

Telogen effluvium: a comprehensive review

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Abstract: Excessive hair shedding is a common and alarming phenomenon, usually complained about by women. The disorder, named telogen effluvium (TE), bears several problems which are discussed in this essay. They are as follows: 1) how profuse a hair loss must be for TE to be diagnosed; 2) its heterogeneity that needs to be properly classified; 3) its distinction from androgenetic alopecia (AGA) with which it is often associated; 4) its main symptom, trichodynia, which is unclear how frequent and how diagnostic could be; 5) why histopathology has been reported to be nonspecific; and 6) its management, from diagnosis to treatment. A common mistake of the dermatologist is to minimize the complaint. Instead, the disorder may have a profound impact on the patients' mind and would require attention, time, and empathy.

Keywords: telogen effluvium, hair, alopecia

An excessive hair shedding, without the formation of a glabrous area, is a common and alarming phenomenon, usually complained about by women. The disorder is so frequent and frightening as to convey urgently the patient to the dermatologist and to extend the complaint even to social blogs on the Web worldwide. The typical statement in such cases is: "I always had a full head of hairs and now I am losing them by the handful". A common mistake of the dermatologist is to minimize it. Instead, the disorder may have a profound impact on the patients' mind and would require attention, time, and empathy.

In this article, I will discuss a little historical recollection of telogen effluvium (TE), as Albert Kligman named the disorder,¹ its classification, clinical presentation, course, and management.

Historical perspective

Sulzberger et al² was the first to take into consideration the unexplained and increasing growth of cases of women complaining about hair loss. In the same article, he described the main accompanying symptom, "the pain in the hair", which later on I named trichodynia.³ Concurrently, Guy and Edmundson⁴ reported on a similar illness in women, emphasizing that they had an intermittent course. Kligman studied TE more extensively, stressing its pathogenetic heterogeneity.¹ Kligman described TE as a

Nonspecific reaction pattern in which the main symptom is the increased shedding of telogen hairs developing 3-4 months after the causing event. Alopecia would occur only when about 40% of hairs have been shed.

Another of Kligman's contributions was the mention of febrile and chronic systemic illnesses, childbirth, major surgery, and emotional strain as possible etiologic

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events. Regrettably, Kligman was unsuccessful in finding any histological inflammatory clues reporting only an increased number of telogen follicles. Whiting introduced the concept of the possible chronicity of the disorder⁵ and confirmed the histopathological findings of Kligman. Headington made an attempt to classify the various forms of TE.⁶ He suggested that TEs could be classified according to 5 different pathogenies, namely (1) immediate anagen release, (2) delayed anagen release, (3) shortened anagen, (4) immediate telogen release, and (5) delayed telogen release.

The problems of TE

Although commonplace, TE bears a number of problems: 1) how profuse a hair loss must be for TE to be diagnosed; 2) its heterogeneity that needs to be more properly classified; 3) its distinction from androgenetic alopecia (AGA) with which it is often associated; 4) its main symptom, trichodynia, which is unclear how frequent and how diagnostic could be; 5) why histopathology has been reported to be nonspecific; and 6) its management, from diagnosis to treatment.

Those problems notwithstanding, most, if not all, articles on TE as a title that have been produced since Kligman's paper have neglected to say what kind of TE they were dealing with and Headington's classification has been ignored even in papers, like those of Whiting, that assert to describe its histopathology and possibly its pathogenesis. As a consequence, the literature on TE is, so far, of modest practical relevance.

How profuse should the hair loss be?

Rarely are subjects with AGA coming to the dermatologist because of hair loss. They complain about the rarefaction of their scalp hair, but do not say that they are actually shedding hair. TE complaint is made especially by women, but, less often also by men. It is doubtful that only women suffer TE. The apparent gender exclusivity may depend on the fact that men keep their hair shorter and fail to notice their shedding, or that they pay less attention to shedding, resigned as they are to become bald. In fact, the typical patient is a lady who always had "a full head of hair" and who, at first sight, she still has. Nonetheless, TE occurs also in patients with AGA, especially if this is of modest severity.

