Hair loss in infancy

J. A. MORENO-ROMERO 1, R. GRIMALT 2

Hair diseases represent a significant portion of cases seen by pediatric dermatologists although hair has always been a secondary aspect in pediatricians and dermatologists training, on the erroneous basis that there is not much information extractable from it. Dermatologists are in the enviable situation of being able to study many disorders with simple diagnostic techniques. The hair is easily accessible to examination but, paradoxically, this approach is often disregarded by non-dermatologist. This paper has been written on the purpose of trying to serve in the diagnostic process of daily practice, and trying to help, for example, to distinguish between certain acquired and some genetically determined hair diseases. We will focus on all the data that can be obtained from our patients’ hair and try to help on using the messages given by hair for each patient. Quite often it is extremely hard to distinguish between abnormality and normality in neonatal hair aspects. We will specially focus in the most common physiological changes that may mislead to an incorrect diagnosis. Specific treatment for those hair diseases that do have one, and basic general approach to improve the cosmetic appearance of hair, will be also be discussed for those hair disturbances that do not have a specific treatment.

KEY WORDS: Child - Alopecia - Hair diseases.

Hair loss in children encompasses a wide range of conditions that can be congenital or acquired. A congenital hair abnormality may be an isolated finding in an otherwise healthy child or may exist as a feature of a clinical syndrome. The clinical presentation of pediatric hair disorders ranges from subtle to disfiguring. A basic working knowledge of normal hair growth is necessary, including the embryology and development of the hair.

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Embryology and normal hair development

The full complement of hair follicles is present at birth and no new hair follicles develop thereafter. Each follicle is capable of producing three different types of hair: lanugo, vellus and terminal. Lanugo hairs are the neonatal non-pigmented, soft, fine hairs with no central medulla; vellus hairs are short, fine, lightly pigmented and they are the hairs found over much of the adult body; terminal hairs are the long, thick, strongly pigmented hairs found in the scalp and eyebrows of adults and children, as well as the axillary and pubic areas of adults and the chest and facial areas of adult males.1

Hair development begins in utero at 9th week, with the follicular units composed of epidermally derived follicles and mesodermally derived papillae. Primary hair follicles first develop on the eyebrows, upper lip and chin. Later, hair follicles develop over the scalp in a frontal to occipital direction and over the body in a cephalocaudal direction. Secondary follicles then form at each side of the primary follicles, producing typical groups of three hairs on follicular units (Mejeres trilos). At 16 weeks of gestation, hair production begins in the follicles. All follicles produce lanugo hair that grows 2-3 cm in length.2 Fine lanugo hair covers the scalp and proceeds to appear elsewhere.
in a cephalocaudal direction, eventually covering the entire fetus. This constitutes the first anagen (growth) wave. At 26-28 weeks of gestation, the body and most of the scalp hair follicles enter catagen and subsequently telogen in a programmed wave in a cephalocaudal direction in the body and a frontal to parietal direction on the scalp. Most of these telogen hairs are shed in utero, although this can be delayed until after birth. A band-like area of occipital hair does not enter telogen until 8-12 weeks after birth. These occipital hairs fall out, producing a well-defined area of alopecia, known as occipital alopecia of the newborn, seen at around 4-8 months of age. It has been recently renamed as transient neonatal hair loss (TNHL) (Figure 1). The duration of growth of the scalp hairs extends, while that of the body hairs shortens to produce hairs of 1 cm in length. These second body hairs grow for 4-8 weeks, then enter telogen, and are shed during the first 3-4 months of life to be replaced by a third coat of hair. Body hair progressively shorten into vellus hair, most of which do not protrude from the follicle. Scalp hair enlarges progressively with each hair cycle into terminal hair. Some infants display intermediate hair from 3 months until the age of 2 years. This hair is coarser than lanugo hairs, but still are sparsely pigmented.

At full term, there are two consecutive waves of hair on the scalp, each running from forehead to occiput. Toward the end of the first year of life, following the first two synchronized waves of telogen, there is a transition to a random mosaic pattern where each hair has its own intrinsic rhythm. This asynchrony continues throughout life unless modified by pregnancy or illness.

At puberty, the level of circulating adrenal androgens increases and elicits a site-specific response from the hair follicles. On the scalp, hairs miniaturize in response to androgens; however, the hairs of the body enlarge, with the hairs of the axillary, pubic, chest and beard regions being more responsive. The hair of these regions change from vellus to terminal hair, contributing to the development of the secondary sex characteristics. Hair leaves the scalp at precisely formed angles. Displacement of the scalp line occurs in a number of syndromes. A congenitally high anterior hairline is seen in myotonic dystrophy. A congenitally low posterior hairline can occur in Turner and Noonan syndromes. A congenitally low anterior hairline is found in Cornelia de Lange syndrome, lipoatrophic diabetes, fetal hidantoin syndrome and Rubinstein-Taybi syndrome.

Alopecia areata

Alopecia areata (AA) is a non-scarring, autoimmune, inflammatory, hair loss on the scalp and/or
body. Recognized subgroups of this disease include those patients with the complete absence of terminal scalp hair (*alopecia totalis*) and those patients with total loss of terminal scalp and body hair (*alopecia universalis*) (Figures 2, 3).[7]

AA is common, the lifetime risk of AA in the general population is estimated to be 1.7%. The disease occurs in both genders and in all age groups, including children. AA presents before 16 years in approximately 20% of patients. In young infants, however, AA has been considered to be quite rare. Recent articles have suggested that this disorder may be more common in neonates and young infants than previously supposed (Figure 4).[8] Thus, AA can be classified as both an acquired and a congenital disorder.

Earlier onset of AA may predispose the patient to progression to more widespread disease. Walker and Rothman[9] reported that onset before puberty is correlated with severity, with 50% of his prepubertal cases developing *alopecia totalis* compared with 23% who had an onset in the postpubertal period. Although the trend toward disease severity in younger patients is well established, it should be emphasized that this cannot predict disease severity in an individual case and does not rule out future hair regrowth.

Before the diagnosis of AA is made in infants with patchy or initially patchy progressive hair loss, several other conditions must be considered. The cause of neonatal occipital alopecia may be synchronized loss of telogen hairs on the occipital scalp at approximately 8-12 weeks of age. Friction or pressure over the bony occipital prominence may contribute to this circumscribed hair loss.[6] Alternatively, perinatal trauma associated with caput succedaneum can cause a pressure-induced alopecia, which often presents as a “halo ring” of hair loss along the occipital ridge. Other causes of circumscribed hair loss to be considered include congenital nevi, congenital triangular alopecia, aplasia cutis congenital, underlying meningocele or cystic lesion, and hair loss associated with complex developmental disorders.[8]

Two rare conditions that are important to consider in the differential diagnosis of total or near-total neonatal/infantile hair loss are atrichia with papular lesions and vitamin-D resistant rickets. Both diseases are characterized by normal hair density at birth, followed by universal loss of hair, usually by 3-15 months of age, with no hair regrowth. Atrichia with papular lesions is characterized by full hair at birth with permanent loss of all scalp and body hair, except eyelashes, which are generally spared, usually during the first 3 months of life. Between the ages of 2 and 26 years, patients develop numerous keratinous, papular cysts resembling milia on the head, torso and extremities, distinguishing them from patients with *alopecia totalis/aloepecia universalis*.[8] The second rare condition to consider is rickets resistant to 1,25-dihydroxyvitamin D. These patients present with loss of some or all scalp, body, and facial hair (with or without loss of eyelashes), typically within the first 15 months of life.Affected children have clinical and radiological signs of rickets, such as bowed limbs, extremity fractures, and diffuse osteopenia, and laboratory abnormalities. In the first months of life, however, it may be difficult to distinguish vitamin D-resistant rickets from AA, because clinical signs of rickets may not yet be apparent.[8]

