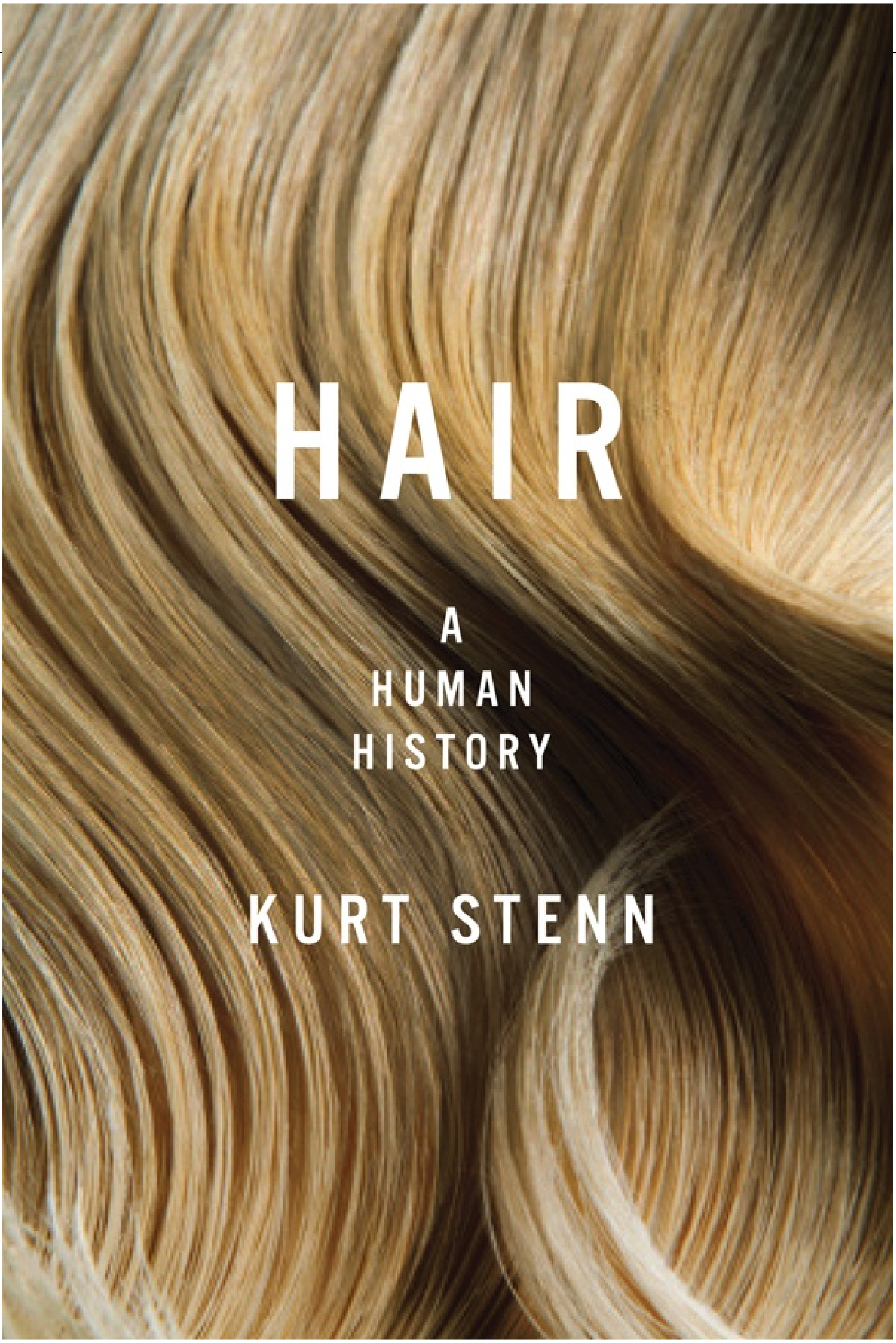

HAIR

A HUMAN HISTORY

KURT STENN

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PEGASUS BOOKS
NEW YORK LONDON

To Judit

“ ’til the rocks melt with the sun”

(after Robert Burns)

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HAIR

FOREWORD

TELLING THE STORY OF HAIR

The idea to write this book came to me in a barber's chair.

I live in a small university town, and although I have a choice of barbershops huddled in sort of collective obeisance before the imposing school gate, I choose to frequent one located in a qui neighborhood on the outskirts. Marked by a traditional red-and-white spiral pole, the shop sits in t adapted living room of a small, white, wooden-framed cottage. The front wall of the room has be replaced by a large window opening onto the street; on the left are four bent-wood waiting seats wi an end table; in the center are two swivel barber chairs, only one of which is ever staffed. The wal are bedecked with golfing paraphernalia: a picture of a golf green with a cluster of four players abo the pin, a photo of Sam Snead with white hat, suspended antique chipping irons, signed pictures, a the like.

