REVIEW

CME CREDIT *EDUCATIONAL OBJECTIVE:* Readers will recognize when hair loss may be the result of a trigger disrupting the normal cycle of hair growth

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Diffuse hair loss: Its triggers and management

ABSTRACT

Diffuse hair loss can affect both sexes at any age. Anything that interrupts the normal hair cycle can trigger diffuse hair loss. Triggers include a wide variety of physiologic or emotional stresses, nutritional deficiencies, and endocrine imbalances. Loss of telogen-phase hairs is the most common. Hair loss during the anagen phase is usually caused by chemotherapy or radiation therapy. Finding the cause, or trigger, of the hair loss requires a thorough history and examination and will enable appropriate treatment. Patient education is key in the management of diffuse hair loss.

KEY POINTS

Early androgenetic alopecia can present as episodic telogen hair shedding, before the distinctive pattern of hair loss is seen.

Telogen effluvium is a sign of an underlying condition and, thus, is not itself a complete diagnosis.

Androgenetic alopecia should not be overlooked as an important cause of diffuse telogen hair shedding.

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DIFFUSE HAIR SHEDDING is distressing. In many cases, the patient notes an increase in hair on the pillow, or when brushing, or in the shower drain.[1] It is usually recognized more readily by women than men.[1,2] However, diffuse hair loss can affect both sexes at any age.

In this article, we review the triggers of diffuse hair loss and outline an approach to diagnosis and management.

THE NORMAL HAIR CYCLE

Scalp hair grows in cycles, with each hair follicle undergoing 10 to 30 cycles in its lifetime.[3] Diffuse hair shedding is the result of a disruption of one phase of the hair cycle,[2,4] ie, anagen (active hair growth), catagen (involution), or telogen (resting) (FIGURE 1). The anagen phase can last 2 to 8 years,[5] the catagen phase lasts 4 to 6 weeks, and the telogen phase lasts 2 to 3 months.[5] The exogen phase (the release of dead hair) coincides with the end of the telogen phase.[6]

Normally, each hair follicle cycles independently, so that while some hairs are growing, others are resting and others are shedding. Thus, the density of the scalp hair and the total number of scalp hairs remain stable. Most people have about 100,000 scalp hairs, and normally 10% to 15% of these are in the telogen phase.[6] Shedding of 100 to 150 telogen hairs per day is normal.[5] Anagen hair loss is never normal.

The most common type of diffuse shedding is telogen effluvium, in which anagen-phase hair follicles prematurely transition to the telogen phase, resulting in a noticeable increase in hair shedding at the end of the telogen

phase 2 to 3 months later.[2,4] Telogen effluvium is a sign of an underlying condition and, thus, is not itself a complete diagnosis.

THE DIFFERENTIAL DIAGNOSIS OF DIFFUSE HAIR LOSS

Telogen hair loss

Telogen effluvium has many triggers, and these determine the characteristics of the telogen hair loss.

Telogen effluvium can be acute (lasting < 6 months), chronic (6 months or more), or chronic-repetitive.[1,7] If a trigger is acute and short-lived, the telogen effluvium will likely be acute and will resolve. If a trigger is ongoing, if repeated or sequential triggers occur, or if a trigger is not reversed, then the telogen hair shedding can be ongoing.[7]

Rule out androgenetic alopecia. Important in the differential diagnosis of telogen hair loss is early androgenetic alopecia (pattern hair loss). Early androgenetic alopecia can present as episodic telogen hair shedding before the distinctive pattern of hair loss is seen.[8] Androgenetic alopecia is a distinct condition, but the signs of telogen hair shedding can be noted.

Shedding of 100 to 150 telogen hairs per day is normal

Anagen hair loss

Anagen hair shedding is due to the premature termination of anagen hair growth or anagen arrest, after an acute, severe metabolic insult.[9] It is most often iatrogenic, caused by treatment with cytotoxic drugs[9,10] or radiation.[9]

Rule out alopecia areata. Important in the differential diagnosis of anagen hair loss is alopecia areata. A detailed history and physical examination to identify the temporal association of possible triggers and any underlying systemic disease should be done in patients with a history of hair shedding. In some cases, further workup is required.

