Papers and Originals

Endocrine Influences on Hair Growth*

ARTHUR ROOK,† M.D., F.R.C.P.

Brit. med. J., 1965, 1, 609-614

I am particularly happy to be given this opportunity of commemorating Dr. Parkes Weber, since I was one of the many young dermatologists to experience personally the benefit of his immense erudition and his kindly eagerness to share it. I met him in 1947 on the first occasion that I presented a case at a meeting in London; he introduced himself and told me much about the condition that I ought to have known, and on many subsequent occasions he helped me with suggestions or with references. So far as I can discover, none of Parkes Weber's writings is concerned primarily with hair, but I hope he would have enjoyed this hesitant excursion of a physician into the realms of comparative physiology. For, although the aim of this lecture is to provide an account of our present knowledge of endocrine influences on hair growth in man, it must lean very heavily on experimental and clinical observations in other mammals. Many of the aspects of hair growth of greatest clinical significance, notably the cyclic activity of the individual follicle, are essentially similar in all species investigated, including man, yet although the main events of the hair cycle have been known for over thirty years they have generally been ignored by clinical endocrinologists, and, until recently, by most dermatologists. Some aspects of the endocrine control of hair growth, on the other hand, while conforming to the same general pattern, show sufficient species variation to impose great caution in applying to man observations in subprimate mammals. However, such observations can both provide us with valuable working hypotheses and suggest the experimental procedures by which they may be tested.

Hair Patterns and Hair Cycles

The hair follicles are formed between the second and fifth months of foetal life as epithelial down-growths which develop in approximately equal numbers in all regions of the body. On the scalp these down-growths are met by a larger number of dermal papillae and are thus able to give rise to a denser population of hair follicles than in other regions (Szabo, 1958). Other regional differences in the density of follicles are the result of dilution by differential growth. The number of follicles is the same in both sexes and in all races investigated. No new follicles are formed after foetal life except as a response to severe local trauma. It follows that since the number of follicles is constant the wide range of hair patterns observed in health and disease must be dependent on the type of hair present in each individual follicle at the moment of examination. The rate of growth of each hair, its shedding and its replacement, and the time-relations of these events are functions of the hair cycle. The type of hair present is independently determined although the two aspects of follicular activity are necessarily related.

It is of great value in clinical practice to make a clear distinction between disturbances of the hair cycle and disturbances of hair pattern, in which certain follicles are producing a type of hair inappropriate to the age and sex of the patient. The distinction not only facilitates the evaluation of the complex factors concerned but is of prognostic importance, for most disturbances of the hair cycle are reversible when the pathological influence is removed, whereas disturbances of hair pattern often are not. The ultimate justification for differentiating the two aspects of follicular activity lies in their very different evolutionary significance. The changing hair patterns are closely linked to the processes of somatic growth, ageing, and sexual maturation, the more elaborate pelage of the mature male serving the purposes of sexual display. The cyclic activity of the hair follicle, on the other hand, is a relic of moulting, originally linked to the reproductive cycle and hence to the seasons, but more or less freed from such associations in man and in some other mammals long domesticated.

It will therefore be convenient first to define the types of hair, then to consider the normal hair cycle before describing the succession of hair patterns throughout life and the endocrine factors which influence them. I shall leave to the last the endocrine influences on the hair cycle because on this aspect of hair growth in man so much remains a matter for speculation.

Types of Hair

Resisting the temptation to discuss the phylogenetic background of the types of hair in man, we must distinguish between lanugo, vellus, and terminal hair. Lanugo is the prenatal hair coat, fine, soft, and silky, sometimes long, unmedullated, and usually unpigmented. The continued formation of lanugo after birth or the reversion to lanugo formation later in life occurs only in certain rare pathological states. Vellus is the fine hair of post-natal life; also soft and unmedullated, but sometimes pigmented, and seldom exceeding 2 cm. in length. Terminal hair is longer, coarser, often medullated, and often pigmented. Vellus and terminal hair cannot be sharply defined, for between them lie a series of hair types usually classified as intermediate. In some follicles the transition from obvious vellus to coarse terminal hair occurs quite suddenly, as in the scalp before birth, or in the pubic region at puberty. In other follicles several generations of intermediate hairs, each slightly coarser than its predecessor, are eventually followed by terminal hair. In some regions of predominantly terminal hair some follicles may continue to produce vellus (Duggins and Trotter, 1951) although the number doing so tends to fall progressively with age. The obvious morphological differences between terminal hair in different body regions—the pubic hair and the scalp, for example—need not concern us, since each follicle is capable, under appropriate stimulation, of producing only lanugo, vellus, or intermediate hairs, or the morphological

* The second Parkes Weber Lecture, given at the Royal College of Physicians of London on 9 October 1964.

