

# Post Graduate Excellence Program on

# ALOPECIA

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Course Code: S.PPDERM16



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# Program Information

## Need assessment

Alopecia or hair loss is a commonly encountered problem worldwide and a cause of significant concern, both for the affected individuals and their family. Several causes of alopecia have been identified; most of these causes are grouped under cicatricial and non-cicatricial alopecia. Alopecia can be due to underlying medical problems. Several diagnostic approaches for alopecia are currently available including trichoscopy and scalp biopsies. Diagnosing the cause of alopecia and treating it to patient's satisfaction can be challenging. It is essential to be familiar with the recommended diagnostic and management approach for alopecia to obtain optimal patient outcomes. This Post Graduate Excellence Program attempts to highlight the current updates related to diagnosis and treatment of different forms of alopecia in dermatological practice.

## Learning objectives

1. To familiarize and offer concentrated exposure to all the various forms of scarring and non-scarring alopecia
2. To update on its currently recommended diagnostic and treatment approaches

## Target participants

Dermatologists

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Dr Goldberg has nothing to disclose in regards to commercial support

## Method of participation in the program

- Study all parts of the educational activity
- Submit the posttest questions with answers, evaluation and request for certificate of participation forms

- A certificate of participation will be issued by Boston University School of Medicine upon completing the evaluation and the posttest with a score of 60% or better.

## Program activity

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## SECTION 1

# Alopecia – Brief introduction, psychological impact and evaluation methods

### ALOPECIA IN CURRENT CLINICAL PRACTICE

Scalp hair is intrinsic to individuals' self-identity and contributes immensely to the overall general appearance.<sup>1</sup> Loss of hair or alopecia is a commonly encountered problem in both men and women worldwide.<sup>2</sup> Several causes of alopecia are known, which include genetic predisposition, diet, trauma, infections, systemic illnesses, drugs, stress, autoimmunity and structural hair defects. Alopecia is categorized into non-cicatricial (non-scarring) and cicatricial (scarring) alopecia (Table 1). Non-scarring alopecia is commonly encountered in dermatological practice and includes androgenetic alopecia, alopecia areata, telogen effluvium, tinea capitis, traction alopecia and trichotillomania. These disorders are associated with non-permanent hair loss and there is potential for hair re-growth after adequate treatment. In contrast, scarring alopecia is rarer and invariably associated with permanent hair loss.<sup>3</sup>

### PSYCHOLOGICAL IMPACT OF ALOPECIA

Although not life-threatening, hair loss, whether patchy or diffuse, significantly affects a person's self-esteem and provokes stress. The psychosocial impact of hair loss on the affected individuals is considerable.<sup>1,2</sup> There is good evidence to show that alopecia is associated with high levels of depression and anxiety. Patients with alopecia have high risk for developing depressive episodes, anxiety disorders, social phobia, or paranoid disorders.<sup>2</sup> This psychological stress has a significant negative impact on the quality of life of affected individuals and results in secondary morbidity. Stress by itself is also a known cause of alopecia. When dealing with patients with hair loss, the primary underlying disorder needs to be satisfactorily managed; however it also appears important to include stress-coping mechanisms in the treatment strategy and therapeutically manage stress for obtaining optimal treatment outcomes.<sup>4</sup>

### EVALUATION APPROACH FOR ALOPECIA IN DERMATOLOGICAL PRACTICE

In patients with alopecia, the significance of a detailed history and meticulous examination of the hair and the scalp cannot be overemphasized. In the patient history, list of medications or any significant systemic disorder (which can be associated

with hair loss) should be enquired. Family history of alopecia, particularly in the first-degree relatives, should be asked for.<sup>3</sup> Patients can be asked to keep a record of daily hair count (by collecting hair lost daily in a bag). A 7-day record can be assessed. Daily hair count can inform the dermatologist if the hair loss is physiological or pathological (normally up to 100 hairs are lost per day). If more than 100 hairs are being lost daily, they should be examined under the microscope for hair shaft and bulb abnormalities.<sup>5</sup>

Scalp examination in a patient with alopecia should include observation for signs of scarring (absence of visible follicular ostia), inflammation, scaling and erythema. The area of the scalp predominantly affected, distribution, length, shape, and density of hairs should also be observed. Furthermore, the integrity of hairs should be examined.<sup>3</sup> Several simple bedside tests can be helpful. The structure and integrity of hair, particularly of the outer cuticle, can be assessed by holding a few hairs between the thumb and index finger of one hand, and passing the thumb and index

**Table 1. Important causes of non-cicatricial (non-scarring) and cicatricial (scarring) alopecia**

#### Non-cicatricial

- Androgenetic alopecia
- Alopecia areata
- Telogen effluvium
- Tinea capitis
- Traction alopecia
- Trichotillomania

#### Cicatricial alopecia

##### Primary

- Primary lymphocytic type (such as lichen planopilaris, central centrifugal cicatricial alopecia)
- Primary neutrophilic type (such as folliculitis decalvans, dissecting cellulitis)
- Primary mixed type (such as acne keloidalis, erosive pustular dermatosis)

##### Secondary

- Severe fungal, bacterial, viral infections
- Burns

**Based on information from:** Shapiro J, Wiseman M, Lui H. Practical management of hair loss. *Can Fam Physician*. 2000 Jul; 46: 1469-1477.

finger of the other hand down the hair towards the root. If the hair resists this movement and ruckles up, the outer cuticle is possibly damaged. The hair pull test involves gently pulling few hairs from the scalp after holding them between the thumb and index finger; if more than 6 hairs (10% of the total pulled hairs) can be extracted from the scalp, the test is positive.<sup>6</sup> A positive hair pull of telogen hair shafts at multiple locations on the scalp indicates a telogen effluvium; a positive pull of telogen hair shafts limited to the crown can be seen in androgenetic alopecia. Another, more labor intensive way of distinguishing a telogen effluvium from androgenetic alopecia is the Wash test or Rebora method. This is a non-invasive technique whereby hair unwashed for 5 days is washed and the shed hairs collected, divided according to length, and counted.<sup>7</sup>

Trichogram is a minimally-invasive technique in which hair cycle-specific morphological characteristics of hair roots is evaluated. For this evaluation, hairs are plucked from a specified site on the scalp fifth day after the last shampoo. About 60-80 hairs are grasped with a hemostat covered with rubber and plucked, twisting and lifting the hair shafts rapidly in the direction of emergence from the scalp. The hair roots are placed on a glass slide and a mounting medium added, before arranging them side by side. These are then evaluated. Anagen hair bulbs are distinguished from telogen hair bulbs and the anagen to telogen ratio calculated. The anagen hair bulbs are darkly pigmented with a 'hockey-stick' appearance; telogen hair bulbs appear less pigmented, and have a club-shaped hair bulb (Figure 1).<sup>5</sup> Trichoscan (a non-invasive method) is a modification of the classical trichogram which combines epiluminescence microscopy with automatic digital image analysis for the measurement of human hair. It involves comparing two close photographs of a well-defined area of the scalp, the second photography taken a few days after the first. Several parameters including hair density, terminal hair density, vellus hair density, anagen hair count, telogen hair count, and mean hair thickness are calculated using special software. It can contribute to the diagnosis of androgenetic alopecia or other causes of diffuse hair loss.<sup>8,9</sup> Trichoscopy (dermoscopy) is another useful non-invasive technique for evaluating patients with hair loss. It allows magnified visualization of the hair and scalp either using a dermatoscope or a videodermatoscope. Videodermoscopy provides more rapid, and higher-resolution viewing compared to conventional dermoscopy; the images can be captured and stored for later use.<sup>5</sup> Note that in clinical practice, the forceful hair pull (trichogram) is seldom done and trichoscan is not readily available.

Most of the above mentioned non-invasive and semi-invasive techniques for hair evaluation are deemed useful for making a diagnosis of alopecia, particularly non-scarring alopecia. Scalp biopsy is sometimes required, especially if scarring is suspected. A scalp biopsy is the "gold standard" test for detecting underlying cause of alopecia. It is useful

**Figure 1. Trichogram - Appearance of anagen and telogen hairs**



Telogen hair showing the hypopigmented, club-shaped cornified bulb with remnants of the cornified epithelial sac

Anagen hair showing the pigmented bulb with 'hockey-stick' appearance

**Source:** Dhurat R, Saraogi P. Hair Evaluation Methods: Merits and Demerits. *Int J Trichology*. 2009 Jul-Dec; 1(2): 108–119.

for diagnosing all cases of scarring and some cases of non-scarring alopecia (which remain undiagnosed despite the use of non-invasive and/or semi-invasive techniques). A 4-mm punch biopsy is taken from the scalp under local anesthesia. In patients with presumed scarring alopecia, biopsy should ideally be taken from an area of inflammation; in those with non-scarring alopecia, biopsy taken from the center of the lesion should be appropriate.<sup>10</sup> Finally blood tests are helpful to exclude secondary causes of alopecia. In women with diffuse alopecia, thyroid function and iron studies need to be evaluated. In women with androgenetic alopecia having virilizing signs such as hirsutism, acne, or irregular menses, evaluation of free testosterone, androstenedione, and dehydroepiandrosterone (DHEA) is advisable.<sup>3</sup>

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## SECTION 2

# Understanding non-cicatricial alopecias and their evaluation approach

## Androgenetic alopecia

### OVERVIEW

Androgenetic alopecia (male and female pattern hair loss), a non-scarring type of alopecia, is the most common form of hair loss encountered by dermatologists in their clinical practice. It is characterized by progressive hair loss in a distinct pattern on the scalp, with gradual reduction in both thickness and length of the hair. Androgenetic alopecia is seen in both men and women. According to available estimates, about 80% men and 50% women develop androgenetic alopecia during their life.<sup>1</sup> Genetic susceptibility can determine the age of onset of hair loss. Thinning and loss of hairs in androgenetic alopecia can start early (in puberty); noticeable hair loss is seen in 30% of men by 30 years and 50% of men by 50 years of age.<sup>2</sup> There is a characteristic pattern of hair loss in men and women; men have gradually receding hair line and loss of hair from the mid-frontal part of the scalp. Women have thinning and loss of hair from the mid-frontal part of the scalp. The central part of the scalp is commonly affected in both genders.<sup>3</sup> Androgens and their effect on follicular miniaturization, alteration in hair cycle dynamics, along with genetic predisposition appear to be the principal underlying causes of androgenetic alopecia.<sup>2,4</sup> Follicular miniaturization is a characteristic feature of androgenetic alopecia although it is seen in alopecia areata as well. However, unlike alopecia areata in which there is potential for hair re-growth, hair loss in androgenetic alopecia is invariably progressive and at best only partially reversible.<sup>5</sup> As with other types of hair loss, androgenetic alopecia has a negative impact on self-esteem and adversely affects the quality of life of the affected individuals.<sup>3</sup> Diagnosis can be suspected based on the characteristic pattern of hair loss and findings of the trichogram and dermoscopy (trichoscopy). A biopsy can be helpful. Several treatment options for androgenetic alopecia are available; topical minoxidil (men and women) and oral finasteride (men) remain the predominantly successful therapeutic agents; hair transplantation may be opted in patients with extensive hair loss who remain refractory to treatment.<sup>4</sup>

### PATHOGENESIS

There is a pronounced influence of genetic factors on the development of androgenetic alopecia, although the exact mechanism is not completely understood. Androgens are the main regulator of human hair growth; thinning and subsequent loss of hair in androgenetic alopecia is mediated by the effect of dihydrotestosterone (DHT) on the hair follicles. It has now been proven beyond doubt that genetic factors determine the susceptibility of follicular response to local androgens. In individuals with a strong genetic predisposition, hair loss starts early while in those with a weak predisposition, onset of hair loss may not be seen until the sixth decade of life.<sup>6</sup> Although recent research has unearthed some new susceptibility genes on chromosomes 3q26 and 20p11 in androgenetic alopecia which suggest that non-androgen-dependent pathways may also be involved in the disease pathogenesis, the effect of DHT on the androgen-sensitive hair follicles is conceivably the primary cause of hair thinning and hair loss in these patients.<sup>7</sup>

Our understanding of the intrafollicular androgen metabolism in the balding scalp of patients with androgenetic alopecia has improved considerably over the last few years. The dermal papilla has an important role to play in the hair growth.<sup>2</sup> Intracellular conversion of testosterone to its more potent metabolite, DHT occurs in the dermal papilla. The potent DHT subsequently activates the pertinent follicular androgen receptors. There is good evidence in support for excess intrafollicular DHT activity in patients with androgenetic alopecia which may either be due to its increased production, reduced degradation, polymorphism of the androgen receptor genes on the hair follicles or due to increase in the number of androgen receptors.<sup>6</sup> It is noteworthy that serum concentration of DHT is not necessarily increased in individuals with androgenetic alopecia. These observations seem to attest the fact that androgen-sensitivity of the hair follicles rather than the systemic DHT concentration is the primary cause of hair loss in androgenetic alopecia.<sup>8</sup> Androgens

seem to have contrasting effects on hair growth depending on the site of the body. While androgens stimulate hair growth in the beard, axillary, and pubic areas, they suppress scalp hair growth in genetically-predisposed individuals.<sup>6</sup> Their inhibitory effect on the dermal papilla results in reduction in the follicular size (follicular miniaturization) which causes thinning of hair; androgens also reduce pigmentation in the scalp hair.<sup>2,6</sup> In the early stages of androgenetic alopecia, selected hair follicles in a single follicular unit undergo DHT-induced miniaturization. Miniaturization of secondary follicles precedes that of primary follicles in a follicular unit. Therefore, in the early stages, visible thinning of the hair in the affected areas can be seen which gradually progresses to complete baldness as the primary follicles in each follicular unit also undergo miniaturization.<sup>9</sup>

