2 inhibits hair growth and is elevated in bald scalp of men with androgenetic alopecia. *Sci. Transl. Med.* **4**, 126ra134 (2012).
105. Lukasik, A., Kozicka, K., Klosowicz, A., Jaworek, A. & Wojas-Pelc, A. The role of family history and its influence on the onset time in female pattern hair loss. *Postepy Dermatol. Alergol.* **38**, 815–818 (2021).
106. Osborn, D. INHERITANCE OF BALDNESS: various patterns due to heredity and sometimes present at birth — a sex-limited character — dominant in man — women not bald unless they inherit tendency from both parents. *J. Heredity* **7**, 347–355 (1916).
107. Heilmann, S. et al. Evidence for a polygenic contribution to androgenetic alopecia. *Br. J. Dermatol.* **169**, 927–930 (2013).
108. Kuster, W. & Happle, R. The inheritance of common baldness: two B or not two B? *J. Am. Acad. Dermatol.* **11**, 921–926 (1984).
109. Redler, S., Messenger, A. G. & Betz, R. C. Genetics and other factors in the aetiology of female pattern hair loss. *Exp. Dermatol.* **26**, 510–517 (2017).
110. Yap, C. X. et al. Dissection of genetic variation and evidence for pleiotropy in male pattern baldness. *Nat. Commun.* **9**, 5407 (2018).
This is a large-scale GWAS study establishing the polygenetic basis of AGA in men.
111. Rexbye, H. et al. Hair loss among elderly men: etiology and impact on perceived age. *J. Gerontol. A Biol. Sci. Med. Sci* **60**, 1077–1082 (2005).
112. Nyholt, D. R., Gillespie, N. A., Heath, A. C. & Martin, N. G. Genetic basis of male pattern baldness. *J. Invest. Dermatol.* **121**, 1561–1564 (2003).
113. Heilmann-Heimbach, S. et al. Meta-analysis identifies novel risk loci and yields systematic insights into the biology of male-pattern baldness. *Nat. Commun.* **8**, 14694 (2017).
114. Hagenaars, S. P. et al. Genetic prediction of male pattern baldness. *PLoS Genet.* **13**, e1006594 (2017).
115. Li, R. et al. Six novel susceptibility loci for early-onset androgenetic alopecia and their unexpected association with common diseases. *PLoS Genet.* **8**, e1002746 (2012).
116. Brockschmidt, F. F. et al. Susceptibility variants on chromosome 7p21.1 suggest HDAC9 as a new candidate gene for male-pattern baldness. *Br. J. Dermatol.* **165**, 1293–1302 (2011).
117. Hillmer, A. M. et al. Susceptibility variants for male-pattern baldness on chromosome 20p11. *Nat. Genet.* **40**, 1279–1281 (2008).
118. Richards, J. B. et al. Male-pattern baldness susceptibility locus at 20p11. *Nat. Genet.* **40**, 1282–1284 (2008).
119. Pirastu, N. et al. GWAS for male-pattern baldness identifies 71 susceptibility loci explaining 38% of the risk. *Nat. Commun.* **8**, 1584 (2017).
120. Henne, S. K., Nöthen, M. M. & Heilmann-Heimbach, S. Male-pattern hair loss: comprehensive identification of the associated genes as a basis for understanding pathophysiology. *Med. Genet.* **35**, 3–14 (2023).
121. Heilmann-Heimbach, S., Hochfeld, L. M., Henne, S. K. & Nothen, M. M. Hormonal regulation in male androgenetic alopecia — sex hormones and beyond: evidence from recent genetic studies. *Exp. Dermatol.* **29**, 814–827 (2020).
122. Fu, P. P. et al. Relationships among direct-acting mutagenicity, nitro group orientation and polarographic reduction potential of 6-nitrobenzo[a]pyrene, 7-nitrobenz[a] anthracene and their derivatives. *Mutat. Res.* **209**, 115–122 (1988).
123. Henne, S. K. et al. Analysis of 72,469 UK Biobank exomes links rare variants to male-pattern hair loss. *Nat. Commun.* **14**, 5492 (2023).
124. Xu, F. et al. Prevalence and types of androgenetic alopecia in Shanghai, China: a community-based study. *Br. J. Dermatol.* **160**, 629–632 (2009).
125. Adhikari, K. et al. A genome-wide association scan in admixed Latin Americans identifies loci influencing facial and scalp hair features. *Nat. Commun.* **7**, 10815 (2016).