† Consultant Dermatologist, Addenbrooke's Hospital, Cambridge.

type of terminal hair to which it is genetically committed. Grafting experiments convincingly demonstrate donor dominance.

Hair Cycle

From the completion of its development in the last month of foetal life each hair follicle undergoes recurring cycles of active growth, regression, and rest (Table I). In most wild mammals the cycles of the follicles in each region of the body are synchronized and waves of activity flow from one or more centres. In man and in the guinea-pig follicular activity is dyssynchronized and neighbouring follicles are normally at different stages of the cycle, the so-called mosaic cycle. It has been said that hair growth in the merino sheep is continuous, but follicular activity is, in fact, of the wave type, but the growing period has been greatly prolonged by natural selection.

TABLE I.—Hair Cycles

Synchronous	{ Wave	Rat, Mouse, Rabbit
	{ "Continuous"	Merino Sheep
Dyssynchronous	mosaic	Guinea-pig, Man

The events of the follicular cycle are currently the subject of intense research for the light they throw on fundamental problems of morphogenesis, and detailed accounts are readily available (Straile *et al.*, 1961; Montagna, 1962; Ebling, 1964). The main stages of the hair cycle are known as anagen, the phase of active growth; catagen, the phase of regression; and telogen, the resting period. This sequence is invariable and irreversible. The follicle in later anagen is committed to catagen; once catagen is induced, spontaneously or pathologically, telogen inevitably follows and is succeeded by a new anagen. As the end of anagen approaches, the melanocytes of the dermal papilla resorb their dendrites and mitotic activity in the matrix ceases. These, the first changes of catagen, are rapidly followed by upward movement of the hair root, which becomes club-shaped (Fig. 1). Beneath the club, which is soon surrounded by a capsule of partially keratinized cells, a strand of epithelial cells, together with the cells of the epithelial sac surrounding the capsule, comprise the hair germ, from which the follicle will later be regenerated. The dermal papilla, which was set free as the club was formed, remains in contact with the epithelial strand. Once catagen is complete telogen begins and there are no further obvious changes until anagen is initiated. The club hair is usually retained until anagen is well advanced, but under certain circumstances may be shed prematurely. In anagen the follicle below the level of the pilosebaceous duct is reconstituted, and a new hair grows up alongside the club hair. The events of catagen and of anagen have been divided respectively into eight and six well-defined stages, the details of which cannot detain us here, but recognition of which could bring much-needed precision to studies of hair growth in man.

The time-relations of the stages of the hair cycle are of great clinical importance. In the young adult human scalp the average duration of anagen is about three years; catagen occupies two weeks or less and telogen three to four months. The duration of anagen shows wide individual variation and may exceptionally be as long as six years or as short as one, but it is always long in relation to telogen. At any given moment 85–95% of scalp follicles are in anagen, 4–14% in telogen, and 1% or less in catagen. The proportion of anagen follicles is highest in childhood (Pecoraro *et al.*, 1964) and lowest in old age, and there are small, relatively constant variations in different regions of the scalp. If we accept 100,000 as a rough estimate of the follicle population of the scalp the daily moult will be in the region of 20–75 hairs. The time-relations of the cycle in other regions of the body have been less carefully studied and many of the available figures are old and of doubtful reliability, but all show a very high proportion of telogen follicles as compared with the scalp.

The very different biological responsiveness of anagen and telogen follicles makes the ratio of one to the other (the A/T ratio) an observation of great diagnostic significance in clinical studies. It will be apparent that the A/T ratio of the normal scalp is high and that of the general body hair low. For research purposes the A/T ratio should be established by biopsy, but in routine clinical work a useful indication is provided by the examination of the roots of plucked hairs under the low power of the microscope. The clubs of telogen hairs are readily distinguished from anagen hairs, but some practice is necessary to achieve a reliable and uniform technique (Maguire and Kligman, 1964).

FIG. 1.—Stages of the hair cycle. (Redrawn from Ebling, 1964.)

Rates of Hair Growth

Scalp hair grows at the rate of about 0.33 mm. daily, somewhat faster on the vertex, and more slowly around the scalp margins (Barman *et al.*, 1962). In other regions of the body the rate ranges from 0.1 mm. on the trunk and limbs to as high as 0.38 mm. on the beard, but there is considerable individual variation (Myers and Hamilton, 1951).