Although significant research on the pathogenesis of AA has taken place, the evidence base for treatment of AA is scant for adults and even less for children. Childhood AA is relatively common and can be psychologically devastating. Although a conservative approach is satisfactory to some, others strongly desire active treatment of their alopecia. Treatment of AA is not well researched in children, but many options for pediatric treatment exist and are commonly used at the present time. Corticosteroids are commonly used for the treatment of AA and are the first-line choice for many dermatologists. Topical corticosteroids are an attractive option for use in...
Hair growth occurs in a 3-phase cycle: anagen growth phase, catagen transitional phase, and telogen resting phase. The duration of the anagen growth phase of scalp hair varies between 2 and 6 years. Individuals with a longer anagen growth phase are able to grow longer hair (Figure 6). Approximately 90% to 95% of scalp hairs are normally in the anagen phase. Catagen transitional phase is characterized by regression of the lower transient half of the hair follicle. Less than 1% of scalp hairs are in catagen transitional phase, which lasts about three weeks. Approximately 5% to 10% of scalp hairs are in telogen resting phase, which lasts about 3 months, after which these hairs are shed. Furthermore, two new phases of the hair cycle have been described named kenogen and exogen. Kenogen indicates the physiological interval of the hair cycle in which the hair follicle remains empty after the telogen hair has been extruded and before a new anagen hair emerges. Kenogen frequency and duration are greater in men and women with androgenetic alopecia. Exogen is the phase of the hair cycle describing the shedding of the club fiber from its epithelial silo within the follicle. Normally, between 40 and 100 hairs are shed daily on a non-shampoo day; twice as many are shed when the hair is shampooed. Shed hair is replaced by new hair that grows from the same follicle.

Children are subject to the same causes of telogen and anagen loss as adults and should have a similar evaluation.

**Disturbances of hair cycle**

Anagen loss

Anagen loss is always abnormal and, with the exception of loose anagen syndrome and alopecia areata, scalp anagen hair loss generally implies a toxic exposure. Hair loss is profound, as up to 90% of scalp hair is normally in anagen, and the loss generally occurs within days to weeks of the insult. The most common and easily recognizable cause
of anagen effluvium is radiotherapy or chemotherapy. Other causes of anagen loss include loose anagen syndrome, alopecia areata and toxic exposure to boric acid or heavy metals (mercury, arsenic, thallium). Very severe protein malnutrition may also give rise to anagen effluvium, as can exposure to colchicine. Loose anagen syndrome does not present as sudden diffuse shedding, and rarely alopecia areata does. Typically, alopecia areata may result in some focal hair loss or findings of exclamation point hairs that may help to distinguish this from the other causes of anagen effluvium.

Loose anagen syndrome

Loose anagen syndrome is characterized by lack of adhesion of the hair shaft to the hair follicle. Since the growing anagen hair is not anchored normally, hairs can be easily and painlessly plucked from the hair follicle. Most hairs do not remain in the follicle for the full duration of anagen and so do not grow to the normal length. Parents indicate that they do not need to cut their child’s hair (Figure 7) because growth stop after it reaches a certain length.

This condition is familial and most likely inherited in an autosomal dominant fashion. The normal-appearing siblings and parents of the affected child may demonstrate easily plucked hair. Loose anagen syndrome may be associated with several types of ectodermal dysplasias.

With light microscopy we can see hair with twisted anagen roots without an inner root sheath. There is a characteristic presence of crumpling of the proximal hair cuticle (ruffling) although this is not confirmative and also occurs in normal hair (Figures 8, 9).

No treatment is necessary, as the hair reverts spontaneously to normal with age. During childhood, gentle handling decreases hair shedding.
Telogen effluvium

The stress on the anagen hair follicle necessary to trigger a telogen effluvium is milder than that with an anagen effluvium and, instead of triggering damage to the matrix, it precipitates an abrupt transformation of anagen to telogen hair.

The diagnosis of telogen effluvium is confirmed by finding a positive hair pull test from multiple areas of the scalp, hair, when examined microscopically, being found to be telogen. In total, 50-100 telogen hair are normally shed per day, reflecting the 10-15% of hair in telogen at any one time. In a telogen effluvium, 100-300 hairs per day are usually shed and 20-50% of the scalp hairs may be in telogen at a given time.4

Telogen effluvium is less common in children than in adults, and in children is more likely to be related to a sudden and transient illness than to the drugs and hormonal fluctuations that commonly trigger this in adults. It must be emphasized that any drug can trigger a telogen effluvium, just as any drug can cause a cutaneous allergic reaction. Different triggering factors may precipitate a telogen effluvium, as can severe febrile illness, trauma, systemic illness, surgery, endocrine disorders, nutritional disorders, starvation, malabsorption, hemorrhage, anemia, severe emotional stress and immunization. The role of low serum ferritin in the cause of diffuse hair shedding is unclear.1 Recently, it has been reported two cases of telogen effluvium occurring in two 11-year-old children following bivalent human papillomavirus (HPV) vaccine administration.17 The two children began to lose their hair following the second HPV vaccine dose. Alopecia worsened following the third vaccine dose and then resolved spontaneously within a few months.

In acute telogen effluvium the shedding resolves in 3-6 months, and the hair may take another 6 months to return to normal density. If the shedding continues past 6 months, it becomes chronic telogen effluvium. This is primarily a condition seen in middle-aged women.18 Chronic diffuse telogen hair loss may occur in children with chronic starvation, especially marasmus with sparse, dry, easily plucked hair. Both hereditary and acquired zinc deficiency lead to sparse, brittle hair. Essential fatty acid deficiency can also produce increased telogen hair shedding. It usually occurs in children with prolonged parenteral alimentation with inadequate

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Figure 8.—Scanning electron microscopy of the distrophyc roots typical of loose anagen hair.

Figure 9.—Scanning electron microscopy of the cuticular ruffling that allows hair to be easily plucked with no pain.
inclusion of supplemental essential fatty acids. Chronic telogen effluvium can also occur in thyroid disorders, pancreatic disease and other causes of malabsorption.

Traumatic alopecia

Trichotillomania

Trichotillomania is defined by the Diagnostics and Statistic Manual of Mental Disorders, 4th edition, (DSM-IV) as “hair loss from a patient’s self-pulling of hair”.19 Trichotillomania is classified as an impulse control disorder, being a self-inflicted compulsion or habit tic to pull or pluck at the hair.

The common presentation of trichotillomania is an unusual pattern of hair loss with very short hairs of irregular length in an area of normal scalp. The scalp and the eyebrows are the most common sites, but any site may be involved. It is usually a non-permanent form of alopecia, but if the same area is persistently plucked, scarring may result, with persistent hair loss.1

Three subsets appear to exist: preschool age children, preadolescents to young adults, and adults.20 In the preschool age population, trichotillomania appears to be similar to a habit, such as nail biting or thumb sucking. These young children tend to have a benign course. Several reviews of childhood trichotillomania relate the onset in young children to stressful situations. The most common age of presentation for trichotillomania is in preadolescents to young adults. Mean age of onset is usually reported between 9 and 13 years of age. There appears to be a female predominance in this group. Overall, these patients tend to have a more chronic and relapsing course of hair pulling. The patient will often deny any role in the hair loss reminiscent of dermatitis artefacta. They are secretive about their behavior, so parents and the patient are often reluctant to accept such a diagnosis. Psychological intervention and counseling may help identify the underlying problem and modify the behavior. Psychiatric referral is recommended in recalcitrant cases.

