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Baldness in Nonhuman Primates*

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Synopsis—Long believed to be a disorder peculiar to the scalp of man, alopecia occurs in some of the other primates. Even discounting the oddities of hair growth patterns in the head of some marmosets, sakis and sakiwinkis from South America, all adult species of uacaris are completely bald. A close look at the head of these animals shows that the bald scalp is covered with short hairs of small diameter. An identical situation occurs in the stump-tailed macaque (*Macaca speciosa*); the scalp of young stump-tails is covered with hair down to the eyebrows. Beginning in adolescence, the forehead becomes gradually "naked" and adult animals have a high, apparently glabrous forehead. Actually, the number of very small hairs on these bald areas is the same as in the haired comparable areas of young animals. The population of hair follicles, then, is not reduced in numbers but the follicles are much smaller and produce very small hairs.

With the diminution in size of the hair follicles, there is a substantial increase in the size of the accompanying sebaceous glands. Such a pattern of development of alopecia is identical with what takes place in some young adult men.

Additional evidences of baldness occur in the orangutan, which, like the stump-tailed macaque, attains a naked forehead as it matures. Inspections of many chimpanzees of all ages also reveal varying degrees of alopecia in a triangle of forehead just above the brows; this appears in adolescent animals and becomes prominent only in some adult animals.

These observations point out that human alopecia has some phylogenetic significance and is not to be considered a disorder or disease.

Introduction

Despite the heroic methods used by some dermatologists in their study of alopecia in human subjects, many factors still limit their re-

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search. The investigator of human subjects must be constantly aware of the moral and legal restrictions that curtail his experiments. Furthermore, man's longevity, the vagaries of his nature and temperament and the near-impossibility of controlling the experimental design and heterogeneity of his genetic makeup render him an unsuitable and often unpleasant subject for experiment.

Investigators have long searched for animal substitutes, but these half-hearted efforts have failed. Hamilton (1), for lack of a better model, studied the wattled starling (*Creatophora carunculata*), the male of which acquires a glabrous, colored tumescent skin during the breeding season in areas of the head that had been feathered during the off season. Female birds, which have a fully feathered head at all times, can be induced to undergo the same changes as those of the males when they are treated with testosterone propionate. These are most interesting observations but their pertinence to the phenomenon of baldness in man is somewhat oblique. Allusions have been made to the South American uacari, the adults of which are all bald, but no one outside our group has observed the histology of their scalp. The contention that these animals are difficult to obtain is simply not true. Actually, they are numerous, but being slow-moving and slow-witted, with a melancholy nature, they rarely survive captivity for very long and hence are poor experimental animals. Most male chimpanzees, after reaching maturity, attain a triangular "bald" area on the forehead, but these formidable animals are expensive and difficult to handle in captivity.

There is now little doubt that the most desirable animal for the study of baldness is the stump-tailed macaque (*Macaca speciosa*). The mature adult animals all have a furrowed forehead covered by small vellus hairs. The "naked" forehead of large adult males may extend to the middle of the calvarium or beyond, but that of females rarely does. Since this bald condition develops in a manner similar to that in man, we have adopted these animals exclusively for the study of alopecia. The lack of greater progress than we now claim can be explained by several factors. First, a great deal of exploratory work still has to be done on normal animals before experimental work can begin in earnest. Also, primates are costly animals, which are used sparingly, thoughtfully and with great deliberateness. Finally, most simian primates are long-lived. For example, stump-tailed macaques do not reach adolescence until 5 years and become bald only after the sixth year.

Since the condition of baldness is best exemplified in the human scalp, we use this as the point of reference. What happens in other

mammals must be comparable to what happens in man. In discussing baldness one must remember that man's scalp is one of the most highly specialized areas of his skin. In most other mammals the scalp shows little difference from the rest of the skin. This is true even in many of the primates.

The Scalp of Man

In the adult human scalp approximately 600 hairs emerge per square centimeter of surface; in the newborn there are about 1000. This means that since no new follicles are formed, the initial ones grow farther apart as the head grows. The number of follicles on the forehead is only somewhat lower than that in the scalp. Also, in *young* men, the number of follicles in the bald areas of the scalp does not differ appreciably from the number in those areas where no clinical evidence of baldness exists. The microscopic anatomy of the scalp and of the forehead is similar, if not identical, and, except for differences in the hair follicles and sebaceous glands, there is no line of demarcation between the two. In four-month old fetuses there is no hairline and hence no distinctive feature between the two areas; hair follicles extend from above the eyebrows over the cranial vault and back. After the fifth month of fetal life, the follicles on the forehead remain approximately the same size while the sebaceous glands attached to them become larger.