The clinical observation that hair growth is increased has little scientific value, and the quantitation of the observation by regularly weighing shavings from a measured area is useful only for purposes of comparison between individuals with the same syndrome. The clinical appearance of increased hairiness may be produced by any of the following factors, alone or in combination: (a) increase in the A/T ratio; (b) delayed shedding of club hairs; (c) increase in shaft diameter—the substitution of terminal hair for vellus; and (d) increased rate of linear

growth. Finally, an increase in pigmentation may give a false impression of increased hairiness. Any planned investigation should include the assessment of A/T ratio, preferably by histological methods, and the use of a technique such as Barman's, in which the shaft diameter as well as the length of daily shavings can be measured (Barman *et al.*, 1962).

Normal and Abnormal Hair Patterns

In man as in other mammals the hair pattern never achieves equilibrium, and changes constantly from the initiation of the first hair cycle during foetal life until death. The genetic constitution and the processes of ageing combine to determine the capacity of the individual follicle to respond to the endocrine changes associated with normal somatic growth, sexual maturation, and senescence. The lanugo, the first pelage, is normally shed *in utero* in the seventh or eighth month and is replaced by vellus in all regions except the scalp and eyebrows and lashes, where coarser intermediate or terminal hair is produced. Certain rare genetic defects determine either the indefinite continuance of lanugo in successive cycles or the replacement of vellus by lanugo after one or more normal cycles. Quite exceptionally this universal growth of lanugo, best termed hypertrichosis lanuginosa, may develop suddenly at any age (Fig. 2). Study of the reported cases (Table II) fails to establish an obvious common factor, but the syndrome is of great theoretical interest in that it demonstrates the capacity of all the follicles, under these peculiar circumstances, to revert after an interval of many years to the production of hair of foetal type.

TABLE II.—Acquired Hypertrichosis Lanuginosa

Author	Sex	Age	
Le Double and Houssay (1912)	M	67	After "influenza"
Ormsby (1930)	F	57	No preceding disease
Le Marquand and Bohn (1951)	M	61	Duodenal ulcer, ulcer of gastric stump, ulcer of jejunal stump
Lyell and Whittle (1951)	F	35	Carcinoma of bladder with metastasis

FIG. 2.—Acquired hypertrichosis lanuginosa of sudden onset in a man aged 67 (Le Double and Houssay, 1912).

The second pelage of the normal infant also has a short growing period, but, from the third pelage onwards, cycles approaching the adult type are slowly established. During childhood there is a progressive increase in shaft diameter, but there is no obvious change in hair pattern until the approach of puberty, when terminal hair replaces vellus, first in the pubic region and then in a fairly regular sequence, over a period of years, in the axillae and on the legs, thighs, forearms, abdomen, buttocks, chest, arms, and shoulders (Reynolds, 1951). The transition from vellus to terminal hair on the face also follows an orderly sequence—upper lip, chin, sides of cheeks, and then the remainder of the beard area. Male and female patterns of body and facial hair differ only in degree (Beek, 1950 ; Thomas and Ferriman, 1957) even in the pubic region, where an acuminate upper border is present in 3 to 4% of normal females

and a horizontal border in about the same percentage of normal males. Although terminal hair on the trunk and limbs is more profuse in the male it tends to become more extensive in distribution in both sexes throughout the years of sexual maturity, and the proportion of females in Britain with some terminal hair on the face reaches about 40% by the age of 50.

The hair pattern is also modified by the opposite process, the replacement of terminal hair by vellus, which first occurs at the frontal hair line at adolescence in 80% of girls and nearly 100% of boys, and produces the characteristic reshaping of the facial outline. This almost universal frontal recession must not be confused with bitemporal recession, which may be evident before the age of 20 and is the first manifestation of male-pattern baldness. During the third decade the replacement of terminal hair by vellus on the vertex may be clinically obvious, and by the age of 50 about 60% of white men show some degree of vertical as well as bitemporal baldness, and in many these bald areas have become confluent. Over 25% of women aged 35 to 40 and 14% aged 40 to 70 show bitemporal recession and about 20% of the latter also show obvious vertical thinning (Beek, 1946). The vellus hairs which replace the terminal hair are small and relatively unpigmented. They have a short anagen and a long telogen, and seldom exceed 2 cm. in length. With advancing age some of these inconspicuous relics may disappear as the number of follicles is progressively reduced (Silvestri, 1956). Other changes in old age have been recently reviewed (Rook, 1965a, 1965b) and cannot be considered in detail here. In general the order of loss of terminal hair on the trunk and limbs, pubes, and axillae reverses that of its appearance, but axillary and pubic hair are lost earlier and more completely in females than in males.