TRIGGERS OF DIFFUSE TELOGEN HAIR LOSS

Triggers of telogen effluvium are numerous.[2,4,11–13]

Physiologic stress

Physiologic stress such as surgical trauma,[4] high fever,[4] chronic systemic illness,[4] and hemorrhage[11] are well known to cause telogen effluvium 2 to 3 months after the insult. Telogen hair shedding can be experienced 2 to 4 months after childbirth (telogen gravidarum).[4]

Emotional stress

The relationship between emotional stress and hair loss is difficult to ascertain, and hair loss itself is stressful to the patient.[14] Historically, acute reversible hair loss occurring with great stress has been reported.[11] However, the relationship between chronic diffuse hair loss and psychological stress is controversial.[11,14] Evidence for this association appears to be weak, as everyday stresses are likely not enough to trigger hair loss.[3,14]

Medical conditions

Both hypothyroidism and hyperthyroidism can cause diffuse telogen hair loss that is usually reversible once the euthyroid state is restored.[9,11] Chronic systemic disorders such as systemic amyloidosis,[14] hepatic failure,[4] chronic renal failure,[4] inflammatory bowel disease,[4,14] and lymphoproliferative disorders[2] can cause telogen hair shedding. Telogen hair loss has also been reported in autoimmune diseases such as systemic lupus erythematosus and dermatomyositis,[14] as well as in chronic infections such as human immunodeficiency virus type 1[9] and secondary syphilis.[11] Inflammatory disorders such as psoriasis, seborrheic dermatitis, and allergic contact dermatitis can all cause diffuse telogen hair loss.[7,15]

Dietary triggers

Nutritional causes of diffuse telogen hair loss are zinc deficiency and iron deficiency.[11,14] Severe protein, fatty acid and caloric restriction with chronic starvation[2,11,14] and crash dieting[12] can also induce diffuse telogen hair loss. Malabsorption syndromes and pancreatic disease can precipitate telogen hair shedding.[11] Essential fatty acid deficiency can also be associated with diffuse telogen hair shedding usually 2 to 4 months after inadequate intake.[11] Vitamin D is an essential vitamin in cell growth, and vitamin D deficiency may be associated with diffuse hair loss.[1,7] Biotin deficiency can result in alopecia, but this is a very rare cause of hair loss.[14]

The hair cycle and diffuse hair loss

The scalp hair grows in cycles of anagen (growth), catagen (involution), telogen (resting), and exogen (release of dead hair) phases. A wide range of triggers can disrupt the normal cycle and lead to diffuse shedding. Diffuse loss of telogen-phase hairs is the most common form of diffuse shedding. Diffuse hair loss during the anagen phase is usually caused by chemotherapy and radiation therapy.