Trichotemnomania

Trichotemnomania (froom Greek temnein, to cut) is hair loss due to cutting or shaving by patients in the context of obsessive-compulsive disorder. Trichotemnomania is not purely voluntary, it is performed to relieve stress. Although it is a conscious act, patients are resistant to admitting their habit. These patients may be embarrassed by their appearance and habit, and have feelings of guilt. The hair is usually cut with scissors or shaved, and the diagnostic key is the presence of follicle openings with filled hair shafts within a healthy-looking scalp.21

Another type of artificial hair loss, which results from perpetual rubbing of the scalp causing fracturing of the hair shafts is called trichotriromania. Trichotriromania presents with bald spots within hair of different length, which may be similar to hair cutting with scissors. White tips are seen at the end of the hair shafts in the form of distal splitting.

Another type of hair loss with associated psychiatric comorbidity is trichodaganomania, which is characterized by the compulsive habit of biting one’s own hair.

In adults a very selective type of trichophagia named trichorrhizophagia has been described, in which the patient exclusively eats the root of the hair he plucked.22

Traction alopecia

Traction alopecia, commonly occurring in females, is due to constant tension placed on the hair during styling, such as tight ponytails or braiding, rollers, or weaving of the hair. Short, broken hairs, folliculitis and follicular papules may be seen. The alopecia is initially reversible if patients can be persuaded to change their hairstyle. Prolonged, continuous traction may cause permanent scarring.1

Androgenetic alopecia in children and adolescents

Androgenetic alopecia (AGA) is the most common type of hair loss in adults. Although there are differences in the age at onset, in both sexes the disease starts after puberty, when enough testosterone is available to be transformed into dihydrotestosterone. The onset of AGA is, therefore, not expected to be seen in pubertal patients without abnormal androgen levels.23 Endocrine evaluation
second study provided data on 448 adolescents with AGA. This group included 341 boys and 107 girls who sought treatment for their thinning hair. Hair loss in this population began between 7 and 17 years of age, with a mean age at onset of 14.8 years in boys and 13.8 years in girls.

A careful clinical assessment is important to confirm the absence of androgen excess. Laboratory tests or endocrine evaluation may be needed.

Minoxidil topical solution appears to be an effective and well-tolerated treatment in adolescents boys and girls with AGA. The percutaneous absorption of minoxidil is similar to that observed in adults. Finasteride has not been studied in the treatment of men younger than 18 years, and thus the safety and efficacy of this drug in the treatment of early onset adolescent AGA has not been determined.

Figure 10.—Androgenetic alopecia in a 13-year-old girl.

Figure 11.—Androgenetic alopecia in a 12-year-old boy.

is strongly recommended in children with AGA.

The occurrence of AGA in healthy prepubertal children has rarely been reported in the literature, but it is probably not exceptional. Tosti et al. reported 20 prepubertal Caucasian children with AGA, 12 girls and 8 boys, age range 6-10 years. In both boys and girls, clinical examination showed hair loss with thinning and widening of the central part of the scalp. In 8 cases frontal accentuation and breach of frontal hairline were also present in the so called Christmas tree pattern. There was a strong family history of AGA in all patients.

AGA in adolescents is not uncommon (Figures 10, 11). There are two studies that have documented the prevalence and early age of onset of AGA. The first study was a multicenter study to assess the prevalence of AGA in 496 randomly selected, healthy boys. Approximately 15% showed early signs of AGA and were rated as having stage 2 or greater hair loss on the Hamilton-Norwood grading scale. The
child may be born with complete absence of scalp and body hair, or the infant may progress to this stage over the first 5 years of life (Figure 12). In another variant of the disease, the neonate is born with lanugo hair, which is shed in the first few months of life and never replaced. Caution should be exercised to ensure that the hair abnormality is isolated, as other associations may be unveiled only with time (Figure 13).

Congenital hypotrichosis is a less severe form of atrichia congenita, where hair is not absent, but it is diffusely thinned. It occurs usually as an isolated defect. Hypotrichosis may not be noticed until the age of two years because of variation in the quality and quantity of hair normally present at birth (Figure 14).

Most cases of congenital hypotrichosis and atrichia congenita are autosomal recessive traits. Several autosomal dominant pedigrees have been identified. When no family history is obtained, a scalp biopsy should be performed to exclude alopecia areata totalis. The biopsy also provides information regarding the follicle architecture and count, and reveals any other cutaneous abnormalities.

There is a very long list of conditions that present with hypotrichosis, but no complete alopecia, in infancy. The hypotrichosis may be secondary to follicular hypoplasia or to faulty hair shaft production and breakage. Many of the ectodermal dysplasias are as-

**Hereditary and congenital hypotrichosis**

*Congenital atrichia and hypotrichosis*

Atrichia congenita is characterized by follicular agenesis or programmed follicular destruction. The
associated with hypotrichosis but, unfortunately, most of the hair shaft abnormalities have not been well characterized; the abnormal hair is generally described clinically only as “brittle”, “sparse” or “lustreless”.

There have been numerous attempts to classify the conditions characterized by congenital alopecia or hypotrichosis. In 1892, Bonnet proposed the first known classification based on embryological principles. It has been widely used until nowadays and roughly divides congenital hypotrichosis with nor-

Figure 15.—Clinicogenetic classification of hypotrichoses. Using three clinical criteria, most patients with hypotrichosis can be assigned to a group of molecularly defined hair disorders. ANE: alopecia, neurological defects and endocrinopathy; ARIH: autosomal recessive ichthyosis with hypotrichosis; DSG4: desmoglein 4; ED: ectodermal dysplasia; EDAR: ectodysplasin A receptor; EDAR-ADD: EDAR-associated death domain; HJMD: hypotrichosis with juvenile macular dystrophy; HRSV: hypotrichosis with recurrent vesicles; KRT85: keratin 85; LIPH: lipase H; LFAR6: lysophosphatidic acid receptor 6; NTS: Netherton syndrome. Adapted from Regina Betz et al.32
mal ectodermal structures from the ones with associated teeth and nail defects. Afterwards, Cockayne and Muller, attempting a more critical analysis, proposed a working classification which allowed the currently named syndromes to be identified, and provided a provisional status for those not yet characterized. In 1981 after the Berlin Congress, Sâlamon proposed a classification for the global problem of hair loss that is considered one of the most useful systems for the study of congenital hypotrichosis.

During the past years, major breakthroughs in genomic techniques have facilitated considerable progress toward unraveling the molecular basis of inherited skin diseases. At present, over 6000 Mendelian disorders are known, of which 560 involve skin abnormalities and are associated with more than 500 unique protein-coding genes. More than 300 inherited disorders featuring hair abnormalities have been catalogued to date, and yet, in a substantial portion of these, no genetic defect has been identified. This new knowledge is now resulting in a reorganization of the classification systems in this group of diseases, which, instead of being solely founded on clinical findings, now integrates both clinical and molecular features. It is now possible to assign most forms of hypotrichosis to one gene (or group of genes) on the basis of a very limited amount of information concerning three clinical features: mode of inheritance, the presence or absence of associated features, and microscopic appearance of the hair shaft. Once these data are available, it is easy to decide about the optimal molecular diagnostic strategy and genetic testing that is likely to lead to the correct diagnosis. (Figure 15).

In this review, we will follow the practical classification based on the clinical observations proposed by Camacho et al. One should be aware, however, that within each of the groups there is a large clinical spectrum and that these are not grouped on a patho-genetic basis. The classification scheme shown in Table I is largely of didactic value.

