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Alopecia: A New Approach to Treatment

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The baffling pathogenesis of hair loss has hindered the development of therapies. A new modality using low-dose corticosteroids plus an anabolic agent has, in a small study, produced good to excellent results. This method, plus tranquilizers, estrogens, and TLC by the physician holds promise.

The female patient views hair loss, or alopecia, as a source of embarrassment and even as a sign of disfigurement. Thus, although it does not endanger her physical well-being, hair loss is a significant threat to the patient's sense of femininity and self-esteem, as well as a frustrating challenge to the clinician.

Why the normal cycle of hair growth (anagen), rest (telogen), and loss (catagen) undergoes alteration or disruption is still poorly understood. Heredity, autoimmune disease, stress, hormonal changes associated with pregnancy and childbirth, certain febrile illnesses, and chemical agents have all been implicated in the various forms of hair loss, but many questions remain unanswered. What controls the cyclicity of the hair follicle? How does testosterone act on the follicle via the skin? Why does hair proliferate in one area and regress in another?

Because the etiologies of alopecia are largely obscure, treatment of this condition has met with only moderate success. Thus, a new approach using low-dose corticosteroids combined with an anabolic agent merits consideration, even though the clinical study group was small.

Classification

Alopecia is divided into three categories, based on the degree and location of hair loss: alopecia areata, alopecia totalis, and alopecia universalis.

Alopecia Areata: This form of hair loss occurs in 17.2/100,000 of the population and usually presents with a well-circumscribed oval-shaped area of hair loss that spreads centrifugally with some degree of rapidity. Occasionally, the initial patches lack a regular outline, and scattered long hairs may be found within the bald areas. Characteristically, the skin of these patchy bald spots is ivory-white and completely hairless; rarely, there may be some erythema or edema. The occurrence

of short, protruding club hairs with frayed points ("exclamation-mark" hairs) in the affected area is pathognomonic of the condition. Under microscopic examination, these hairs have an irregular diameter and a poorly pigmented attenuated bulb (due to atrophy of the hair root), which is unlike the club-shaped tips of telogen hairs.

Another important feature of alopecia areata is the predominance of hair follicles in a state of arrested anagen. In an interesting study using hairs plucked successively from concentric rings surrounding developing

fast take

Alopecia areata is characterized by the presence of short, protruding club hairs with frayed points, the so-called "exclamation mark" hairs. This finding, combined with rapid onset and a classical clinical appearance of well-circumscribed bald areas, without inflammation or scaling, easily distinguish alopecia from other dermatologic disorders.

lesions, Eckert and colleagues found that, at an early stage, 100 per cent of the hairs removed from the center of the patch were club hairs, and that the number of telogen hairs increased outwardly from the epicenter. Thus, a simple hypothesis for the pathogenesis of alopecia areata may be a transitory failure of the hair matrix, resulting in the premature shedding of anagen hair.

Alopecia Totalis: This condition, a severe form of alopecia areata, results in total loss of scalp hair. It develops slowly in 5–10 per cent of patients with alopecia areata and is observed more frequently in children.

Alopecia Universalis: This virtually complete loss of all body hair, including eyebrows and eyelashes, is the worst manifestation of the disease.

Prognosis depends on the extent of the disease: full hair regrowth may be expected when the lesions are few, while only 2.5 per cent of alopecia totalis patients manifest even short periods of complete hair regrowth; relapses are frequent. Alopecia universalis carries the worst prognosis.

Diagnosis

The diagnosis of alopecia is based mainly on clinical appearance. Rapid onset, well-circumscribed areas of baldness, and the absence of inflammation or scaling easily differentiate alopecia from other dermatologic disorders.

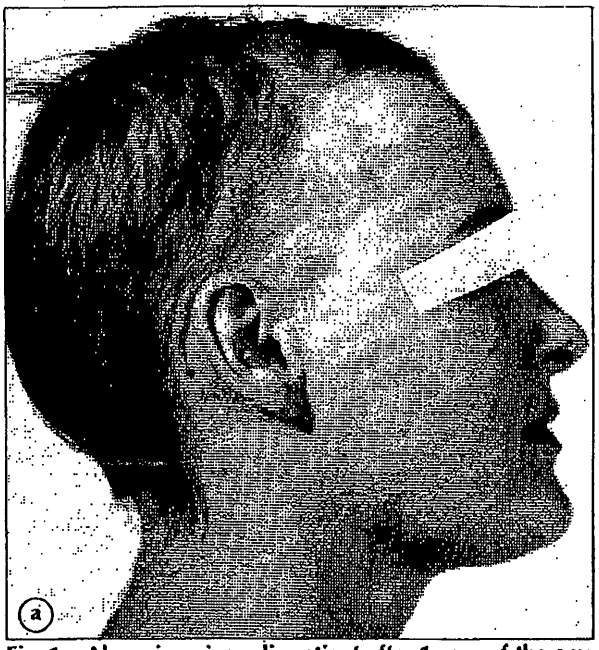

Fig. 1a. Alopecia universalis patient after 1 year of therapy. Before treatment there was a 90 per cent loss of head hair, and complete absence of eyebrows and body hair. Her eyelashes, axillary and pubic hair were scanty.

