10 Telogen effluvium

A telogen effluvium (TE) occurs when abnormally large numbers of anagen hairs from all areas of the scalp enter the telogen phase (1). This may be caused by some sort of endogenous stress to the follicles, such as a metabolic disturbance, nutritional deficiency, or serious systemic illness. Other cases of TE are "physiologic" and not indicative of disease. Some of the many possible causes are listed in Table 10.1. In response to the etiologic insult, many hairs prematurely enter the catagen phase. This is a committed step for follicles, and having entered catagen they must proceed through the telogen phase and ultimately exogen (shedding).

Headington proposed five functional subtypes of TE distinguishable by different perturbations of follicular cycling that ultimately result in increased shedding of telogen club hairs (10). These subtypes may account for the many different types of triggers and slight variations in presentation and symptom duration that can be experienced by patients with TE.

CLINICAL FINDINGS

TE is probably the most common form of hair loss associated with systemic disease, especially chronic and debilitating conditions (11). However, only the most dramatic cases of TE, resulting in a greater than 25% hair loss, are likely to come to clinical attention. An apparent reduction of hair density is often not appreciated until a substantial amount of hair has been lost—some authors claim that a 50% reduction in density is required for clinically obvious thinning (10,12). The majority of drugs that have been associated with alopecia (with the important exception of anticancer medicines, other toxins, and biologic immunomodulatory agents) cause hair loss through the mechanism of a telogen effluvium (13).

Physiological forms of TE include postpartum and neonatal hair loss. During pregnancy, numerous follicles are artificially maintained in the anagen state under the influence of gestational hormones. This is reflected in the lower telogen counts that occur in the second two trimesters of pregnancy (1,14). After parturition, numerous follicles synchronously enter the catagen/telogen phase, followed by synchronous shedding of hairs approximately three months later. An analogous drug-induced effluvium can be seen after discontinuation (and occasionally after the initiation) of estrogenic oral contraceptives due to synchronized shifting of follicles into or out of an artificially prolonged anagen stage (13).

TE of the newborn represents the nearly universal shedding of scalp hair during the first six months of life. This may occur rapidly, resulting in obvious alopecia, or may proceed slowly and imperceptibly. In either case, large numbers of anagen hairs enter telogen within a period of months. It is presumed that changes in the hormonal milieu precipitated by childbirth contribute at least partially to the effluvium in the infant. The telogen counts can be elevated beyond what is typically seen in adult TE, with observations in the 70th percentile(1); this is presumed to be due to the synchronization of the majority of the follicles in the first pelage of the neonate (1).

Many adult women suffer from an ongoing TE with no definable precipitating event (15). Effluvium lasting more than 6 months has been termed "chronic telogen effluvium" and is a diagnosis of exclusion (15). Many or most of these women experience an insidious onset of disease. The course is frequently self-limited, although the condition may last for years prior to

Table 10.1 Causes of Telogen Effluvium

Physiological (not pathological)
Physiological effluvium of the newborn
Postpartum telogen effluvium

Injury or stress (pathologic)
Postfebrile (extremely high fevers, e.g., malaria)
Severe infection
Severe chronic illness
Severe, prolonged psychological stress
Postsurgical (implies major surgical procedure)
Hypothyroidism, hyperthyroidism, and other endocrinopathies
Crash or liquid protein diets; starvation

Drugs
ACE-inhibitors (e.g., captopril, enalapril, ramipril) (2)
allopurinol (2)
amphetamines (2)
androgens (2)
Anticoagulants (especially heparin) (1)
Antithyroid (propylthiouracil, methimazole)
Anticonvulsants (e.g., phenytoin, valproic acid)
Antifungals (e.g., terbinafine, fluconazole, itraconazole, clotrimazole) (2)
Antihistamines (e.g., cimetidine, ranitidine)
Antiretrovirals (e.g., indinavir, acyclovir) (3,4)
Beta-blockers (e.g., metoprolol, propranolol) (2)
Dopamine agonists (e.g., pramipexole, bromocriptine, pergolide) (5)
Ethambutol (2)
Dopamine precursor (levodopa) (5)
Fibrates (clofibrate, fenofibrate) (2)
Heavy metals
Interferons (6)
Leflunomide (2)
Lithium (especially if induces hypothyroidism) (2)
Minoxidil (either initiation or discontinuation of) (2,7)
Nicotinic acid (2)
Nonsteroidal anti-inflammatories (e.g., naproxen, ibuprofen) (2)
Oral contraceptives (either initiation or discontinuation of) (8)
Retinoids, vitamin A and its derivatives (acitretin, etretinate, isotretinoin) (2,9)
Salicylates (2)
Serotonin re-uptake inhibitors (e.g., fluoxetine) (2)
Spironolactone (2)
Tricyclic antidepressents (e.g., amytriptiline, doxepin) (2)

spontaneous resolution. This form of TE is speculated to result in part from a shortened duration of the anagen phase (10).