Endocrines and Hair Patterns

The analysis of the complex interplay of genetic and endocrine factors which determine this succession of patterns can be attempted with greater knowledge but less assurance than twenty-five years ago, but the most useful framework on which to hang the available facts is still the old classification proposed by Danforth and modified by Garn (1951) (Table III).

TABLE III.—Hormonal Classification of Hair Patterns (Modified from Garn, 1951)

Non-sexual Hair	
Not dependent upon steroid hormones	
Scalp, eyebrows, eyelashes,	
Forearms and lower legs	
Ambosexual Hair	
Dependent upon female levels of steroid hormones	
Lower pubic triangle	Axillae
Some limb hair	
Male Sexual Hair	
Dependent upon male levels of steroid hormones	
Upper pubic triangle	Ears
Beard	Body hair
	Nasal tip

The anterior pituitary influences hair patterns mainly indirectly through its dependent endocrine glands ; but growth hormone, and probably also luteotrophin, can affect the hair follicle directly. Growth hormone appears to be responsible for the increase in hair-shaft diameter, which continues throughout life in many regions of the body and is not inhibited by castration. A marked reduction in the size of the hair follicles followed hypophysectomy in rats, and injection of a pituitary extract induced an increase in follicle size above normal (Snow and Whitehead, 1935). In the rat, in the absence of growth hormone the pelage remains infantile and steroid hormones are unable to modify the type of hair produced (Mohn, 1958). Recent more detailed study in the rat of the pituitary factors involved (Rennels and Callahan, 1959) suggests that while growth hormone induces the slow increase in follicle size the more rapid and specific change from infantile to adult pelage, corresponding to the development of ambosexual hair in man, is due to the direct action of luteotrophin on the follicles. Similar mechanisms are possibly concerned in

man, but the evidence is purely circumstantial. The hypopituitary dwarf may be totally hairless, and in Sheehan's syndrome axillary and pubic hair are lost and the scalp hair becomes very sparse. The coarsening of the hair in acromegaly may be attributable to the increased output of growth hormone, but it is also reported in a syndrome without acromegaly with overproduction of luteotrophin (Forbes *et al.*, 1954).

The hair of the lower pubic triangle and the axillae and some hair on the limbs appear in both sexes at or soon after puberty. In the female, androgens of suprarenal origin are normally responsible; in Addison's disease this hair does not develop. In the male, testicular androgen can replace suprarenal androgen, for normal hair growth occurs in Addison's disease. In ovarian agenesis no ambosexual hair growth occurs, although there is no change in hair pattern following ovariectomy after puberty (Summers, 1949). Hair growth is not induced by oestrogens alone and ovarian androgens are presumably implicated. Wide individual variations in pattern at any age are usually correctly attributed to genetically determined variation in follicular response to levels of hormonal stimulation normal for the age and sex, but this explanation should not be too readily accepted without supporting evidence. In the rare syndrome known as premature pubarche (Silverman *et al.*, 1952; Arnal *et al.*, 1961) the patient, usually a girl, develops pubic and sometimes axillary hair during early childhood, even as early as the first year, although breast development and the menarche occur at the normal age. This syndrome has been cited as an example of abnormal end-organ response, but the recent report of two cases (Zurbrugg and Gardner, 1963) in which fractionation of the urinary C19 steroids was undertaken, showing levels of androsterone six and four times and of etiocholanolone three and two and a half times higher than in controls, illustrates the danger of premature conclusions.

Male sexual hair patterns are produced by male levels of androgen, the capacity of each follicle to produce terminal hair being genetically determined but influenced by the age of the patient. We have already noted the progressive extension of male sexual hair during the years of sexual maturity. The importance of the age factor is further illustrated by the fact that, in young boys with androgen-producing tumours, although ambosexual and male sexual hair may develop prematurely, the different sites are involved successively at intervals and the full pattern of male maturity is not seen.

In women with virilizing syndromes the pattern of male sexual hair is again determined by the genetic constitution and the age of the patient. The wide individual variation in the capacity of the follicles to respond to a potent androgen has recently been confirmed (Maguire, 1964) by the repeated subcutaneous injection of a long-acting testosterone ester into a single site in the beard area of five post-menopausal women. Two produced a vigorous growth of terminal hair at the injection site in four months, two a sparse growth in one year, and one no growth whatever. In the many women with terminal hair in part of the male sexual pattern but without genital virilism—so-called constitutional hirsutism—genetically determined susceptibility of certain follicles to female levels of circulating androgen has been assumed, and such a mechanism probably underlies the great majority of cases. However, the modern techniques of hormone assay are elucidating disorders of steroid biosynthesis, sometimes genetically determined, which may result in hirsuties with minimal or no genital virilization.