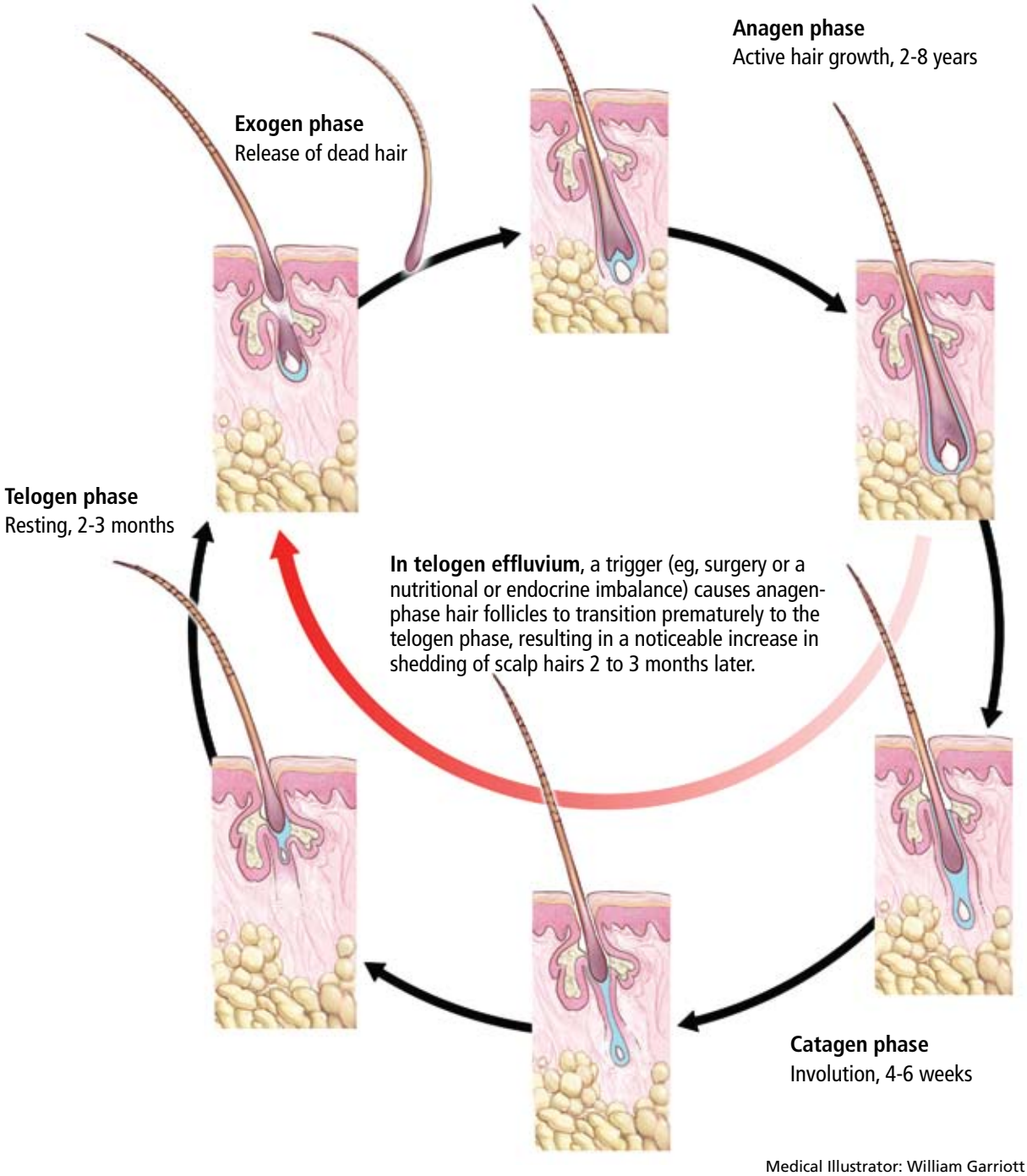

FIGURE 1

TABLE 1

Taking the history: Identifying triggers of diffuse hair loss

Duration of hair shedding
Episodic or continuous hair shedding
Estimation of percentage hair lost
Identification of triggers and their temporal relationship to the hair shedding
Recent surgery, fever, illness, childbirth, psychological stress
History of chronic disease, malignancy, infection, autoimmune disease, liver or renal disease
Menstrual history
Hair care procedures
Dietary history and weight loss noted
Family history of androgenetic alopecia, alopecia areata, autoimmune disease, thyroid disorder
Medication history including over-the-counter drugs and botanicals
History of radiation therapy or exposure to heavy metals

Androgen excess, as in polycystic ovarian syndrome, can cause diffuse or patterned hair loss

Drugs that cause hair loss

Drugs can cause telogen hair loss that starts about 12 weeks after starting the drug and continues while on the drug.[10] Dosing changes can also precipitate hair shedding.[7] Any medication or over-the-counter product the patient is taking should be suspected in hair loss.

Drugs known to cause telogen effluvium are oral contraceptive pills, androgens, retinoids, beta-blockers, angiotensin-converting enzyme inhibitors, anticonvulsants, antidepressants, and the anticoagulants heparin and warfarin (Coumadin).[10,14] Changing or stopping any oral contraceptive can precipitate telogen hair shedding.[10,14] Oral contraceptives containing an androgenic progestin and hormonal replacement therapy with high-dose progesterone can cause telogen hair shedding with or without patterned alopecia.[7,11,14]

IDENTIFYING THE TRIGGERS

Normal hair shedding usually goes unnoticed. However, at the onset of telogen effluvium, hair shedding increases by 25%.[7]

To determine the true trigger of telogen hair loss, the relationship between the trigger and the hair loss must be reproducible, with improvement of the hair shedding following correction of or removal of the trigger, and deterioration on rechallenge.[3]

In acute telogen effluvium, ie, the acute onset of telogen hair loss 2 to 3 months after an acute, short-lived triggering event,[4] a detailed history is important to determine an accurate timeline. No trigger can be identified in some cases.[2] Regrowth is not visible for 4 to 6 months.[7] If the trigger is identified and removed, recovery can be expected to be complete.[4,7]

In chronic diffuse telogen hair loss, ie, telogen hair loss lasting more than 6 months,[3,14] a range of triggers can precipitate the hair loss. It can be due to idiopathic chronic telogen effluvium. It can also be secondary to prolonged, sequential, or repeated triggers, such as a nutritional deficiency or underlying systemic disorder, and shedding can be less pronounced than in acute telogen effluvium.[7]

Chronic telogen effluvium is an idiopathic condition with telogen hair shedding lasting longer than 6 months, and with a fluctuating chronic course over many years without an identifiable trigger.[16,17] These patients can present with a full head of hair or with bitemporal recession and no widening of the midline part.[16,17] Histologic study shows no miniaturization of the hair follicles.[17] The diagnosis of chronic telogen effluvium is made by the exclusion of causes of diffuse telogen hair loss, including androgenetic alopecia.