The early stage of androgenetic alopecia is akin to a *localized* form of chronic TE (10). The affected hairs of the balding (typically vertex and frontal) scalp experience a marked reduction in the length of anagen. A much higher proportion of hairs are thus entering telogen at any given time. Hair shedding is only obvious during the early stages of the balding process, when large, terminal hairs are being shed. As androgenetic alopecia becomes more chronic, the hairs miniaturize and the turnover and shedding of vellus telogen hairs is not apparent.

Patients with acute forms of TE notice hair loss about three or four months after the precipitating event. This corresponds to the time it takes for a hair to move through catagen and the early stages of telogen. Scalp hair density may appear normal to outside observers, despite the patient's complaint of profuse hair loss. If alopecia is clinically obvious, the loss appears diffuse and affects all parts of the scalp equally (Figs. 10.1 and 10.2). A gentle hair pull yields several hairs with the depigmented, cornified, clubbed morphology of telogen hair roots (Fig. 10.3). Dystrophic anagen hairs are not expected in a diagnosis of TE; if they are found, this may point to a diagnosis of alopecia areata incognita (16). A forcible hair pluck produces a mixture of normal anagen (dysmorphic due to plucking but not dystrophic) and telogen hairs, as well as an occasional catagen hair (Fig. 10.4).

In TE the percentage of telogen hairs will be increased to more than 20%, a criterion without which this diagnosis cannot be established with certainty. Counts between 15% and 20% can be regarded as "suspicious." In the typical case of TE,

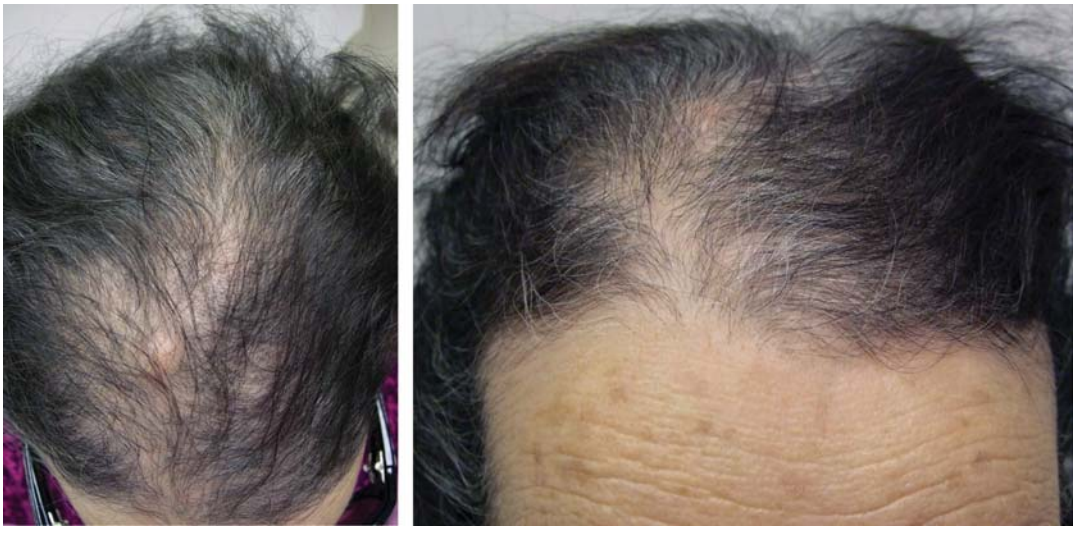

Figure 10.1 This patient with chronic *Mycobacterium avium intracellulare* lung infection treated with combination drug therapy including ethambutol, complained of diffuse thinning of the hair throughout her scalp.