The overwhelming importance of the hereditary factor in hirsuties has been emphasized by Hamilton and Terada (1963), but no genetic investigations have been reported. It seems probable that there are many distinct genotypes. Male-pattern alopecia, in which the interplay between genotype, endocrine activity, and ageing determines the degree and pattern of hair loss, has, however, attracted the attention of

the geneticists. This form of baldness results in the progressive replacement of terminal hair by vellus and ultimately a reduction in the number of hair follicles. Although complete agreement has not been reached it is probable that a pair of sex-influenced factors is concerned (Snyder and Yingling, 1935) (Fig. 3). Both men and women of genotype BB become bald, the women some years later than the men. Men but not women of genotype Bb become bald, but with genotype bb no baldness develops in either sex. It follows that women of genotype Bb will develop male-pattern baldness with male levels of androgen of pathological origin. Those of genotype bb will not do so no matter how great the degree of androgenic stimulation.

MALE	BB	Bb	bb
FEMALE	BB	Bb	bb

FIG. 3.—Inheritance of male-pattern baldness. Baldness will develop in individuals of the ringed genotypes.

Castration before puberty prevents male-pattern baldness (Hamilton, 1942). Castration later prevents further extension of the baldness, but there is no regrowth of terminal hair in the frontal and temporal regions and only rarely some partial regrowth on the vertex (Hamilton, 1960). Changes of hair pattern, involving as they do a change in the calibre of the hair shaft and therefore a structural change in the follicle, are usually not spontaneously reversible on the removal of the endocrine stimulus which induced them; however, no generalization is applicable to all cases and the factors determining reversibility or irreversibility are obscure, except, of course, in those male-pattern alopecias of long duration in which many follicles have disappeared. Clinical observations suggest that the age of the patient and the duration of the change in pattern may be relevant factors. Hirsuties in women with virilizing syndromes is usually not reversed by operative removal of the source of excess androgen. A rare familial syndrome has been reported (Cedercreutz, 1939) in which a most conspicuous growth of coarse hair regularly developed in the region of the eyebrows during the second month of pregnancy. This embarrassing incentive to good behaviour always disappeared completely after childbirth. It is interesting that the facial hypertrichosis sometimes induced by cortisol is usually spontaneously reversible, as is the very rare generalized hypertrichosis which has followed severe emotional shock (Robinson, 1955), whereas male-pattern hirsuties following stress usually persists.

Endocrines and the Hair Cycle

It has been calculated that 25% of hairs must be shed from the human scalp before clinically apparent hair loss is produced. It is perhaps for this reason that the very common disturbances of the hair cycle are so often overlooked and have been little studied. Hair cycles in wild animals are linked to sexual cycles which in temperate climates are determined by the photoperiod. The mechanisms controlling the hair cycle have been most thoroughly studied in the common laboratory animals, particularly the rat, rabbit, and guinea-pig. Theoretically the events of the hair cycle could be modified in several ways. The duration of the resting-phase, telogen, could be increased or reduced by retarding or advancing the initiation of anagen in resting follicles. The duration of anagen might be prolonged or shortened, the rate of hair growth might be increased or decreased. Finally, the rate of loss of club hairs from resting and early anagen follicles might be influenced. Most of these possible modifications of the cycle have been observed in the experimental animal, and, although there are some important species differences, there is

striking general similarity in the pattern of response (Davis, 1963; Ebling, 1964; Ebling and Johnson, 1964a, 1964b). The very large volume of research may be briefly and incompletely summarized, at the risk of oversimplification, before we consider its implications for man.

Each follicle has its own intrinsic rhythm, which is subjected to systemic adjusting mechanisms. Not all follicles even of the same type will respond to the same degree, and the age of the individual will further modify the response. Hypophysectomy accelerates the initiation of anagen in resting follicles. A.C.T.H. will inhibit this acceleration, but not in the adrenalectomized animal. Adrenalectomy also accelerates initiation, and this effect is inhibited by cortisone. Thyroidectomy delays initiation, and the administration of thyroxine advances it until toxic doses are given (Chang and Feng, 1929), when initiation is again delayed. This means that in both hyperthyroidism and hypothyroidism the ratio of telogen to anagen hairs is increased. In some species the rate of hair growth is also increased by thyroxine. Gonadectomy advances the initiation of hair growth in resting follicles and oestradiol and testosterone delay it. In female rats spaying accelerates and oestradiol retards the shedding of club hairs, but neither gonadectomy nor implantation of testosterone has any such effect in males. Spaying increases and oestradiol reduces definitive hair length in female rats and oestradiol reduces it in males, although it is not influenced by castration or by testosterone. Pregnancy retards spontaneous replacement. There are very few observations on experimental diabetes, but replacement is retarded in alloxan diabetes in the rat (Mohn, 1958).