Assessing the "normal" daily hair loss is not easy. We found the modified wash test (MWT) a very useful tool. The reader may find its details elsewhere.^{7,8} In brief, after 5 days of abstention from shampooing, the patient is

invited to wash his/her hair in a basin whose bottom is covered by a filtering napkin and to count all hairs that have been lost during soaping and rinsing, neglecting those that are lost afterward in the drying procedure. The hairs shorter than 3 cm, which, according to Rushton,⁹ are to be considered vellus hairs, are counted apart. The method is apparently simplistic, but it is easily accepted by the patients, provides important information and, instead of histopathology, may be repeated every month to monitor the disorder.¹⁰ Prepubertal children who, because of the absence of 5 alpha reductase, must be considered as "normal" from the AGA point of view at least, shed under standardized condition, only 10.68 ± 3.91 hairs every 5 days,¹¹ a number very far from the 100 a day claimed elsewhere to be the "normality".¹²

TE can be taken into consideration when hair shedding exceeds 100 hairs every 5 days.¹³ Such a number varies greatly, the median being around 300 hairs, but exceptionally exceeding even 1,000 hairs. The common hair shedding of AGA is instead in between 10 and 100 hairs. The hairs shorter than 3 cm are the markers of the severity of AGA. Ten percent is a tolerable prevalence.

How can TE be properly classified?

The first attempt to classify TE has been made by Headington.⁶ Its classification, however, has never been applied possibly because of its difficulty. I tried to produce a friendlier classification, dividing TEs in three pathogenetic types: (1) premature teloptosis, (2) collective teloptosis, and (3) premature entry into the telogen phase. Those types share in common the copious shedding of hairs. In some cases, some of the types mentioned earlier may overlap.¹⁴

Type I: premature teloptosis

Premature teloptosis may be analogous to Headington's immediate telogen release. It occurs after treatment with topical all-*trans* retinoic acid and with salicylic acid,^{15,16} both used in medicated shampoos, but also in the first weeks of minoxidil medication.¹⁷ Both acids have been proven to damage cadherins that keep the exogen hair moored to the follicle. Retinoic acid disintegrates both desmosomes and hemidesmosomes¹⁸ and, by disrupting cell-to-cell adhesion, promotes a premature dislodgment of the exogen hair. A similar mechanism can be surmised for minoxidil lotion. To explain the autumnal hair shedding populace is often complaining about is more difficult. It would be the intense exposure to UV rays in the previous summer to cause the cadherin disruption and the

shedding two-three months later. In fact, in the cataract, UV radiation has been proven to downregulate desmosomal protein desmoglein-2.¹⁹

Proinflammatory cytokines, like TNF- α , may be putative endogenous causes of desmoglein breaking down. Dandruff is often incriminated by patients to cause their hair to fall, a suspicion that is too often cast-off by dermatologists. However, TNF- α has been proven to downregulate E-cadherin causing cell-cell junction disruptions²⁰ and high TNF- α levels have been recovered from dandruff scalps.²¹

Type 2: collective teloptosis

Collective teloptosis may be equivalent to Headington's delayed anagen and telogen releases. In adults, the hair cycle is individual, namely, each hair follows its natural course independently from the nearby one. However, there are physiological or drug-induced settings in which the hair cycles get synchronized. Any event that causes hair loss results, therefore, in an alarming shedding that recalls a molt.

Neonatal hair loss

In neonates, the occipital hairs enter collectively the telogen phase close to delivery and fall 8–12 weeks later in what it is used to name transient neonatal hair loss.²²

Postpartum TE

During the last trimesters of pregnancy, a number of hair follicles are in anagen and enter the telogen phase simultaneously after delivery.^{23,24} Two to 3 months after delivery, a molt-like shedding may develop in about 20% of the women.

Noncytostatic drugs

Cycle synchronization may occur also in the course of long-lasting medications with estrogens. The pill may induce collective teloptosis when it is interrupted. Minoxidil and finasteride do the same and may induce collective teloptosis 3–4 months after the medication is stopped.

Type 3: premature entry into the telogen phase

This type may be equivalent to Headington's immediate anagen release. The anagen phase is stopped prematurely, and the hairs quicken their normal progression to telogen. In this phase, they remain for 3 months before being displaced.

Pathophysiology

The anagen phase may be interrupted by an arrest of the keratinocyte mitoses in the hair matrix. Whatever the operating

agency, when an antimetabolic insult occurs on an ordinary cell, the result is subject to only two factors: the strength of the insult (ie, the dosage of a drug) and/or its time extent. In contrast with other epithelial targets, however, the hair follicle is a dynamic target. Hair keratinocytes, in fact, go through periodic and regular phases of mitotic activity and rest. The eventual result of the insult depends, therefore, on two additional factors: the stage of the hair cycle in which the insult finds the hair follicle and on the coexistence of factors which modify the normal length of the cycle phases (most often AGA).