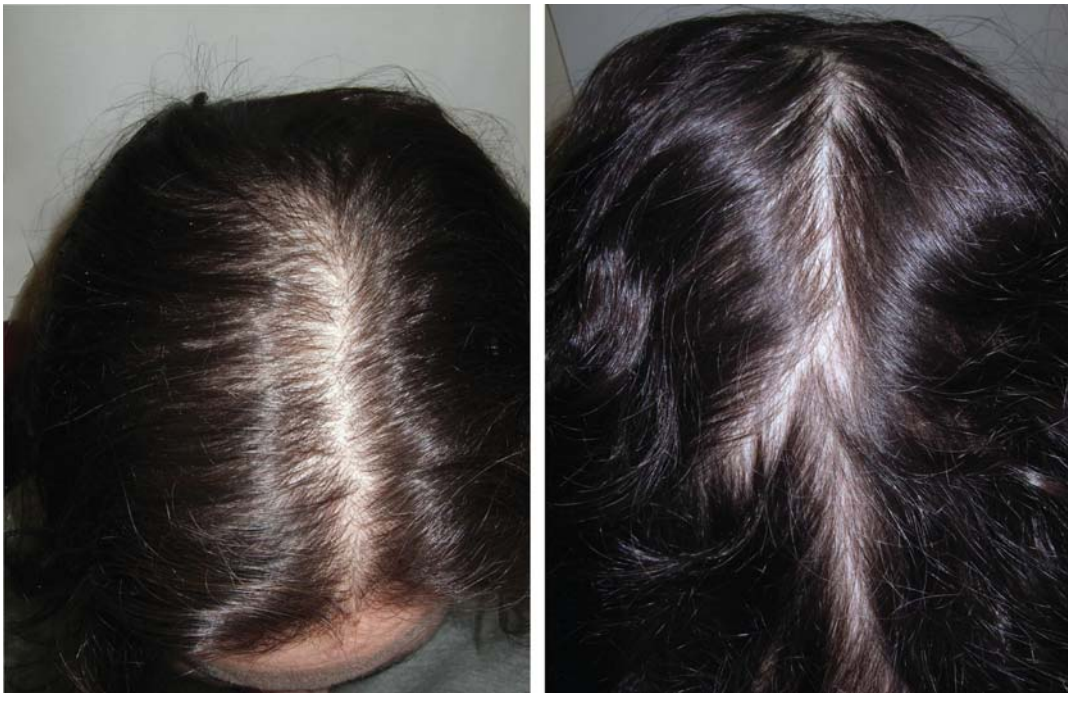

Figure 10.2 This patient demonstrates the typical pattern of telogen effluvium with diffuse thinning of hair over the entire scalp, such that the part width is equally widened over the frontal scalp and crown (*left panel*) and the posterior vertex and occiput (*right panel*).

the telogen count does not exceed 50%. However, exceptions to this rule can occur, and a unique case of effluvium following heparin administration with a telogen count of 80% has been documented (1). Figures exceeding 80% are inconsistent with a simple case of TE. The vast majority of cases we have seen have counts less than 50%.

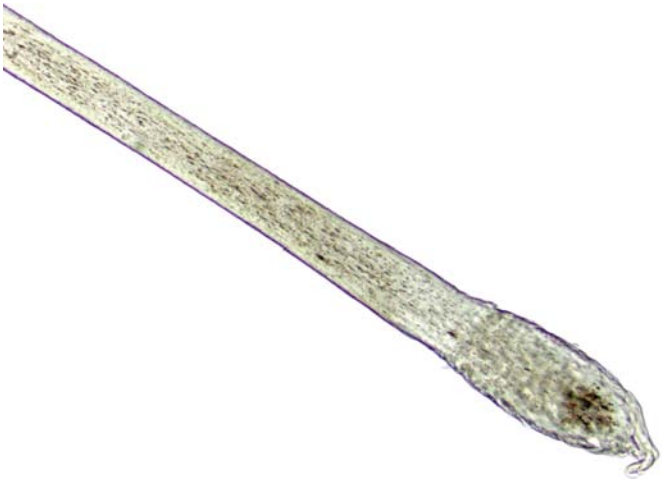

Figure 10.3 An example of a forcibly plucked or gently pulled late telogen hair. The club is depigmented and completely cornified.

Figure 10.4 Portion of a forcible hair pluck (trichogram) obtained from the scalp of a young woman with telogen effluvium. There is a mixture of normal-appearing anagen and telogen bulbs, but the telogen bulbs are overrepresented (nine telogen bulbs are visible in this image). When all hairs were counted, the telogen count was 35%.