126. Janivara, R. et al. Uncovering the genetic architecture and evolutionary roots of androgenetic alopecia in African men. *HGG Adv.* **6,** 100428 (2025).
127. Kim, I. Y. et al. The first broad replication study of SNPs and a pilot genome-wide association study for androgenetic alopecia in Asian populations. *J. Cosmet. Dermatol.* **21**, 6174–6183 (2022).
128. Liang, B. et al. Genetic variants at 20p11 confer risk to androgenetic alopecia in the Chinese Han population. *PLoS ONE* **8**, e71771 (2013).
129. Ong, J. S. et al. Uncovering the complex relationship between balding, testosterone and skin cancers in men. *Nat. Commun.* **14**, 5962 (2023).
130. Li, W. Q., Cho, E., Han, J., Weinstock, M. A. & Qureshi, A. A. Male pattern baldness and risk of incident skin cancer in a cohort of men. *Int. J. Cancer* **139**, 2671–2678 (2016).
131. Stanganelli, I. et al. Dermoscopy of scalp tumours: a multi-centre study conducted by the International Dermoscopy Society. *J. Eur. Acad. Dermatol. Venereol.* **26**, 953–963 (2012).
132. Norwood, O. T. Male pattern baldness: classification and incidence. *South. Med. J.* **68**, 1359–1365 (1975).
133. Hamilton, J. B. Patterned loss of hair in man; types and incidence. *Ann. N. Y. Acad. Sci.* **53**, 708–728 (1951).
134. Ludwig, E. Classification of the types of androgenetic alopecia (common baldness) occurring in the female sex. *Br. J. Dermatol.* **97**, 247–254 (1977).
135. Carmina, E. et al. Female pattern hair loss and androgen excess: a report from the multidisciplinary Androgen Excess and PCOS Committee. *J. Clin. Endocrinol. Metab.* **104**, 2875–2891 (2019).
136. Olsen, E. A. Female pattern hair loss. *J. Am. Acad. Dermatol.* **45**, S70–S80 (2001).
137. Gupta, M. & Mysore, V. Classifications of patterned hair loss: a review. *J. Cutan. Aesthet. Surg.* **9**, 3–12 (2016).
138. Kerkemeyer, K. L. et al. Female pattern hair loss in men: a distinct clinical variant of androgenetic alopecia. *J. Am. Acad. Dermatol.* **85**, 260–262 (2021).
139. Abbasi, A. & Avram, M. Retrograde androgenetic alopecia. *Dermatol. Surg.* **47**, 1521–1522 (2021).
140. Mortimer, P. S., Gummer, C., English, J. & Dawber, R. P. Acquired progressive kinking of hair. report of six cases and review of literature. *Arch. Dermatol.* **121**, 1031–1033 (1985).
141. Norwood, O. T. Whisker hair. *Arch. Dermatol.* **115**, 930–931 (1979).
142. Levy, L. L. & Emer, J. J. Female pattern alopecia: current perspectives. *Int. J. Womens Health* **5**, 541–556 (2013).
143. Lee, W. S. et al. A new classification of pattern hair loss that is universal for men and women: basic and specific (BASP) classification. *J. Am. Acad. Dermatol.* **57**, 37–46 (2007).
144. Olsen, E. A. & Whiting, D. A. Focal atrichia: a diagnostic clue in female pattern hair loss. *J. Am. Acad. Dermatol.* **80**, 1538–1543 e1531 (2019).
145. Miteva, M. & Tosti, A. Hair and scalp dermatoscopy. *J. Am. Acad. Dermatol.* **67**, 1040–1048 (2012).
This is a foundational study establishing diagnostic potential of trichoscopy, a non-invasive quantitative method for diagnosing AGA.
146. Herskovitz, I., de Sousa, I. C. & Tosti, A. Vellus hairs in the frontal scalp in early female pattern hair loss. *Int. J. Trichology* **5**, 118–120 (2013).
147. Dhurat, R. & Saraogi, P. Hair evaluation methods: merits and demerits. *Int. J. Trichology* **1**, 108–119 (2009).
148. Bienenfeld, A. et al. Androgens in women: androgen-mediated skin disease and patient evaluation. *J. Am. Acad. Dermatol.* **80**, 1497–1506 (2019).
149. Lee, A. T. & Zane, L. T. Dermatologic manifestations of polycystic ovary syndrome. *Am. J. Clin. Dermatol.* **8**, 201–219 (2007).
150. Khutsishvili, N. et al. Trichoscopy — a valuable tool for identifying conditions mimicking androgenetic alopecia. *Int. J. Dermatol.* **63**, 23–31 (2024).
151. Hordinsky, M. Scarring alopecia: diagnosis and new treatment options. *Dermatol. Clin.* **39**, 383–388 (2021).