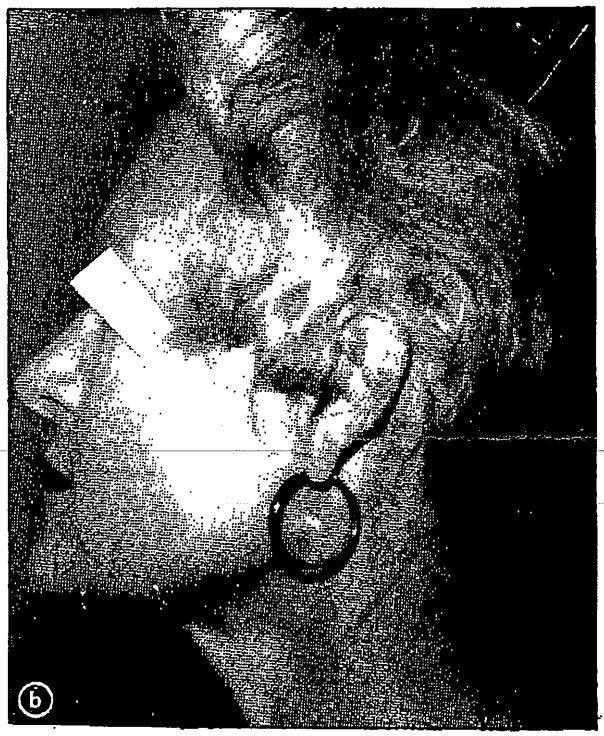

Fig. 1b. The patient, 21 years later. She received cortisone, 50 mg/day, which was gradually reduced to 25 mg/day; prednisone, 7.5 mg/day, was then substituted and gradually reduced to 2.5 mg/day. Corticoid therapy was discontinued 5 years ago. Concomitant therapy, from the beginning to the present, included subcutaneous pellet implantation of 50 mg of estradiol, and 75 mg of testosterone, with cyclic 7-day courses of a progestin to assure regular withdrawal of menstrual periods.

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On histologic examination, lymphocytic cell infiltration surrounding the dermal papilla is a prominent feature. The affected area is characterized by a nonspecific inflammatory infiltrate of the hair follicle, and a round-cell "swarm of bees" type of infiltration around the hair bulb. The sebaceous glands are unaffected, and the surrounding skin is histologically normal.

Another type of hair loss, male-pattern baldness, should not be confused with alopecia. In the former, heredity and an inappropriate response to circulating androgen play a primary role; in the latter, the causes are largely unknown. The predominant role of testosterone in male-pattern baldness is manifested in women suffering from congenital adrenal hyperplasia and androgen-producing tumors.

Possible Causes

Autoimmune Disease: This condition is most frequently suggested as a cause of hair loss. High or low titers of circulating autoantibodies and anti-smooth-muscle antibodies have been reported in several studies of patients with alopecia. Kern and co-workers found the same type of histologic abnormalities: perifollicular infiltrates and thickened connective tissue sheaths around the follicles. They also measured higher antibody levels for thyroglobulin, parietal cells, adrenal cells, and thyroid cells. No antibodies against hair follicle cells were found. The leukocyte count was normal in most patients, and neither thyroid nor adrenal disease was present at the time. However, according to Van Scott, the primary immunologic mechanism was degenerative change in the connective tissue surrounding the blood vessels that supply the dermal papilla, leading to a decrease in hair matrix volume.

fast take

Causes: Autoimmune disease is named more often than any other factor as a cause of hair loss. Cancer chemotherapeutic drugs, stress, high doses of vitamin A and hormonal changes postpartum are also implicated. Most forms of alopecia are reversible with treatment.

Psychogenic or Emotional Stress: Frequently, patients correlate the onset of alopecia with a stressful situation or an emotionally upsetting event. There is little doubt that in susceptible individuals emotional disturbances are strong promoters, if not initiators, of excessive hair loss. A condition, sometimes referred to as telogen alopecia, (the loss of telogen hair) has been shown to be stress related. Although there is usually a latent period

Fig. 2a. Alopecia areata in a 31-year-old hysterectomized woman.