Treatment is aimed at identifying the cause of the TE and ameliorating the condition when possible. A thorough history addressing the potential triggers of various physiologic conditions, symptoms, disease states, and medications in the preceding three months is imperative. This is followed by appropriate physical exam and laboratory testing as guided by the history. When one or more of the medications closely associated with TE are being taken by the patient, a dialog with the primary prescribing physician and a search for alternative agents is a worthwhile endeavor. Vitamin A supplements should be limited, hormone therapies stabilized and diets should be balanced (17). The relationship of iron deficiency to alopecia, and TE in particular, has been a topic of ongoing investigation (18). Recent studies support that iron deficiency, although common in women in general, is not more common in patients with chronic TE as compared with patients with female pattern hair loss or control patients (19). There are no solid data to support the contention that iron supplementation in iron-deficient patients improves hair regrowth. Nevertheless, many clinicians provide iron supplementation with a goal of achieving a serum ferritin greater than 40 μg/L in otherwise healthy individuals. Topical minoxidil may hasten regrowth, but the medication can itself lead to a temporary effluvium upon initiation of use, due to conversion of telogen follicles into exogen in preparation for new anagen hair growth (13). Furthermore, discontinuation of minoxidil can lead to a synchronized transition of follicles (previously maintained in anagen by the drug) into telogen, with subsequent shedding after 2–3 months (13). Reassurance and stress management are important aspects of counseling patients with TE (20).

HISTOLOGICAL FINDINGS

Just as in androgenetic alopecia, the histological diagnosis of TE depends more on *quantitative* than *qualitative* features (21). The only abnormality in a "pure" case of TE is an increase in the percentage of terminal telogen follicles (Fig. 10.5). Therefore, the total number of hairs in the specimen will be normal, but there will appear to be a reduced number of terminal hairs when counted at the level of the subcutis or the deep reticular

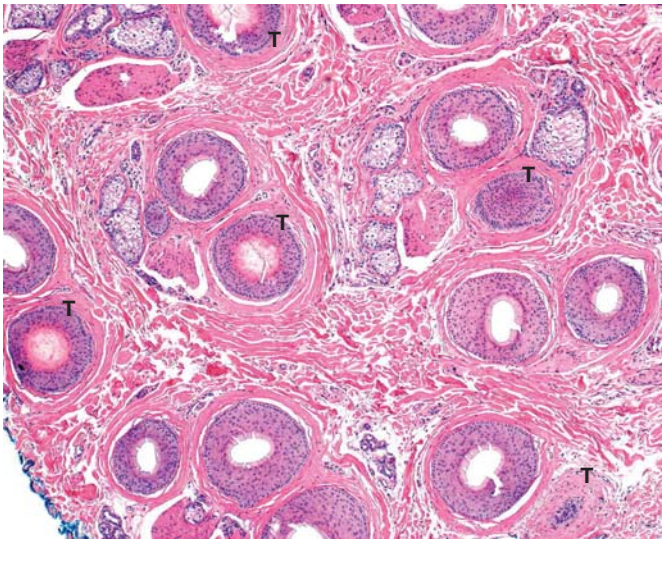

Figure 10.5 In this specimen from a patient with telogen effluvium, 15 terminal follicles can be identified; of these, five are in the catagen/telogen phase (labeled "T"). This is a catagen/telogen percentage of approximately 33%, within the typical range seen in telogen effluvium.

dermis. Fibrous "streamers" (stelae) replace the "missing" terminal hairs at this level (Figs. 10.6–10.8). These streamers lie deep to the bulbs of the terminal telogen hairs, which are found in the mid-dermis. The telogen hairs are increased in number, and the telogen count (number of terminal telogen hairs divided by the total number of terminal hairs) will be greater than 20% (Figs. 10.6–10.8).

It is important to realize, however, that a telogen count lower than 20% does *not* exclude the diagnosis of TE. If a patient's normal telogen count happens to be 5%, a telogen count of 15% would be clearly abnormal for that patient. Unfortunately, we do not know the "baseline" telogen counts for specific individuals, so numbers less than 20% must be regarded as equivocal. In cases of chronic, low-grade TE, values are