152. Miteva, M. & Tosti, A. Dermoscopy guided scalp biopsy in cicatricial alopecia. *J. Eur. Acad. Dermatol. Venereol.* **27**, 1299–1303 (2013).
153. Miteva, M. & Tosti, A. Pathologic diagnosis of central centrifugal cicatricial alopecia on horizontal sections. *Am. J. Dermatopathol.* **36**, 859–864 (2014).
154. Quadrelli, F., Cedirian, S. & Piraccini, B. M. Trichoscopy of frontal fibrosing alopecia in Caucasians: a review. *Skin. Appendage Disord.* **10**, 439–442 (2024).
155. Svigos, K., Yin, L., Fried, L., Lo Sicco, K. & Shapiro, J. A practical approach to the diagnosis and management of classic lichen planopilaris. *Am. J. Clin. Dermatol.* **22**, 681–692 (2021).
156. Zinkernagel, M. S. & Trueb, R. M. Fibrosing alopecia in a pattern distribution: patterned lichen planopilaris or androgenetic alopecia with a lichenoid tissue reaction pattern? *Arch. Dermatol.* **136**, 205–211 (2000).
157. Griggs, J., Trueb, R. M., Gavazzoni Dias, M. F. R., Hordinsky, M. & Tosti, A. Fibrosing alopecia in a pattern distribution. *J. Am. Acad. Dermatol.* **85**, 1557–1564 (2021).
158. Freites-Martinez, A. et al. Endocrine therapy-induced alopecia in patients with breast cancer. *JAMA Dermatol.* **154**, 670–675 (2018).
159. Kang, J., Lee, J. W. & Kwon, O. Efficacy of low-dose oral minoxidil in the management of anticancer therapy-induced alopecia in patients with breast cancer: a retrospective cohort study. *J. Am. Acad. Dermatol.* **88**, 1170–1173 (2023).
160. Freites-Martinez, A. et al. Assessment of quality of life and treatment outcomes of patients with persistent postchemotherapy alopecia. *JAMA Dermatol.* **155**, 724–728 (2019).
161. Olsen, E. A., Bettencourt, M. S. & Cote, N. L. The presence of loose anagen hairs obtained by hair pull in the normal population. *J. Investig. Dermatol. Symp. Proc.* **4**, 258–260 (1999).
162. Cantatore-Francis, J. L. & Orlow, S. J. Practical guidelines for evaluation of loose anagen hair syndrome. *Arch. Dermatol.* **145**, 1123–1128 (2009).
163. Blume-Peytavi, U. et al. S1 guideline for diagnostic evaluation in androgenetic alopecia in men, women and adolescents. *Br. J. Dermatol.* **164**, 5–15 (2011).
164. Liu, L. P. et al. Factors associated with early-onset androgenetic alopecia: a scoping review. *PLoS ONE* **19**, e0299212 (2024).
165. Campese, V. M., Stein, D. & DeQuattro, V. Treatment of severe hypertension with minoxidil: advantages and limitations. *J. Clin. Pharmacol.* **19**, 231–241 (1979).
166. Gupta, A. K. & Charrette, A. Topical minoxidil: systematic review and meta-analysis of its efficacy in androgenetic alopecia. *Skinmed* **13**, 185–189 (2015).
167. Goren, A., Castano, J. A., McCoy, J., Bermudez, F. & Lotti, T. Novel enzymatic assay predicts minoxidil response in the treatment of androgenetic alopecia. *Dermatol. Ther.* **27**, 171–173 (2014).
168. Messenger, A. G. & Rundegren, J. Minoxidil: mechanisms of action on hair growth. *Br. J. Dermatol.* **150**, 186–194 (2004).
169. Shorter, K., Farjo, N. P., Picksley, S. M. & Randall, V. A. Human hair follicles contain two forms of ATP-sensitive potassium channels, only one of which is sensitive to minoxidil. *FASEB J.* **22**, 1725–1736 (2008).
This study established the mechanism of action of minoxidil in human hair follicles.
170. Ohko, K. et al. Skin and hair abnormalities of Cantu syndrome: a congenital hypertrichosis due to a genetic alteration mimicking the pharmacological effect of minoxidil. *J. Dermatol.* **47**, 306–310 (2020).
171. Jimenez-Cauhe, J. et al. Hair follicle sulfotransferase activity and effectiveness of oral minoxidil in androgenetic alopecia. *J. Cosmet. Dermatol.* **23**, 3767–3773 (2024).
172. Gupta, A. K., Talukder, M. & Shemer, A. Efficacy and safety of low-dose oral minoxidil in the management of androgenetic alopecia. *Expert. Opin. Pharmacother.* **25**, 139–147 (2024).