Changes in hair cycle dynamics are also seen in androgenetic alopecia, an effect which may also be androgen-mediated. In patients with androgenetic alopecia there is progressive shortening of the anagen phase of each hair cycle (possibly under the influence of DHT) while the telogen phase remains either constant or shortens.<sup>6</sup> Shortening of the anagen phase of each hair cycle, constant or shortened telogen phase along with longer latency period between the telogen shedding and anagen regrowth results in progressive shortening of hairs. Progressive reduction in the hair size, along with thinning and depigmentation of scalp hairs occurs in most patients with androgenetic alopecia, although at a variable rate, and ultimately results in a bald scalp.<sup>2,6</sup>

Follicular miniaturization is a feature of alopecia areata as well. An intriguing question is why follicular miniaturization in androgenetic alopecia is irreversible or only partially reversible compared to that in alopecia areata where it is almost completely reversible. Current evidence shows that “irreversibility or partial reversibility” of hair loss in androgenetic alopecia may be related to degeneration of the arrector pili muscles. It has been shown that arrector pili muscles undergo degeneration and infiltration with fatty tissue in androgenetic alopecia. This loss of structural integrity of the arrector pili muscles results in its detachment from the primary follicle.<sup>10</sup> Recent studies have shown that preservation of the arrector pili muscle may be associated with reversible hair loss while loss of attachment between the arrector pili muscle and the hair follicle may be associated with irreversible or partially reversible hair loss.<sup>9</sup>

Some researchers have recently proposed a “follicular microinflammation” concept to explain hair loss in patients with androgenetic alopecia. According to them, perifollicular microinflammation is an essential feature of androgenetic alopecia and may have a contributory role in hair loss.<sup>6</sup> This hypothesis stems from observation of perifollicular infiltration with activated T-cells around the follicular infundibulum in scalp biopsies of patients with androgenetic alopecia.<sup>11</sup> It appears plausible that follicular inflammation induces deposition of collagen and resultant thickening of the perifollicular sheath. This promotes perifollicular fibrosis, and

sometimes destruction of the affected follicles in advanced cases.<sup>12</sup> The concept, however, remains debatable.

## CO-ASSOCIATED DISEASES

Androgenetic alopecia has been linked to cardiovascular diseases. This association is not new and has been known to researchers for more than four decades.<sup>13</sup> Several recent studies have shown that subjects with androgenetic alopecia are at an increased risk of coronary artery disease (CAD).<sup>14</sup> The frequently reported concurrence of androgenetic alopecia with prominent cardiovascular risk factors such as hypertension, dyslipidemia, insulin resistance and metabolic syndrome may account for its high cardiovascular risk. Androgenetic alopecia has a strong association with hypertension. Hypertension is known to occur more frequently in men and women with androgenetic alopecia than in those without.<sup>15,16</sup> Although the precise underlying cause remains unknown, genesis of hypertension in androgenetic alopecia may be secondary to smooth muscle proliferation effects of androgens in the blood vessels and their role in activation of the mineralocorticoid receptors. In addition to hypertension, dyslipidemia – particularly high triglyceride and low HDL cholesterol concentrations – has been frequently reported in patients with androgenetic alopecia. Insulin resistance also is known in many patients with androgenetic alopecia, particularly in those with an early-onset disease, and increases their risk of developing metabolic syndrome.<sup>17</sup> These observations may necessitate a thorough cardiovascular, blood pressure and lipid evaluation in patients with androgenetic alopecia, at least in those with early-onset and severe forms of the disease, to mitigate their supposedly high cardiovascular risk.

Some studies have linked androgenetic alopecia in men with the risk of benign prostatic hyperplasia (BPH), although the association remains debatable. A study<sup>18</sup> which evaluated subjects with early-onset androgenetic alopecia and compared them to healthy controls showed a higher mean prostate volume, a higher International Prostate Symptom Score (IPSS), a higher prostate-specific antigen (PSA) concentration, and a significantly lower maximum urinary flow rate in patients with androgenetic alopecia compared to those without. In fact, some investigators believe that early-onset androgenetic alopecia may be an early marker of BPH. Another study<sup>19</sup> suggested a possible association between vertex androgenetic alopecia in men and increased risk of early-onset prostate cancer. The precise underlying mechanism remains to be established. There are also reports of possible association between androgenetic alopecia in women and risk of polycystic ovarian syndrome.<sup>20</sup>

## CLINICAL FEATURES

Androgenetic alopecia is characterized by distinct pattern of hair loss in men and women which is easily recognizable and facilitates diagnosis. Male pattern baldness is associated with variable degree of recession of the bitemporal hair line. Most affected individuals initially show receding temporal hair

**Figure 1. Androgenetic alopecia in a woman with thinning of hairs seen along the part line**



Courtesy: Dr Lynne Goldberg, Boston University School of Medicine

line on both sides, which is followed by thinning of hair over the vertex. As hair loss continues, a complete bald patch over the vertex ensues which enlarges circumferentially and joins the receding bitemporal hair line. Thinning and subsequent loss of hairs may start early, usually at puberty, in genetically-susceptible individuals; while it may be delayed in those who are less susceptible.<sup>2</sup> The Norwood-Hamilton scale is commonly used to assess the severity of male pattern baldness. Female pattern hair loss presents as slow midfrontal hair thinning which may or may not be associated with increased shedding of the hairs.<sup>20</sup> In some women, initially the dividing line in the middle of the hair becomes prominent (line sign); Figure 1. The ponytail holder frequently becomes loose or the women need to pull the hair more often through the use of rubber band.<sup>21</sup>

Three different patterns of hair loss are typically described in women with androgenetic alopecia:<sup>20,21</sup>

1. Diffuse thinning of the crown (biparietal and vertex region) with preservation of the frontal hairline (Ludwig's type)
2. Thinning of the crown and vertex with frontal accentuation, also known as the "Christmas tree pattern" (described by Olsen)
3. Thinning of the hair in the latero-frontal region of the scalp and the vertex; associated with bitemporal recession, similar to male pattern baldness (Hamilton type).

Women with female pattern hair loss may also report features of hyperandrogenism such as irregular menses, acne, infertility, and hirsutism.<sup>20</sup> Also, some patients with androgenetic alopecia have burning, pain, discomfort, and/or

or paresthesia of the scalp, often referred to as trichodynia. Patients with androgenetic alopecia report trichodynia less frequently than those with telogen effluvium.<sup>22</sup>

## DIAGNOSIS

The diagnosis of androgenetic alopecia is usually made based on a detailed history and clinical evaluation of the scalp; the pattern of hair loss is characteristic, with initial thinning and subsequent loss of hair seen primarily over the bitemporal area and the vertex in men and the crown in women. The hair pull test in the affected region of the scalp is negative, except in the active phase of the disease. A positive pull test in most regions of the scalp should raise suspicion of telogen effluvium.<sup>4</sup>

Scalp trichoscopy is being routinely used to diagnose androgenetic alopecia. It confirms the diagnosis and differentiates androgenetic alopecia from other diseases with similar manifestations. Scalp trichoscopy is also used for staging the disease severity and evaluating response to treatment.<sup>1</sup> In early stages of the disease, trichoscopy shows evidence of hair shaft diameter diversity of more than 20% and peripilar sign, seen as a subtle brown halo, which reflects perifollicular inflammation. "Yellow dots" can also be seen.<sup>22</sup> The peripilar sign is often considered the commonest sign on scalp trichoscopy in Asians with androgenetic alopecia.<sup>4</sup> Additionally, trichoscopy shows hair follicles with single hair unlike normal unaffected follicles which bear up to 4 terminal hairs. Pearly "white dots", suggestive of hypertrophied sebaceous glands, may be seen in long standing cases of androgenetic alopecia.<sup>22</sup>

Rakowska et al<sup>23</sup> proposed a criteria for differentiating female pattern hair loss from chronic telogen effluvium based on trichoscopy criteria. Major criteria included ratio of (1) more than four yellow dots in four images (70-fold magnification) in the frontal area, (2) lower average hair thickness in the frontal area compared to the occiput and (3) more than 10% of thin hairs (below 0.03 mm) in the frontal area. Minor criteria encompass increased frontal to occipital ratio of (1) single-hair pilosebaceous units, (2) vellus hairs and (3) perifollicular discoloration. Fulfillment of two major criteria or one major and two minor criteria allowed a diagnosis of female pattern baldness based on trichoscopy with 98% specificity.

Scalp biopsy is not routinely required and is only performed in cases with difficulty in diagnosis. Laboratory evaluation in women with female pattern hair loss to rule out hormonal dysfunction, particularly polycystic ovarian syndrome, may be done when deemed suitable.<sup>4</sup>

# Alopecia areata

## OVERVIEW

Alopecia areata is another common non-scarring form of alopecia. It affects 1–2% of men and women; and is characterized by either patchy or diffuse hair loss involving the scalp and/or other parts of the body.<sup>1</sup> Alopecia areata has an unpredictable course. While a subset of the affected patients recover spontaneously, in others the disorder pursues a more chronic and fluctuating course inundated with remissions and relapses.<sup>2</sup> In the latter subset of patients, recurrent episodes of hair loss result in multiple well-demarcated bald patches on the scalp which may coalesce into large lesions, and in some cases may involve the entire scalp.<sup>3</sup> Spontaneous resolution followed by regrowth of hair in the bald patch is seen in about 50-80% cases of alopecia areata. In approximately 5% cases, multiple localized bald patches form which progress to involve the entire scalp; loss of hair on the entire body is seen in 1% cases.<sup>1,3</sup>

Depending on the severity of hair loss several clinical forms of alopecia areata have been described; important clinical forms include patchy hair loss (alopecia areata focalis or commonly called patchy alopecia areata); loss of hair on the entire scalp including the eyebrows and eyelashes (alopecia areata totalis); loss of all or nearly all hair from the body (alopecia areata universalis). An exhaustive list of different clinical forms of alopecia areata is shown in Table 1.<sup>1</sup> Considerable work done in this field has improved our understanding of the pathogenesis of alopecia areata although the precise mechanism still remains uncertain. There is plenty of support for an autoimmune basis of the disease. It has been suggested that alopecia areata develops due to an autoimmune attack directed against the hair follicles in genetically-susceptible individuals, with several environmental factors acting as triggers to the disease development and progression.<sup>3</sup> Alopecia areata has a significant emotional impact and similar to androgenetic alopecia, adversely affects the quality of life.<sup>2</sup> Diagnosis is based on clinical examination, the pull test and findings on trichoscopy. Scalp biopsy is sometimes required, especially when the alopecia is diffuse. Several treatment options for alopecia areata are available; however its management is often frustrating both for the dermatologist and the patient because of the unpredictable course of the disease and mixed response to treatment.<sup>1,4</sup>

## PATHOGENESIS

The pathogenesis of alopecia areata is multifactorial and complex. Despite extensive research done over the past few decades investigators have not been able to unravel intricacies involved in the mechanism of its development. However, there is compelling evidence to show that an aberrant autoimmune T-cell response directed against the hair follicles, possibly in genetically-susceptible individuals, accounts for variable

**Table 1. Different clinical forms of alopecia areata**

Clinical form	Manifestations
Alopecia areata focalis	Patches of hair loss on the scalp or other body parts
Alopecia areata totalis	Loss of all hair from the scalp (including eyebrows and eyelashes)
Alopecia areata universalis	Loss of all or almost all hair from the body
Alopecia areata diffusa (alopecia areata reticularis)	Diffuse or reticular hair loss where no separate bald patches can be distinguished
Alopecia areata marginata (ophiasis)	Snake-shaped hair loss pattern seen along the posterior occipital and temporal margins of the scalp
Ophiasis inversus	Inverse pattern of hair loss, originates from the center and progresses to the margins of the scalp

**Based on information from:** Brzezińska-Wcisło L, Bergler-Czop B, Wcisłowski D, Lis-Świątek A. New aspects of the treatment of alopecia areata. Postepy Dermatol Alergol. 2014 Aug; 31(4): 262-265.

degree of hair loss in patients with alopecia areata.<sup>3,5</sup> Hair follicles are an immune protected site due to the absence of major histocompatibility complex (MHC) expression on their surface. This so called “immune privilege” is seen during the active (anagen) phase of the hair cycle; however it is lost during the regression (catagen) and the resting (telogen) phases. Alopecia areata is characterized by collapse of this “immune privilege” in hair follicles during the anagen phase of the hair cycle. The underlying cause for loss of this “immune privilege” remains unknown although it has been posited that a predominant proinflammatory milieu around the hair follicles may be the inciting event. The role of several inflammatory mediators has been studied in this regard. One such inflammatory mediator, interferon (IFN) gamma, has been shown to upregulate MHC class I expression in cultured hair follicles, and therefore may be a crucial player in the disease pathogenesis. There are also reports of *in vivo* production of IFN gamma in response to several viral infections, raising the possibility that these infections can also trigger the development of alopecia areata.<sup>6</sup> A history of a pre-existing viral infections (such as Epstein-Barr virus and varicella zoster infections) before the onset of hair loss episodes in some patients with alopecia areata seem to validate this assumption.<sup>7,8</sup>

Upon breakdown of the “immune privilege”, MHC class I molecules with peptides (antigens) are expressed on the hair follicles. The autoantigen expressed by MHC class I and targeted by the T-cells appears to be melanogenesis-related protein. It triggers a CD8+ cytotoxic T-cell autoimmune response against the hair follicles. This is followed by antigen

presentation by the exposed MHC class II molecules which incite a secondary CD4+ T cell-mediated response on the hair follicles.<sup>9</sup> It is believed that this distinct follicular response to inflammatory insults associated with collapse of the “immune privilege” results in the development of alopecia areata. Histopathologically as seen on scalp biopsy, an accumulation of lymphocytes around the bulb of hair follicles is sometimes seen. This peribulbar congregation of lymphocytes, which include CD4+ and CD8+ T-cells along with the natural killer (NK) cells, is often referred to as a “swarm of bees”.<sup>6</sup> It is noteworthy that perifollicular infiltration of the lymphocytes spares the “bulge region” of the hair follicle (unlike that in cicatricial alopecias). Since the “bulge region” is the site of follicular stem cells, hair follicles retain their potential for regrowth in alopecia areata.<sup>10</sup> In addition to perifollicular lymphocytic infiltration, scalp biopsies of many patients with alopecia areata also demonstrate follicular miniaturization, a hallmark of androgenetic alopecia which also contributes to thinning and loss of hairs in these patients.<sup>11</sup> Affected hair follicles in alopecia areata prematurely terminate the anagen phase and regress resulting in predominance of hair follicles in the catagen/telogen phase.<sup>10,11</sup> Telogen hairs, being loosely attached to the scalp, shed resulting in episodes of hair loss.