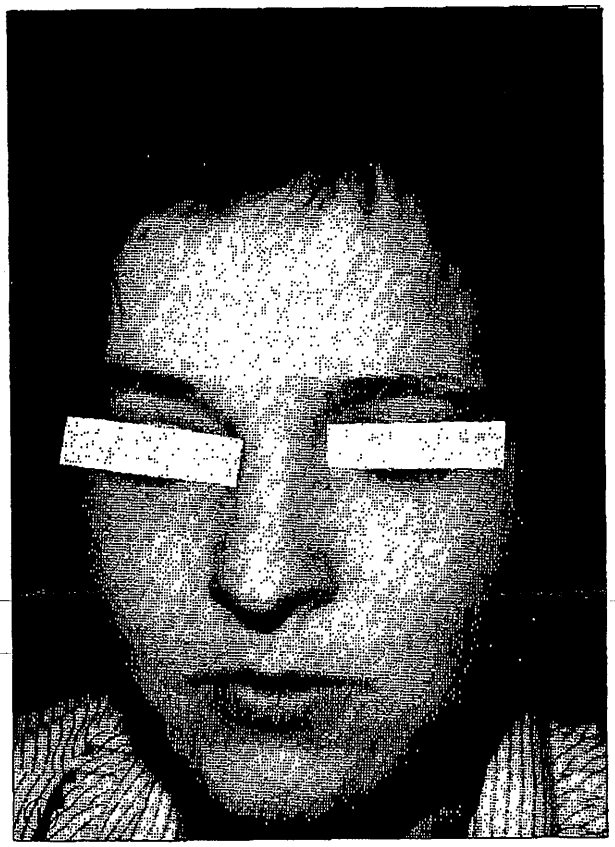

Fig. 2b. Same patient 1 year later. There is marked hair regrowth, which continued to improve with 4-6 mg/day of methylprednisone, and concomitant subcutaneous pellet implants of 25 mg estradiol and 75 mg of testosterone.

of 2–4 months, hair loss may be obvious earlier. Whether alopecia following serious febrile illnesses, such as typhoid, is caused by stress or an agent associated with the illness is not yet known.

Postpartum Hair Loss: Temporary alopecia occurs with varying degrees of severity in most parturient women. There is typically a latent period of 4–16 weeks, and onset within a few days of delivery strongly suggests a preexisting cause. In these patients, alopecia represents a delay in the normal anagen/telogen conversion, resulting in a temporary increase in the number of anagen hairs changed to telogen hairs in the postpartum period. The precise hormonal mechanism is unknown. There are conflicting data concerning the reoccurrence of alopecia with consecutive pregnancies, but the majority of investigators find no consistent relationship. Complete hair regrowth has been observed in about 50 per cent of patients.

Drug-Induced Alopecia: Hair loss associated with chemical agents is being seen with increasing frequency. Since these drugs are designed to attack cells indiscriminately in their most active phase of replication, cells of bone marrow, gastrointestinal and germinal epithelium, hair follicles, skin and embryonic tissue may be equally affected. However, not all chemotherapeutic agents cause alopecia, and the reasons for this are unclear. Doxorubicin leads to hair loss within 3 weeks in more than 80 per cent of patients. Cyclophosphamide, vincristine, methotrexate, and 5-fluorouracil also induce significant hair loss. Since anagen hair is chiefly affected, hair loss is observed where the anagen count is highest. The affected hair is irregularly narrowed, fragile, and breaks off at its narrowest point as soon as it emerges from the follicle, giving the characteristic appearance of "chemotherapy hair." The observed hair loss is temporary and regrowth occurs when therapy is discontinued.

A significant number of nonchemotherapeutic drugs, such as heparin and the coumarin derivatives, also cause telogen alopecia. Thallium used in treating tinea capitis, colchicine for hyperuricemia, as well as propranolol, trimethadione, methysergide, clofibrate, and lithium carbonate cause a moderate degree of hair loss. Megadoses of vitamin A and antithyroid drugs may lead to diffuse, but reversible, hair loss. The only drug-induced irreversible telogen alopecia is caused by high doses of androgens given to genetically predisposed individuals.

Treatment

Since alopecia requires long-term systemic treatment before results are evident, hair pieces or wigs are recommended to minimize the psychic trauma.