Androgenetic alopecia typically presents as well-defined, patterned scalp hair loss in patients with a family history of androgenetic alopecia. Diffuse hair loss over the vertex and widening of the central part in women, with or without frontal accentuation ("Christmas-tree" pattern), is characteristic.[14,18]

The functional mechanism of patterned hair loss is related to a shortening of the anagen phase and a progressive miniaturization of the hair follicles.[18] In some instances, androgenetic alopecia may present as diffuse scalp hair loss with episodic increases in telogen hair shedding.[8,14] This presentation can be

mistaken for other causes of diffuse telogen hair loss.[14]

Although, most women with patterned hair loss have normal androgen levels,[14] androgen excess disorders such as polycystic ovarian syndrome can cause diffuse scalp hair loss or patterned hair loss.[7,18] Laboratory testing can exclude other causes of telogen hair loss, and an androgen screen should be performed in women who present with signs of androgen excess, such as irregular menstrual periods, hirsutism, or acne.[18] Scalp biopsy can confirm the diagnosis of androgenetic alopecia.[14]

ANAGEN HAIR LOSS: KEY FEATURES

Anagen hair loss, the result of interruption of the anagen hair cycle, presents as abrupt anagen hair shedding with a severe diffuse scalp alopecia.[9] A serious insult to the hair follicles can cause up to an 80% loss of scalp hair.[7] The time course for anagen effluvium is usually rapid compared with telogen effluvium, occurring within days to weeks of the insult to the hair follicles.[9] The hair-pull test (see below) is positive for dystrophic anagen hairs with tapered ends.[9] If the insult ceases, hair growth restarts again within weeks.

Causes of anagen effluvium include cancer therapies and alopecia areata

Antimitotic chemotherapeutic agents induce arrest of the anagen phase and present a toxic insult to the rapidly dividing hair matrix.[9] Hair loss usually begins 1 to 2 weeks after chemotherapy is started and is most noticeable by 1 to 2 months.[19] The scalp hair is usually most affected, but all body hair including eyelashes and eyebrows can be affected.[10]

Other triggers of anagen hair loss include radiation,[9] heavy-metal poisoning, and boric acid poisoning.[19] Radiation has also been known to cause telogen hair loss and permanent hair loss.[9,10]

Alopecia areata is another cause of anagen hair shedding.[9] This autoimmune condition of the hair[20] can cause patchy hair loss, complete hair loss of the scalp (alopecia totalis), or complete loss of scalp and body hair (alopecia universalis).

THE IMPORTANCE OF THE HISTORY IN IDENTIFYING TRIGGERS

A careful history is key to identifying triggers in any patient with diffuse hair loss (TABLE 1). The duration of the hair shedding and whether the shedding is continuous or episodic should be noted. The patient should also estimate the percentage of hair lost.

The history should concentrate especially on events in the 3 months before the start of the hair loss in the case of telogen hair loss. A history of recent illness or surgery should be recorded. A dietary history is also helpful.[21] A detailed drug history including new medications or over-the-counter supplements should be recorded, as should any change in dosages.

As mentioned above, other important factors include recent chemotherapy or radiation therapy, a family history of pattern hair loss such as androgenetic alopecia, oral contraceptive use, and hormone replacement therapy.

PHYSICAL EXAMINATION

Given the complexity of the diagnosis of diffuse hair loss, the clinical examination is of great importance. The scalp should be examined for degree and pattern of hair loss. The hair shafts should be assessed for length, diameter, and breakage.[21] The scalp should be examined for inflammation, erythema, and scaling.[21]

Educating the patient is an essential part of management

The hair-pull test should be done in all patients with hair loss.[22] This involves gentle traction from the base to the tips of a group of 25 to 50 hairs. Normally, only 1 or 2 hairs are dislodged.[1] However, in shedding conditions, 10 to 15 hairs can be dislodged.[1] Light-microscopy helps differentiate the pulled hairs into telogen hairs or dystrophic anagen hairs.[1] Hair shaft microscopy can also indicate nutritional deficiencies.[11]

A daily count of shed hair can sometimes be useful,[22] as can a hair collection.[7] A hair collection is done by the patient at home over 2 weeks.[7] The shed hair is collected daily at one specific time, usually in the morning, and is placed in dated envelopes. It is important to note the dates of shampooing.[7] Daily hair collections of more than 100 hairs per day suggest effluvium.[7] Hairs can then be examined and identified as telogen hairs or anagen hairs.