The inhibitory role of stress on hair growth has been a long-standing subject of debate. These observations have fuelled interest in understanding the role of neuropeptides in the development of alopecia areata. More than fifty neuropeptides have been identified, chiefly substance P, neuropeptide Y, somatostatin and neuropeptidin. It is believed that these neuropeptides also induce a proinflammatory response.<sup>12</sup> Animal-based studies have shown that stress-associated neuropeptide may be associated with perifollicular inflammation, breakdown of “immune privilege” of the hair follicles, premature termination of hair growth and catagen phase induction, thus having a possible contributory role in the development of alopecia areata.<sup>10</sup>

## CO-ASSOCIATED DISEASES

The general rule of science stating that “correlation does not always imply causation” was proposed long back and since then has stood the test of time. However, the pragmatic view is that frequent co-occurrence of two diseases should lend support to their common pathophysiology or origin. Alopecia areata frequently co-occurs with many other autoimmune diseases, such as thyroid disorders (particularly hypothyroidism), vitiligo, pernicious anemia, diabetes mellitus, myasthenia gravis, autoimmune polyendocrine syndrome type I and celiac disease.<sup>13</sup> Several studies<sup>14,15</sup> have evaluated the frequency of co-association of alopecia areata with autoimmune thyroid disorders. A study<sup>14</sup> which compared patients with alopecia areata to healthy controls showed significantly higher prevalence of thyroid autoantibodies in alopecia areata patients compared to healthy controls (25.7% vs. 3.3%). These results were in agreement with those of another study<sup>15</sup>

**Figure 2. Coexistence of loss of hair (due to alopecia areata) and loss of pigment (due to vitiligo) in a patient's scalp**



**Source:** Ramot Y, Thomaïdou E, Mali A, Zlotogorski A. An Extraordinary Colocalization of Alopecia Areata and Vitiligo. *Int J Trichology*. 2010 Jul-Dec; 2(2): 108-109.

performed around the same time and which also evaluated patients with alopecia areata and showed its frequent co-association with thyroid disorders. Hypothyroidism was the most common co-associated thyroid disorder in these patients (seen in 14% patients). It therefore seems prudent to screen thyroid function in all patients with alopecia areata and investigate for the presence of thyroid autoantibodies, even in the absence of manifestations of a thyroid disorder.<sup>14</sup> Similar to thyroid disorders, vitiligo – another autoimmune disorder – also frequently coexists with alopecia areata. According to reports, about 12.5% patients with vitiligo have co-associated alopecia areata and up to 8% of alopecia areata patients have co-existing vitiligo. The two are often associated with other autoimmune disorders. In addition to being co-associated, certain case reports have demonstrated their colocalization as well (Figure 2).<sup>16</sup> Similarly co-existence of alopecia areata and type 1 diabetes, another autoimmune disorder, has also been reported although their simultaneous development appears to be a rare phenomenon.<sup>17</sup> Alopecia areata has been reported more frequently in patients with lupus erythematosus compared to the general population (10% vs. 0.4%, respectively) and is also known to coexist in patients with myasthenia gravis (4%).<sup>18,19</sup> Atopy is also strongly correlated with alopecia areata. Studies have shown higher frequency of co-occurrence of atopic dermatitis in patients with alopecia areata than in those without. The risk of atopic dermatitis appears to be particularly high in patients with alopecia areata totalis and alopecia areata universalis compared to those with localized patches of alopecia.<sup>20</sup> Its co-association with other atopic disorders such as asthma and allergic rhinitis is also known.<sup>21</sup> Therefore, it should be noted that hair loss occurring in patients with autoimmune disorders and in those with history of atopy (or any atopic disorder) should be highly suggestive of alopecia areata.<sup>22</sup>

**Figure 3. Alopecia areata with localized patches of hair loss**



Courtesy: Dr Lynne Goldberg. Boston University School of Medicine

## CLINICAL FEATURES AND PROGNOSTIC FACTORS

Onset of hair loss in alopecia areata starts early; most affected patients are < 30 years of age. However, any age group can be affected.<sup>23</sup> Men and women appear to be equally affected. Alopecia areata can have variable clinical presentations depending on the extent of hair loss. Most commonly, it presents with well-demarcated round bald patches on the scalp (Figure 3). Exclamation mark hairs (short hairs that taper towards the scalp surface) are characteristically seen on the periphery of these patches. Hair loss can occur in a single, self-limiting episode with subsequent hair re-growth seen in 50-80% cases; in other cases, hair loss may recur at varying intervals over many years leading to several bald patches on the scalp which coalesce and may involve the entire scalp.<sup>3</sup> In addition to the scalp, hair from the eyebrows and eyelashes can be lost.<sup>23</sup> Changes in the nails are seen in about 7- 66% patients with alopecia areata. Nail pitting is common. Other nail changes may include longitudinal ridging, thin and brittle fingernails and toenails and trachonychia.<sup>3,24</sup>

Hair loss has a considerable negative impact on the psychological status of patients with alopecia areata. It is commonly co-associated with various psychiatric

**Table 2. Some poor prognostic markers in alopecia areata**

- Early onset of hair loss
- Extensive hair loss
- Bald patches persisting for more than 1 year
- Positive family history
- Ophiasis variant
- Co-existing nail changes
- History of atopy
- Down syndrome

**Based on information from:**

1. Brzezińska-Wcisło L, Bergler-Czop B, Wcisło-Dziadecka D, Lis-Świąty A. New aspects of the treatment of alopecia areata. *Postepy Dermatol Alergol.* 2014 Aug; 31(4): 262-265.
2. Spano F, Donovan JC. Alopecia areata Part 1: pathogenesis, diagnosis, and prognosis. *Can Fam Physician.* 2015 Sep; 61(9): 751-755.

co-morbidities, including mood disorders and anxiety.<sup>25</sup> Depression is known to occur in up to 50% and obsessive compulsive disorder in about 36% of children and adolescents with alopecia areata. Generalized anxiety disorder is also known to occur in about 39% of patients with this disorder.<sup>26</sup> Some poor prognostic factors in patients with alopecia areata include early onset of alopecia; extensive hair loss; bald patches persisting for more than 1 year, ophiasis variant of alopecia areata; positive family history, alopecia areata with co-associated nail changes, and atopy (Table 2).<sup>1,3</sup>

## DIAGNOSIS

The diagnosis of alopecia areata can be suspected on clinical grounds based on the pattern of hair loss; well-demarcated bald patches with a normal skin and preserved follicular ostia are highly suggestive. The hair pull test is positive when the disease is active.<sup>3,23</sup> Trichoscopic evaluation may reveal “yellow dots” which represent degenerated follicular keratinocytes and sebum within the affected follicles. “Black dots” are also seen within the “yellow dots” and represent stubs of hair (cadaverized hair), that are fractured before emergence from the scalp. Additionally, broken hairs and short vellus hairs are also seen. While “black dots” are known to correlate well with the disease activity, “yellow dots” correlate well with the disease severity.<sup>24,27,28</sup> A scalp biopsy may be required when the diagnosis is uncertain.<sup>3</sup>

## Telogen effluvium

### OVERVIEW

Telogen effluvium is another type of non-scarring alopecia and one of the most common causes of diffuse hair loss, especially in women. Several triggers for its development, including physiological and mental stressors, are known. The precise pathogenic mechanism remains unknown, however alteration in hair cycle dynamics in response to various stimuli (triggering event) has been proposed as the

principal underlying cause. In telogen effluvium, scalp hairs undergo synchronized termination of the anagen phase and entry into the telogen phase. The telogen hairs (club hairs) initially remain firmly attached to the scalp but undergo excessive shedding about 2-3 months after the triggering event.<sup>1</sup> Both acute and chronic forms of telogen effluvium are known. While acute telogen effluvium can affect both men and women, chronic telogen effluvium is seen almost exclusively

in women. Acute telogen effluvium has an abrupt onset, with scalp hair shedding starting around 2-3 months after a triggering event and lasting for about 6 months; the disorder is self-limiting. In contrast, chronic telogen effluvium has an insidious onset and a fluctuating disease course (hair shedding lasting for more than 6 months) inundated with frequent remissions and relapses.<sup>2</sup> In addition to the scalp, hair loss is seen in other parts of the body as well.<sup>1-3</sup> There is no specific treatment of this disorder. Reassurance and counseling is required in most cases.<sup>1,2</sup>

## TRIGGERING EVENTS

Several triggers for telogen effluvium have been identified which include, although are not limited to, emotional stress, fever, systemic illness, major surgery, trauma, postpartum (telogen gravidae), and extensive hemorrhage.<sup>1,4</sup> Five functional types of telogen effluvium depending on the type of alteration in the hair cycle have been described:<sup>1,2</sup>

- **Immediate anagen release:** Follicles prematurely terminate anagen phase and enter into the telogen phase; hair shedding occurs 2-3 months after a triggering episode. It commonly follows emotional stress and febrile illness
- **Delayed anagen release:** Follicles remain for a prolonged period in the anagen phase, followed by their entry into the telogen phase when excessive shedding of hair occurs. The mechanism of post-partum hair loss
- **Immediate telogen release:** Shortening of the telogen phase (under the influence of medications) and premature entry of hair follicles into the anagen phase resulting in excessive loss of exogen hairs. It can be seen within a few weeks after starting minoxidil therapy
- **Delayed telogen release:** There is prolonged telogen phase and delayed transition of hair follicles into the anagen phase. This is common cause of seasonal shedding of hair in humans or telogen effluvium following travel from low- to high-daylight environment
- **Short anagen phase:** Idiopathic shortening of the anagen phase and recurrent shedding of telogen hairs. The main cause of chronic telogen effluvium

Recently it has been suggested that chronic telogen effluvium can also be a result of reduction in the variance of the anagen phase across all follicles. This may represent the sixth functional type of telogen effluvium.<sup>5</sup>

## CLINICAL FEATURES

Acute telogen effluvium can be seen in both men and women; hair shedding starts abruptly and usually occurs 2-3 months after a triggering episode. Not all patients can recall the triggering event. There is diffuse loss of hair, although less than 50% of the total scalp hair is affected.<sup>1</sup> About 100-1000 hairs may be lost per day; patients note excessive loss of hair usually while combing or washing their hair. Clumps of hair can be easily pulled out from the vertex or even the scalp margins. Scalp examination reveals no signs of inflammation and/or follicular miniaturization. Hair shedding in acute telogen effluvium is self-limiting and does not persist beyond

6 months.<sup>1-3</sup> Chronic telogen effluvium is predominantly seen in middle-aged women (30-60 years). It has an insidious onset and a prolonged disease course (> 6 months) associated with remissions and relapses. A triggering cause for hair loss may or may not be identified.<sup>2</sup> Scalp examination shows hairs with normal thickness; short hairs in the frontal and marginal regions of the scalp can be seen.<sup>2</sup> Some patients with telogen effluvium may report pain, burning, discomfort, and/or paresthesia of the scalp (trichodynia).<sup>6</sup>

Telogen effluvium is an important cause of diffuse hair loss in women and needs to be differentiated from other causes of diffuse hair loss in them, two of the most important being female pattern hair loss (androgenetic alopecia) and diffuse alopecia areata. Female pattern hair loss is associated with gradual thinning of the hairs along the central part line or frontotemporal recession, followed by hair loss.<sup>3</sup> Trichodynia may be reported in these patients as well although as a symptom it is reported more commonly by patients with telogen effluvium.<sup>6</sup> Diffuse alopecia areata in women has an abrupt onset, usually after periods of psychological stress or a systemic illness, and is characterized by a mild to moderate decrease in density of hairs throughout the scalp. Patches of baldness on the scalp may be present. Loss of hair in many of these women starts early (less than 20 years of age). Nails may also be affected.<sup>3</sup>