In contrast, the follicles of the scalp proper become progressively larger while their sebaceous glands remain approximately the same size and thus relatively smaller. Also, the few wisps of smooth muscle fiber formerly attached to the follicles on the presumptive forehead practically disappear whereas the arrector pili muscles attached to the terminal follicles of the scalp become stouter. Scalp and forehead, then, become distinct at about the fifth fetal month. After birth, the hair follicles at the margin of the "scalp" continue to become involuted for two or three years until the receding hair line assumes whatever familial pattern the child has inherited. This phenomenon is the exact mechanism adapted by the follicles later when alopecia develops. In the "precocious" alopecia of men, the hair follicles become involuted, but the total population of hairs in bald areas remains relatively unaltered. All human beings, then, are to some degree bald. The balding scalp of adult men repeats the process in the forehead of infants.

What happens later in old men and women is a different phenomenon. In senescence not only does the number of involuted follicles increase but many follicles disappear outright. Even in those old men and

women who show no clinical signs of baldness there is a mosaic pattern of senile alopecia, that is, a "thinning" of the hair does occur. Kligman (2) has pointed out that as many as 70% of the hairs from the scalp may be lost before clinical signs of alopecia become apparent. In discussing baldness, then, one must distinguish between the "precocious" type that develops in mature men and the "senile" type that develops in men and women of advanced years.

In comparing human baldness with that in subhuman primates, only the "precocious" type is of interest. Being a degenerative phenomenon, senile alopecia is less significant.

The Stump-Tailed Macaque

Since only few readers may be acquainted with these animals, a brief description is in order.

They are muscular, heavy-bodied and short-limbed. Their hair is variably dark gray-brown, turning almost black on the mid-back, with a contrasting white on the underparts. The eyebrows consist of sparse, relatively coarse hairs, some of which are vibrissae, crowding toward the midline. They have a naked, furrowed forehead (Figs. 1, 2, 3, 4) which, in fully grown adult males, is 3 or 4 inches across and anywhere from 2½ to 5 inches in height. This naked area is much smaller in adult females. The naked forehead and scalp are usually reddish, actually hemangiomatous, and spattered with black and brown pigmented spots. Around the bald scalp grow long straight hairs that form a distinct crown, giving the animal an appearance of dignity. This hair may be 4 to 6 inches long in the males and 3 to 5 inches long in the females. Three to 4 inches long "mutton chops" grow from the jaws, and on the chin is a goatee about 3 inches. On the face, muzzle, and other apparently naked areas grow short sparse hairs (Fig. 3). The long hairs of the crown, the nape, the extensor surface of the arms, dorsal thoracic and lumbar regions form a handsome mane, 5 or more inches long. The hairs on the ventral surface are white and finer and sparser than those on the back. In the axilla, very long reddish hairs grow in distinct rows. Just medial to the cavum axillae is a narrow strip of naked pink skin, similar to that found on the inguinal fold.

The clipped skin is pinkish white with blue or brown maculae scat tered at random. In male animals the skin of the mons, scrotum and medial sides of the thighs is usually red.

Both male and female animals, but particularly male, have greasy hair and dandruff on the hairy scalp but seldom elsewhere.