173. Peterson, R. E., Imperato-McGinley, J., Gautier, T. & Sturla, E. Male pseudohermaphroditism due to steroid 5-α-reductase deficiency. *Am. J. Med.* **62**, 170–191 (1977).
174. Kaufman, K. D. et al. Finasteride in the treatment of men with androgenetic alopecia. Finasteride Male Pattern Hair Loss Study Group. *J. Am. Acad. Dermatol.* **39**, 578–589 (1998).
A foundational study establishing clinical efficacy of finasteride for the treatment of AGA in men.
175. Perez-Mora, N., Velasco, C. & Bermudez, F. Oral finasteride presents with sexual-unrelated withdrawal in long-term treated androgenic alopecia in men. *Skinmed* **13**, 179–183 (2015).
176. Etzioni, R. D. et al. Long-term effects of finasteride on prostate specific antigen levels: results from the Prostate Cancer Prevention Trial. *J. Urol.* **174**, 877–881 (2005).
177. Marberger, M. J. Long-term effects of finasteride in patients with benign prostatic hyperplasia: a double-blind, placebo-controlled, multicenter study. PROWESS Study Group. *Urology* **51**, 677–686 (1998).
178. Ding, Y. et al. Dutasteride for the treatment of androgenetic alopecia: an updated review. *Dermatology* **240**, 833–843 (2024).
179. Choi, G. S. et al. Long-term effectiveness and safety of dutasteride versus finasteride in patients with male androgenic alopecia in South Korea: a multicentre chart review study. *Ann. Dermatol.* **34**, 349–359 (2022).
180. Gupta, A. K., Bamimore, M. A., Wang, T. & Talukder, M. The impact of monotherapies for male androgenetic alopecia: a network meta-analysis study. *J. Cosmet. Dermatol.* **23**, 2964–2972 (2024).
181. Trueb, R. M., Gavazzoni Dias, M. F. R. & Dutra Rezende, H. Suicidality and psychological adverse events in patients treated with finasteride. *Skin. Appendage Disord.* **7**, 524–526 (2021).
182. Ali, A. K., Heran, B. S. & Etminan, M. Persistent sexual dysfunction and suicidal ideation in young men treated with low-dose finasteride: a pharmacovigilance study. *Pharmacotherapy* **35**, 687–695 (2015).
183. Piraccini, B. M. et al. Efficacy and safety of topical finasteride spray solution for male androgenetic alopecia: a phase III, randomized, controlled clinical trial. *J. Eur. Acad. Dermatol. Venereol.* **36**, 286–294 (2022).
184. Rodriguez-Cuadrado, F. J., Pinto-Pulido, E. L. & Fernandez-Parrado, M. Mesotherapy with dutasteride for androgenetic alopecia: a concise review of the literature. *Eur. J. Dermatol.* **33**, 72 (2023).
185. Nohria, A., Desai, D., Paez-Garcia, M. S., Lo Sicco, K. I. & Shapiro, J. Outcomes of androgenetic alopecia treated with dutasteride mesotherapy: a case series. *JAAD Case Rep.* **54**, 53–58 (2024).
186. Ong, M. M., Avram, M., McMichael, A., Tosti, A. & Lipner, S. R. Antiandrogen therapy for the treatment of female pattern hair loss: a clinical review of current and emerging therapies. *J. Am. Acad. Dermatol.* **93**, 749–760 (2025).
187. Orentreich, N. Autografts in alopecias and other selected dermatological conditions. *Ann. N. Y. Acad. Sci.* **83**, 463–479 (1959).
188. Maletic, A., Dumic-Cule, I., Zic, R. & Milosevic, M. Impact of hair transplantation on quality of life. *Aesthetic Plast. Surg.* **48**, 1825–1830 (2024).
189. Stoneburner, J. et al. Contemporary management of alopecia: a systematic review and meta-analysis for surgeons. *Aesthetic Plast. Surg.* **44**, 97–113 (2020).
190. Liu, F. et al. The relationship between self-esteem and hair transplantation satisfaction in male androgenetic alopecia patients. *J. Cosmet. Dermatol.* **18**, 1441–1447 (2019).
191. Jimenez, F., Alam, M., Vogel, J. E. & Avram, M. Hair transplantation: basic overview. *J. Am. Acad. Dermatol.* **85**, 803–814 (2021).
192. Jimenez, F., Vogel, J. E. & Avram, M. CME article Part II. Hair transplantation: surgical technique. *J. Am. Acad. Dermatol.* **85**, 818–829 (2021).
193. Bernstein, R. M. & Rassman, W. R. Follicular transplantation. patient evaluation and surgical planning. *Dermatol. Surg.* **23**, 771–784 (1997).