## DIAGNOSIS

Telogen effluvium can be suspected based on the typical history of the patient and his/her scalp examination findings. A typical patient of telogen effluvium is a woman with a history of "head full of hair" followed by onset of excessive hair shedding (often described as "hair fall by the handful", particularly while washing, shampooing or combing hair). Pain or burning sensation on the scalp (trichodynia) may also be reported. While a precipitating cause may be identified in patients with acute telogen effluvium that in chronic telogen effluvium frequently remains unidentified.<sup>1,2,7</sup> A hair pull test is strongly positive and more than 10% of the total hairs can be pulled out easily from the scalp during the acute phase of the disease. Microscopic evaluation of the shed hairs show homogeneous thickness and the follicles in the telogen phase.<sup>3</sup> A trichogram shows > 25% of the plucked hairs in the telogen phase in the acute disease state; the anagen:telogen ratio is significantly reduced. Trichoscopic findings include reduced hair density with presence of empty follicles. There is absence of hair diameter variability and peripilar halo (unlike in androgenetic alopecia). Scalp biopsy is not routinely required; however it may help differentiate telogen effluvium from other notable causes of diffuse alopecia (androgenetic alopecia and diffuse alopecia areata). Scalp biopsy in patients with telogen effluvium shows telogen follicles in excess of 15% of the total scalp hair. Iron deficiency and hypothyroidism are considered the two most common precipitating causes of telogen effluvium. Therefore in patients with suspected telogen effluvium, serum ferritin and thyroid function assessment (T4 and TSH) is advisable.<sup>3,4</sup>

# Tinea capitis

## OVERVIEW

In addition to androgenetic alopecia, alopecia areata and telogen effluvium, tinea capitis is another non-scarring type of alopecia. It is seen predominantly in children.<sup>1</sup> Most cases of tinea capitis are reported in the prepubertal age group (pre-school and school-going children). In fact, tinea capitis is designated the most common dermatophyte infection in children. Adults are infrequently affected. Its rapidly increasing burden in the general population, particularly in children, has made it a “modern day epidemic”. The two genera of dermatophytes most commonly implicated as causes of tinea capitis are *Trichophyton tonsurans* and *Microsporum canis*.<sup>2</sup> Other causes include *Microsporum audouinii*, *Trichophyton soudanense*, and *Trichophyton violaceum*. *T. tonsurans* appears to be the most common cause of tinea capitis followed by *M. canis*. Tinea capitis has variable clinical types; seborrheic dermatitis-like tinea capitis, non-inflammatory black dot type tinea capitis, kerion, and favus. The seborrheic dermatitis-like tinea capitis presents as patchy or diffuse white adherent scales on the scalp similar to dandruff. There is no apparent hair loss. Non-inflammatory black dot type tinea capitis presents as well-demarcated areas of baldness with hair broken at or below the level of scalp surface, giving the characteristic appearance of black dots. Kerion presents as single or multiple tender, inflamed, alopecic nodules with pustules on their surface. Many patients with kerion additionally have fever and occipital

lymphadenopathy which may aid the diagnosis. Favus is a rare type of inflammatory tinea capitis characterized by typical honey-colored, cup-shaped, follicular crusts called scutula. It can lead to scarring and permanent hair loss.<sup>3</sup>

## DIAGNOSIS

Clinical diagnosis of tinea capitis should be confirmed by mycological examination. Potassium hydroxide (KOH) preparation and examination under the microscope is required for making the diagnosis, which is confirmed by fungal culture.<sup>2</sup> Specimens for microscopy and culture should be taken from the margins of the infected area, which corresponds to the active zone of the lesion.<sup>3</sup> The hair shaft itself (and not scalp scrapings) needs to be sent; for obtaining hair samples forceps, surgical blade, or brushing hair, may be used. The hair shafts obtained are mounted in 10-20% KOH solution (with or without dimethyl sulfoxide) and examined under the microscope for fungal hyphae and spores. Cultures usually take a longer time; the first evidence of fungal growth is seen in 7-10 days, and cultures are held a full month before being declared negative. Wood's lamp examination may be beneficial in diagnosing ectothrix dermatophytes such as *M. canis* and *M. audouinii*; hairs show a bright yellow-green fluorescence when these dermatophytes are present. Wood's lamp, however, is not helpful for diagnosing endothrix dermatophytes such as *T. tonsurans*.<sup>3</sup> Therefore, while a positive Wood's lamp examination confirms a diagnosis of tinea capitis, a negative result does not rule out its diagnosis.<sup>2</sup>

# Trichotillomania

## OVERVIEW

Trichotillomania is a chronic impulse control disorder characterized by pulling out one's own hair, resulting in progressive non-scarring hair loss. It is usually seen in adolescents and young adults.<sup>1</sup> The median age of onset of trichotillomania is about 12 years, with a female predilection of 3.5:1. Adults with trichotillomania often have co-associated psychiatric disorders such as anxiety, mood and personality disorders. The part of the scalp most often affected is the vertex; although other regions of the scalp, face, and body may also be involved. The classic dermatological presentation of trichotillomania is an irregularly-shaped patch on the scalp with reduced hair density. The patch is most often seen in easily accessible areas of the scalp.<sup>2</sup> In the affected region of the scalp, short, broken hairs of variable lengths are seen. Hair

pulling in or beyond the vertex creates a typical tonsure pattern which is also known as the Friar Tuck sign.<sup>3</sup> It is important to differentiate trichotillomania from alopecia areata and tinea capitis, which also present with non-scarring patches of hair loss. Patches of baldness in alopecia areata are usually completely devoid of hair; the hair pull test is positive. In contrast, trichotillomania has patches of reduced hair density and the hair pull test is negative. Microscopic and Wood's light examination can be helpful to rule out tinea capitis, and sometimes a biopsy can be helpful to exclude alopecia areata, especially when the patient does not admit to manipulating the hair.<sup>4</sup> Trichoscopic findings in trichotillomania include scalp with reduced hair density, broken hairs, short vellus hairs, coiled hairs, trichoptilosis, yellow dots, black dots, and exclamation mark hairs.<sup>3</sup>

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## Case study 1

A 22 year old woman presents with hair loss on the back of her neck. It was noticed by her hairdresser. She had a small area of hair loss on her temple as a child that resolved spontaneously. She has no known medical history. The area is asymptomatic. Examination reveals a large area of alopecia on her occiput with some regrowth of fine, pigmented hairs on either side. There is no scale. There is no hair loss elsewhere.

### 1) What is the best diagnosis?

- A) Traction alopecia
- B) Alopecia areata
- C) Female pattern hair loss
- D) Telogen effluvium
- E) Lichen planopilaris

### 2) Which of the following is true?

- A) Close inspection would reveal loss of follicular ostia
- B) This type of hair loss is permanent
- C) This pattern of hair loss is called ophiasis
- D) Spontaneous regrowth never occurs in this disease
- E) Children and young adults are rarely affected

### 3) This disease can be associated with:

- A) Nail changes
- B) Autoimmune diseases
- C) Vitiligo
- D) Diabetes
- E) All of the above



Courtesy: Dr Lynne Goldberg, Boston University School of Medicine

Answers: 1) B, 2) C, 3) E

## SECTION 3

# Understanding cicatricial alopecias and their evaluation approach

### CICATRICIAL ALOPECIA

Cicatricial alopecia, also commonly referred to as scarring alopecia, is a relatively uncommon group of hair disorders characterized by a perifollicular inflammatory infiltrate, particularly targeting the “bulge region” of the hair follicle, leading to eventual destruction of the pilosebaceous units with replacement by fibrous tissue. Permanent hair loss ensues.<sup>1-3</sup> Hair loss in cicatricial alopecia is permanent due to destruction of the epithelial stem cells which reside in the “bulge region” of the outer root sheath of hair follicle at the level where the arrector pili muscle inserts.<sup>2</sup>

Follicular destruction in cicatricial alopecia may be primary or secondary. In primary cicatricial alopecia, the hair follicle is the main target for the inflammatory destructive process; scalp biopsy shows preferential destruction of the follicular epithelium and/or its associated adventitial dermis with variable sparing of the intervening dermis. In contrast, secondary cicatricial alopecia results from incidental damage to the hair follicle from a non-follicle directed injurious process, including infiltrative and inflammatory diseases. Examples would be loss of hair in sarcoidosis of the scalp or in a scar from a traumatic injury. Follicular scarring in these diseases is a result of their close proximity to the primary site of injury on the scalp.<sup>3</sup> The diagnostic hallmark of cicatricial alopecia is visible loss of follicular ostia and destruction of the hair follicle on histopathologic examination.<sup>3,4</sup> A workshop sponsored by the North American Hair Research Society in 2001<sup>1</sup> classified primary cicatricial alopecia based on the predominant cellular infiltrate seen in scalp biopsy specimen; lymphocytic, neutrophilic, and mixed types of primary cicatricial alopecia (Table 1). Lymphocytic cicatricial alopecia mainly includes lichen planopilaris, classic pseudopelade (Brocq), central centrifugal cicatricial alopecia, chronic cutaneous lupus erythematosus and keratosis folliculitis spinulosa decalvans; neutrophilic cicatricial alopecia includes folliculitis decalvans and dissecting cellulitis/folliculitis; mixed type includes acne keloidalis and erosive pustular dermatosis.<sup>1,2</sup>

### Primary lymphocytic cicatricial alopecias, their clinical presentations and histopathological findings

The subtypes of primary lymphocytic cicatricial alopecias primarily include lichen planopilaris, classic pseudopelade

**Table 1. A common classification scheme for primary cicatricial alopecias**

#### Lymphocytic

- Lichen planopilaris
- Classic pseudopelade (Brocq)
- Central centrifugal cicatricial alopecia
- Chronic cutaneous lupus erythematosus
- Alopecia mucinosa
- Keratosis folliculitis spinulosa decalvans

#### Neutrophilic

- Folliculitis decalvans
- Dissecting cellulitis

#### Mixed

- Acne keloidalis
- Acne necrotica
- Erosive pustular dermatosis

#### Non-specific

##### Based on information from:

1. Olsen EA, Bergfeld WF, Cotsarelis G, Price VH, Shapiro J, Sinclair R, Solomon A, Sperling L, Stenn K, Whiting DA, Bernardo O, Bettencourt M, Bolduc C, Callendar V, Elston D, Hickman J, Ioffreda M, King L, Linzon C, McMichael A, Miller J, Mulinar F, Trancik R; Workshop on Cicatricial Alopecia. Summary of North American Hair Research Society (NAHRS)-sponsored Workshop on Cicatricial Alopecia, Duke University Medical Center, February 10 and 11, 2001. *J Am Acad Dermatol.* 2003 Jan;48(1):103-10.
2. Ross EK, Tan E, Shapiro J. Update on primary cicatricial alopecias. *J Am Acad Dermatol.* 2005 Jul;53(1):1-37.

(Brocq), central centrifugal cicatricial alopecia, chronic cutaneous lupus erythematosus and keratosis folliculitis spinulosa decalvans. Lichen planopilaris is considered a follicular variant of lichen planus, although the clinical appearance differs. Three forms of lichen planopilaris are recognized: classic lichen planopilaris, Graham-Little syndrome, and frontal fibrosing alopecia. Patients with lichen planopilaris often have pruritus, burning and tenderness in the scalp region, and increased hair shedding. Most affected patients are adults, with the typical age of onset of the disease being 40-60 years. Women are more frequently affected than men. Scalp lesions may be single or multiple, discrete or confluent, and commonly involve the vertex and parietal area (Figure 1). Careful inspection reveals perifollicular erythema and scale, especially when the disease is active.

**Figure 1. Confluent areas of lichen planopilaris on the crown**



Courtesy: Dr Lynne Goldberg, Boston University School of Medicine

Anagen hairs can be pulled out easily in active lesions. Histopathological examination of the scalp biopsy reveals perifollicular lymphocytic inflammation and fibrosis with thinning of follicular epithelium, loss of sebaceous glands, and eventual follicular loss.<sup>5-7</sup> Frontal fibrosing alopecia differs clinically from lichen planopilaris, although they share the same histology. It involves the frontal hairline and is often associated with loss of eyebrows.

Pseudopelade of Brocq is another subtype of primary lymphocytic cicatricial alopecia. It derived its name Brocq in 1888 for its likeness to “la pelade”, or hair loss of alopecia areata. It is a rare form of alopecia which occurs as discrete, irregular-shaped, and slightly depressed patches of hair loss, primarily in the parietal and vertex regions of the scalp. Irregular-shaped bald patches in pseudopelade are in contrast to well-demarcated round or oval patches in alopecia areata. Middle-aged women are usually affected. Early histopathological findings include a lymphocytic infiltrate around the infundibulum and absence of sebaceous glands. Late in the disease, concentric lamellar fibroplasia and eventual replacement of follicles by fibrous tissue can be seen.<sup>8</sup>

Central centrifugal cicatricial alopecia includes previously known terms such as “hot comb alopecia,” “follicular degeneration syndrome,” and “pseudopelade” in African-Americans and “central elliptical pseudopelade” in Caucasians. Classically this form of alopecia has been known to affect

**Is pseudopelade a true separate entity of cicatricial alopecia?**

Some authors question whether pseudopelade is a true entity, and consider it a late stage of lichen planopilaris or other scarring alopecia

**Based on information from:** Amato L, Mei S, Massi D, Gallerani I, Fabbri P. Cicatricial alopecia; a dermatopathologic and immunopathologic study of 33 patients (pseudopelade of Brocq is not a specific clinico-pathologic entity). *Int J Dermatol.* 2002 Jan;41(1):8-15.