**Generalized congenital alopecia**

*Genodermatoses with non-scarring hypotrichosis*

**Genodermatoses with skeletal alterations**

*Trichorhinophalangeal syndrome.*—Trichorhinophalangeal syndrome (TRPS) comprises a distinctive combination of hair, facial and bone abnormalities with autosomal dominant inheritance.

1. **Trichorhinophalangeal syndrome type I.** Type I TRPS is clinically characterized by the presence of a variable congenital hypotrichosis, piriform (pear-shaped) nose, coniform epiphysis, subnasal fold, thin lips, prognatia, and mandibular hypoplasia. The hair alterations consist of diffuse alopecia with a broad forehead and a partial alopecia of the lateral third of the eyebrows. Scanning electron-microscopic studies of the hair shaft can reveal flattened hair with an elliptoid transverse section pattern. Mechanical behavior of the hair might be abnormal with a significant increase in the viscous parameter, indicating a decreased intermolecular bridging within the keratin matrix.

2. **Trichorhinophalangeal syndrome type II (Lang-en-Giedion syndrome).** Patients with TRPS type II usually present hypotrichosis of the scalp hair, piriform nose and redundant skin as the type I, plus multiple cartilaginous exostosis. In a recent article Lu et al. described associated alterations to this syndrome including aplasia of the epiglottis and congenital nephrotic syndrome.

3. **Trichorhinophalangeal syndrome type III.** TRPS type III is a newly defined clinical entity inherited as an autosomal dominant trait and clinically characterized by growth retardation, craniofacial abnormalities, severe brachydactyly and sparse hair. In addition, absence of mental retardation and cartilaginous exostoses are required for the diagnosis of TRPS type III. Other associated abnormalities include a short stature, a thin upper lip and a prominent lower lip, a pear-shaped nose, stubby fingers and toes with cone-shaped epiphyses and sparse scalp hair.

**Dubowitz syndrome.**—First described in 1965, Dubowitz syndrome (DS) is characterized by a peculiar face, eczema, small stature and mild microcephaly. The cutaneous findings consist of an eczematous eruption affecting the face and flexural areas. Scalp hair is sparse and brittle and commonly affects the lateral eyebrows. Patients affected by DS have a moderate mental deficiency with a tendency toward hyperactivity, short attention span, stubbornness and shyness. They have also been characterized by their high-pitched weak cry.

**Hallermann-Streiff syndrome.**—Hallerman-Streiff syndrome is a rare congenital anomaly characterized...
by a peculiar bird face, mandibular and maxillary hypoplasia, dyscephaly, congenital cataracts, microphthalmia, hypotrichosis, skin atrophy, and short stature. Dental abnormalities are present in 80% of the cases and include malocclusion, crowding, severe caries, supernumerary and neonatal teeth, enamel hypoplasia, hypodontia, premature eruption of primary dentition, agenesis of permanent teeth, and anterior displacement or absence of condyles.

Genodermatoses with ectodermal alterations

ECTODERMAL DYSPLASIAS

The ectodermal dysplasias (EDs) are a heterogeneous group of conditions primarily affecting the hair, teeth, nails, and skin, and are classified according to the tissue(s) affected. EDs are rare diseases with an estimated incidence of 7/10,000 births. Of the 170 EDs described so far, fewer than 30 have been explained at the molecular level with the identification of the causative gene.

The term ectodermal dysplasia was originally applied to anhidrotic ectodermal dysplasia in which hair, teeth, nails and sweat glands are defective. The classification proposed by Freire-Maia in 1977 was based on a primary defect of ectodermal derivatives. Conditions in which the ectodermal changes are secondary, as in xeroderma pigmentosum are thus excluded from the EDs. According to the Freire-Maia classification, subgroup 1 is a hair dysplasia, subgroup 2 a dental dysplasia, subgroup 3 a nail dysplasia, subgroup 4 a sweat gland defect, and subgroup 5 a defect of other ectodermal structures.

Solomon and Keuer in 1980 defined subgroups of the EDs based on what ectodermal structures were affected (Table II).

Anhidrotic ectodermal dysplasia (Christ-Siemens-Touraine syndrome).—In this X-linked syndrome sweat glands and other ectodermal-derived appendages are absent or few in number. The full syndrome only occurs in males. Scalp and body hair is short, fine and very sparse and often bright in colour, but may increase in quantity after puberty. Eyebrows and eyelashes may also be sparse or absent but may be relatively little affected. The prominent square forehead, saddle nose, thick lower lip and the pointed chin produce a distinctive face. The skin around the eyes is finely wrinkled and may be pigmented. The teeth may be absent or few in number, and characteristically the canines and incisors are conical shaped. The absent or reduced sweating leads to heat intolerance, and unexplained pyrexia may be the presenting symptom in infancy. Carrier females may be clinically normal but may show in some degree one or more of the features of the syndrome as conical teeth, hypotrichosis or heat intolerance. Otherwise apparently normal carriers may show dermatoglyphic abnormalities, the presence of which may be a value in diagnosis.

EEC syndrome (ectrodactily, ectodermal dysplasia and cleft lip and palate).—The association of ectrodactyly (lobster-claw deformity), ectodermal dysplasia, and cleft lip and palate is a well defined autosomal dominant syndrome.

Reported EEC syndrome cases show sparse hair, malformed teeth with early caries, ectrodactyly, cleft lip and/or palate, lacrimal duct stenosis and kidney abnormalities, but not all defects are present in all affected individuals within a single family.

Hypotrichosis with juvenile macular dystrophy (HJMD).—Becker et al. described two sisters in a

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**Table II.—Ectodermal dysplasia subgroups proposed by Solomon and Keuer.**

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<td>Anhidrotic ectodermal dysplasia</td>
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<td>Xeroderma-Talipes-Enamel defect syndrome</td>
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Family of consanguineous parents with diffuse hypotrichosis of the head and visual impairment in the context of a tricho-ocular malformation of an ectodermal dysplasia. This entity is an autosomal recessive disorder. Mutations in the P-cadherin (CDH3) gene have been shown to underlie HJMD. Because P-cadherin is expressed not only in the hair follicle, but also in retinal pigmented epithelium of the eye, disruption of P-cadherin would lead to macular dystrophy of the retina.\textsuperscript{45}

Hypotrichoses with aminoacid metabolism alterations, ectodermal dysplasia.—Among the aminoacid metabolism alterations occurring in hypotrichoses there are hair-shaft structure defects, hypercysteine ahr and glucosuria.

Hypotrichosis, hair-shaft structure defects, hypercysteine hair and glucosuria.—Blume-Peytavi \textit{et al.}\textsuperscript{46} reported of two Turkish siblings with fragile and sparse scalp hair associated with glucosuria without diabetes or kidney disease. Clinical examination revealed normal physical and mental development, and an analysis of plucked hairs showed dysplastic and broken hair shafts. Polarizing microscopy and scanning electron microscopic studies revealed torsion, irregularities and impressions of the hair shaft, as seen in \textit{pili torti}, trichorrhexis nodosa and pseudomonilethrix. Analysis of the amino-acid composition of the hair demonstrated a significant reduction of sulphonic cysteic acid and an elevated cysteine and lanthionine content.

\textit{Other genodermatoses with hypotrichosis}.—Other genodermatoses with hypotrichosis include kid syndrome (keratitis, ichthyosis and deafness).

KID syndrome (keratitis, ichthyosis, deafness).—The KID syndrome is a congenital ectodermal disorder that affects not only the epidermis, but also other ectodermal-derived tissues such as the corneal epithelium and the inner ear. In a classic review,\textsuperscript{47} 61 patients who met the criteria for this syndrome were identified. All had cutaneous and auditory abnormalities, and 95\% of them also had ophthalmologic defects. The most frequent clinical features were neurosensory deafness (90\%), erythrokeratoderma (89\%), vascularizing keratitis (79\%), alopecia (79\%), and reticulated hyperkeratosis of the palms and soles (41\%).