194. Limmer, B. L. Elliptical donor stereoscopically assisted micrografting as an approach to further refinement in hair transplantation. *J. Dermatol. Surg. Oncol.* **20**, 789–793 (1994).
195. Rassman, W. R. et al. Follicular unit extraction: minimally invasive surgery for hair transplantation. *Dermatol. Surg.* **28**, 720–728 (2002).
This study established the minimally invasive hair transplantation procedure.
196. Gupta, A. K. et al. Innovations hair restoration surgeons have made to adapt to the challenges of follicular unit excision. *J. Cosmet. Dermatol.* **19**, 1883–1891 (2020).
197. Umar, S. et al. No-shave long hair follicular unit excision using an all-purpose skin-responsive device. *Clin. Cosmet. Investig. Dermatol.* **16**, 3681–3691 (2023).
198. Park, J. H., You, S. H., Kim, N. R. & Ho, Y. H. Long hair follicular unit excision: personal experience. *Int. J. Dermatol.* **60**, 1288–1295 (2021).
199. Trivellini, R., Perez-Meza, D., Renaud, H. J. & Gupta, A. K. Preview long hair follicular unit excision: an up-and-coming technique. *J. Cosmet. Dermatol.* **20**, 3422–3426 (2021).
200. Jimenez, F. & Ruifernandez, J. M. Distribution of human hair in follicular units. A mathematical model for estimating the donor size in follicular unit transplantation. *Dermatol. Surg.* **25**, 294–298 (1999).
201. Salanitri, S., Goncalves, A. J., Helene, A. Jr. & Lopes, F. H. Surgical complications in hair transplantation: a series of 533 procedures. *Aesthet. Surg. J.* **29**, 72–76 (2009).
202. Williams, K. L. Jr. & El-Maghraby, S. Complications with follicular unit excision. *Facial Plast. Surg.* **40**, 234–244 (2024).
203. Kaiser, M. A. et al. Platelet rich plasma combination therapies for treatment of androgenetic alopecia: a systematic review. *J. Cutan. Aesthet. Surg.* **16**, 169–177 (2023).
204. Lai, D., Zhou, S., Cheng, S., Liu, H. & Cui, Y. Laser therapy in the treatment of melasma: a systematic review and meta-analysis. *Lasers Med. Sci.* **37**, 2099–2110 (2022).
205. English, R. S. Jr., Ruiz, S. & DoAmaral, P. Microneedling and its use in hair loss disorders: a systematic review. *Dermatol. Ther.* **12**, 41–60 (2022).
206. Adil, A. & Godwin, M. The effectiveness of treatments for androgenetic alopecia: a systematic review and meta-analysis. *J. Am. Acad. Dermatol.* **77**, 136–141.e5 (2017).
207. Avci, P., Gupta, G. K., Clark, J., Wikonkal, N. & Hamblin, M. R. Low-level laser (light) therapy (LLLT) for treatment of hair loss. *Lasers Surg. Med.* **46**, 144–151 (2014).
208. Sheen, Y. S. et al. Visible red light enhances physiological anagen entry in vivo and has direct and indirect stimulative effects in vitro. *Lasers Surg. Med.* **47**, 50–59 (2015).
209. Mai-Yi Fan, S., Cheng, Y. P., Lee, M. Y., Lin, S. J. & Chiu, H. Y. Efficacy and safety of a low-level light therapy for androgenetic alopecia: a 24-week, randomized, double-blind, self-comparison, sham device-controlled trial. *Dermatol. Surg.* **44**, 1411–1420 (2018).
210. Zhang, Y., Su, J., Ma, K., Fu, X. & Zhang, C. Photobiomodulation therapy with different wavebands for hair loss: a systematic review and meta-analysis. *Dermatol. Surg.* **48**, 737–740 (2022).
211. Juhasz, M. L. W., Lo Sicco, K. & Shapiro, J. The utility of platelet-rich plasma for the treatment of alopecia. *J. Drugs Dermatol.* **19**, 736–741 (2020).
212. Stevens, J. & Khetarpal, S. Platelet-rich plasma for androgenetic alopecia: a review of the literature and proposed treatment protocol. *Int. J. Womens Dermatol.* **5**, 46–51 (2019).
213. Nouh, A. H., Abdelaal, A. M. & Fathy, A. E. S. Activated platelet rich plasma versus non-activated platelet rich plasma in the treatment of alopecia areata. *Skin. Appendage Disord.* **9**, 42–49 (2023).
214. Chuah, S. Y. et al. Efficacy of platelet-rich plasma in asians with androgenetic alopecia: a randomized controlled trial. *Indian. J. Dermatol. Venereol. Leprol.* **89**, 135–138 (2023).