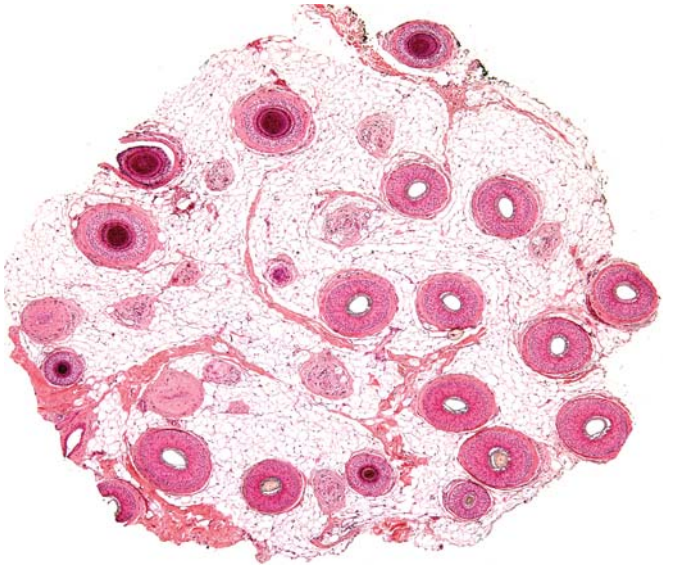

Figure 10.6 Telogen effluvium sectioned within the subcutis. At first glance the total follicular count might seem decreased for this Caucasian patient, however, when the catagen/telogen follicles (2) and numerous streamers (11) are counted along with the anagen follicles (19), the total follicular count is normal (32 total follicles). The catagen/telogen percentage is approximately 40%.

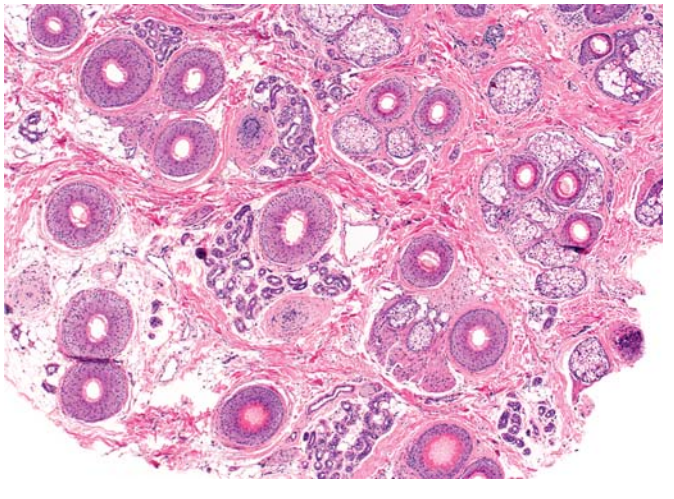

Figure 10.7 This telogen effluvium specimen, sectioned at the level of the dermal/subcutaneous junction, also demonstrates a reduced number of terminal anagen hairs. The terminal anagen hairs present are all roughly similar in diameter. Catagen/telogen hairs are seen, as well as several stelae (underlying additional catagen/telogen hairs). The total follicular number is normal but the percentage of telogen hairs is elevated to 36%.

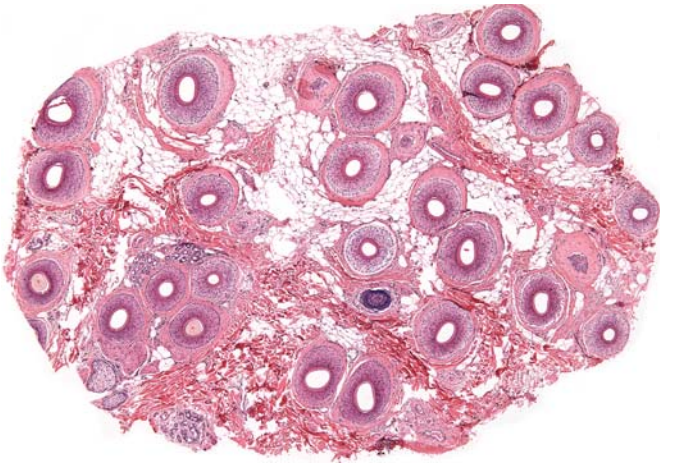

Figure 10.8 This case of telogen effluvium, also sectioned at the dermal/subcutaneous junction, is slightly subtler. In this section there are 25 anagen follicles, three catagen/telogen follicles, and four stelae (underlying telogen follicles). The catagen/telogen percentage is 22%.