In the same article, the authors state that the KID acronym does not accurately define this entity, since the disorder is not an ichthyosis, because scaling is not the main cutaneous feature. In addition, not all patients have keratitis. They suggest that this syndrome should be included under the general heading of congenital ectodermal defects as a keratodermatous ectodermal dysplasia (KED).

Genodermatoses with hypotrichosis and tumors.—Genodermatoses with hypotrichosis and tumors include Rombo syndrome, Bazex-Dupré-Christol’s syndrome, hereditary hypotrichosis simplex.

Rombo syndrome.—First described by Michaëlsen in 1981,\textsuperscript{48} Rombo syndrome is an autosomal dominant disease clinically characterized by hypotrichosis affecting the eyelashes and yellowish follicular facial papules. They also present cyanotic lips and multiple tricoepiteliomata and basal cell carcinomas.\textsuperscript{49}

Bazex-Dupré-Christol’s syndrome.—Bazex-Dupré-Christol’s syndrome (BDCS) is an X-linked dominant disorder of the hair follicle characterized...
by follicular atrophoderma, multiple basal cell carcinomas, hypotrichosis, milia, and localized hypohidrosis. Follicular atrophodermas are follicular depressions (‘ice pick marks’) seen most commonly on the dorsum of the hands and elbows. In a recent article Kidd et al. described a Scottish family with this syndrome, with five affected members through three generations. The reported patients showed hypohidrosis confined to the face, coarse hair, dry skin, milia, and follicular atrophoderma. All the adults had a history of multiple basal cell carcinomas. None of them presented any skeletal feature suggestive of Gorlin’s syndrome. The authors thus suggest that the BDCS should be considered as a differential diagnosis in patients with early onset or familial basal cell carcinomas. In 1994 Goeteyn et al. described 20 affected patients of a large family across four generations with typical features of the BDCS. However, the clinical picture in that family differs with regard to gender and age, confirming an X-linked inheritance.

Hereditary hypotrichosis simplex.—Hereditary hypotrichosis simplex (HHS) is an uncommon group of familial hypotrichias and atrichias, usually non-scarring, which are not associated with other dysplasias neither with internal abnormalities. HHS is an autosomal dominant hair disorder which is characterized by progressive loss of hair starting in the middle of the first decade of life. HHS can be largely classified into the scalp limited form (HHSS) and the generalized form (GHHS) in which facial and body hairs are also affected (Figure 16).

HHSS was previously mapped to chromosome 6p21, and subsequently, heterozygous nonsense mutations in the CDSN gene have been identified in patients with HHSS. Interestingly, it has recently been shown that homozygous mutations in the CDSN gene underlie an inflammatory type of generalized peeling skin syndrome, which is characterized by erythema with peeling of the cornified layer on the whole body. It is also known that mutations in other genes functionally related with CDSN can show some hair phenotypes. Of these, Netherton syndrome is an autosomal recessive disorder characterized by ichthyosiform erythroderma, atopic manifestation and the hair shaft anomaly called bamboo hair (trichorrhexis invaginata). The Netherton syndrome is caused by mutations in the SPINK5 gene. More recently, it has been reported that recessively inherited mutations in the ST14 gene underlie ichthyosis with hypotrichosis syndrome.

The generalized form of HHS (GHHS) was previously mapped to chromosome 18p11.32-p11.23. Recently, a heterozygous mutation in the APCDD1 gene has been identified in families with GHHS.

Recently described syndromes (non-classified disorders).—In the last decade, several new hypotrichotic syndromes have been described with the title of “A new genodermatosis?” or “A new syndrome?” These have yet to be classified and included into the older classification schemes.

Congenital ichthyosis with follicular atrophoderma.—Lestringant et al. described five Emirati sibs (three girls and two boys), aged between 4 and 18 years, with normal stature, diffuse congenital ichthyosis, patchy follicular atrophoderma, generalized and diffuse non-scarring hypotrichosis, and marked hypohidrosis. Steroid sulfatase activity, assessed in the two boys, was found to be normal. Electron microscopic studies of ichthyotic skin did not show any specific abnormality. The patients were thought to have Bazex syndrome; however, ichthyosis is not a component of Bazex syndrome. They concluded that congenital ichthyosis with follicular atrophoderma represents a new autosomal recessive genodermatosis.

Congenital atrichia, palmoplantar hyperkeratosis mental retardation, and early loss of teeth

Steijlen et al. reported four siblings with congenital atrichia, palmoplantar hyperkeratosis, mental retardation, and early loss of teeth. The pedigree in that family suggested an autosomal recessive trait. This combination of findings has not been previously reported and is therefore considered to be a new genetic entity.

Keratoderma, hypotrichosis and leukonychia totalis

Basaran et al. reported three relatives with congenital hypotrichosis, characterized by trichorrhexis nodosa and trichoptilosis, dry skin, keratosis pilaris and leukonychia totalis. The described patients also developed a progressive transgrediens type of palmoplantar keratoderma, and hyperkeratotic lesions on the knees, elbows and perianal region.
Alopecia-mental retardation syndrome associated with convulsions and hypergonadotropic hypogonadism

Devriendt et al. reported two brothers with total congenital alopecia, mental retardation, childhood convulsions and hypergonadotropic hypogonadism. The authors believe that this association which has not previously been reported represents a new autosomal recessive condition.

Universal congenital alopecia

Complete or partial congenital absence of hair may occur either in isolation or with associated abnormalities. Most of the families with isolated congenital alopecia have been reported to follow an autosomal-recessive inheritance. In an attempt to map the gene for the autosomal recessive form, Nothem et al. performed genetic linkage analysis in a large inbred family from Pakistan where affected individuals showed a complete absence of hair. They mapped the gene for this hereditary form of isolated congenital alopecia on chromosome 8p21-22 (ALUNC [alopecia universalis congenitalis]). In a more recent article, they reported an homozygous missense mutation in the human hairless gene. In addition, they found that the human hairless gene undergoes alternative splicing and that at least two isoforms generated by alternative usage of exon 17 are found in human tissues. Interestingly, the isoform containing exon 17 is the predominant isoform expressed in all tissues except the skin, where they observed exclusive expression of the shorter isoform. The authors speculate that this tissue-specific difference in the proportion of hairless transcripts lacking exon 17 sequences could contribute to the tissue-specific disease phenotype observed in individuals with this type of isolated congenital alopecia.

Atrichia with papular lesions

Atrichia with papular lesions (APL) is a rare autosomal recessive disorder characterized by early onset of complete hair loss, which is followed by papular eruptions due to formation of dermal cysts. It has been shown that loss-of-function mutations in the hairless gene (HR) underlie APL.

Previously, it has been reported patients with congenital hypotrichosis and milia. This patient presents with coarse sparse hair and multiple milia on the face, chest, axillae and pubic region. There are no abnormalities of teeth and nails. Polarizing light microscopy of hair shows an increased diameter of the hair shaft. Rapelanoro et al. reported a large four generations family where individuals presented with congenital hypotrichosis and multiple self-healing milia.

Marie-Unna hereditary hypotrichosis

Typically, affected patients are born with normal to adequate, normal to coarse hair. With increasing age, the hair becomes increasingly coarse and wiry, and has classically been likened to an “ill-fitting wig” or “horse’s mane”. Patients most commonly have decreased or absent eyebrows, eyelashes, and body hair, including secondary sexual hair. Patients often demonstrate a progressive, nonscarring loss of scalp hair that begins around puberty, particularly in the vertex and scalp margins. The condition may eventually result in only a sparse fringe of remaining hair along the scalp periphery.