**Figure 2. Severe loss of hair on the vertex in a patient with central centrifugal cicatricial alopecia**



Courtesy: Dr Lynne Goldberg, Boston University School of Medicine

middle-aged women from African-American ethnicity, although men may also be affected. Genetic susceptibility and traumatic hair styling involving heat and chemicals have been suggested as possible causes. The disease typically starts in the central part or the vertex of the scalp (Figure 2). Affected patients may experience scalp pruritus and tenderness. The lesion usually enlarges centrifugally with time; hence its name. Certain parts of the affected scalp may be smooth and shiny and have absence of follicular orifices on close inspection, helping to differentiate it from female pattern hair loss and alopecia areata. Histopathological examination reveals loss of hair follicles and sebaceous glands, with broad hyalinized fibrous tracts that may contain naked hair shafts.<sup>9,10</sup>

Cutaneous lupus erythematosus can be a dermatological manifestation of systemic lupus erythematosus, an autoimmune multisystemic disease, or it can occur in the absence of systemic involvement. It is further subdivided into acute, subacute and chronic cutaneous (discoid) lupus erythematosus. Discoid lupus erythematosus is the most common form of chronic cutaneous lupus erythematosus. It occurs more frequently in women compared to men; most affected patients are in their fourth to fifth decade of life. A typical lesion begins as a well-demarcated, erythematous, scaly macule or papule that gradually expands and develops into an indurated discoid (coin-shaped) plaque with an active border and central scarring (Figure 3). Scales are adherent to the plaque and the plaque may extend into the hair follicles causing scarring, disfigurement, and irreversible alopecia. Histopathologically, superficial and deep perivasicular and periappendageal lymphocytic inflammation is present, along with follicular plugging, interface dermatitis, and increased dermal mucin. Sebaceous glands are absent.<sup>11</sup>

Keratosis follicularis spinulosa decalvans is an uncommon type of scarring alopecia associated with follicular hyperkeratosis, followed by scarring and permanent hair loss. It is predominantly an X-linked disorder; however, sporadic

**Figure 3. Central scarring and depigmentation in a patient with treated discoid lupus erythematosus**



Courtesy: Dr Lynne Goldberg, Boston University School of Medicine

**Figure 4. Inactive patch of scarring alopecia in a patient with treated folliculitis decalvans**



Courtesy: Dr Lynne Goldberg, Boston University School of Medicine

and autosomal dominant inheritance patterns are also known. It is characterized by hair loss in the scalp and eyebrows in the setting of widespread keratosis pilaris. Male heterozygotes are more frequently affected compared to female heterozygotes in families having an X-linked inheritance pattern. Onset of the disease is early in life (infancy or childhood) with development of follicular keratosis, first on the face and then on other parts of the body including the trunk and the limbs. This is followed by patches of alopecia on the scalp, eyebrows, and eyelashes followed by scarring. Some patients may have photophobia, the onset of which coincides with the skin manifestations. Palmoplantar keratoderma may also be present.<sup>12,13</sup>

#### **Primary neutrophilic cicatricial alopecias, their clinical presentations and histopathological findings**

There are two major types of primary neutrophilic scarring alopecias, folliculitis decalvans and dissecting cellulitis of the scalp, also known as perifolliculitis capitis abscedens et suffodiens. Folliculitis decalvans is a subtype of primary neutrophilic cicatricial alopecia characterized by destructive, suppurative folliculitis. The precise etiology is unknown although host predisposition to *S. aureus* infection, either due to local or system immune deficit, has been cited as a possible cause of its development. Folliculitis decalvans is seen mainly in young and middle-aged adults (Figure 4). Both men and women can be affected. Lesions are typically seen over the vertex and occipital area and present as follicular pustules, with perifollicular erythema and lack of ostia. Affected part of the scalp may have hemorrhagic crusts and erosions. Once treated, the pustules resolve and perifollicular scale remains, making it difficult at times to distinguish from lichen planopilaris. A helpful clue is tufting of more than three hair shafts (emerging from the same follicular orifice). Histology displays a mainly neutrophilic inflammatory infiltrate at the level of the follicular infundibulum in early

lesions and additionally some lymphocytes and plasma cells and interfollicular fibrosis in advanced lesions.<sup>14</sup>

Dissecting cellulitis, (perifolliculitis capitis abscedens et suffodiens) occurs predominantly in African-American men who are between 20-40 years of age. Women and children are less frequently affected. It can occur in association with acne conglobata and hidradenitis suppurativa, which together comprise the follicular occlusion triad. The lesions include follicular pustules, nodules, abscesses and sinuses in the affected part of the scalp that progresses to scarring (Figure 5). Histopathology shows occlusion of the follicular ostium followed by a deep perifollicular inflammatory infiltrate with predominant neutrophils, histiocytes, and lymphocytes.<sup>15,16</sup> The depth of the infiltrate distinguishes it from folliculitis decalvans.

#### **Primary mixed cicatricial alopecias, their clinical presentations and histopathological findings**

Acne keloidalis, also known as acne keloidalis nuchae, is a chronic inflammatory disorder predominantly affecting the posterior aspect of the neck and occipital region of the scalp. It frequently affects black men of African descent and is characterized initially by the presence of small flesh-colored to reddish-brown, follicular papules in the nape of the neck and the occiput. Some patients may have burning or pain in the affected regions. With time the papules coalesce forming pustules, keloidal plaques, and folliculitis with tufting of hairs. Histologically, there is a peri- and intrafollicular lymphoplasmacytic infiltrate and dermal fibrosis. Sebaceous glands are absent.<sup>17,18</sup> Erosive pustular dermatosis is a chronic, relapsing pustular dermatosis of the scalp which presents with cicatricial alopecia. Local trauma has been implicated as a possible triggering cause. It is mainly seen in the elderly; women are more often affected compared to men. Patients

**Figure 5. Multiple pustules and nodules in a patient with dissecting cellulitis**



Courtesy: Dr Lynne Goldberg. Boston University School of Medicine

have sterile pustules, erosions and crusted lesions on the scalp. Skin of the affected region is atrophic. Histopathological findings are non-specific.<sup>19,20</sup>

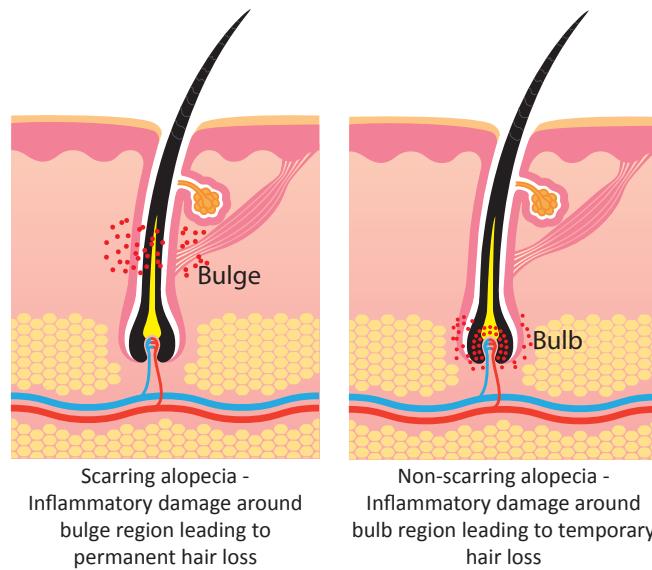
### PATHOGENESIS

The pathogenesis of cicatricial alopecia is poorly understood. Our understanding of cicatricial alopecias received a major boost in the early 1990s with the identification of stem cells in the “bulge region” of the hair follicle.<sup>21</sup> The “bulge region” is the area where the arrector pili muscle inserts in the hair follicle, and is the site of pluripotent follicular stem cells. These stem cells undergo coordinated differentiation to regrow the lower hair follicle during normal telogen-anagen cycling, and restore and renew the upper follicle, including the sebaceous gland and adjacent epidermis. They therefore appear to play a central role in follicle cycling and are vital for the maintenance of hair follicle integrity.<sup>22</sup> Since follicular inflammation in primary cicatricial alopecia is mainly seen to involve the “bulge region”, damage and loss of its resident follicular stem cells appears to be the main cause of permanent hair loss in this disorder (Figure 6).<sup>23</sup> Immunohistochemical studies using antibodies, including those targeting cytokeratin 15 in the “bulge region” of the hair follicle, have shown absence of follicular bulge stem cells associated with moderate to severe inflammation in cicatricial alopecia. This confirms the role of inflammation-mediated damage of the stem cells in the “bulge region”.<sup>23</sup> This inflammation and subsequent damage is followed by replacement of the “bulge region” with fibrous tissue that impairs the ability of hairs to replace their epithelial components, leading to permanent hair loss.<sup>22</sup> Since “immune privilege” protects the hair follicle against immune-mediated damage, it is plausible that collapse of “immune privilege” may be an early event in the development of cicatricial alopecia.<sup>24</sup> However, there is now good evidence to show that inflammation-induced loss of stem cells from the “bulge region” of the hair follicle cannot alone explain the

different morphological and pathological hair changes seen in primary cicatricial alopecia.<sup>22</sup>

Recent studies on primary cicatricial alopecia utilize the asebia mouse, a well-studied animal model of cicatricial alopecia with a spontaneous mutation linked to deficiency of stearoyl CoA desaturase-1. This is a rate-controlling enzyme required for the formation of mono-unsaturated fatty acids from saturated fatty acids. Studies have shown that deficiency of stearoyl CoA desaturase-1 in the asebia mouse induces lipid abnormality in the sebaceous glands causing their hypoplasia, reduced sebum secretion, adipose tissue atrophy of the subcutis, a dermal inflammatory reaction and eventual scarring, which possibly destroys the hair follicle.<sup>4,25,26</sup> In 2009, a group of investigators made a seminal contribution to our understanding of the link between lipid metabolism defects and cicatricial alopecia. They used gene array analysis and real-time PCR and demonstrated downregulation of PPAR gamma – a ubiquitous nuclear hormone receptor which has a central role in lipid homeostasis – in lichen planopilaris. Furthermore, they showed that in mouse models, targeted deletion of PPAR gamma in follicular stem cells induced scalp and hair phenotype similar to the scarring alopecia in lichen planopilaris.<sup>27</sup> These findings seem to suggest that PPAR gamma may be required for the maintenance of functional epithelial stem cell compartment in murine hair follicles; its downregulation induces scalp and hair changes similar to those seen in scarring alopecia (lichen planopilaris). That the same mechanism may be active in humans with scarring alopecia seems an attractive proposition and should warrant

**Figure 6. Scarring vs non-scarring alopecia**



**Diagrammatic representation based on information from:**

- Dogra S, Sarangal R. What's new in cicatricial alopecia? *Indian J Dermatol Venereol Leprol.* 2013 Sep-Oct;79(5):576-90.
- Pozdnyakova O, Mahalingam M. Involvement of the bulge region in primary scarring alopecia. *J Cutan Pathol.* 2008 Oct;35(10):922-5.

more intensive search to identify the precise role of lipid abnormalities and peroxisome biogenesis in the pathogenesis of primary cicatricial alopecia.

A role for neurogenic inflammation and apoptosis in the pathogenesis of primary cicatricial alopecia has also been suggested. Psycho-emotional stress upregulates nerve growth factor and substance P. There is resultant induction of neurogenic inflammation characterized by a perifollicular inflammatory infiltrate, degranulation of perifollicular mast cells, reduced hair matrix keratinocyte proliferation and their increased apoptosis; these apoptotic matrix keratinocytes prematurely enter the catagen phase. The presence of a dense network of substance P positive nerve fibers in the “bulge region” of the hair follicle provides credence to the role of neurogenic inflammation in the genesis of permanent hair loss in scarring alopecia.<sup>4,28</sup> The observation of apoptotic keratinocytes in hair follicles of primary cicatricial alopecia also supports the role of apoptosis in the pathogenesis of this disorder.<sup>28</sup>

Finally, environmental factors, such as scalp trauma and infection, have been studied as triggers of cicatricial alopecia. Scalp trauma has been linked to hair loss in some types of scarring alopecia; however, its definitive role in the pathogenesis of primary cicatricial alopecia needs further exploration in clinical trials.<sup>29</sup> Scalp infections, particularly those due to *S. aureus*, have also been linked to some forms of scarring alopecia. *S. aureus* has been implicated in the pathogenesis of folliculitis decalvans.<sup>14</sup> Familial cases of primary cicatricial alopecia are also known and certain genetic factors may also increase susceptibility to primary cicatricial alopecia.<sup>4</sup>

## DIAGNOSTIC APPROACH TO CICATRICIAL ALOPECIA

History and examination provide important clues to the diagnosis of primary cicatricial alopecia. Disease onset is usually in the adult age. Onset of primary cicatricial alopecia in childhood and the elderly is rare. Ethnicity is also an important determinant to the risk for some types of cicatricial alopecias. Central centrifugal cicatricial alopecia, acne keloidalis nuchae and dissecting cellulitis of the scalp are commonly seen in individuals belonging to African-American ethnicity. A magnified view of the affected part of the scalp using trichoscopy shows absence of follicular ostia which confirms a diagnosis of cicatricial (scarring) alopecia. Noting the site of baldness on the scalp, pattern of alopecia, and follicular and interfollicular stigmata (such as perifollicular erythematous and violaceous papules, follicular plugging and/or atrophy) may be useful in suggesting a diagnosis.<sup>2</sup> Trichoscopy may show white and milky-red areas lacking follicular openings; these findings differentiate cicatricial alopecia from non-cicatricial alopecia.<sup>30</sup> A scalp biopsy taken from the center of a bald patch confirms diagnosis of cicatricial alopecia; when taken from the periphery or area of inflammation, it can suggest the underlying pathogenesis.<sup>2</sup>

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## Case study 2

This trichoscopic photograph is of a 48 year old man with several areas of hair loss on his scalp. It had started with bumps, and in the past he was treated with multiple courses of antibiotics with some improvement by his primary care provider. He has no involvement elsewhere. Examination reveals a smooth scalp surface, mild perifollicular scale, and multiple hair shafts emerging from follicular ostia.