These observations may be applied to man only with the very greatest caution. The essential similarity of the morphological events of the hair cycle in all mammals has been emphasized. We know that in other mammals in which domestication has modified seasonal and sexual cycles the normal adjustment of the follicular cycle has retained its essential features. It is possible that it has done so in man. Unfortunately almost all the published accounts of the disturbances of hair growth in human endocrine disorders totally ignore the existence of the hair cycle and are therefore difficult to interpret. Many of the changes observed in man resemble those in experimental animals, and there is some evidence that the underlying mechanisms are similar. There are other changes which we cannot yet begin to explain.

In congenital cretinism lanugo may be retained for some months and scalp hair is sparse and dry. In myxoedema scalp and body hair may be sparse. These changes are entirely compatible with retardation of the initiation of anagen, and we have found a marked increase in the telogen count in plucked hairs in two cases in adults. However, such findings are not constant (Smith *et al.*, 1959). The response of alopecia in myxoedema to effective management of the hypothyroid state is sometimes excellent but sometimes disappointing. Personal experience suggests that in the cases which fail to respond satisfactorily a mild diffuse hypothyroid alopecia has unmasked a pre-existing irreversible alopecia of male pattern.

The cause of the growth of long fine hair on the back and shoulders and the outer aspects of arms and legs in some children with hypothyroidism (Perloff, 1955) is equally obscure. This inconstant but characteristic sign is always reversed by thyroxine treatment. Prolongation of anagen or an increased rate of linear growth could produce this effect.

On hyperthyroidism we are no better informed. Some degree of diffuse alopecia is present in about 40% of cases (Sainton and Simmonet, 1931). No histological studies have been published. Recovery usually follows control of the hyperthyroidism.

Bilateral ovariectomy is not an unusual operation, and even bilateral orchidectomy is an occasional surgical necessity, yet no observations have been reported on the effects of these

procedures on the hair cycles as distinct from the hair patterns. Diffuse thinning of the scalp hair is not unusual in uncontrolled diabetes, but no observations have been published. The two patients I have had the opportunity of investigating both showed high telogen counts.

The changes in pregnancy have also not been adequately investigated. An increase in the percentage of anagen hairs has been reported (Lynfield, 1960; Kligman, 1961), but without biopsy studies we do not know whether this increase is due to prolongation of anagen or to failure of retention of club hairs. In the rat, oestradiol both retards the shedding of club hairs and delays the initiation of anagen in resting follicles. These findings are therefore contradictory and much further work is needed in man.

In some degree in all women and to a clinically significant degree in many the stress of childbirth initiates hair loss of a distinct type, telogen effluvium (Kligman, 1961), which is not yet known to occur in other mammals. Childbirth, fever, and other physical or emotional stress induce a great many or all anagen follicles prematurely to enter catagen and therefore to shed their hairs some three months later, when they are, of course, immediately replaced. Clinically the patient may be aware only of increased hair fall or she may temporarily become almost bald. The mechanism by which the follicles are precipitated into catagen is unknown. Adrenaline has some direct effect on the hair follicles of rats, retarding the initiation of anagen, but it does not influence growth once it has started (Mohn, 1958). Although adrenaline depresses the mitosis rate in surface epidermis it has, in rodents, no effect on the mitotic activity of hair follicles (Bullough and Laurence, 1964).

A very distinctive abnormality of follicular activity is alopecia areata, which we must consider briefly because its incidence is significantly increased in hyperthyroidism and in other disturbances of thyroid function and because it shows a paradoxical response to corticosteroids. The defect in alopecia areata is probably genetically determined and hyperthyroidism is one of several stimuli which may raise it above the clinical threshold. During the active stages of the disorder the hair follicles in the affected patches fail to proceed far beyond the third stage of anagen—inner root sheath is formed and projects upwards as a cone, but the matrix can form only a very imperfect hair or keratinous debris. The follicle is small and lies high in the dermis, and the normal relations between papilla and matrix are disturbed.