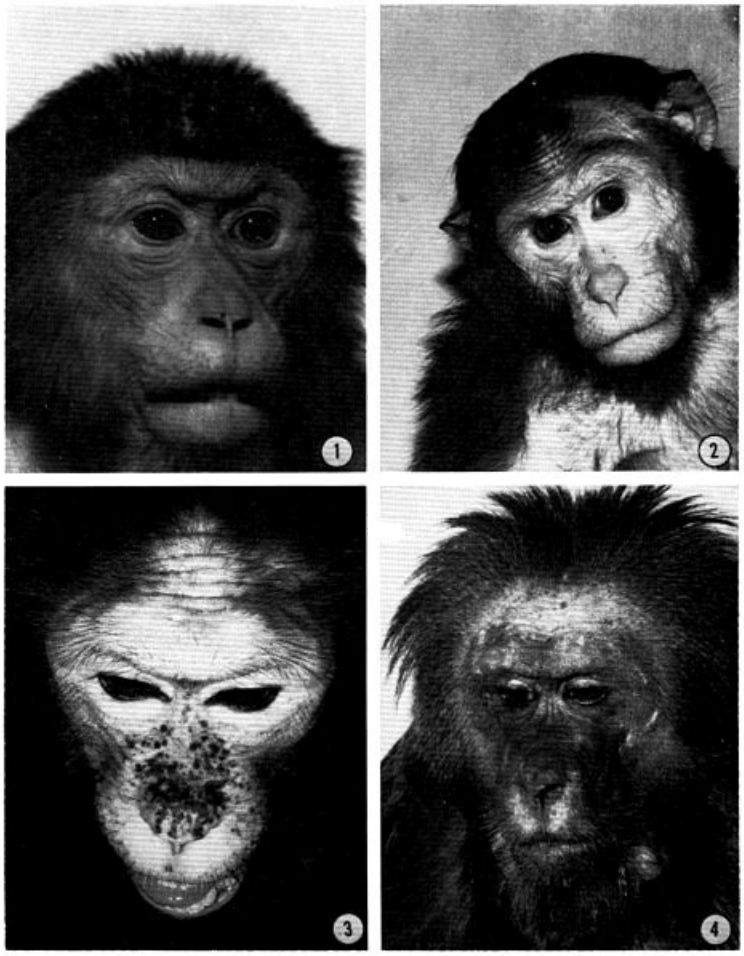


Figure 1. Immature female animal with fully haired forehead
Figure 2. Young male stump-tail with "sparsely haired" forehead
Figure 3. Forehead and scalp of a young adult male showing nearly "naked" forehead
Figure 4. Adult male stump-tail with a "naked" forehead and muzzle

Despite their name (*speciosa*, beautiful, comely), they are rather filthy animals with a strong body odor compounded of fecal encrustation and the secretion of skin glands. A curious characteristic of infant stump-tails is the appalling musky odor, strongly reminiscent of that of the unwashed human axilla. Young animals gradually lose this aura and acquire the different, but equally offensive odor of the adult animals.

The sparse pelage of infant and juvenile animals is generally a pale russet color or creamy white with pink skin showing through it. This

Figure 5. Docile young male enjoying an embrace from his handler

fur is gradually replaced by a darker, coarser, and longer one as the animals grow and attain maturity. The forehead and face, definitely haired in young animals (Figs. 1, 2), become gradually naked after adolescence (Figs. 3, 4).

All animals show some sexual dimorphism in their hair. The hairs of males are everywhere coarser and longer than those of the females. Baldness in the males may advance to the middle of the calvarium and beyond but in the females it does not reach the fronto-parietal suture. The males always have more dandruff and a greasier scalp. The males have longer hairs on the tragus of the pinna and a much longer tuft of hairs from a fleshy eminence opposite the scaphoid fossa of the ear. Only the goatee of the males grows from a caruncular eminence at the base of the chin. The bare areas in the inguinal fold are larger in the female.

Those who may plan to use stump-tailed macaques in their laboratory but who are inexperienced in handling monkeys should be forewarned. When young, these animals are relatively docile and even affectionate (Fig. 5). In adulthood, however, their temperament is unpredictable and mercurial. When annoyed, adult males become treacherous, display fits of temper, and even bite their own hands or feet. An adult stump-taled macaque can be formidable and should be managed only by skillful handlers.

The Hair Follicles

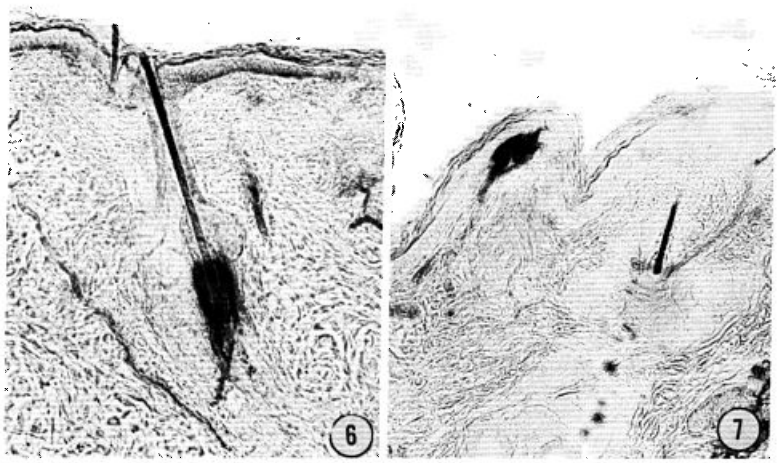
Hair follicles generally grow in groups of two or three, with one apocrine sweat gland associated with each group; on the face the follicles usually grow singly. In those scalp areas that are still covered with long hairs, the groups consist of one or two large terminal and one or two vellus hairs. The bald forehead and scalp are covered with a sparse population of vellus hairs with an occasional terminal hair scattered among them. Although the follicles in the bald areas are notably reduced in size, most still have arrectores pilorum muscles attached to them; true vellus follicles have no muscle. Terminal hair follicles have a small bulge for the attachment of stout muscles. In quiescent "vellus" follicles the muscle, when present, is attached to the epithelial capsule around the club hair, below which is the small hair germ. Quiescent terminal follicles are about one-half the length of the growing ones, the small, eccentric hair germ extending only a short distance below the bulge.