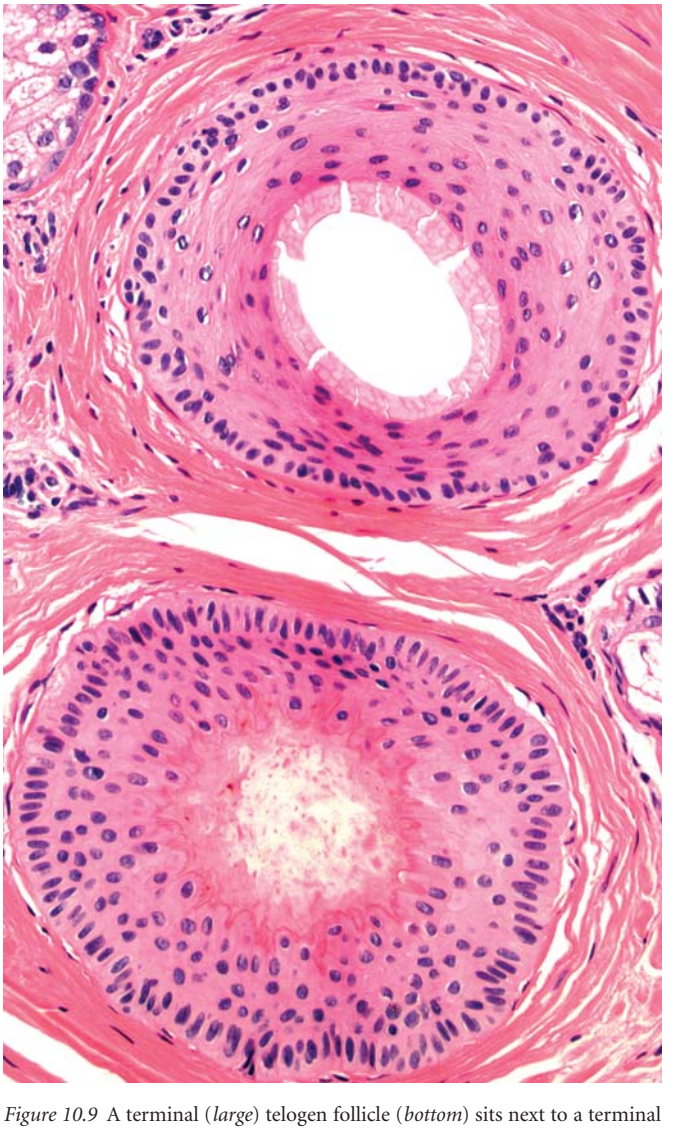

Figure 10.9 A terminal (*large*) telogen follicle (*bottom*) sits next to a terminal anagen follicle (*top*) in a high power view of a biopsy from a patient with telogen effluvium. The sizes of the two follicles are comparable.

often lower than typically seen in acute effluvium, in the range of 15%–20%; Whiting cites an even lower range of 10%–20%, with an average of 11% (15).

The size of hairs is not affected in TE. Abnormally high numbers of terminal anagen hairs are converted into terminal telogen hairs which regress normally leaving streamers behind, but miniaturization does not occur (Figs. 10.9 and 10.10). Therefore, the terminal:vellus hair ratio is normal (greater than 2:1) (Figs. 10.11 and 10.12).

In a simple case of TE, all parts of the scalp are affected equally, resulting in truly diffuse hair loss. In fact, all body hair is affected by the disease. This is clinically demonstrable by thinned eyebrows, pubic hair, and axillary hair. If paired biopsy specimens (frontal and occipital scalp) are obtained, the histological findings will be very similar at both sites; this is in contrast to androgenetic alopecia, which preferentially affects the frontal and/or vertex scalp while the occipital scalp remains normal.

TE is a non-inflammatory form of hair loss, and accordingly, no significant inflammatory infiltrate is found. In particular, peribulbar inflammation and inflammation affecting the lower two-thirds of the follicles is *absent* (Fig. 10.13). If inflammation (or miniaturization) is found, the patient may, in fact, have the diffuse form of alopecia areata known as alopecia areata incognita (see chap. 15 for more information), a potential diagnostic pitfall, as the clinical presentations can be remarkably similar.