On physical examination, gentle hair pull may result in extraction of multiple anagen hairs. Light microscopic examination may reveal hair shafts that are deeply pigmented and vary in diameter. Hairs may also be twisted or bent at odd angles. Histologic findings include a significantly reduced number of follicles per unit area that are often atrophic. A mild to moderate inflammatory infiltrate with limited fibrosis and scarring may be present.

Marie-Unna hypotrichosis was mapped to chromosome 8p21.3, where the hairless gene (HR) is located. It is related to upregulation of the expression of this gene.

Genodermatoses with scarring alopecia

Happle syndrome

Gobello et al. described a 13-year-old girl with chondrodysplasia punctata, associated with ichthyosis...
arranged along Blaschko’s lines, follicular atrophoderma, cicatricial alopecia and coarse, lustreless hair. The patient also showed a congenital cataract in the right eye, dysplastic facial appearance and symmetrical shortening of the tubular bones. The pathogenetic concept of functional X-chromosome mosaicism introduced by Happle is used to name this syndrome.

**Localized congenital alopecia**

*Congenital triangular alopecia.*—Congenital triangular alopecia (CTA), also known as temporal triangular alopecia, is an unilateral or, less frequently, bilateral patch of non-cicatricial and non-inflammatory alopecia in the frontotemporal region. Although CTA is a congenital trait, it is usually noticed by the family when the child is above 2 years of age. Only about 74 cases have been reported, probably because the lesion is benign and nonprogressive. An estimated frequency of 0.11% is reported by García-Hernández et al. Most cases are sporadic but the trait may affect, by way of exception, several members of a family. The hair loss is described as a “triangular”, “oval” or “lance-t-shaped” temporal patch, covered only by vellus hair. Recently, it has been described a central hair tuft in CTA as a typical feature of this disorder in a substantial proportion of cases.

CTA usually occurs as an isolated anomaly but also several congenital diseases have been associated: phakomatosis pigmentovascularis, Down syndrome, Dandy-Walker malformation, mental retardation and seizure, congenital heart diseases, and bone and tooth abnormalities, multiples lentigines and café-au-lait patches.

*Aplasia cutis congenita (Adams-Oliver syndrome and other associations).*—Aplasia cutis congenita is a part of heterogeneous group of disorders characterized by the absence of a portion of skin in a localized or widespread area of the scalp at birth. It most commonly manifests as a solitary defect on the scalp, but sometimes it may occur as multiple lesions. Aplasia cutis is a congenital condition in which skin, bone and dura can be absent. The majority of cases affects the scalp and are limited to the dermis and epidermis. Vertex aplasia cutis typically ranges in size from 0.5 to 3 cm. Ultrasound and magnetic resonance imaging are helpful diagnostic tools for determining the extension of the lesion.

**Table III.—Classification of hair shaft disorders.**

<table>
<thead>
<tr>
<th>Classification of Hair Shaft Disorders</th>
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<tr>
<td>Hair shaft dysplasia with hair fragility</td>
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<tr>
<td>Monilethrix</td>
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<tr>
<td>Pseudomonilethrix</td>
</tr>
<tr>
<td>Pili torti</td>
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<tr>
<td>Corkscrew hair</td>
</tr>
<tr>
<td>Menkes’ syndrome ( kinky hair)</td>
</tr>
<tr>
<td>Trichorrhexis invaginata (Netherton’s syndrome)</td>
</tr>
<tr>
<td>Trichothiodystrophy</td>
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<tr>
<td>Trichonodosis</td>
</tr>
<tr>
<td>Trichorrhexis nodosa</td>
</tr>
<tr>
<td>Bubble hair</td>
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<tr>
<td>Loose anagen hair</td>
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<tr>
<td>Hair shaft dysplasia without hair fragility</td>
</tr>
<tr>
<td>Pili annulati (ringed hair)</td>
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<tr>
<td>Woolly hair</td>
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<tr>
<td>Woolly hair nevus</td>
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<tr>
<td>Acquired progressive kinking of the hair</td>
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<tr>
<td>Diffuse partial woolly hair</td>
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<tr>
<td>Acquired partial curly hair</td>
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<tr>
<td>Uncombable hair (Pili canaliculi)</td>
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</table>

**Adams-Oliver syndrome.**—Adams-Oliver syndrome depends on the association of aplasia cutis with terminal digital abnormalities namely shortening of fingers and toes, absence of phalange or more rarely the absence of the entire extremity. A literature review revealed a rate of 13.4% for congenital heart malformations in individuals with Adams-Oliver syndrome, suggesting that cardiac anomalies are a frequent manifestation of this syndrome. Thus, all patients with Adams-Oliver syndrome should be evaluated for cardiac abnormalities.

**Aplasia cutis congenita, high myopia, and cone-rod dysfunction.**—Recently Gershoni-Baruch et al. reported two siblings with congenital nystagmus, cone-rod dysfunction, high myopia, and aplasia cutis congenita on the midline of the scalp vertex. The authors consider this familial oculocutaneous condition as a new unique autosomal recessive disorder.

**Nevus sebaceous.**—Nevus sebaceous of Jadassohn is a benign, congenital hamartoma of the folliculo-sebaceous apocrine unit and epidermis that often presents at birth, appears to regress in childhood, and grows during puberty, suggesting possible hormonal control. In childhood, the lesion consists of a circumscribed hairless yellow-orange-colored, waxy, pebble-like, papule or plaque often linear or round or irregular. In puberty the lesion becomes verrucous and nodular. Nevus sebaceous may develop tumors...
in adulthood particularly, syringocystadenoma papiliferum and benign hair follicle tumors. Basal cell carcinoma has been observed in about 5% of cases.

**Hair shaft disorders**

This refers to malformations of the hair shaft. They are most likely due to single gene defects. Most of these are congenital, and may be hereditary, whereas others are acquired. They may be localized or generalized and the defect may be simply local or it may be a key diagnostic sign of a genodermatosis.\(^{70}\) It is often difficult to draw a clear line between hypotrichoses and hair shaft disorders, as patients with diseases primarily resulting from abnormal hair structure often also manifest clinically with hypotrichosis.

The patients presents with an abnormality or change in hair texture, appearance, manageability or ability to grow hair long. A key feature of the clinical evaluation is to determine if there is hair fragility with hair breakage (Table III).

**Hair shaft abnormalities with increased fragility and breakage**

**Monilethrix (beaded hair)**

Monilethrix is a distinctive rare hair shaft disorder due to a mutation in the type II hair cortex keratins hHb6 and hHb1. When inherited as a dominant trait, Monilethrix is usually due to mutations in genes encoding hair keratins, including *KRT81*, *KRT83*, and *KRT86*. When inherited as a recessive trait, Monilethrix is caused by mutations in *DSG4*, encoding desmoglein 4.

It is named after the resemblance of the affected hair to a string of beads. The beaded appearance of the hair can be visualized by the naked eye, or with a dermatoscope, as alternating wide and constricted segments along the hair shaft. The hair breaks spontaneously or as a result of friction. The scalp is the main site affected, especially in the occipital region, but hair all over the body may be affected. The hair appears short (a few millimetres) and beaded, so that shortly after it has emerged from the follicle it is fractured at the constrictions. It is accompanied by local hyperkeratosis follicularis and it is also a common finding on the upper back and shoulders.