**1) What is the best diagnosis?**

- A) Central centrifugal cicatricial alopecia
- B) Alopecia areata
- C) Folliculitis decalvans
- D) Dissecting cellulitis of the scalp
- E) Lichen planopilaris

**2) Which of the following is false?**

- A) Antibiotics should never be used for treatment
- B) This type of hair loss is permanent
- C) This pattern is called tufting
- D) This disorder is mediated by neutrophils
- E) This patient likely exhibited pustules at some point in his disease

**3) Cicatricial alopecias should be suspected when the exam reveals:**

- A) Loss of follicular orifices
- B) Scalp nodules
- C) Scalp pustules
- D) Perifollicular erythema and scale
- E) All of the above



**Courtesy:** Dr Lynne Goldberg, Boston University School of Medicine

**Answers:** 1) C, 2) A, 3) E

## SECTION 4

# Management options of alopecia

### MANAGEMENT OF ALOPECIA

Alopecia can include either localized or diffuse hair loss from the scalp and/or other body parts. Notwithstanding the extent of hair loss and its cause, alopecia is a cause of significant stress and psychological disturbance for the affected individuals. Taking a detailed history and performing a meticulous examination of the hair and scalp is crucial in

patients with alopecia. The distribution of hair loss, density of hair and presence or absence of inflammation, erythema, scale and scarring should be noted. Additional detailed work-up may include a “hair pull-test”, trichoscopy and scalp biopsy, when required. Depending on the type of alopecia, treatment options may differ. A detailed discussion on the management options for different types of alopecia is discussed below.

## Androgenetic alopecia

### MANAGEMENT OPTIONS

Androgenetic alopecia is a disorder characterized by progressive, characteristic pattern of hair loss in men and women. Early identification and prompt initiation of management can stem further hair loss and facilitate mild-to-modest hair growth.<sup>1</sup> Several treatment options for androgenetic alopecia are available. Topical minoxidil (5% solution or foam; 1 ml or 1/2 capful twice daily) is approved and recommended for the treatment of mild-to-moderate androgenetic alopecia in men above 18 years of age; in women above 18 years of age, topical 2% minoxidil, 1 ml twice daily or 5% minoxidil foam, 1/2 capful once daily can be used. Men with androgenetic alopecia can also derive treatment benefits from oral finasteride, a 5 alpha-reductase inhibitor. Along with topical minoxidil, oral finasteride is also an approved treatment option for male pattern baldness; it is recommended at a dose of 1 mg daily (either as monotherapy or in combination with topical minoxidil). Oral dutasteride, another 5 alpha-reductase inhibitor, is an alternative but unapproved treatment option which can be used at a dose of 0.5 mg daily. There is no sufficient evidence to recommend the use of topical finasteride in men and women with androgenetic alopecia. Although hormonal therapy (antiandrogens, estrogens or antiestrogens) has also been evaluated in androgenetic alopecia and yielded mixed results, it is not currently recommended for management. Surgery, especially follicular unit transplantation, can be considered in men and women with sufficient donor hair along with medical treatment.<sup>2</sup> Camouflage methods are an essential part of treatment regimen, and include keratin fibers to coat the hair and scalp, and masking lotions to darken the scalp.

#### Minoxidil

Minoxidil was first introduced in the early 1970s as an oral antihypertensive medication. Studies showed its association with hypertrichosis which prompted its subsequent use as

a topical formulation for treating progressive hair loss in androgenetic alopecia. Several possible explanations have been propounded for its effects in arresting hair loss and promoting hair growth; these include a vasodilator effect, modulation of potassium channel conductance in the dermal papilla, an increase in the expression of vascular endothelial growth factor (VEGF) mRNA in the dermal papilla, and activation of cytoprotective prostaglandin synthase-1.<sup>2,3</sup> By modulating potassium channel conductance in the dermal papilla, minoxidil induces hyperpolarization of the cell membranes. This, along with its vasodilator effect, increases blood, oxygen and nutrient supply to the hair follicles. Under minoxidil treatment, follicles in the telogen phase are shed and replaced by the new thicker anagen hairs.<sup>3</sup> Topical minoxidil is currently one of the most successful treatment options with the best level of evidence in both male and female androgenetic alopecia. Several studies performed over the last few decades in patients with androgenetic alopecia have shown its benefits in promoting cosmetically acceptable hair growth.

A placebo-controlled study<sup>4</sup> included men with androgenetic alopecia and assigned them to 12-months treatment with either topical minoxidil (2% or 3% solution) or placebo. Patients assigned to placebo were crossed over to 3% minoxidil treatment after 4 months. The study results showed new hair growth at the end of the study in 82% men (2% minoxidil group), 78% men (3% minoxidil group), and 83% men (switched from placebo to 3% minoxidil). Growth of non-vellus hairs at 4 months was significantly greater in patients using minoxidil compared to those who used placebo.<sup>4</sup> Similar treatment benefits with minoxidil were obtained in another placebo-controlled study,<sup>5</sup> which treated women with androgenetic alopecia using either topical 2% minoxidil solution or placebo for 32 weeks. Results of this study showed minimal-to-moderate hair growth in 60% women who used minoxidil compared to 46% women who used placebo. At the

study end, mean non-vellus hair count in the minoxidil group was again greater than that in the placebo group (195 hairs vs. 177 hairs, respectively). In both these studies, minoxidil was not associated with any serious adverse events.

Lower strength (2%) and higher strength (mainly 5%) minoxidil solutions have been compared in androgenetic alopecia for their potential to induce new hair growth.<sup>6-8</sup> In men with androgenetic alopecia, 5% minoxidil solution has shown superiority over 2% minoxidil.<sup>7</sup> In one such study<sup>7</sup> which compared 2% and 5% minoxidil solutions in men with androgenetic alopecia, 5% minoxidil was associated with early response to treatment and more significant increase in non-vellus hair count after 48 weeks compared to 2% minoxidil. Hair regrowth was 45% more in the 5% minoxidil group compared to 2% minoxidil group after 48 weeks. Similarly, superiority of 5% over 2% minoxidil solutions in female androgenetic alopecia has also been demonstrated.<sup>8</sup> Recently, minoxidil has been incorporated in a foam formulation. A study<sup>9</sup> compared 5% minoxidil foam applied once daily to 2% minoxidil solution applied twice daily and showed the 5% foam to be better tolerated; the foam was associated with lesser incidence of side-effects such as pruritus and hypertrichosis.

Currently, topical minoxidil is the proven mainstay of treatment for androgenetic alopecia. There are clear benefits of using higher strength minoxidil over its conventional 2% preparation. It is recommended to use 5% topical minoxidil, wherever possible, at least in male androgenetic alopecia. Treatment benefits in terms of hair growth are usually evident about 6 months after starting treatment in both men and women. It is important to continue treatment indefinitely.<sup>2</sup> Facial hypertrichosis, which is sometimes seen with topical minoxidil solution and may be bothersome in women, can be prevented by applying the solution directly to the scalp as a thin layer and not using more than the suggested amount. To restrict itching and dermatitis with topical minoxidil, concomitant topical corticosteroids can be used.<sup>10</sup>

## Finasteride and dutasteride

Dihydrotestosterone (DHT) has a central role to play in the pathogenesis of androgenetic alopecia. Finasteride is a type II selective 5 alpha-reductase inhibitor. It reduces DHT concentration and thereby inhibits miniaturization of hair follicles. Oral finasteride was approved in 1997 as the first oral treatment option for male pattern baldness. Treatment benefits of oral finasteride are well-documented in androgenetic alopecia; it reverses the balding process and can promote new hair growth.<sup>11-13</sup> In a 2-year placebo-controlled study<sup>12</sup> that included men with androgenetic alopecia having predominantly vertex hair loss, oral finasteride at a dose of 1 mg/day showed significantly better hair count in the vertex area (compared to placebo) at the end of 1 and 2 years of treatment. Similar positive outcomes with finasteride were reported in another study<sup>13</sup> which included men with androgenetic alopecia with loss of hair mainly in

the anterior/mid area of the scalp. The results of this study again showed significantly greater hair count in the frontal scalp in finasteride-treated patients (at a dose of 1 mg/day for 1 year) compared to those who received placebo. These studies confirm good hair growth with oral finasteride in both frontal and vertex parts of the scalp. Dose comparison studies<sup>14</sup> have shown 1 mg/day oral dose of finasteride is optimal for treating male pattern baldness and deriving benefits without the risk of bothersome side-effects seen with higher doses. Its long-term efficacy and ability to provide durable growth of scalp hair after 5 years of treatment has also been established.<sup>15</sup> Despite these well-documented benefits in men, studies in the past did not show similar treatment efficacy of oral finasteride in women with androgenetic alopecia.<sup>16,17</sup> In one such double-blind, placebo-controlled trial<sup>16</sup> in which postmenopausal women with androgenetic alopecia were randomized to treatment with either 1 year of finasteride or placebo, no significant difference in the change in hair count between finasteride and placebo could be shown.<sup>16</sup> However, a recent Cochrane systematic review<sup>18</sup> on the treatment of androgenetic alopecia in women concluded that some of these randomized trials which failed to demonstrate treatment benefits of oral finasteride in female pattern hair loss were associated with possible bias, and therefore treatment recommendations could not be based upon them. Currently oral finasteride (1 mg/day) has received approval and is universally an acceptable treatment option in male androgenetic alopecia; it remains an unapproved treatment option in postmenopausal women with androgenetic alopecia as its treatment benefits in them remain equivocal.<sup>2</sup> Its use in women of childbearing age is not recommended due to potential effects on the developing fetus.

### Oral finasteride in women with androgenetic alopecia

A large study involving the use of oral finasteride at a dose of 1 mg/day did not show improvement in androgenetic alopecia in women; some small case series and case reports have however shown that women can benefit from higher doses ranging from 2.5 to 5 mg/day.

**Based on information from:** Dinh QQ, Sinclair R. Female pattern hair loss: Current treatment concepts. *Clin Interv Aging*. 2007 Jun; 2(2): 189-199.

Dutasteride is another 5 alpha-reductase inhibitor approved for prostatic hyperplasia in men. It inhibits both type I and type II 5 alpha-reductase enzymes leading to more potent enzymatic blockade. Dutasteride therefore also reduces follicular DHT concentration and is expected to promote clinically meaningful hair growth similar to finasteride. Some studies<sup>19,20</sup> which have compared dutasteride with finasteride in androgenetic alopecia have demonstrated either similar or better treatment outcomes with dutasteride than finasteride. A recent study<sup>19</sup> in men with androgenetic alopecia which compared treatment with oral dutasteride, finasteride and placebo showed dutasteride at 0.5 mg/day significantly increased hair count and improved hair growth at week 24 compared with finasteride and placebo. Similar results were obtained from a recent retrospective analysis<sup>20</sup>

of studies which evaluated 3 years of treatment with oral dutasteride (0.15 mg/day) and finasteride (1.25 mg/day) in women with androgenetic alopecia; dutasteride was shown to be similarly effective as finasteride for increasing hair thickness and slowing hair loss. Dutasteride was significantly better than finasteride in women below 50 years with hair loss mainly at the central and vertex regions of the scalp. Therefore in patients of androgenetic alopecia not responding optimally to treatment with oral finasteride, adding dutasteride can improve hair density.<sup>21</sup> Notwithstanding these positive outcomes, currently dutasteride is not first-line therapy and is a treatment alternative in patients with androgenetic alopecia who do not respond after 6 months of finasteride treatment.<sup>22</sup> It should be used with extreme caution, if at all, in women of childbearing age.

### **Oral finasteride vs. topical minoxidil and their combination**

Both oral finasteride at 1 mg/day and 5% topical minoxidil (solution and foam) are approved in male androgenetic alopecia. Additionally, topical minoxidil (2% and 5%) is approved in female androgenetic alopecia. A limited number of studies, most performed in men with androgenetic alopecia, have compared topical minoxidil vs. oral finasteride, and furthermore evaluated treatment benefits with their combination. Most studies have demonstrated oral finasteride to be superior to topical minoxidil for restricting progressive hair loss and promoting new hair growth in male androgenetic alopecia. Their combination seems to impart enhanced efficacy.<sup>23-25</sup> A recent study<sup>25</sup> evaluated men with androgenetic alopecia and assigned them to three treatment groups; oral finasteride 1 mg daily, topical minoxidil 5% solution, or combined oral finasteride 1 mg daily and topical 5% minoxidil for 12 months. At the end of 12 months of treatment, improvement in terms of hair growth was seen in 80.5%, 59%, and 94.1% of men treated with finasteride, 5% minoxidil and their combination therapy, respectively. Therefore, while oral finasteride appears to be superior to topical minoxidil, their combination is conceivably associated with the best treatment response.