A number of specific treatment regimens (Table 1) have been used for alopecia, with varying degrees of success. Phenol, rubefacients (e.g., tincture of cantharides or nicotinic acid derivatives), ultraviolet light, and dinitrochlorobenzene (DNCB) sensitization all appear

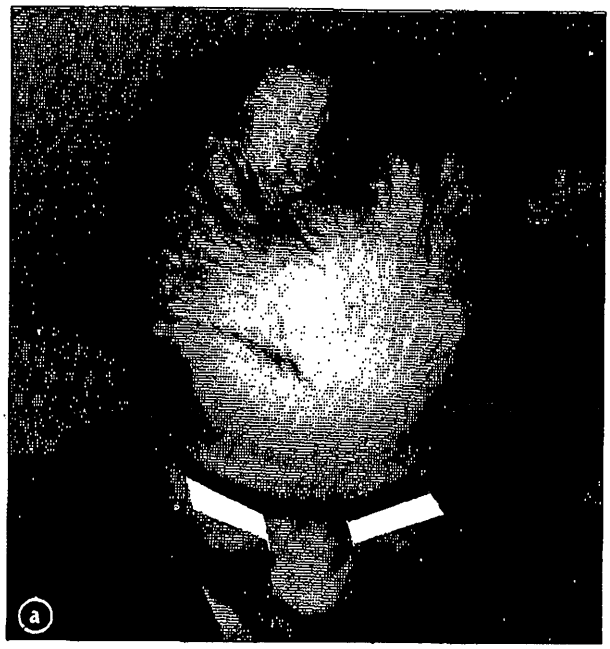

Fig. 3a. Alopecia areata in a 25-year-old woman.

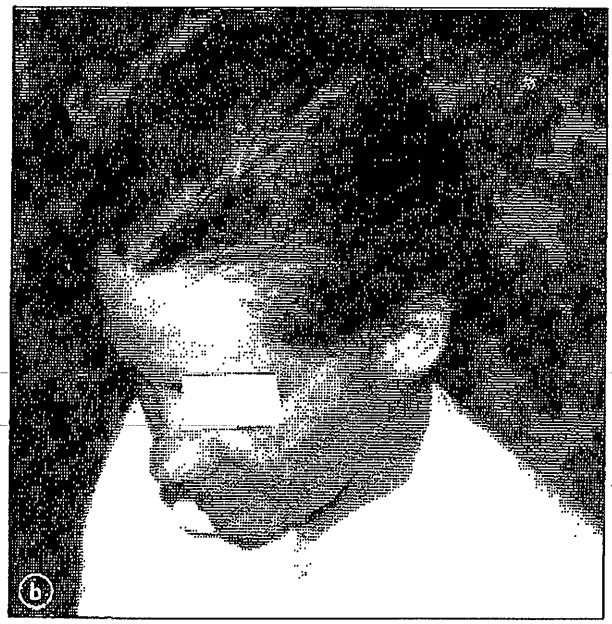

Fig. 3b. Same woman 9 months later, following treatment with 4 mg/day of methylprednisone.

to act via local vasodilation, followed by tissue hyperemia, which is believed to stimulate hair growth. Corticosteroids and psoralen (PUVA) probably exert their therapeutic effect via the autoimmune system. As for the other treatments listed in the Table, there is no universally accepted explanation for their mode of action.

Corticosteroids are currently the most frequent treatment method. One of the modes of administration, intralesional corticosteroid injection, is too painful for routine use. Systemic administration of high dosages, alone or with simultaneous local applications, has been fairly successful, although relapses are frequent. The duration and type of corticosteroid used have varied. Prednisone is generally recommended: 20–30 mg/day, for 4–6 weeks, followed by alternate-day therapy and/or treatment-free periods. Some clinicians, however, use comparatively short courses of prednisone at dosages rarely exceeding 30–40 mg/day, in combination with local treatment.

Table 1 Treatments for Alopecia

Corticosteroids:	Local
	Intralesional
	Systemic
	In conjunction with anabolic agent
Phenol	
Rubefacients	
Ultraviolet light	
DNCB sensitization (dinitrochlorobenzene)	
Psoralen (PUVA)	
Diaminodiphenylsulfone	
Zinc sulfate	
Penicillin	
Aloe	
Topical estrogens	
Tranquilizers	

A New Approach: We believe treatment with chronic and/or high doses of corticosteroids carries many risks; therefore, we have employed a much lower dosage regimen along with anabolic agents.

Our study consisted of 13 female patients: 8 with alopecia areata, 2 with alopecia totalis, and 3 with alopecia universalis in the incipient stage. Treatment was started at the first visit, and patients were seen at 6-month intervals thereafter.