One morning several years ago, when it was my turn, I settled in the chair as usual; the barb covered me with a white cape, followed by a tissue-paper collar.

"So, what's it today, Doc?"

"Short. Light trim. The usual, but not my brows."

Though on occasion both of us share family stories—the wife, the kids—we have spoken little ov the years. For the most part, we sit and enjoy the silence between the clip of his scissors and the ti of the wooden clock on the back wall. So I was rather surprised one day when he asked, "Say, Do what do you do?"

"I'm a university physician."

"Yeah, I know that, but what kind? I mean, what do you do?" He held up his clipper and fixed h gaze on me.

"I do research on hair."

His eyes widened and his face broke into a smile. "Aw, come on, Doc!"

"No, I really do," I replied.

"Okay, if you say so." He shrugged, still unsure if I was teasing him or not, and went back to work

Hair as a body part meriting serious cultural and scientific attention is—and has been througho history—a foreign concept to many people, including my barber. For him, hair is limited to the stu on your head, which you position properly to get the right look. There is only one way of thinki about hair and that's it.

Since then, I have noticed that many people adhere to this limited and myopic view. They a unaware of the bigger picture. They see little to no relationship between hair and fur, hair and histor hair and health, or hair and basic biology. They are unaware that hair has played a role in the Weste settlement of North America, in Middle Age European trade, in modern criminology, in religion, art, in orchestral instruments, and now in modern biological research. They are unaware that there a many people throughout history who have worked with hair in very different ways, well beyond t barber or salon worker. They are unaware of the advances in science that promise new, more effecti tools for hair care: tools to put hair follicles where none now grow, tools to curl hair that is no incorrigibly straight, or tools to uncurl hair that is corkscrew rigid.

These realizations prompted me, a lifelong hair-follicle scientist, to write a book giving the who picture of hair and the part hair has played, and continues to play, in human life. Hair evolved as a environmental barrier for our primitive ancestors. When modern humans lost body hair, the appropriated the skin and hair of neighboring mammals for cover. With time, man found wide uses fo animal hair, far beyond cloth. Hair, because of its unique properties, has shaped human evolutio social communication, history, industry, economics, forensics, and art. The topic is expansiv describing not only the role of body hair in sending social messages but also the impact of hair o human history, economic growth, artistic expression, forensics, archeology, science, and industry.

The common thread and focus of this book is the hair shaft, the beautiful straight or curled filame that decorates the skin surface. I tell the story from the perspective of people who have a particul interest and investment in hair, who know and exploit different features of hair, each of whom looks the use and significance of hair in his or her own distinctive way. For the hair-loss patient or th bearded cleric, what’s most important is the message hair sends. For the fur trader and wool worke it’s hair’s insulating and cloth-making properties. For the paleontologist, it’s the role hair has playe in protecting mammalian life. For the cell biologist, it’s the ability of the hair follicle to re-for itself; for the violinist, it’s the bow; for the criminologist, it’s the incriminatory or exculpator evidence; for the cosmetician and wigmaker, it’s the means for building a social message; and for th artist, it’s the medium for sculpture. Because each sees hair differently, in terms of function an impact, each refers to the same essential properties using different words; for example, “fur,” “wool “beard,” and “hank” refer variously (depending on the speaker) to an assemblage of hair, whi “whisker,” “fiber,” “bristle,” and “shaft” refer to individual hairs. From the viewpoint of the biologis all these words refer to the same structure, though they recognize differences in size, shape, an growth density. From the standpoint of this book, as I address the larger question of how hair ha impacted the history of man, I will take the biologist’s perspective and refer to all these fibers a “hair” or “hair shaft.”

What’s described here is only the glimpse of a much larger story, for in all fairness each group o hair workers deserves its own book of equal or greater size. While exploring the diverse world of hai I traveled widely and met extraordinary people—wig makers, artists, luthiers, criminologists, an others—on a journey that has taken me to medical clinics, patient support groups, molecular biolog laboratories, dinosaur museums, fur merchant associations, sheep farms, textile mills, and hair a exhibitions. In the telling, I have sacrificed the comprehensive for the panoramic. Accordingly, no only have I omitted many people who work with hair, but I emphasized the Western European an North American experience, knowing full well that I could have told the same story from an Asian o African perspective. I made these decisions based on my own personal knowledge and on my attemp to limit the book to a length attractive to the average reader. I have tried to simplify the science an keep those descriptions pithy and illustrative. For the more inquisitive reader, I offer an extensiv glossary, chapter notes, and references.

A recurring theme throughout is that all hairs, from wherever they arise—human, sheep, beave platypus, or porcupine—are alike, though they vary in degree: long or short, stiff or soft, black white, sticky or smooth. So, a hair is a hair from wherever it comes. But, to begin, we must ask: Wh exactly is hair and from where does it come?