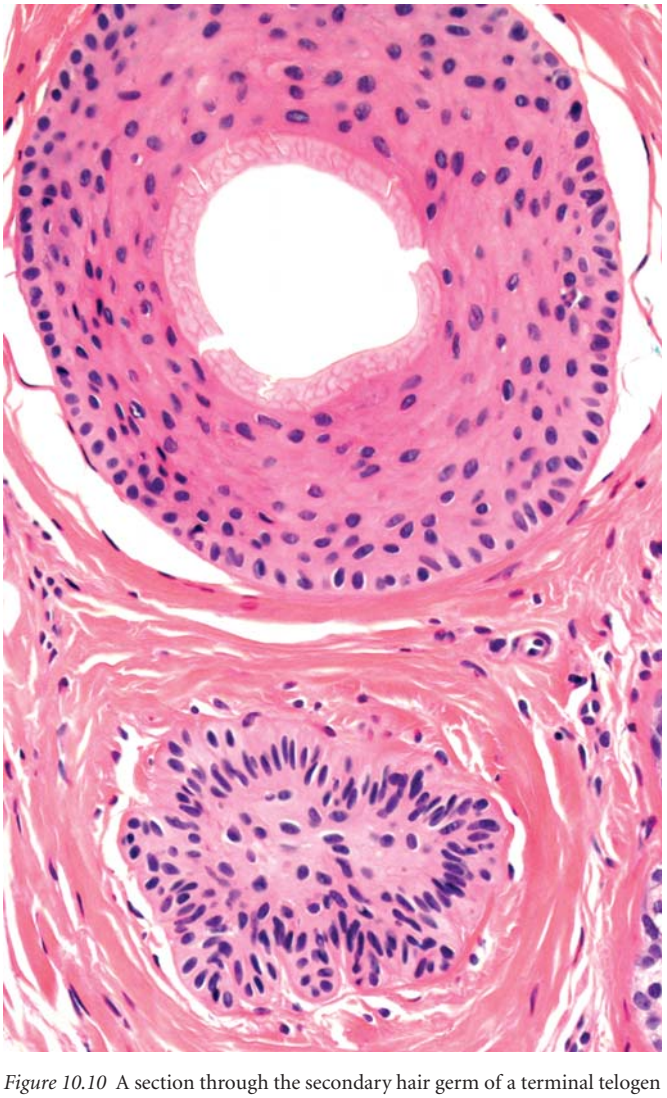

Figure 10.10 A section through the secondary hair germ of a terminal telogen hair (inferior) sits next to a terminal anagen follicle (superior) in a high power view of a biopsy from a patient with telogen effluvium. The condensed structure of the secondary hair germ is smaller than the terminal anagen follicle, but this does not represent miniaturization.

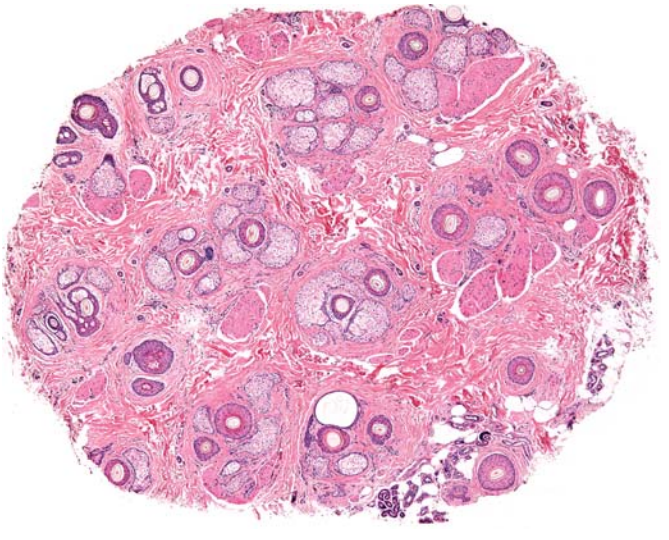

Figure 10.11 Telogen effluvium is characterized by an increase in the percentage of catagen/telogen hairs without a decrease in the overall size of hairs. The terminal: vellus hair ratio in this section taken at the level of the sebaceous glands where vellus hairs are evident, is much greater than 2:1.

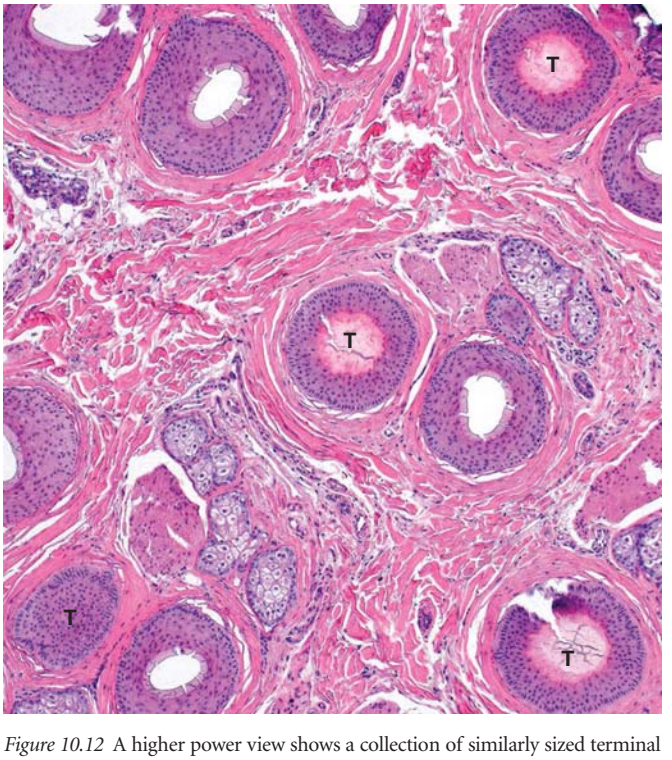

Figure 10.12 A higher power view shows a collection of similarly sized terminal telogen hairs (T) and terminal anagen hairs without evidence of miniaturization.