The phase of the cycle is in which the insult finds the follicle is of paramount importance. If the follicle is in a subphase with the topmost mitotic activity (anagen I–V), a great deal of mitoses would be blocked and the hair would be shed as a dystrophic hair. Conversely, if the follicle is coming near the end of the anagen phase (anagen VI), in which mitoses are already abating, the result would be the simple quickening of the normal progress to telogen. As a mitotically inactive phase, telogen becomes a sanctuary for the insulted hair to take refuge and to remain for 3 months before being shed.^{25,26} Of course, if the insult is strong or lasts enough, the hair fall would be massive and both of dystrophic and telogenic type.

The hair follicle behaves in the same two ways if the insult is generated either by an antimetabolic drug or by T lymphotoxicity, like in alopecia areata. In this disease, both ways of shedding can be seen. In some cases, the profuse telogenic shedding may prevail without forming a definite bald patch (alopecia areata incognita²⁷), a diagnosis that is made when MWT detects a few dystrophic hairs.²⁸

When AGA coexists, the ratio between the length of anagen and the one of telogen becomes a critical factor for the quality of the hair's response to the insult. If this ratio is low, as in AGA in which the anagen length is abbreviated, the probabilities that the insult finds keratinocytes with a high mitotic rate are reduced. As AGA is very common among Caucasians, therefore, the anagen/telogen length ratio is characterized in most patients by the prevalence of the telogen duration. TE would be therefore the usual way of shedding.

In brief, the same mitosis-blocking insult may cause anagen effluvium or TE independently from its quality. Even a combination of both effluvia is possible.

Etiology

The premature arrest of mitosis may occur because of drugs provided with cytostatic activity, because of nutritional insufficiencies, and, possibly, because of lymphocytotoxic activity.

Drug-induced TE

Many drugs are responsible or are allegedly credited of hair loss. The reader then may be interested in broadening this issue may find details in another paper of mine.²⁹ With a few exceptions (retinoic acid, for example) only drugs with an antimetabolic activity can produce anagen or telogen effluvia or both. Because of their toxic effect on the hair's matrix, most of the 90 chemotherapeutic drugs that are presently administered induce hair to fall. Heparin sodium and heparinoids, do it as well in more than 50% of the patients. Again, hair fall as anagen or telogen effluvia independently from the type of the drug, but rather resulting from the 4 factors mentioned earlier, specifically, the strength and length of the insult, the phase of the hair cycle in which the hair follicle is when the insult strikes it, and the co-occurrence with AGA.

TE due to nutritional or micronutrient deficiencies

Nutritional insufficiencies may cause hairs to shed, especially in the setting of chronic anorexia. Hair shedding has been described to be dystrophic,³⁰ or hair shafts are defined as being dry and brittle,³¹ but, again, how hairs are shed is the result of the four factors cited earlier. It is difficult, however, to understand exactly what the cytostatic mechanism could be. A recent study³² has reviewed the literature concluding that adding the diet with low doses of vitamin C and D improve TE. No data are presently provided to suggest zinc, riboflavin, folic acid, or vitamin B12 prescription, except perhaps the uncontrolled study of Cheung et al who found that a large proportion of TE patients had deficiencies in ferritin, vitamin D, and zinc.³³ Severe diet and iron deficiency have been claimed to be triggering causes with higher risk of association with AGA.³⁴ The literature does not support either vitamin E or biotin supplementation. Conversely, an excess of vitamin A can contribute to hair loss, and cases of TE have been reported in patients supplemented with selenium. As for iron and/or ferritin, an old tradition incriminates their deficiency for hair loss, but there are also authoritative controlled studies that deny any importance to iron deficiency.³⁵

TE due to lymphocytotoxicity ('autoimmune' TE)