### **Hormonal therapies**

Hormonal therapy – antiandrogens and estrogens (or antiestrogens) – has also been evaluated as an alternative treatment options in androgenetic alopecia. Oral antiandrogens, such as spironolactone and cyproterone acetate, have been mainly assessed in female androgenetic alopecia.<sup>2</sup> Oral spironolactone (usually at doses of 100-200 mg/day) may reduce hair loss and though not FDA approved, may be considered an alternate treatment option in female androgenetic alopecia, particularly in those not responding to approved front-line medications. Its antiandrogenic effects however may increase risk of menstrual irregularities and breast tenderness. Cyproterone acetate is another antiandrogen with antigenadotropic and weak progesterone

activity. It blocks DHT receptor binding and when used at an oral dose of 50 mg/day can reduce hair loss in some women with androgenetic alopecia, particularly in those with signs of hyperandrogenism. It is also associated with antiandrogenic side-effects such as menstrual irregularities and decreased libido. It is not available in the US. Flutamide is a non-steroidal selective antiandrogen that inhibits binding of androgens with its pertinent receptors. Oral flutamide (at a dose of 250 mg/day) can also improve hair growth in androgenetic alopecia, and therefore may be considered an alternate treatment option, mainly in those with normal androgen levels.<sup>10</sup> However, it is not often used due to its side effect profile. Topical estrogens have also been evaluated in men and women with androgenetic alopecia. Currently there is no concrete evidence of benefit with topical fluridil, fulvestrant and alfatradiol and therefore these agents are not recommended for routine use in androgenetic alopecia.<sup>2</sup>

### **Other treatment options**

Prostaglandin analogs are considered hair growth stimulants due to their association with hypertrichosis. Latanoprost, a prostaglandin analog, is known to stimulate growth of eye lashes and is currently being evaluated for its role in scalp hair growth. Since seborrheic dermatitis can aggravate hair loss in androgenetic alopecia, antimicrobials such as ketoconazole- or pyrithione zinc-containing shampoos may be expected to increase hair growth, at least in some patients with androgenetic alopecia.<sup>2</sup> A study<sup>26</sup> which compared 2% ketoconazole shampoo to a non-medicated shampoo (along with 2% minoxidil) in androgenetic alopecia showed similar improvement in hair density in both treatment groups. Platelet-rich plasma (PRP) extracted from whole blood can be used for its growth factors and stimulatory mediators. Injections of PRP are a novel method for treating various types of alopecia. Its role and treatment benefits however need verification in clinical trials.<sup>27</sup> Various aminoacids, micronutrients and vitamins are also known to have some role in hair growth and nutrition. Zinc and copper improves hair nutrition; cysteine, biotin and niacin are believed to be important for hair growth. Topical and oral formulations containing mixture of these minerals and vitamins are being evaluated in different types of alopecia.<sup>2</sup> Laser treatment for androgenetic alopecia is also rapidly becoming popular. It can stimulate hair growth and appears to be promising alternate treatment option in male and female androgenetic alopecia. Several devices are FDA approved. However studies are of relatively short duration and their use requires further evaluation in clinical trials.<sup>28</sup> Several other treatment options are also in different stages of evaluation in androgenetic alopecia.

### **Surgical treatment**

Many patients with androgenetic alopecia opt for hair transplantation surgery. This is done to improve hair density and is used in combination with medical therapy, which slows

further hair loss. It involves surgical movement of hair from the occipital (donor) scalp to areas of genetic loss (recipient scalp). It is used in addition to and not in place of medical therapy.<sup>10</sup> Follicular unit transplantation, the movement of several hair follicles together as a unit, is the gold standard for hair transplantation surgery in androgenetic alopecia. There are two ways in which donor hair can be harvested: strip harvesting and follicular unit extraction.<sup>29</sup> Each technique has its own advantages and disadvantages; the surgical option

chosen may vary according to the patient. These are methods of harvesting hair follicles; both utilize transplantation of follicular units. Hair transplantation surgery may require multiple sittings, is time consuming and expensive. Follicular neogenesis, or follicular cell implantation, is a new technique which involves utilizing the inherent properties of cultured hair follicle cells to induce de novo hair growth in balding scalp. It is still in its early stages and requires further evaluation in clinical trials.<sup>30</sup>

## Alopecia areata

### MANAGEMENT OPTIONS

Alopecia areata is an important non-scarring form of alopecia. It can either occur as a single self-limiting episode leading to an oval well-circumscribed bald patch on the scalp; or the disease may follow a chronic progressive course resulting in multiple confluent patches of alopecia. Several treatment options have been evaluated for their role in stimulating hair re-growth in patients with alopecia areata with variable results. Furthermore, data on their long-term efficacy and impact on quality of life is scarce.<sup>1</sup> It is prudent to individualize treatment of alopecia areata according to the patient. Treatment options should be chosen keeping a consideration of the patient's age and rapidity of hair loss. Corticosteroids, minoxidil, topical and systemic immunomodulators, anthralin, oral and topical psoralen plus ultraviolet A (PUVA) therapy, prostaglandin analogs, and topical retinoids have been used in alopecia areata with variable success.<sup>2</sup> The National Alopecia Areata Foundation (NAAF.com) is an excellent resource for patients and providers.

#### Corticosteroids

Corticosteroids have anti-inflammatory effects. Intralesional corticosteroids have been widely used by dermatologists for hair re-growth in alopecia areata and are considered the front-line treatment option, particularly in patchy alopecia. The most commonly used intralesional corticosteroid is triamcinolone acetonide. Different concentrations of triamcinolone acetonide, ranging from 2.5-10 mg/mL, have been used for injecting in the bald patches on the scalp and face. The injections are repeated every 4–6 weeks. Multiple intralesional injections of triamcinolone may cause transient scalp atrophy and hypopigmentation; these side-effects should be looked for when using this treatment option and the concentration and volume adjusted accordingly. Hair growth is usually evident weeks to months after starting intralesional corticosteroids.<sup>2</sup> Topical corticosteroids are also widely used in alopecia areata although their efficacy in this indication has not been unequivocally proven. They are considered less effective than intralesional triamcinolone. In adults, potent class 1 corticosteroids are used for application although in

children a lesser strength is appropriate. They are deemed more effective for hair growth in localized patches of alopecia. In patients with alopecia totalis and alopecia universalis their treatment benefits are suspect.<sup>2,3</sup> Hair growth may start between 6 weeks to 6 months after treatment with topical corticosteroids. Relapses after stopping treatment are high.<sup>2</sup> Systemic corticosteroids, particularly oral systemic steroids, are also used in select patients with alopecia areata. Although they can induce remission, treatment is often required for a prolonged period of time which increases the risk of steroid-associated adverse effects. Corticosteroid pulse therapy was introduced to obviate the risk of prolonged treatment with oral steroids and has been shown to benefit some patients with severe alopecia areata, particularly when treatment is started within 3 months of disease onset.<sup>4</sup> Various pulse regimens of corticosteroids have been used in alopecia areata. Relapse is frequently seen after dose reduction and stopping treatment with systemic steroids, which restricts their utility in patients with alopecia areata.<sup>2,3</sup>

#### Minoxidil

Minoxidil has shown potential to stem hair loss and promote hair regrowth. Topical minoxidil has been used off label for promoting hair growth in alopecia areata and is a useful adjunct to the first-line treatment options.<sup>2</sup> It appears to have some treatment benefits in patchy alopecia, although not in extensive alopecia.<sup>3</sup> Unlike corticosteroids, minoxidil does not reduce inflammation but promotes hair growth. Evidence of hair growth is usually seen 3-6 months after minoxidil treatment. When treating alopecia areata, it is preferable to use minoxidil along with other treatment options, rather than as monotherapy.<sup>2,3</sup> The 5% strength is preferred. Concomitant use of minoxidil with systemic steroids can restrict post-corticosteroid hair loss.<sup>5</sup>

#### Topical immunotherapy

Topical immunotherapy with contact sensitizers has been widely used in patients with alopecia areata. Along with intralesional corticosteroids, it is a front-line treatment option in alopecia areata. It appears to be particularly useful

in patients with extensive alopecia (hair loss in more than 50% of the scalp area) and in those with refractory alopecia areata. These agents have a unique mechanism of action. By sensitizing the scalp and inducing allergic contact dermatitis, they alter the pathogenic inflammatory response in alopecia areata and thereby induce hair growth.<sup>6</sup> Dinitrochlorobenzene (DNCB) was the first topical sensitizer to show potential for hair growth in patients with alopecia areata; other agents which belong to this class which are currently used with variable success are squaric acid dibutylester (SADBE) and diphenylcyclopropenone (DPCP).<sup>7</sup> Among these, DPCP is one of the most commonly used contact sensitizer for alopecia areata management. A cotton-tipped applicator saturated with 2% DPCP in acetone is applied to a coin-sized area on the scalp. The area on which the medication is applied should neither be washed nor exposed to sunlight for 48 hours. Starting 2 weeks later, application with a dilute concentration of DPCP is repeated weekly. An allergic response on the area of application indicates that sensitization has occurred. The dose concentration is adjusted to maintain a mild dermatitis after application.<sup>8</sup> Studies which have used topical DPCP in patients with chronic extensive alopecia areata have shown partial or complete hair growth in 71.4% patients at the end of 6 months of treatment.<sup>9</sup> Similarly, application of incremental concentrations of SADBE for 20 weeks in patients with alopecia areata has shown excellent response (defined as > 75% hair regrowth) in 68% patients.<sup>10</sup> However, despite good response, relapses are frequent after stopping topical immunomodulators. There is evidence to show that more than half the patients treated with either DPCP or SADBE experience or are likely to experience recurrence of hair fall after stopping treatment. Topical immunotherapy is additionally associated with bothersome side-effects such as eczema, blistering, contact leukoderma and urticarial reaction.<sup>2</sup>

### **Anthralin**

Anthralin, a synthetic substance similar to coal tar, also appears to have some treatment benefits in patients with alopecia areata. It acts by provoking dermatitis of the scalp although unlike topical immunomodulators, which primarily induce allergic contact dermatitis, anthralin promotes an irritant contact dermatitis. Its precise mechanism of action

however remains obscure. Topical anthralin creams and ointments are used in both children and adults.<sup>2</sup> Anthralin needs to be applied in a concentration sufficiently strong (usually 0.5-1%) to evoke irritant contact dermatitis. Its low-dose regimens are not deemed beneficial for hair growth.<sup>11</sup> Patients are advised to apply topical anthralin daily on the scalp and remove it with shampoo after 10-15 minutes. The application time is increased weekly until a constant low-grade irritation is observed.<sup>2</sup> Response to anthralin treatment in patients with alopecia areata is variable; combining it with topical minoxidil may improve treatment response.<sup>12</sup> Some patients may develop severe irritation and staining of skin and clothes when using anthralin; patients should be counseled about these adverse effects prior to starting treatment.<sup>3</sup>

### **Other treatment options**

Systemic immunomodulators (methotrexate, sulfasalazine, and cyclosporine) have also been used in some patients with alopecia areata. They may be considered in selected patients with alopecia areata, particularly in those with extensive disease and those who do not respond to conventional first-line agents.<sup>2</sup> Oral and topical psoralen plus ultraviolet A (PUVA) therapy has also been used as an alternative treatment modality for extensive, difficult-to-treat alopecia areata.<sup>13</sup> However, it has not been shown to be significantly effective, with success rate of 6.3% for alopecia areata focalis, 12.5% for alopecia areata totalis and 13.3% for alopecia areata universalis.<sup>14</sup> PUVA-turban therapy is a method of administering dilute psoralen solution selectively to the scalp of patients. It lacks the systemic side-effects of oral psoralen and is therefore a well-tolerated, alternative treatment option for alopecia areata.<sup>15</sup> Similarly, 308-nm Excimer laser is also considered an effective and safe treatment option for patchy alopecia areata.<sup>16</sup> Ophthalmic prostaglandin and prostamide analogs are associated with hypertrichosis.<sup>17</sup> In patients with alopecia areata involving the eye lashes, prostaglandin analogs (latanoprost and bimatoprost) may be considered, although their treatment benefits, if any, need to be further evaluated for this indication.<sup>2</sup> Topical retinoids also have an adjunctive role to play in the treatment of alopecia areata. However, lack of clarity on its precise mechanism of action and limited published studies evaluating its role in alopecia areata prevents a definitive conclusion to be drawn on its treatment benefits.<sup>3</sup>

## **Telogen effluvium**

### **MANAGEMENT OPTIONS**

Telogen effluvium is a self-limiting disorder characterized by periods of diffuse non-scarring hair loss. Hair shedding usually occurs for about 3-6 months and thereafter re-growth of hair starts.<sup>1</sup> Complete recovery is usually the rule in telogen effluvium although it may take variable time,<sup>2</sup>

and sometimes patients do not reach 100% of pre-effluvium density. Counseling and reassuring the patients about the benign nature of the disorder is important. It should be emphasized to the patient that this disorder only involves periodic hair shedding and not actual hair loss; therefore total baldness of the scalp does not usually occur.<sup>3</sup> Several causes (triggers) of telogen effluvium are known. They should be

identified and if present, satisfactorily treated.<sup>1</sup> Serum iron and vitamin D2 deficiency are seen in some patients with telogen effluvium and may have a role in the disease development.<sup>4</sup> It is recommended to keep serum ferritin (a measure of iron stores) above 40-70 mg/dL in patients with telogen effluvium. Low iron stores, when present, should be treated with oral ferrous sulfate or gluconate at a dose of 300 mg two to four times a day, depending on degree.<sup>1,2</sup>

In telogen effluvium, hair shafts synchronously enter into the telogen phase. The end of the telogen phase at the time of hair shedding corresponds to the exogen phase. Pharmacological treatment of telogen effluvium should aim to prolong anagen, inhibit entry into telogen phase, and shorten exogen. Unfortunately, there is no approved pharmacological treatment which can inhibit telogen phase or induce anagen

in telogen follicles.<sup>1</sup> Minoxidil prolongs the anagen phase of the hair follicles.<sup>5</sup> In addition, experimental studies have shown its effects in counteracting stress-induced inhibition of hair growth.<sup>6</sup> These findings support a promising role of minoxidil in telogen effluvium because both physical and mental stress has been implicated as its cause.<sup>2</sup> At least theoretically, topical minoxidil may seem to be a reasonable treatment option in telogen effluvium and it may be worth evaluating its role. Drugs such as beta-blockers, antithyroid drugs, and anticoagulants, which induce catagen phase, should be avoided in patients with telogen effluvium. Catagen-inducing endocrine disorders such as thyroid dysfunction, hyperprolactinemia and hyperandrogenism should also be treated appropriately. Deficiencies of iron and zinc, which induce catagen phase, if present, should also be corrected.<sup>1,2</sup>