Sinus hair follicles are found in the median aspect of the eyebrows, on the mystacial areas, on the lower lip, and on the chin scattered among the follicles of the goatee.

Although grossly the transitional area between the bald and nonbald portions of the scalp appears to be abrupt, in histological sections it is surprisingly gradual. The normal-sized terminal hair follicles grow sparsely, having among them numerous vellus types or intermediate follicles. Farther back, on the temporal and occipital areas, where the terminal hairs grow longest, there is an appreciable population of small follicles. Even on the back of the trunk and nape, where the hairs form the mane, and elsewhere nearly every hair group contains small ones.

In the scalp and face every follicle, large or small, has a complex of sensory nerves that compose the follicle nerve end-organ (Fig. 6). This is found around the pilary canal between the bulge and duct of the sebaceous glands. These nerves, reactive for both butyryl- and acetylcholinesterase, are arranged in both a perpendicular and a horizontal direction. Elsewhere, not all of the follicles have such an abundant nerve supply. The sinus hair follicles are enveloped by very fine nerves that swirl around the upper portion, just below the sebaceous glands.

In the forehead and eyebrows, the bald areas of the scalp and in some parts of the naked face, cholinesterase-containing nerve fibers are found in the papillary layer of the dermis that accompanies the underside of the epidermis for some distance. These terminate at the base of some of the epidermal ridges in small bulbous endings or in small bodies that resemble mucocutaneous end-organs (Figs. 7, 8).



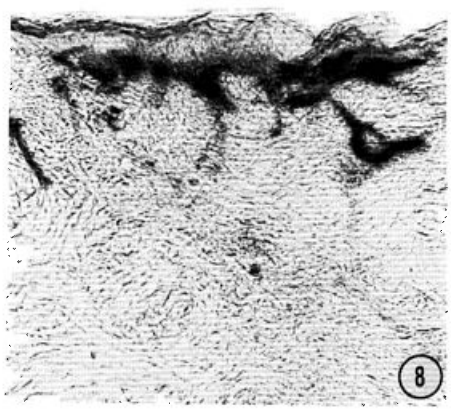


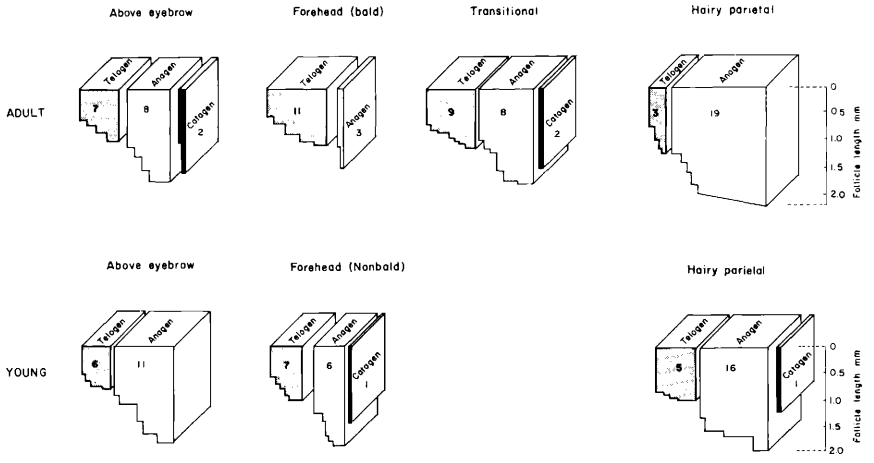
Figure 6. Butyrylcholinesterase activity in the hair follicle end-organ from the scalp
Figure 7. Butyrylcholinesterase activity in small bulbous endings that resemble mucocutaneous endorgans from the bald scalp
Figure 8. More extensive mucocutaneous-like end-organs from the bald scalp

Uno *et al.* (3) have made a detailed quantitative study of the populations and sizes of hair follicles in young and adult stump-tailed macaques. They have also dissected out intact hair follicles from the surrounding connecting tissue to measure accurately their size and to study (to be reported later) their enzyme content, eliminating the contamination of surrounding tissues.