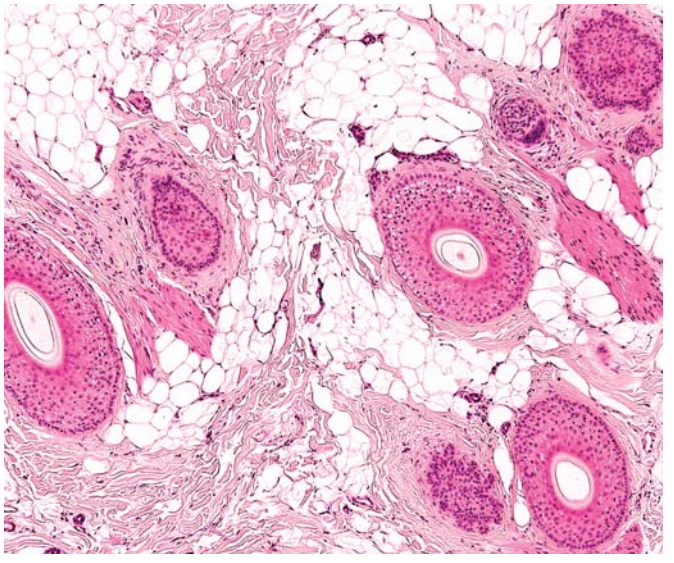

Figure 10.13 In this section through the subcutaneous fat there are three anagen follicles, three catagen/telogen follicles, and a single bulb; there is no inflammation to account for the shift, concordant with a diagnosis of telogen effluvium.

Telogen Effluvium in Summary

Clinical correlation: a patient reports diffuse hair loss/increased shedding of hair into the brush or comb, on the pillow, or in the shower drain. A history of a precipitating event (approximately 3 months prior to onset of hair loss) is often obtainable, such as childbirth, major surgery or severe illness, use of certain medications, etc. Many cases of chronic TE do not have an identifiable cause.

Histological findings:

- ❖ Normal *total* number of follicles
- ❖ Increased *percentage* of terminal catagen/telogen hairs (rarely exceeds 50%)
- ❖ Normal size of follicles (miniaturization is not a feature) and, therefore, a normal terminal: vellus hair ratio
- ❖ Presence of fibrous "streamers" indicating conversion to telogen hairs
- ❖ Absence of significant inflammation
- In chronic TE the catagen/telogen rate can be quite variable because of a waxing and waning course

Histological Differential diagnosis:

- **Acute traction alopecia:** shares with TE normal follicular size and count with an increased catagen/telogen shift. Trichomalacia and pigment casts (not features of TE) may occasionally be found. The clinical history is especially important
- **Trichotillomania:** also demonstrates normal follicular size and counts, and frequently shows an increased catagen/telogen percentage. Incomplete, disrupted follicular anatomy is diagnostic but not always present
- **Androgenetic alopecia:** can show a slight shift to the catagen/telogen phase but miniaturization of follicles is also present
- **Postoperative (pressure-induced) alopecia:** shows a massive conversion into the catagen/telogen phase, far surpassing the typical 20–50% range of TE. Trichomalacia, vascular thrombosis and fat necrosis can be seen in this entity but not in TE. The clinical history is also distinctive
- **Alopecia areata:** demonstrates a higher catagen/telogen shift (typically well above 50%) than TE; miniaturization is a prominent feature in alopecia areata (especially with chronic disease)
- **Psoriatic alopecia and TNF-alpha-inhibitor associated psoriasiform alopecia:** also show very elevated catagen/telogen percentages (typically > 50%), however they have additional findings (most notably inflammation) that help to distinguish them from TE

⚠ Pitfalls

- The diffuse variant of alopecia areata (alopecia areata incognita) is a deceptive clinical mimic of TE; careful evaluation of the histopathology is required.
- New onset TE not uncommonly unmasks the early stages of androgenetic alopecia. Paired biopsies from both involved (e.g., frontal or crown) and normal-appearing (e.g., occipital) scalp may be required to evaluate for the presence of one (or both) of the two diseases.

Abbreviation: TE, telogen effluvium.

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