Severity is highly variable and as a result there is a spectrum of clinical presentations, ranging from near normal hair, to hair that is no able to grow more than a few millimetres. At birth the hair is normal but after the first shedding the replacement hairs are beaded, fragile and break easily, arising from hyperkeratotic follicular papules. The age of onset is variable and may be delayed until the teenage years.

There is no effective treatment for monilethrix. Retinoids, glycolic acids and minoxidil may be helpful in some cases. Monilethrix may improve with the years. Patients are advised to protect the fragile hair from excessive combing, styling or friction.

**Pseudomonilethrix**

This defect is inherited, also as a dominant trait. It involves a distinctive hair fragility to compulsive, sustained treatment of the hair by the normal actions of brushing and combing. This leads to diffuse or localized hypotrichosis with images of false nodes (flattened areas of irregular distribution) in the hair shaft. It is not accompanied by hyperkeratosis follicularis. It affects several members in the same family. It is a very rare defect, not to be confused with iatrogenic or acquired pseudomonilethrix. Iatrogenic pseudomonilethrix is the same defect caused by previous improper handling of the hair, generally caused by applying excessively strong pressure with the fingers or forceps when taking samples of hair which is also dysplastic for microscopic observation.

**Pili torti**

Pili torti is a hair with a twisted appearance which shows regular angulations on its longitudinal axis. The hair does not grow long and is easily broken, patchy hair breakage and coarse stubble are typically seen in the occiput and temporal areas due to friction. The twisted arrangement of this hair usually leads to a distinctive shine depending on the incidence of the light on this area.

It is a familial defect of dominant inheritance which may be isolated or associated with other conditions (Beare, Bazex, Crandall and Björnstad syndromes).\(^{71}\)

Atypical forms of pili torti have been found in Menkes syndrome (kinky hair) or isolated angulations in other hair dysplasias. It is commonly associ-
ated with other congenital defects and therefore, if identified, further evaluation for possible neurological and ectodermal disorders is an important part of the clinical evaluation.

There is a range of heterogeneous disorders where half and three-quarter twists on the hair are seen at irregular intervals rather than the 180° turns seen in pili torti. Acquired twisting is also invariably seen at the edge of a scarring alopecia where the hair follicle is distorted by the scarring process.¹

CORKSCREW HAIR

This atypical acquired form of pili torti is clinically characterized by thick, dark scalp hairs that are coiled into a unique double spiral. It may be associated with ordinary pili torti. Corkscrew hair has been associated with ectodermal dysplasia.⁷²

MENKES SYNDROME (KINKY HAIR)

Menkes disease is a multisystemic lethal disorder due to impaired copper transport and metabolism with pili torti. As a result, this produces a general complex syndrome dominated by neurological signs, accompanied by hypothermia, psychomotor retardation, quadriplegia, deafness, herniation, nanism, etc. These children have very distinctive facial features (partridge profile) and their hair is light, very fine, sparse and fragile. Death usually occurs at an early age due to neurological alterations. The kinky hair is a polydysplastic hair with images of irregular pili torti, as well as images of monilethrix and/or trichorrhexis nodosa.⁷³, ⁷⁴

TRICHOHRXESIS INVAGINATA (NETHERTON’S SYNDROME)

Netherton’s syndrome is caused by mutations in SPINK5. As with monilethrix, the primary abnormality involves a defect of keratinization of the hair shaft, allowing intussusception of the harder, keratinized distal portion of the hair into the softer proximal segment. This gives the typical bamboo appearance under light microscopy, or the hair can resemble a tulip if breakage of the distal hair shaft occurs (Figure 17).⁷⁵

Trichorrhexis invaginata can rarely occurs in traumatized, otherwise normal hair or with other congenital hair shaft dysplasias. Usually, however, is associated with Netherton’s syndrome, an autosomal recessive inherited disorder that consists on the triad of ichthyosis, atopic diathesis and trichorrhexis invaginata. The diagnosis of Netherton’s syndrome should always be entertained in “red scaly babies” who have sparse hair.

There is no specific treatment for trichorrhexis invaginata. Avoidance of trauma is important in this condition. Similar to the management of monilethrix, the only treatment available is cosmetic. Retinoids and photochemotherapy have been reported to be of some value and the condition may spontaneously improve with age.

TRICHOITHIODYSTROPHY

Trichothiodystrophy (TTD) is a term that describes cystine-deficient brittle hair.⁷⁶ Hair is an important clinical marker for this rare inherited disorder with a wide variety of phenotypes that range from brittle hair only to a neuroectodermal symptom complex with severe intellectual and development impairment. It can be accompanied
Trichorrhexis nodosa is the most common defect of the hair shaft leading to hair breakage. Trichorrhexis nodosa describes a congenital or acquired defect. The affected hairs develop a disruption in the cuticle permitting cortical fiber damage, fracture and fraying that resembles a nodal swelling. The nodes can be sited proximally or distally in the hair shaft. Distal nodes generally indicate hair weathering. Proximal nodes indicate increased hair fragility and increased susceptibility to weathering suggestive of an underlying hair shaft abnormality (Figure 18). Although congenital trichorrhexis nodosa can occur as an isolated finding or with teeth and/or nail abnormalities, its presence in an infant or young child should trigger a search for an underlying metabolic problem. It can be associated with argininosuccinic aciduria, citrullinaemia and it can also be present in Menkes disease.

Wheathering refers to the structural damage of the hair shaft caused by external forces. These forces may be cosmetic in nature, such as shampooing, grooming or styling, or environmental, such as UV radiation, wetting and natural friction. Acquired nodes resembling trichorrhexis nodosa are seen in severe wheathering of the hair.

Management of congenital and acquired trichorrhexis nodosa os prevention of injury to the hair shaft. Avoidance of unnecessary hairdressing procedures and styling products is advised. Protection from sunlight exposure is also recommended.

**Bubble hair**

This is an acquired abnormality of the hair shaft due to the presence of air bubbles within the shaft. This phenomenon seems to be caused by the direct effect of excessively high temperatures from styling with blow dyers or curling irons. It is seen above all in women in the form of localized hypotrichosis plaques or as a focal area of unruly and fly-away area in the vertex.

**Hair shaft abnormalities without increased fragility**

**Pili annulati (ringed hair)**

Ringed hair is, together with bubble hair, a disease that affects the hair medulla. It consists of the pres-
ence of alternating dilatations of the medulla, which is shown clinically by the ringed appearance of the hair. After detailed observation, a series of light and dark bands are visible on the hair. There is no fragility, and the hair can grow long.

Observation with light microscopy reveals that in fact there is a regular alternating pattern of light and dark bands (dilatations of the medulla filled with air).

Pili annulati is inherited in an autosomal dominant fashion and may also appear sporadically. It constitutes an esthetic defect which may be well-accepted by the patient, depending on the fashion.\(^{45}\)

**Woolly Hair Syndrome**

Woolly hair is defined as hair which is thinner than normal, curly and flat. It is normally found in the white race, as the hair of black individuals is usually flat and curly, but of normal size.