PART ONE

SHAPING THE SHAFT

1

THE FIRST FIBERS

The first hairs arose in a reptilelike, mammalian ancestor.

All biological forms at any level—whether societal, cellular, or organismal—must separa themselves from the outside in order to survive: Each must have a wall. At the societal level, that wa shields a kingdom from its enemies. At the cellular level, the membrane, another type of wa surrounds, defines, and contains the cell nucleus and cytoplasm. At the organismal level—be it fro chicken, or monkey—that wall is skin. Our story must therefore start with mammalian skin, not on because hair grows out of skin, but also because hair enhances the wall-like properties of skin b buffering it from trauma, protecting it from temperature extremes, and sensing the environme before actual contact.

All organs, like the hair shaft (the hair fiber) and its follicle (the hair root that gives rise to t fiber), are made of three different cell types. The first is a bachelor cell, which tends to live alo without making long-lasting relationships with other cells. These cells wander about the body, most within vessels as blood cells, carrying freight or messages, but always traveling and functioning alon Eggs and sperm are examples of such cells, and they remain single for a long time; in fact, their job- finding a partner—could not be consummated if they were dragging along one or several petula little brother or sister cells.

The second type is a cell that manufactures cell matrix, the soupy or solid materials that surrou cells. By means of the matrix, such cells provide the undergirding for all body tissues and organs; th generate collagen, elastin, bone, and cartilage. Relevant to skin, these cells give rise to a collagen-ri layer of the deep skin called dermis.

The third type of cell makes up epithelium. These cells characteristically bind tightly to o another. They are highly social beings; if separated, they become fidgety, seeking to link up to one more neighbors. As they stick firmly to one another, they make up a good cover for any biologic plane, such as the surface layer of the heart or lung or the outmost layer of the skin. At the same tim they form the core of many three-dimensional organs, such as the salivary gland, liver, and kidne Because epithelial tissues are made essentially of cells alone, they are, in general, soft and need out structural support, such as bone, cartilage, and collagen. Thus, when epithelial cells form a sheet, su as the epidermal covering of the skin, they need a supportive underlying layer: the dermis.

The mammalian skin surface, then, is made of a multilayered epithelium, the epidermis, which li over a thick, leathery tissue, the dermis. Infiltrating the dermis are cells, nerves, and vessels, whic nourish the skin. The hair fiber coming out of the skin arises in a hair follicle, a fingerlike dow growth of the epidermis. In humans, the first hair follicle forms in the fetus as a bud at the base of t primitive epidermis. This bud projects down into the dermis as an extension of the epidermis and nurtured and supported by the dermis.

~~The completely mature hair follicle consists of epithelial cell layers except for a small collag~~enou nubbin within its base called the dermal papilla. The epithelial layers of the follicle look like collapsible telescope with three sleeves. The innermost sleeve is solid and forms the hair shaft, t outmost sleeve serves as a cellular wall separating the hair follicle from the dermis, and the midd layer holds and molds the shaft on its way out. Growing off the central hair follicle is a muscle, whic pulls the follicle and its shaft upward after a fright or a chill, and a sebaceous (or oil) gland, whic squirts greasy liquid onto the surface of the hair shaft as it grows out.

Except for the palms, soles, and some special regions (such as the lips, anus, and glans penis), ha is present on all skin surfaces. Nevertheless, humans have been referred to as the “naked ape” becaus unlike other mammals, most human skin is covered by short, thin, lightly pigmented, and soft hairs— like the hair on your forehead, barely noticeable.

So if that’s what hair is, the next question is this: Why did we and other mammals acquire hair the first place? From where did it arise and how has it helped humans become *sapiens*?

The origin of hair is based on the evolution of animal life.

Life itself appeared on earth about three and a half billion years ago, surprisingly soon after t formation of the planet, a billion years earlier. The first life-forms were unicellular—simple, singl and independent. The next evolutionary step, which took two billion years, involved the formation soft and jellylike multicellular organisms; these could survive and flourish anywhere as long as the were floating in water. For them to leave a liquid environment and move onto land, however, they ha to acquire a supporting structure of some sort: Either the cells on the outside had to harden or the cel on the inside had to provide a framework. The former became an exoskeleton, a surface armor, whic is seen in house flies, crayfish, and snails; the latter became an internal framework, a skeleton with segmented backbone, as seen in tree frogs, rattlesnakes, wombats, and humans. The earlie backbones, or vertebrae, appeared in primitive fish about five hundred million years ago. It wou require another one hundred million years before the vertebrates took a deep breath and made th fateful evolutionary step out of the oceans and onto dry land.