Their results are shown in Figs. 9 to 12. Here are recorded the actual representative populations and sizes of hair follicles on the lower

Table I

NUMBER AND LENGTH OF HAIR FOLLICLE



(Fig. 9) and upper forehead (Fig. 10), the transitional area (Fig. 11), and the hairy scalp in the parietal area (Fig. 12). The summation of these results is presented in Table I. The first and third sets of trichograms in the table show the number of hair follicles per 1.6 mm^2 of surface found in different areas of the scalp of adult and young animals, respectively. The foreheads of young and adult animals have a scantier population of follicles than the other areas. Most of the follicles in the alopecic forehead of adult animals are very short and quiescent; in the "hairy" forehead of young animals, the follicles vary widely in size, but their number is about the same as in the adult animals. These trichograms also show the actual lengths of the follicles in telogen, anagen and catagen.

The proportion of anagen to telogen hair follicles in the various scalp areas in young and adult animals is significant. In the bald forehead telogen hair follicles predominate, whereas in the area about half the follicles are in anagen and half in telogen. These follicles are distributed almost identically in both young and adult animals. In both cases the forehead has more telogen than anagen follicles than the other two areas.

Figure 13 shows the different types and sizes of hair follicles in the different areas of the scalp. In the parietal area most of the follicles in anagen are about 2 mm long. Some of the anagen follicles in the transitional area, in the area above the eyebrow, and in most of the bald area are about 1 mm.

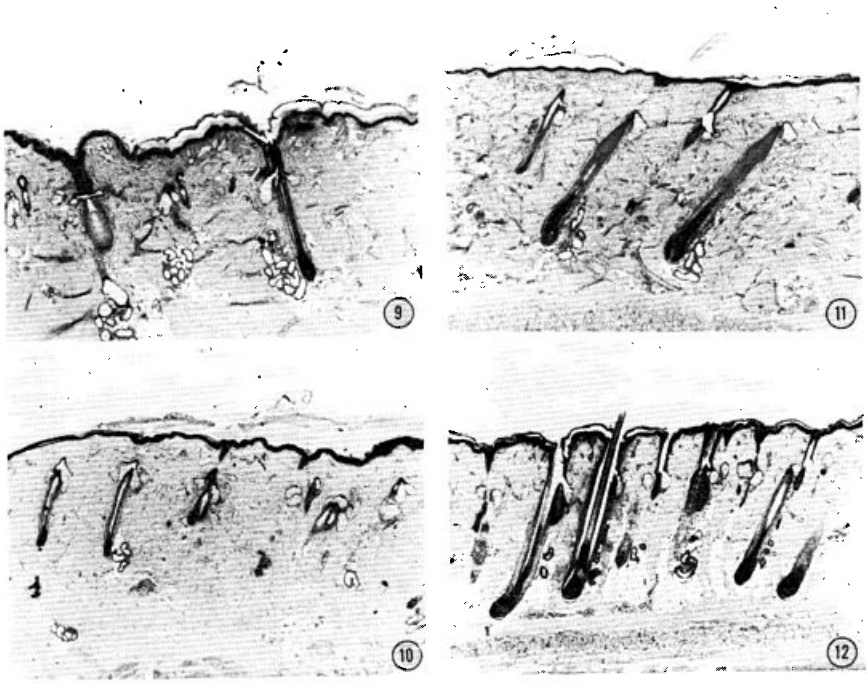


Figure 9. Forehead just above the eyebrow showing one each of anagen and telogen type of terminal hair follicle and some vellus follicles

Figure 10. Bald area of forehead showing 3 telogen and 2 anagen type of vellus follicles

Figure 11. Transitional area between bald and hairy areas showing 2 each of guard and vellus hair follicles

Figure 12. Parietal hairy area showing many terminal hair follicles in anagen

The short follicles, called vellus follicles, are not limited to the bald area but are found in the transitional areas and elsewhere. However, whereas true vellus hair follicles are nonerectile, having no arrector pili muscle attached to them (4), many of the vellus follicles in the bald scalp of stump-tails still have muscle fiber attached, the follicles having arisen from an involution of terminal hair follicles.