There are other striking changes, including a lymphocytic infiltrate, during the early stages. Cortisone systemically or by local injection will temporarily, and for as long as it is administered, remove the inhibition and allow normal growth to proceed. This response is paradoxical, for cortisone is without benefit or harmful in other forms of alopecia in man, and in all other mammals investigated it will delay the initiation of anagen in resting follicles. The endocrine associations are not the least interesting aspect of this mysterious disorder.

Future Research

It will be abundantly clear that we have little reliable knowledge of the factors which influence the follicular cycle in man either in health or in disease and that there are still many surprising gaps in our knowledge of some of the normal hair patterns. Much of the research required is of the old-fashioned observational variety, supplemented by such histological studies and modifications of some of the elegant techniques of the experimental zoologists as can be carried out with the minimum of discomfort and inconvenience to our patients. Such investigations will give valuable information provided that they are planned with a full understanding of the events of the hair cycle and of the essential difference

between disturbances of the hair cycle and disturbances of hair pattern.

In conclusion, I am tempted to quote a former President of this College. John Ayrton Paris (1785–1856) wrote in 1822: "For any problem which involves the phenomenon of life is unavoidably embarrassed by circumstances so complicated in their nature, so fluctuating in their operation, as to set at defiance any attempt to appreciate their influence."

Summary

The differentiation of two aspects of follicular activity is phylogenetically sound and clinically useful. The recurrent cycles of active growth, regression, and rest in the individual hair follicle represent the seasonal moulting cycles of other mammals. The sequence of hair patterns throughout life, which depends on the calibre of the hair produced by each follicle, is linked to the processes of somatic growth, sexual maturation, and ageing.

Disturbances of hair pattern are usually produced by excessive or deficient stimulation of follicles by androgens or by somatotrophin, or by genetically determined defects in follicular response. Most such disturbances are incompletely reversed by removal of the endocrine stimulus.

Disturbances of hair cycles involve modification of the relative duration of the phases of the cycle and are most characteristically determined by excess or deficiency of glucocorticosteroids or thyroid hormones. They are usually completely reversible.

Scientifically planned investigations on hair cycles in man have seldom been undertaken, and conclusions based on comparative studies are tentative.

REFERENCES

- Arnal, M., Dresch, C., and Prader, A. (1961). *Helv. paediat. Acta.*, **16**, 186.
Barman, J. M., Pecoraro, V., and Astore, I. (1962). *Arch. argent. Derm.*, **12**, 55.
Beck, C. (1946). *Dermatologica (Basel)*, **93**, 213.
Beck, C. H. (1950). *Ibid.*, **101**, 317.