215. Sasaki, G. H. The effects of lower vs higher cell number of platelet-rich plasma (PRP) on hair density and diameter in androgenetic alopecia (AGA): a randomized, double-blinded, placebo, parallel-group half-scalp IRB-approved study. *Aesthet. Surg. J.* **41**, NP1659–NP1672 (2021).
216. Shapiro, J., Ho, A., Sukhdeo, K., Yin, L. & Lo Sicco, K. Evaluation of platelet-rich plasma as a treatment for androgenetic alopecia: a randomized controlled trial. *J. Am. Acad. Dermatol.* **83**, 1298–1303 (2020).
217. Ocampo-Garza, S. S., Fabbrocini, G., Ocampo-Candiani, J., Cinelli, E. & Villani, A. Micro needling: a novel therapeutic approach for androgenetic alopecia, a review of literature. *Dermatol. Ther.* **33**, e14267 (2020).
218. Pei, D. et al. Efficacy and safety of combined microneedling therapy for androgenic alopecia: a systematic review and meta-analysis of randomized clinical trials. *J. Cosmet. Dermatol.* **23**, 1560–1572 (2024).
219. Abdi, P. et al. Efficacy and safety of combinational therapy using topical minoxidil and microneedling for the treatment of androgenetic alopecia: a systematic review and meta-analysis. *Arch. Dermatol. Res.* **315**, 2775–2785 (2023).
220. Jia, L., Xiong, J., Guo, R., Li, Y. & Jiang, H. A comprehensive review of microneedling as a potential treatment option for androgenetic alopecia. *Aesthetic Plast. Surg.* **46**, 2979–2994 (2022).
221. Vathananai, W. & Jimenez, F. What do we know about hair growth induced by wounding and its therapeutic applications? *Dermatol. Surg.* **49**, 995–1000 (2023).
222. Oak, A. S. W. & Cotsarrelis, G. Wound-induced hair neogenesis: a portal to the development of new theapies for hair loss and wound regeneration. *Cold Spring Harb. Perspect. Biol.* https://doi.org/10.1101/cshperspect.a041239 (2023).
223. Wu, Y. F. et al. Enhancing hair follicle regeneration by nonablative fractional laser: assessment of irradiation parameters and tissue response. *Lasers Surg. Med.* **47**, 331–341 (2015).
224. Choi, Y. M., Diehl, J. & Levins, P. C. Promising alternative clinical uses of prostaglandin F2α analogs: beyond the eyelashes. *J. Am. Acad. Dermatol.* **72**, 712–716 (2015).
225. Blume-Peytavi, U., Lonnfors, S., Hillmann, K. & Garcia Bartels, N. A randomized double-blind placebo-controlled pilot study to assess the efficacy of a 24-week topical treatment by latanoprost 0.1% on hair growth and pigmentation in healthy volunteers with androgenetic alopecia. *J. Am. Acad. Dermatol.* **66**, 794–800 (2012).
226. Melo, D. F. et al. Efficacy of botulinum toxin in male androgenetic alopecia: a triple-blind, randomized clinical trial. *J. Am. Acad. Dermatol.* **91**, 996–998 (2024).
227. Shon, U., Kim, M. H., Lee, D. Y., Kim, S. H. & Park, B. C. The effect of intradermal botulinum toxin on androgenetic alopecia and its possible mechanism. *J. Am. Acad. Dermatol.* **83**, 1838–1839 (2020).
228. Pan, L. & Li, C. Exosome therapy for androgenetic alopecia: balancing potential with standardization challenges. *Aesthetic Plast. Surg.* https://doi.org/10.1007/s00266-025-04981-y (2025).
229. Harada, K. et al. Efficacy of autologous dermal sheath cup cell transplantation in male and female pattern hair loss: a single-arm, multi-center, phase III equivalent clinical study. *J. Dermatol.* **50**, 1539–1549 (2023).
230. Rossi, A. et al. A preliminary study on topical cetirizine in the therapeutic management of androgenetic alopecia. *J. Dermatol. Treat.* **29**, 149–151 (2018).
231. Ong, M. M., Ricardo, J. W. & Lipner, S. R. Hair-raising costs: evaluating botulinum toxin treatment for androgenetic alopecia. *J. Am. Acad. Dermatol.* **92**, e25–e26 (2025).
232. Tsuboi, R. et al. Autologous cell-based therapy for male and female pattern hair loss using dermal sheath cup cells: a randomized placebo-controlled double-blinded dose-finding clinical study. *J. Am. Acad. Dermatol.* **83**, 109–116 (2020).
233. Huang, C. H., Fu, Y. & Chi, C. C. Health-related quality of life, depression, and self-esteem in patients with androgenetic alopecia: a systematic review and meta-analysis. *JAMA Dermatol.* **157**, 963–970 (2021).