The Sebaceous Glands

A description of sebaceous glands is included here because they show some sexual dimorphism, being larger in male animals, and because they change character in the balding scalp.

Relatively small in the skin of the trunk, they can attain the size of sebaceous follicles on the face, lips, chin and bald forehead, and scalp

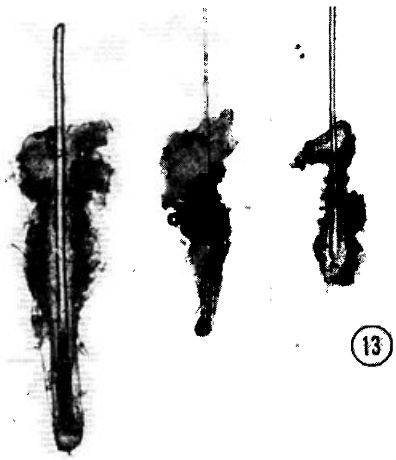


Figure 13. Microdissected hair follicles: on the left is an anagen, terminal follicle, 2.2 mm in length; in the middle an anagen, vellus follicle, 1.2 mm; and on the right a telogen, terminal follicle, 0.8 mm

Figure 14. Large sebaceous gland "follicle" from the bald forehead

(Fig. 14). The glands are everywhere larger in the male than in the female.

Melanocytes often surround the ducts of the glands, which in some areas may be remarkably pigmented. In the glands of the forehead and scalp and those on the chin and lips, small dendritic melanocytes are often insinuated between the peripheral cells of the acini, imparting some melanin granules to the sebaceous cells. Distinct melanin granules may be found even in some mature cells and in the sebum.

Discussion

Since there is no structural demarcation between the forehead and the scalp, even in man, except for the presence of terminal hairs, a "naked" forehead indicates that alopecia has occurred. When the hairline recedes, as it does in most human beings, there is no way of differentiating between what was originally forehead and what was scalp. Thus, every human being and every adult stump-tail is partially bald.

Stump-tails, even in those scalp areas with an apparently dense pelage, have an appreciable number of vellus hair follicles. Furthermore, in some males, probably older animals, baldness advances to the occiput and beyond. The presence of naked expanses of skin on the anterior axillary border and the inguinal folds, the sparse pelage of the ventral areas and the presence everywhere of vellus type follicles, coupled with the development of true alopecia, suggest that the stump-tailed macaques may be undergoing a general loss of hair cover. The luxuriant growth of hairs on the occiput, nape, back and shoulders, and the goatee are no doubt protective devices, but they are also definitely ornamental. These phenomena may be comparable to those that might have taken place in man as he evolved from a heavily furred creature.

Aside from theoretical implications, the gradual diminution of the size of the follicles of the forehead and scalp in stump-tailed macaques is similar to what takes place in human infants at the "hair line" and later when pattern alopecia develops.

Another similarity between the bald human scalp and the bald scalp of the stump-tails is the presence of special nerve end-organs underneath the epidermis. These are identical with those described by Montagna and Giacometti in man (5) and may arise from the follicle end-organs released when the follicles became atrophied. These structures are not present in young animals.

It is significant that the distribution of hair follicles in the scalp is almost identical in young nonbald animals and in adult ones. In both groups, hair follicles are normally least numerous in the forehead.

Since baldness is the result of a transformation of terminal hair follicles to vellus ones, something must be said about these follicles. Noback (6) identified vellus hairs as those that grow from follicles having no erectile tissue. Danforth (7) believed that the vellus hair follicles from the forehead undergo no changes from childhood to old age. During the development of baldness and with the onset of old age, however, vellus hair follicles vary greatly in size, depending on their location (8, 9, 10).

Hence, a sharp distinction between vellus and terminal hair follicles cannot be made on the basis of length alone. Also, the vellus follicles that develop from terminal ones during the process of baldness may still have wisps of arrectores pilorum muscles attached to them.

Although the aging process in man causes a progressive degeneration of the follicles as well as of the bodily organs in general, baldness in young men (as in the stump-tailed macaques) can be attributed only to the transformation described here.

Now that we have an experimental animal model for the study of alopecia, we may look forward to some progress in our understanding of this interesting biological phenomenon.

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