This form is the most frequent case for trichologists and shares many features in common with alopecia areata

incognita, including the occurrence of a few dystrophic anagen hairs in the MWT. Of course, it is distinguished from classic alopecia areata for the absence of any glabrous areas. In fact, it is possible that TEs described in many articles without being properly classified are nothing else but cases of "autoimmune" TE. Tentatively, this condition can be labeled "autoimmune" because of its similarity with alopecia areata and because is frequently associated with other autoimmune diseases. In fact, circulating anti-thyroperoxidase antibodies and Hashimoto's thyroiditis may be encountered in up to 60% of the cases.^{36,37} Less frequent is the co-occurrence of other thyroid autoimmune diseases, or of Sjögren syndrome, inflammatory bowel disease, or autoimmune atrophic gastritis. Emotional stress commonly precedes alopecia areata and TE episodes as well, and, in mice, has been attributed to peribulbar inflammation (neurogenic?) via substance P-dependent pathways.³⁸ In fact, stress level, TH1/TH2 cytokine balance, and hair parameters proved to change significantly in a stressful situation.³⁹ Trichodynia can be complained about in 14% of the AA cases as well.⁴⁰ In TE, the trichodynamic areas are the very same from which hairs are coming out.⁴¹ Also, corticotropin-releasing factor receptor antagonists have been found to revert alopecia in mice that overexpress corticotropin-releasing factor and exhibit phenotypes of chronic stress, including alopecia.⁴² Finally, antithyroperoxidase antibodies and possible Hashimoto's thyroiditis have been often observed in alopecia areata as well.⁴³

Other mechanisms

An inflammation of the small papillary or peripapillary vessels possibly related to circulating immunocomplexes may be envisaged in TEs occurring in the setting of systemic lupus erythematosus and in postfebrile TE (PFTE), as even a XVI century communication suggests.⁴⁴

Clinical presentation

Postpartum TE

Postpartum TE develops 2–4 months after childbirth, habitually lasting 2 months, infrequently longer, and only very rarely becoming chronic, and is usually followed by full recovery.¹ From the pathogenetic point of view, the synchronization of the hair cycles during gestation, conceivably because of the scalp-wide curtailing of the anagen phase, is the critical cause, but by no means is postpartum TE a physiological phenomenon. In fact, it occurs only in about 20% of the women and not even in all pregnancies

of the same woman, but almost always at the first delivery. Possibly, the arrest of mitoses is in relationship with the emotional strain of delivery, which is maximum at the first delivery.

Autoimmune TE

Typically, the patient is a lady who reports having had a “full head of hair” but noted that it “began suddenly” to “come out by the handful”. Usually, and differently from AGA, the patient is accurate in giving the date of onset of her hair loss. Also, frequently she complains about a “pain in the hair” (trichodynia),^{3,45,46} a symptom that should be asked for because the patients are shy to confess it spontaneously. In some cases, the disorder is attributable to an emotional stress that occurred three months before its onset, but in other cases either the lady prefers not to reveal her stressing events often lost in her past or they are chronic and irremediable. Customarily, she is a well-being person without signs of anorexia or nutritional insufficiencies, and often, her TE is chronic/intermittent. As stated by Kligman, alopecia is not observed. However, it may be present in a discrete form in areas normally spared by AGA, especially the supra-auricular area (personal observation).

Postfebrile TE

Although mentioned by Kligman¹ and sequaciously cited in all chapters of hair loss, PFTE is exceptionally encountered in the daily trichological practice, but it has been common during the influenza epidemic that developed worldwide after the war 1914–18. It follows, after 2 to 6 weeks, the onset of a high fever. According to Sabouraud (cited by A. Savill⁴⁷), the fever must be between 39° and 39.5° (ie, 103°F) continuing for about 6 weeks. The amount of hair fall is great, but patients never become quite bald.⁴⁷ Pathogenesis is obscure, but a vasculitis of the small papillary or peripapillary vessels can be surmised.

Clinical course

TE course may be acute or chronic when its duration exceeds 6 months. Of course, some of the forms described above cannot be chronic. A typical acute course is that of post-partum TE. In the autoimmune TE, instead, the course is characteristically chronic, with intermittent episodes of improvement.¹⁰ The severity of any relapse can be assessed by MWT,^{7,10} but it is often impossible to establish its possible cause. Intermittency, however, is important especially because the spontaneous recovery

that can intervene in the course of any chronic TE may be erroneously credited to the therapy. This may explain some of the “successes” of popular treatments which cannot be but placebos and make any controlled study difficult to undertake.

Forms depending on interacting mechanisms

Two different pathogenetic mechanisms may interact.¹⁴ Postpartum TE is an example. A collective teloptosis may in fact coexist with an autoimmune form. From this point of view, the possible coexistence of TE with postpartum thyroiditis, which develops occurs in about 5% of the new mothers,⁴⁸ has never been investigated.