LABORATORY EVALUATION AND SCALP BIOPSY

A laboratory workup can identify triggers or causes of diffuse telogen hair loss. This should include the following:

- A complete blood count and serum ferritin level to look for anemia and iron deficiency
- A thyroid-stimulating hormone and thyroxine (T_4) level to detect thyroid disease
- A serum zinc level to detect zinc deficiency
- A comprehensive metabolic panel to exclude chronic renal or liver disease.

If the history and physical examination suggest lupus erythematosus or syphilis, serologic testing can be ordered. Also, an androgen screen should be performed if signs of hyperandrogenism are present[18] or if a hormonal cause for the telogen hair loss is suspected.

Scalp biopsy is helpful in most cases of hair loss.[21] Lack of identifiable triggers, chronic hair loss, miniaturized hair shafts, and failure to exclude alopecia areata are all indications for scalp biopsy.[1,2]

Two 4-mm biopsy specimens are recommended to provide for adequate horizontal and vertical sectioning.[7] Terminal and vellus hair counts can be done, and the anagen-to-telogen hair ratio can be calculated. In acute telogen effluvium, a reversal of the normal anagen-to-telogen ratio can be seen.[23] Miniaturization of the hair shafts and low terminal-to-vellus hair counts are seen in androgenetic alopecia.[23] Characteristic peribulbar lymphocytic inflammation can be seen in alopecia areata.[20]

Changing or stopping an oral contraceptive can cause telogen hair shedding

MANAGEMENT: THE IMPORTANCE OF PATIENT EDUCATION

The most important aspect in the management of telogen effluvium is educating the patient about the natural history of the condition. The normal hair cycle should be explained, as well as the relationship between triggers and the timing of hair loss. For example, in telogen effluvium, shedding usually is noted 2 to 3 months after a trigger, although it can in rare cases begin as soon as 2 weeks after a trigger.[7]

To help identify triggers, a health diary or calendar can be useful. The patient should be instructed to record any stresses, hospital admissions, surgical procedures, new medications, dosage changes, or other potential triggers of hair loss.[1,7]

The patient should understand that, once the trigger is identified and removed or treated, the shedding settles but can continue for up to 6 months.[1] Regrowth can be noted 3 to 6 months after the trigger has been removed, but cosmetically significant regrowth can take 12 to 18 months.[1,7]

In acute telogen effluvium, if the trigger can be identified and removed, the shedding is short-lived and no further treatment is required.[1,4] Patients can be reassured that they are unlikely to go bald.

Adequate nutrition is essential. If a drug is suspected, it should be ceased or changed for at least 3 months to determine whether it is a contributing factor.[3] Any underlying scalp inflammation (for example, seborrheic dermatitis or psoriasis) should be treated with an anti-dandruff shampoo and a topical corticosteroid.[1,7]

Chronic diffuse telogen hair loss is more complex because multiple sequential or repetitive triggers can be involved.[7] Nutritional deficiencies, thyroid disease, systemic illnesses, and infections should be treated.

For acute telogen effluvium, chronic diffuse telogen hair loss, and chronic-repetitive telogen effluvium, biotin and zinc replacement can support hair regrowth.[1,7]

No specific medical treatment exists for telogen effluvium, but applying the topical hair-growth promoter minoxidil (Rogaine) 2% and 5% to the scalp once a day can be useful in chronic diffuse telogen hair loss and chronic telogen effluvium[7] (W. F. Bergfeld, personal communication, November 12, 2008).

In men, medical treatment of androgenetic alopecia includes topical minoxidil 2% or 5% and oral finasteride (Propecia).[18] Women can also use topical minoxidil; however, only the 2% solution is approved by the US Food and Drug Administration for female androgenetic alopecia.[18] Antiandrogens such as spironolactone (Aldactone) are used off-label for females with androgenetic alopecia. Antiandrogens cause feminization of the male fetus; hence, all women of childbearing years should be on a reliable form of contraceptive.[18] Small studies

show spironolactone combined with an oral contraceptive can be useful in the treatment of androgenetic alopecia in women.[18,24]

Anagen hair loss is usually managed with observation and support, as the cause will be obvious from the history. If no iatrogenic cause can be found for anagen hair loss, then other causes such as alopecia areata and heavy-metal poisoning should be investigated and the underlying condition treated.

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