- Bullough, W. S., and Laurence, E. B. (1964). *Symp. zool. Soc. Lond.*, **12**, 1.
Cedercreutz, A. (1939). *Acta derm.-venereol. (Stockh.)*, **20**, 704.
Chang, H.-C., and Feng, T.-P. (1929). *Chin. J. Physiol.*, **3**, 57.
Davis, B. K. (1963). *Acta endocr. (Kbh.)*, **44**, Suppl. No. 85, p. 9.
Duggins, O. H., and Trotter, M. (1951). *Ann. N.Y. Acad. Sci.*, **53**, 569.
Ebling, F. J. (1964). In *Progress in the Biological Sciences in Relation to Dermatology*, edited by A. Rook and R. H. Champion. Cambridge University Press, London.
— and Johnson, E. (1964a). *Symp. zool. Soc. Lond.*, **12**, 97.
— (1964b). *J. Endocr.*, **29**, 193.
Forbes, A. P., Henneman, P. H., Griswold, G. C., and Albright, F. (1954). *J. Clin. Endocr.*, **14**, 265.
Garn, S. M. (1951). *Ann. N.Y. Acad. Sci.*, **53**, 498.
Hamilton, J. B. (1942). *Amer. J. Anat.*, **71**, 451.
— (1960). *J. clin. Endocr.*, **20**, 1309.
— and Terada, H. (1963). In *The Hirsute Female*, edited by R. B. Greenblatt, p. 20. Thomas, Springfield, Ill.
Kligman, A. M. (1961). *Arch. Derm.*, **83**, 175.
Le Double, A.-F., and Houssay, F. (1912). *Les Vélus*. Vigot, Paris.
Le Marquand, H. S., and Bohn, G. L. (1951). *Proc. roy. Soc. Med.*, **44**, 155.
Lyell, A., and Whittle, C. H. (1951). *Ibid.*, **44**, 576.
Lynfield, Y. L. (1960). *J. invest. Derm.*, **35**, 323.
Maguire, H. C. (1964). *Lancet*, **1**, 864.
— and Kligman, A. M. (1964). *J. invest. Derm.*, **42**, 77.
Mohn, M. P. (1958). In *The Biology of Hair Growth*, edited by W. Montagna and R. A. Ellis, p. 336. Academic Press, New York.
Montagna, W. (1962). *The Structure and Function of Skin*, 2nd ed. Academic Press, New York.
Myers, R. J., and Hamilton, J. B. (1951). *Ann. N.Y. Acad. Sci.*, **53**, 562.
Ormsby, O. (1930). *Arch. Derm.*, **21**, 663.
Paris, J. A. (1822). *Pharmacologia*, 5th ed. London.
Perloff, W. H. (1955). *J. Amer. med. Ass.*, **157**, 651.
Pecoraro, V., Astore, I., Barman, J., and Araujo, C. I. (1964). *J. invest. Derm.*, **42**, 427.
Rennels, E. G., and Callahan, W. P. (1959). *Anat. Rec.*, **135**, 21.
Reynolds, E. L. (1951). *Ann. N.Y. Acad. Sci.*, **53**, 576.
Robinson, R. C. V. (1955). *Arch. Derm.*, **71**, 401.
Rook, A. (1965a). In *Comparative Physiology and Pathology of Skin*, edited by A. Rook and G. Walton. Blackwell, Oxford.
— (1965b). *Geront. clin. (Basel)*. In press.
Sainton, P., and Simonnet, H. (1931). *Ann. Méd.*, **29**, 263.
Silverman, S. H., Migeon, C., Rosenberg, E., and Wilkins, L. (1952). *Pediatrics*, **10**, 426.
Silvestri, U. (1956). *G. geront.*, Suppl. 5, p. 203.
Smith, J. G., Weinstein, G. D., and Burr, J. M. (1959). *J. invest. Derm.*, **32**, 35.
Snow, J. S., and Whitehead, R. W. (1935). *Endocrinology*, **19**, 88.
Snyder, L. H., and Yingling, H. C. (1935). *Hum. Biol.*, **7**, 608.
Straile, W. E., Chase, H. B., and Arsenaault, C. (1961). *J. exp. Zool.*, **148**, 205.
Summers, V. K. (1949). *Acta med. scand.*, **136**, 105.
Szabo, G. (1958). In *The Biology of Hair Growth*, edited by W. Montagna and R. A. Ellis. Academic Press, N.Y.
Thomas, P. K., and Ferriman, D. G. (1957). *Amer. J. phys. Anthropol.*, **15**, 171.
Zurbrugg, R. P., and Gardner, L. I. (1963). *J. clin. Endocr.*, **23**, 704.

Virus Isolations From Throats of Children Admitted to Hospital with Respiratory and Other Diseases, Manchester 1962–4

A. HOLZEL,* M.D., D.C.H.; L. PARKER,† M.A., B.M., M.C.PATH.; W. H. PATTERSON,‡ M.D., D.C.H.
D. CARTMEL,§ M.B., D.C.H.; L. L. R. WHITE,|| M.D., B.SC., D.C.H.; ROSEMARY PURDY,¶ A.I.M.L.T.
K. M. THOMPSON,¶ F.I.M.L.T.; J. O'H. TOBIN,¶ M.A., B.M., DIP.BACT., M.C.PATH.

Brit. med. J., 1965, **1**, 614–619

Recently we reported (Holzel *et al.*, 1963) the isolation of 36 strains of respiratory syncytial (R.S.) virus from children with acute respiratory infections admitted to Booth Hall Children's Hospital during January to April 1962. The strains were isolated by the direct inoculation with throat swabs of cell cultures kept in an incubator in the hospital admission-room.

Since then routine throat swabs dealt with in this way have been obtained from the majority of infants and children admitted to the medical wards of this hospital.

Our principal aim in this two-year study from April 1962 to March 1964 was to delineate so far as is possible the role of specific viral agents in the seasonal pattern of respiratory infection in children admitted to hospital.

Children with and without respiratory disease were studied in order to assess the clinical significance of the viruses isolated, as regards both their frequency of occurrence in patients without respiratory symptoms and their association with non-respiratory illness.

* Reader in Child Health, University of Manchester.

† Consultant Bacteriologist, Booth Hall Children's Hospital, Manchester.

‡ Consultant Paediatrician, Booth Hall Children's Hospital, Manchester.

§ Resident Medical Officer, Booth Hall Children's Hospital, Manchester.

|| Consultant Pathologist, Booth Hall Children's Hospital, Manchester.

¶ From the Public Health Laboratory, Withington Hospital, Manchester.