234. Cash, T. F. The psychology of hair loss and its implications for patient care. *Clin. Dermatol.* **19**, 161–166 (2001).
This paper established the effect of AGA on quality of life.
235. Frith, H. & Jankowski, G. S. Psychosocial impact of androgenetic alopecia on men: a systematic review and meta-analysis. *Psychol. Health Med.* **29**, 822–842 (2024).
236. Davis, D. S. & Callender, V. D. Review of quality of life studies in women with alopecia. *Int. J. Womens Dermatol.* **4**, 18–22 (2018).
237. Elsaie, L. T. et al. Cross sectional quality of life assessment in patients with androgenetic alopecia. *Dermatol. Ther.* **33**, e13799 (2020).
238. Zhuang, X. S., Zheng, Y. Y., Xu, J. J. & Fan, W. X. Quality of life in women with female pattern hair loss and the impact of topical minoxidil treatment on quality of life in these patients. *Exp. Ther. Med.* **6**, 542–546 (2013).
239. Vastarella, M. et al. Efficacy and safety of oral minoxidil in female androgenetic alopecia. *Dermatol. Ther.* **33**, e14234 (2020).
240. Yamazaki, M. et al. Oral finasteride improved the quality of life of androgenetic alopecia patients. *J. Dermatol.* **38**, 773–777 (2011).
241. Nilforoushzadeh, M. A., Golparvaran, M. & Yekaninejad, M. S. Assessment of quality of life and self-esteem in male patients with androgenetic alopecia before and after hair transplantation. *J. Cosmet. Dermatol.* **22**, 2283–2287 (2023).
242. Pappalardo, A., Kim, J. Y., Abaci, H. E. & Christiano, A. M. Restoration of hair follicle inductive properties by depletion of senescent cells. *Aging Cell* **24**, e14353 (2025).
243. Uchiyama, M. Primary cicatricial alopecia: recent advances in evaluation and diagnosis based on trichoscopic and histopathological observation, including overlapping and specific features. *J. Dermatol.* **49**, 37–54 (2022).
244. Bao, A. et al. Low-dose metformin and profibrotic signature in central centrifugal cicatricial alopecia. *JAMA Dermatol.* **160**, 1211–1219 (2024).
245. Kim, M. J. et al. Minoxidil-loaded hyaluronic acid dissolving microneedles to alleviate hair loss in an alopecia animal model. *Acta Biomater.* **143**, 189–202 (2022).
246. Kaiser, M., Abdin, R., Gaumond, S. I., Issa, N. T. & Jimenez, J. J. Treatment of androgenetic alopecia: current guidance and unmet needs. *Clin. Cosmet. Investig. Dermatol.* **16**, 1387–1406 (2023).
247. Lee, J. et al. Hair-bearing human skin generated entirely from pluripotent stem cells. *Nature* **582**, 399–404 (2020).
248. Abaci, H. E. et al. Tissue engineering of human hair follicles using a biomimetic developmental approach. *Nat. Commun.* **9**, 5301 (2018).
249. Motter Catarino, C., Cigaran Schuck, D., Dechiario, L. & Karande, P. Incorporation of hair follicles in 3D bioprinted models of human skin. *Sci. Adv.* **9**, eadg0297 (2023).
250. Wu, X., Scott, L. Jr., Washenik, K. & Stenn, K. Full-thickness skin with mature hair follicles generated from tissue culture expanded human cells. *Tissue Eng. Part. A* **20**, 3314–3321 (2014).
251. Higgins, C. A., Chen, J. C., Cerise, J. E., Jahoda, C. A. & Christiano, A. M. Microenvironmental reprogramming by three-dimensional culture enables dermal papilla cells to induce de novo human hair-follicle growth. *Proc. Natl Acad. Sci. USA* **110**, 19679–19688 (2013).
252. Jeong, S., Na, Y., Nam, H. M. & Sung, G. Y. Skin-on-a-chip strategies for human hair follicle regeneration. *Exp. Dermatol.* **32**, 13–23 (2023).
253. Nguyen, D. D. et al. Investigation of suicidality and psychological adverse events in patients treated with finasteride. *JAMA Dermatol.* **157**, 35–42 (2021).
254. Gubelin Harcha, W. et al. A randomized, active- and placebo-controlled study of the efficacy and safety of different doses of dutasteride versus placebo and finasteride in the treatment of male subjects with androgenetic alopecia. *J. Am. Acad. Dermatol.* **70**, 489–498 e483 (2014).
255. Olsen, E. A. et al. Summation and recommendations for the safe and effective use of topical and oral minoxidil. *J. Am. Acad. Dermatol.* **93**, 457–465 (2025).
256. Ntshingila, S., Oputu, O., Arowolo, A. T. & Khumalo, N. P. Androgenetic alopecia: an update. *JAAD Int.* **13**, 150–158 (2023).