## Tinea capitis

### MANAGEMENT OPTIONS

Tinea capitis is predominantly a disorder of childhood, seen mainly in the preadolescent (pre-school and school age) children. While most cutaneous dermatophyte infections respond to topical treatment, those on the scalp (tinea capitis) require systemic oral antifungals in nearly all patients for optimal response. Topical antifungals may be used as adjuncts to systemic therapy. Treatment in tinea capitis is needed for as long as 6-8 weeks.<sup>1,2</sup> Oral griseofulvin has remained the mainstay of its treatment for several years.<sup>1</sup> The introduction of new systemic antifungal agents (itraconazole, terbinafine, and fluconazole) significantly revolutionized management of tinea capitis, and provided dermatologists with new therapeutic options to choose from (Table 1). The effectiveness of newer systemic antifungal agents has been shown to be either comparable or greater than griseofulvin against tinea capitis. They however achieve response with shorter treatment duration. They are also safe to use, with most side-effects being minor and self-limiting.<sup>3,4</sup> Currently, griseofulvin and terbinafine are the FDA-approved systemic antifungals for tinea capitis, although other agents (itraconazole and fluconazole) can also be used off-label and provide good treatment efficacy.<sup>4</sup>

### Griseofulvin

Griseofulvin, a metabolic product of *Penicillium* spp, is primarily a fungistatic agent. The exact mechanism of its fungistatic action remains unknown. It has good antifungal activity against *Trichophyton*, *Microsporum* and *Epidermophyton* species. After treatment discontinuation, griseofulvin does not persist for long time periods in cutaneous tissue (compared to the newer systemic antifungal agents), which necessitates longer treatment durations. The standard length of treatment for tinea capitis with oral

griseofulvin is 6-8 weeks; infections caused by *M. canis*, being often recalcitrant, may require a longer duration of treatment. Two formulations of griseofulvin are available; microsized and ultramicrosized, based on the particle size of the active ingredient.<sup>5</sup> The dose of microsized griseofulvin preparation for tinea capitis is 20-25 mg/kg/day; higher doses (25 mg/kg/day) may be required in infections by *M. canis*. Ultramicrosized griseofulvin preparation is administered at a dose of 10-15 mg/kg/day.<sup>6</sup> Griseofulvin is an FDA-approved treatment for tinea capitis and has remained its gold standard treatment for a considerable period of time. Its good treatment efficacy in tinea capitis has been maintained for the last several years, although it needs to be given up to 8 weeks for

**Table 1. Different systemic antifungal agents for treating tinea capitis, their dose and duration**

Antifungal agent	Treatment dose and duration
Griseofulvin	Microsized 20-25 mg/kg/day Ultramicrosized 10-15 mg/kg/day Duration – Usually 6-12 weeks
Itraconazole	Capsules 5 mg/kg/day Oral solution 3 mg/kg/day Duration – Continuous daily regimen 2-6 weeks; pulse regimen (2-3 pulses)
Terbinafine	4-5 mg/kg/day OR 10-20 kg: 62.5 mg 20-40 kg: 125 mg > 40 kg: 250 mg Duration – <i>Trichophyton</i> spp – 2-4 weeks; <i>Microsporum</i> spp. – 8-12 weeks
Fluconazole	Daily dose: 5-6 mg/kg/day Weekly dose: 8 mg/kg, once weekly

**Based on information from:** Kakourou T, Uksal U; European Society for Pediatric Dermatology. Guidelines for the management of tinea capitis in children. *Pediatr Dermatol.* 2010 May-Jun;27(3):226-8.

an optimal response.<sup>5,7</sup> It still continues to be the treatment of choice for *Microsporum* species.<sup>6</sup> Headache, gastrointestinal upset and occasionally rash can occur after griseofulvin administration.<sup>5</sup>

### Itraconazole

Itraconazole is a broad spectrum triazole antifungal agent. It is one of the new systemic antifungals which exhibits both fungistatic as well as fungicidal activity. Itraconazole has good treatment efficacy against both *Trichophyton* and *Microsporum* spp.<sup>2</sup> It has a high affinity for keratin and therefore achieves high concentration in the stratum corneum.<sup>8</sup> Itraconazole is available as capsules and oral solution. It can be given as a daily continuous dose or intermittent pulse dosing (one pulse of 5 mg/kg/day for 1 week with 2 weeks off between the first and the second pulses and 3 weeks between the second and third pulses). The recommended dose of itraconazole for tinea capitis is 5 mg/kg/day (as capsules) or 3 mg/kg/day (as oral solution) given either as daily dosing or by repeat pulsing. When given as daily doses, treatment may be required for 2-6 weeks; on the other hand, 2-3 pulses may provide an optimal antifungal response.<sup>6</sup> Oral itraconazole solution is associated with higher risk of gastrointestinal upset compared to capsule preparations.<sup>8</sup> Itraconazole has demonstrated good effectiveness and safety in the treatment of tinea capitis. It is particularly effective for treating tinea capitis caused by *M. canis*, which is otherwise difficult to manage.<sup>9</sup>

### Terbinafine

Terbinafine is an allylamine, a new generation of antifungal agents. It has good fungicidal activity against all the dermatophytes.<sup>2</sup> Usually *Trichophyton* infections respond better to terbinafine compared to *Microsporum*. The major advantage of terbinafine is its short treatment duration.<sup>10</sup> Oral terbinafine is available as 250 mg tablets. The standard single daily dose is 62.5 mg in children < 20 kg; 125 mg in children between 20-40 kg; and 250 mg in children ≥ 40

kg. Alternatively, a dose of 4-5 mg/kg/day can be used. The total treatment duration is usually 4 weeks, although shorter durations (2 weeks) have also been reported to be effective. Higher doses and longer duration of treatment (up to 8-12 weeks) may be required for infections caused by *M. canis*.<sup>6</sup> Studies have shown that a 4-week course of terbinafine is comparable to 8-week course of griseofulvin for clearing tinea capitis infections. However, for treating infections caused by *Microsporum* spp., terbinafine appears inferior to griseofulvin.<sup>10</sup> When compared with the newer antifungals, terbinafine appears to be marginally more effective than both itraconazole and fluconazole. It is usually safe with a low incidence of adverse events; most of these, including gastrointestinal disturbance, cutaneous eruptions, and weight gain, are transient and self-limiting in nature.<sup>1</sup>

### Fluconazole

Fluconazole is a fungistatic bis-triazole agent used for treating superficial and deep mycoses. It is distinguished from other azoles by its water solubility. Fluconazole is available as tablet and oral suspension. Its recommended dose for treating tinea capitis is 5-6 mg/kg/day for 4-6 weeks. Alternatively, once-weekly 8 mg/kg pulse dosing for 8-12 weeks can also be used.<sup>2,6</sup> Fluconazole is comparable to griseofulvin for clearing tinea capitis infection and reducing its transmission rates. It is however less effective than griseofulvin against *M. canis*.<sup>11,12</sup> Its side-effects are similar to other azole antifungal agents.<sup>2</sup>

### Topical antifungals

Topical antifungals are usually used as adjunctive treatment options for tinea capitis. They are not absorbed systemically and act by direct contact with the fungus. Shampoos, lotions and creams containing selenium sulfide, zinc pyrithione, and/or ketoconazole are available and used along with oral antifungals. For optimal results, these agents should be applied once daily on the affected region of the scalp. One week of treatment with topical antifungals may be necessary to decrease shedding of fungus.<sup>2</sup>

## Trichotillomania

### MANAGEMENT OPTIONS

Trichotillomania is primarily an impulse control disorder. Its treatment is challenging and primarily requires counseling or rarely a psychiatric referral. Both psychotherapy and hypnotherapy have been used. Dronabinol (a cannabinoid agonist) and N-acetylcysteine (a glutamate modulator) are new treatment options that are being used to control compulsive behavior in patients with trichotillomania.<sup>1</sup> Habit

reversal training, which targets the obsessive compulsive behavior in these patients that causes them to tear out their hair, is conceivably the most effective behavioral therapy for trichotillomania.<sup>2</sup> Treatment response, however, is overall inconsistent and relapses are frequent. Bimatoprost, a synthetic prostaglandin analog, has recently been used to treat eyelash madarosis associated with trichotillomania with some success.<sup>2</sup>

# Cicatricial alopecia

## MANAGEMENT OPTIONS

Primary cicatricial alopecias are one of the most difficult disorders to treat as they are characterized by permanent loss of hair shaft. Their treatment is therefore challenging and oftentimes frustrating. The aim of treatment should be to stem the progression of the disease and improve symptoms. A thumb rule to follow is that lymphocytic cicatricial alopecia should be primarily treated with immunosuppressive agents; while neutrophilic cicatricial alopecia should be treated mainly with antimicrobial agents, isotretinoin or dapsone.<sup>1,2</sup> The Cicatricial Alopecia Research Foundation (CARFintl.org) is an excellent resource for patients and providers.

### Lymphocytic cicatricial alopecia

Patients with lymphocytic cicatricial alopecia are treated primarily with systemic and/or topical immunosuppressive agents. Treatment in the active state should include a systemic immunomodulator such as hydroxychloroquine sulfate or an anti-inflammatory antibiotic such as doxycycline, along with topical and/or intralesional corticosteroids. For patients who remain symptomatic despite treatment or those who have rapidly progressing disease, oral corticosteroids (such as prednisone) or second-line systemic immunomodulators such as cyclosporine or mycophenolate mofetil can be used.<sup>3,4</sup>

Hydroxychloroquine has proven efficacy in slowing the progression of discoid lupus erythematosus of the scalp, lichen planopilaris, and frontal fibrosing alopecia.<sup>4</sup> It is usually administered orally at a dose of 200 mg twice daily after performing baseline labs, a glucose-6-phosphate dehydrogenase level and an ophthalmological examination.<sup>5</sup> Possible adverse effects include hyperpigmentation, hematological changes and ophthalmological damage. Periodic monitoring for retinopathy during hydroxychloroquine treatment is important, especially after several years on therapy.<sup>6,7</sup>

Intralesional and potent topical corticosteroids are also considered front-line treatment options in primary lymphocytic cicatricial alopecia, particularly during the active stage of the disease. Topical corticosteroids used are fluocinonide 0.025%–0.05% and clobetasol solution or gel. The intralesional corticosteroid used is triamcinolone acetonide at a concentration of 5-10 mg/cc. It is particularly effective in discoid lupus erythematosus of the scalp and lichen planopilaris/frontal fibrosing alopecia.<sup>4</sup> Intralesional corticosteroid is also effective for treating central centrifugal cicatricial alopecia; it is injected at the periphery of the affected area on the scalp monthly for the first 6 months; and thereafter symptomatically.<sup>8</sup>

Second-line treatment options in lymphocytic cicatricial alopecia are used in patients not responding to first-line therapy. Cyclosporine, a systemic immunomodulator, is used orally at a dose of 3-5 mg/kg/day; for practical purposes a dose of 300 mg/day is used. Mycophenolate mofetil, another

systemic immunomodulator, is an alternate treatment option. A routine baseline blood count and liver function test is important prior to starting treatment. The dose of mycophenolate is 500 mg twice daily initially for the first month; after the first month, complete blood count and liver function tests are repeated, and the dose is increased to 1 gm twice daily for 5 months. Oral retinoids are effective in some patients but are poorly tolerated. In patients of lichen planopilaris and frontal fibrosing alopecia with severe symptoms and rapidly progressive disease, oral corticosteroids such as prednisone at a dose of 25–40 mg/day for 2–4 months may be required.<sup>6</sup> Topical minoxidil can be used in some patients with primary cicatricial alopecia, particularly in those with central centrifugal cicatricial alopecia, with the hope of preventing further scarring and encouraging growth of recovering follicles.<sup>9</sup>

The role of PPAR gamma in the maintenance of functional epithelial stem cell compartment in murine hair follicles has been shown; furthermore, its downregulation induces scalp and hair changes similar to those seen in scarring alopecia (lichen planopilaris). Given this experimental role of PPAR gamma in cicatricial alopecia, its modulators (PPAR gamma agonists) such as thiazolidinediones or glitazones may be expected to improve symptoms in lichen planopilaris. These drugs are still being evaluated for their role in lichen planopilaris; however early results demonstrate some clinical and histologic improvement associated with their use.<sup>3</sup>

### Neutrophilic cicatricial alopecia

Topical and systemic antimicrobials are front-line treatment options in neutrophilic cicatricial alopecias. In mild cases of folliculitis decalvans, topical clindamycin can be used. For most cases, oral antibiotics are preferred. Many different antibiotics have been used, and sometimes repeated courses are necessary. For those that do not respond, combination therapy with rifampicin and clindamycin has been reported to be beneficial. Rifampicin achieves high concentration in the hair follicles and can sterilize *S. aureus*, even when the organism is intracellular. It is always used in combination with another antimicrobial agent, typically clindamycin, due to issues with resistance.<sup>6</sup> Both medications are used at a dose of 300 mg twice daily for 10 weeks.<sup>10</sup>

Dapsone may also be effective in some patients. Combination treatment with isotretinoin, corticosteroids, and clindamycin has also been used with some success.<sup>11</sup> Oral isotretinoin at a dose of 0.5-1 mg/kg daily for 6-11 months is beneficial in dissecting cellulitis and results in a good treatment response.<sup>6</sup> It has also been used in folliculitis decalvans. Surgical correction of cicatricial alopecia and laser hair removal has been used for patients with intractable symptoms from neutrophilic scarring alopecia who would rather sacrifice their hair than live in pain. In general, hair transplantation is not utilized in this setting.<sup>12</sup>

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## Cicatricial alopecia

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