Woolly hair may be localized, diffuse, congenital or acquired. The congenital diffuse form can be inherited in an autosomal dominant pattern or, less frequently, an autosomal recessive fashion. It is well known that the surface of the hair shaft cuticle is covered by a lipid layer which is believed to play a role in protecting the hair shaft as a barrier. However, additional roles of lipids in the hair follicle had remained unknown. Kazantseva *et al.*\(^{85}\) have reported that a large deletion mutation in the lipase H (*LIPH*) gene causes an autosomal recessively-inherited hypotrichosis in isolated Russian populations. Importantly, it has recently turned out that *LIPH* mutations also show the woolly hair phenotype, thus the *LIPH* gene can be regarded as a causative gene for not only hypotrichosis, but also autosomal recessive woolly hair.\(^{45}\)

Woolly hair can occur as an isolated finding or in association with various genetic syndromes. There may be associated ocular defects, deafness, keratosis pilaris atrophicans, enamel hypoplasia and Noonan syndrome. Congenital localized woolly hair nevus occurs sporadically. It is characterized by a discrete area of tightly curled hair in an otherwise normal scalp. In about half the reported cases, woolly hair nevus is associated with linear nevi. The pigmentary or epidermal nevi are usually on the neck, arms or trunk, and not on the scalp. In general, it is an isolated finding, but woolly hair nevus has been reported to occur with neurological defects, ocular abnormalities, bone disorders, and other mesodermal defects.

Acquired progressive woolly hair may herald the onset of androgenetic alopecia or be observed as a side effect of etretinate drug treatment.

There is no specific treatment and in the congen-
Uncombable hair (pili canaliculi)

Uncombable hair syndrome presents with characteristic unruly hair that is difficult to style and has the appearance of standing away from the scalp. It affects young individuals or children with abundant hair. The hair is arranged in bundles pointing in different directions which make it impossible to manage or comb. It is also known as “spunglass hair”. Usually it is a dominant familial condition which may be sporadic. Cases of localized uncombable hair have also been described.

In all cases the clinical aspect of uncombable hair involves a characteristic hair shaft dysplasia: pili canaliculi. On light microscopic examination, the shaft may have a canal-like longitudinal groove along one or two facets. When hair cross-sections are examined the characteristic triangular or kidney-shaped appearance of the hair shaft is diagnostic (Figures 20, 21).

Table IV.—Conditions associated with focal scarring hair loss in children.

<table>
<thead>
<tr>
<th>Condition</th>
<th>Details</th>
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<tbody>
<tr>
<td>Ankyloblepharon-ectodermal defects-cleft lip/palate syndrome</td>
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<tr>
<td>Aplasia cutis congenita</td>
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<tr>
<td>— Single anomaly</td>
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<tr>
<td>— Associated with other anomalies</td>
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<tr>
<td>1) Associated with limb abnormalities</td>
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<td>2) 46 XY genotype/gonadal dysgenesis</td>
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<tr>
<td>3) “Lumpy” scalp syndrome</td>
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<td>4) Trisomy 13</td>
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<td>5) 4p syndrome</td>
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<tr>
<td>6) Ectodermal dysplasia of Carey</td>
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<td>7) Ectodermal dysplasia of Tufelli</td>
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<tr>
<td>8) Hallerman-Streiff syndrome</td>
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<tr>
<td>9) ANOTHER syndrome</td>
<td></td>
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<tr>
<td>10) Focal dermal hypoplasia</td>
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<tr>
<td>Birth trauma</td>
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<tr>
<td>Congenital ectodermal dysplasia of the face</td>
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<tr>
<td>Conradi-Hünermann chondrodysplasia punctata</td>
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<tr>
<td>Epidermal or organoid nevus</td>
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<tr>
<td>— CHILD syndrome (congenital hemi dysplasia with ichthyo-siform erythroderma and limb defects)</td>
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<tr>
<td>Epidermolysis bullosa</td>
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<tr>
<td>Hallerman-Streiff syndrome</td>
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<td>Incontinentia pigmenti</td>
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<tr>
<td>Keratosis follicularis spinulosa decalvans</td>
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<tr>
<td>Kerion</td>
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<tr>
<td>KID syndrome (keratitis, ichthyosis, deafness)</td>
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<tr>
<td>Neoplasia</td>
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<td>Prolonged pressure</td>
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<tr>
<td>Primary cutaneous disease</td>
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<tr>
<td>Tufted folliculitis</td>
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ital diffuse form, the hair may relax from curly to waxy with age.¹

Acquired progressive kinking of the hair

Acquired progressive kinking of the hair is a non-familial acquired form of curly hair. It primarily affects young males near puberty (Figure 19). Multiple areas of hair gradually becomes kinky, mainly affecting the occipital area. It does not seem to be related to external causes and it gradually evolves into androgenetic alopecia. A localized form in the temporal regions is known as circumscribed symmetric allotrichia (“whisker hair”). Cases of acquired curling of hair can be drug induced (retinoids).³⁶
There is a spontaneous tendency to improve over time. The use of a shampoo with zinc piritione and silicone-based conditioners may help in managing the hair.\textsuperscript{70, 86}

**Scarring alopecia**

Scarring alopecia can be either focal or diffuse. In an infant, there are four main causes of focal scarring hair loss: trauma (including prolonged pressure), aplasia cutis congenita, underlying nevus (or neoplasia) or as a part of a syndrome (Table IV).

The most common primary cicatricial alopecias, \textit{i.e.}, lupus erythematosus, lichen planopilaris, folliculitis decalvans and pseudopelade of Brocq, are rare in children. However, the group of disorders characterized by keratosis pilaris and scarring alopecia, termed keratosis pilaris atrophicans, typically have their onset in childhood. One of these, keratosis follicularis spinulosa decalvans begins with keratosis pilaris in infancy and is accompanied by photophobia, corneal changes and progressive alopecia of the scalp, eyebrows and/or eyelashes.\textsuperscript{4}

**Conclusions**

The psychological and cosmetic importance of hair is immense in our society. Disruption in the normal appearance of hair can predispose to low self-esteem and negative body image. A detailed clinical history and examination accompanied by hair microscopy is essential for accurate diagnosis of the condition. In pediatric hair disorders it is important that the parents are given a clear understanding of the etiology and natural history of the disease and are offered genetic counseling if the disease is hereditary.

Unfortunately, for many hair disorders there is no effective, reliable therapy; in reversible conditions such as infections, treatment is mandatory. Some conditions are amenable to surgical correction. Cosmetic solutions such as wigs can provide satisfactory camouflage if surgery is not an option and medical therapies fail.\textsuperscript{1}

**Riassunto**

**Alopecia infantile**

Le patologie dei capelli rappresentano una frazione importante dei casi osservati dai dermatologi pediatrici, sebbene i capelli abbiano rivestito sempre un aspetto secondario nella formazione di pediatri e dermatologi, partendo dal presupposto erroneo che non sia possibile ricavare una grande quantità di informazioni da essi. I dermatologi si trovano nell’invisibile posizione di poter studiare numerosi disturbi attraverso tecniche diagnostiche semplici. I capelli si prestano facilmente a essere analizzati; paradossalmente, però, tale approccio è spesso trascurato dai medici non dermatologi. Obiettivo del presente articolo è stato quello di cercare di contribuire al processo diagnostico nella pratica quotidiana, aiutando a distinguere, ad esempio, tra alcune patologie dei capelli acquisite e altre determinate geneticamente. Presteremo particolare attenzione a tutti i dati che sono stati ottenuti dai capelli dei nostri pazienti e cercheremo di mettere a frutto le informazioni ricavate dai capelli per ciascun paziente. Spesso, è estremamente difficile distinguere tra normalità e anomalia nell’aspetto dei capelli neonatali. Ci concentreremo in particolare sulle alterazioni fisiologiche più comuni che potrebbero condurre a una diagnosi erronea. Discuteremo anche dei trattamenti specifici per le patologie dei capelli che è possibile trattare e dell’approccio basilare generico per migliorare l’aspetto estetico dei capelli in quei disturbi che non hanno un trattamento specifico.

**Parole chiave:** Età pediatrica - Alopecia - Capelli, malattie.

**References**

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Conflicts of interest.—The authors certify that there is no conflict of interest with any financial organization regarding the material discussed in the manuscript.