Oral systemic and local corticosteroids in ointment form were used as treatment modalities; intralesional corticosteroid injections were employed in an occasional patient, but later abandoned because of pain or poor results. Oral preparations included cortisone in 1 patient (50 mg/day, gradually reduced to 25 mg/day), prednisone in 5 patients (5–10 mg/day), and methylprednisolone in 7 patients (4–6 mg/day). The duration of therapy varied from patient to patient, but was continued until satisfactory hair growth was achieved. Then the medication was gradually withdrawn.

Corticosteroids were administered with an anabolic

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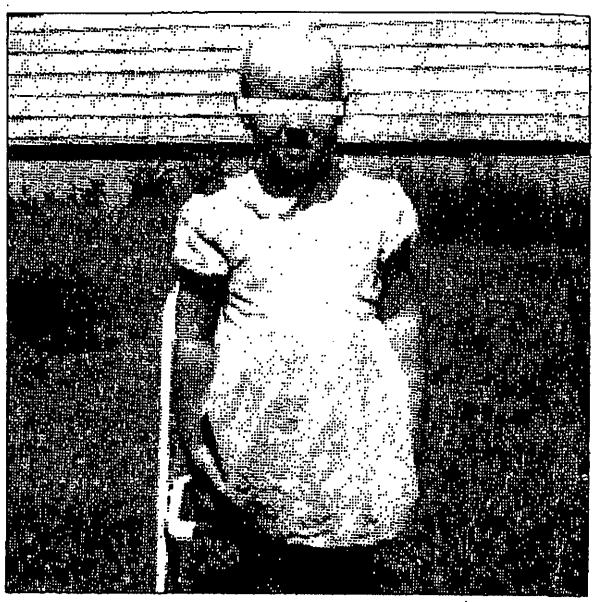

Fig. 4. Alopecia in a 4-year-old girl with almost total loss of head hair, and complete absence of eyebrows, eyelashes, and body hair.

steroid, either in an oral form, such as stanozolol or by subcutaneous implantation of a 75 mg pellet of pure crystalline testosterone, and 1 or 2 pellets of estradiol (25 mg) at 6-month intervals. Anabolic agents were chosen for their psychotonic action as a mood elevator, helpful in women experiencing the emotional upheaval following hair loss, and for their ability to counterbalance the catabolic effects of long-term corticosteroid therapy. It should be emphasized, however, that corticosteroids are the primary method of treatment, since they apparently suppress the underlying autoimmune disorder.

fast take

An alternative therapy was evaluated in a study of 13 women using low-dose corticosteroids administered with an anabolic agent. The latter was chosen for its action as a mood elevator, and for its ability to counterbalance the catabolic effects of long-term corticosteroid therapy. There were no adverse reactions to corticoids or anabolic steroids: results were comparable, and probably better, than with other modalities.

Treatment was assessed on a scale of 100 per cent improvement by both patient and examiner. Of 8 patients afflicted with alopecia areata, results were excellent in 1 (95 per cent improvement), moderately good in 5 (about 50 per cent improvement), and poor in 1 (25 per cent improvement). One patient relapsed, although

moderately good results were produced by further therapy.

Of the 2 patients with alopecia totalis, 1 had excellent results and the other, a recent patient, has shown decided improvement in a few months. Of the 3 patients with incipient alopecia universalis, 1 had 100 per cent hair regrowth; another did not respond until after the simultaneous local application of 10 mg of prednisone and 2 mg of an oral anabolic agent (stanozolol); the third, a young child, responded well over a 5-year period while on therapy but relapsed within a year after corticosteroids were discontinued. No untoward effects occurred from the dosages of corticoids and anabolic steroids used in this study.

The simultaneous use of oral corticosteroids and anabolic steroids achieved results that were at least comparable to, and probably better than, most other approaches.

Treatment is not too complex. Family physicians, general practitioners, and gynecologists with endocrinologic orientation may readily undertake the long-term management of alopecia. Administration of relatively small doses of corticosteroids, mild tranquilizers, tender loving care, and supportive therapy with estrogens and/or mild anabolic agents have proved rewarding for many victims of alopecia. □

Hair Physiology

Hair is embryologically derived from the mechanoreceptor units in the hinge regions between the scales of certain reptilian species. It is composed of fibrous protein, which undergoes rapid keratinization and intracellular coherence to form hair fiber. Hair follicles, like other rapidly proliferating tissues, are constantly cycling.

Anagen

This is the first phase of the cycle, when hair is synthesized from a follicle during a period ranging from a few weeks to several months. Approximately 85 per cent of scalp hair follicles are in anagen.

Telogen

The next phase is telogen, the resting period, which lasts several weeks and may be identified by its typical clubbed hair root. Unlike scalp hair, most follicles from other areas of the body are in telogen.

Catagen

Catagen is the final phase of the cycle during which telogen hair is shed.

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