Acknowledgements

This work was supported in part by grants from W.M. Keck Foundation (WMKF-5634988 to M.V.P.), Chan Zuckerberg Initiative (AN-0000000062 to M.V.P.), NIH (R01-AR079150 and P30-AR075047 to M.V.P.), L'Oreal USA (228736/C250233 to M.V.P.), AbbVie Inc. (00306355.0 to M.V.P.) and clinical fellowship from a CIRM training grant (EDUC4-12822 to Y.L.).

Author contributions

Introduction (M.V.P.); Epidemiology (C.A., O.K., Y.L. and M.V.P.); Mechanisms/pathophysiology (Y.L., S.-J.L., S.H.-H. and M.V.P.); Diagnosis, screening and prevention (A.T., S.H.-H., Y.L. and M.V.P.); Management (E.C.E.W., F.J., Y.L. and M.V.P.); Quality of life (C.A., F.J. and M.V.P.); Outlook (Y.L., C.A., S.H.-H., E.C.E.W., S.-J.L. and M.V.P.).

Competing interests

M.V.P. and Y.L. are inventors on patent applications related to hair loss treatment filed by the University of California, Irvine. M.V.P. is co-founder and Chief Scientific Officer at the Amplifica Holdings Group, Inc., and has received consultation fees from Oddity Labs and L'Oréal. A.T. has received consultation fees from DS Laboratories, Almirall, Thirty Madison, Eli Lilly and Company, Pfizer, Myovant Sciences, Bristol Myers Squibb, Ortho Dermatologics and Sun Pharmaceutical. C.A. has received consultation fees from Eli Lilly and Company, Pfizer, Olaplex and Myovant Sciences; has authored an UpToDate section on central centrifugal cicatricial alopecia; and directs the Ethnic Skin Program at Johns Hopkins University, funded by an educational grant from Janssen. S.H.-H. has received salary payments from Life & Brain GmbH. S.-J.L. has received clinical trial funds from Eli Lilly and Company. O.K. has received consultation fees from Eli Lilly and Company and has received clinical study funds from Eli Lilly and Company, Pfizer and AbbVie. E.C.E.W. and F.J. declare no competing interests.

Informed consent

The authors affirm that human research participants provided written informed consent for publication of the images in Figs. 4, 5, 6 and 7.

Additional information

Peer review information *Nature Reviews Disease Primers* thanks P. Suchonwanit, M. Talukder, R. Trüeb, R. Dhurat and the other, anonymous, reviewer(s) for their contribution to the peer review of this work.

Publisher's note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Springer Nature or its licensor (e.g. a society or other partner) holds exclusive rights to this article under a publishing agreement with the author(s) or other rightsholder(s); author self-archiving of the accepted manuscript version of this article is solely governed by the terms of such publishing agreement and applicable law.

© Springer Nature Limited 2025

[1]Department of Developmental and Cell Biology, University of California, Irvine, Irvine, CA, USA. [2]Sue and Bill Gross Stem Cell Research Center, University of California, Irvine, Irvine, CA, USA. [3]Center for Complex Biological Systems, University of California, Irvine, Irvine, CA, USA. [4]Dr. Phillip Frost Department of Dermatology and Cutaneous Surgery, University of Miami Miller School of Medicine, Miami, FL, USA. [5]National Skin Centre, Singapore, Singapore. [6]Skin Research Institute of Singapore, Singapore, Singapore. [7]Institute of Human Genetics, School of Medicine & University Hospital Bonn, University of Bonn, Bonn, Germany. [8]Department of Dermatology, Johns Hopkins School of Medicine, Baltimore, MD, USA. [9]Mediteknia Skin & Hair Laboratory, Las Palmas de Gran Canaria, Spain. [10]Facultad de Ciencias de La Salud, Universidad Fernando Pessoa Canarias, Las Palmas de Gran Canaria, Spain. [11]Clinica CDI/Ruber Internacional, Madrid, Spain. [12]Department of Biomedical Engineering, College of Medicine and College of Engineering, National Taiwan University, Taipei, Taiwan. [13]Department of Medical Research and Department of Dermatology, National Taiwan University Hospital, Taipei, Taiwan. [14]Department of Dermatology, College of Medicine, National Taiwan University, Taipei, Taiwan. [15]Research Center for Developmental Biology and Regenerative Medicine, National Taiwan University, Taipei, Taiwan. [16]Genomics Research Center, Academia Sinica, Taipei, Taiwan. [17]Department of Dermatology, College of Medicine, Seoul National University, Seoul, Korea. [18]Genomic Medicine Institute, Seoul National University, Seoul, Korea. [19]Laboratory of Cutaneous Aging and Hair Research, Clinical Research Institute, Seoul National University Hospital, Seoul, Korea. [20]Institute of Human Environment Interface Biology, College of Medicine, Seoul National University, Seoul, Korea.