Another case of interaction is the alleged seasonal hair loss. Summertime UV irradiation may cause a premature teloptosis later in the fall, but a synchronization factor (AGA?) should be regarded as a co-factor (collective teloptosis).

How can chronic TE be distinguished from AGA?

How often chronic TE is associated with AGA is difficult to say, but given the high frequency of AGA among Caucasians, it must be a common observation.

Clinically, when AGA is obvious there would be no difficulty to recognize it. Modest cases are more troublesome, but trichoscopy is of a major help. The ratio between the hair density at the vertex and that at the occiput should be less than 1.⁴⁹ MWT is a simpler and invaluable diagnostic tool providing a measure of the respective severities. The prevalence of vellus hairs that exceeds 10% indicates AGA that deserves treatment. Instead, a 10% vellus prevalence is tolerable.

How frequent trichodynia is and what is its significance?

Trichodynia was observed by Sulzberger² as a distinctive symptom of TE and later confirmed.³ Its presence in cases of AGA^{49,51} is probably due to the association of the two disorders. Its prevalence is around 20%, occurs in sites where hairs are actually shedding and it may be regarded as a sign of severity of the disorder and of the fact that TE is going to continue for further three months at least. In general, trichodynia is a complex symptom, varying from pruritus to a needle prick.

Why has histopathology been reported to be non-specific?

The histopathology of the acute forms is non-specific and resembles that of normal scalp.⁵² In chronic TE, only an increased number of telogen hairs is detected. Signs of perifollicular inflammation have never been observed. This may be due to a belated biopsy, namely when the noxious event is no longer active because of the well-known three-month lag.

How can TE patients be managed?

The most difficult patient to be managed is the one who comes complaining about shedding her hairs “by the handful”. Dermatologists should be aware that she needs at least half an hour of visit. The patient is deeply anxious, in some cases, she reports not to sleep or to wake up in the night her first thought being her hair. It is highly advisable not to disregard those patients, to be cautious in their management and not to discard the possibility of asking for a psychiatric advice. Cases of suicide are exceptional but have been regrettably observed.

The first thing to do is to assess the severity of the hair loss. MWT is indispensable first to know whether the shedding is actually present. It is important to remember that a 3-month-lag is always present and because of this lag the patient may come when the cause of TE has already ceased to be active. Second, to assess the severity of hair loss, and, lastly, to monitor its course.

To assess the severity of the hair shedding, a “pull test” could be sufficient, but very rarely is the patient coming without having shampooed the day before and sometime even the very same day, making the pull test unreliable. As a rule, when the patient has not shampooed for some days and the pull test is intensely positive, the number of hairs collected at the MWT exceeds 300.

Trichoscopy is highly advisable. Not only it may make the patient aware of the severity of her problem, but it provides another indispensable clue to understand if the patient has only TE, only AGA or a combination of both. Trichoscopy should be done in three areas: the frontal, the occipital, and above the ears. The presence of vellus hairs, the absence of couples, or triads of hairs coming out from the same hair canal are useful indications of AGA. Conversely, noticing a sparseness of hair in the zone above the ears, a zone always spared by AGA, even the most severe; is a clue of chronic TE.

Treatment depends of course on the type of TE. In the case, which is most common, of autoimmune TE, the patient, for what it is worth, is invited to understand

what stressful event might have occurred three months before the onset of the hair shedding and possibly, to remove its cause. Then, if this is impossible, as it is the rule, a clobetasol foam can be used which is very easy to apply. Controlled studies on its use are difficult to undertake, because of the three-month lag and the typical intermittency of chronic TE and the consequent need of a too large number of subjects. In the absence of any approved treatment, clobetasol foam is my preferred attempt to do something vaguely rational. Corticosteroid creams are in general declined by the patients because they make the hairs dirty and lotions are difficult to be dosed. Systemic corticosteroids are usually unadvisable for TE needs to be treated for a long time and because of the unavoidable side-effects that are disproportionate to the severity of the original disorder. In fact, the treatment must last at least three months, and the patient should be informed not to expect any improvement before and invited to monitor the severity of her shedding once a month by MWT. It may be, however, that a spontaneous recovery occurs before the canonical three months. In such cases, the patient should not stop corticosteroids lest a possible rebound effect but to taper them gradually. Minoxidil has been suggested, but its capacity to synchronize the hair cycles does not advise its use.

Disclosure

The author reports no conflicts of interest in this work.

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