With the appearance of the vertebrates, a dramatic change occurred in the structure of skin: Th outer epithelial layer transformed from a single layer of cells to a multilayer of cells. This was pivotal event for our topic because the hair shaft and the hair follicle consist of packed cells that cou only have derived from a multilayered structure. While the lobster, an invertebrate, has oth redeeming features, there is no way he or his cousins the locusts (or their distant relatives, th earthworms) could make a hair shaft because their surface epithelium is single-layered. Th invertebrates are able to augment their skin surface with noncellular materials, such as mucus (in th case of slugs), shells (for periwinkle) or chitinous materials (for beetle skin), but they do not have th wherewithal to produce a tissue of piled up, tightly adherent, epithelial cells like we vertebrates do.

If we extend our family lineage back about three hundred million years, we would be hard press to recognize any family resemblance to the vertebrates existing at the time. However, th morphological and molecular records are clear: We mammals share an ancestor with the reptiles, a as-yet unknown creature called a “stem reptile.” The relationship is driven home by the example the duck-billed platypus, which is classified as a primitive mammal. This semi-aquatic denizen eastern Australia lays eggs, suckles its babies with a form of milk, and grows hair. In terms c classification, the platypus is a contradiction: mammals have hair, make milk, but don’t lay eggs; the birth live young. It’s very revealing that some of the platypus genes are common to mammals, othe to birds, and yet others to reptiles. This animal represents one very early point in the evolutiona crossroad. Its genome reflects the traits making up the first, most primitive mammals, as well as wh remains from our reptilian predecessor, whose descendants sired all the great landed vertebrates: th reptiles, dinosaurs, birds, and mammals.[1]

~~Our skin and its appendages reflect at least to some extent what this ur-forebear bestowed~~ on u When animals left the primordial seas for land, their skin had to protect them from a wholly new, n always friendly environment: dry air, electromagnetic radiation (strong light), oxygen toxicit physical trauma, and extreme temperature fluctuations. This necessitated dramatic changes in th epidermis; it acquired thickness, strength, and water barrier properties. With time, discrete regions o the epidermis projected upward and folded down upon themselves, thereby amplifying their protectiv properties. In fish and reptiles, these raised portions formed flat and broad-shaped scales. In birds an mammals, they formed pointed growths—filaments that extended beyond the skin surface. For bird that filament branched and evolved into a feather; for mammals, that filament remained threadlike: hair.

Over the years, ideas concerning the origin of hair have varied widely. One current school propose that hair evolved from the stem reptile’s scales, a notion suggested by the fact that there are sma hairs sitting in the hinge region of the scaly tail-skin of most rodents. A second hypothesis sugges that the shaft arose within a gland and initially served a role directing oily secretions from the glan onto the skin surface. This idea is based on the observation that all follicles have oil glands, that th cuticle layer of the hair shaft is structured to scoop oils to the skin surface, and that the earlie animals needed oil on their skin to prevent water loss. A third theory, which is not exclusive of th first two, considers that hair arose from hairlike sensory structures seen on the skin of some living fi and amphibians. These structures serve to alert the fish of an environmental danger, such as the wat pulse of an approaching predator or the presence of an adjacent sharp rock.

In fact, there’s a lot of evidence that the hair follicle and its shaft play important sensory role Studies in mice suggest that each hair type has its own distinct sensory system so that different hai provide different types of sensation. While all hairs are invested with nerves and thus capable perceiving movement, there are large and uniquely sensitive hairs found on the upper lip of mo mammals. These whiskers are so important to mouse sensation that they have been elevated to th status of a “sensory organ”; in fact, they have inherent erectile properties, which, when stimulate draw the prominent shafts to attention. For a mouse probing the world at night, its whiskers serve valuable antennae reconnoitering the terrain well before a tender nose arrives.

Hair is an important sensory device for humans as well. In a common life experience, small hairs o the outstretched arm accurately perceive a close-passing person or a zephyr riding in with the tide on warm summer day. People are also able to detect bedbugs more efficiently on an unshaven arm than shaved one.[2]

In recent years, we have learned that in addition to its rich supply of nerves, the hair follicle surrounded by dermal cells, which, under the proper conditions, can act like nerves. These cel contain proteins also found in nerve cells, and when they are isolated and grown in tissue culture, the can become neural. In fact, when Dr. Robert Hoffman and his research team transplanted these cel into a paralyzed rat, the cells not only supported nerve repair but they also integrated into new formed nerves that allowed the rat to recover function.[3]

Hair also plays a role in temperature control. A turtle on a log, with up-stretched head catching th early morning sun, reminds us that reptiles do not have an internal means of generating heat. From i cool and protected bower in a deep stream, the turtle awakes from its slumber, moseys onto a floatin log, and into a beam of strong morning sun; there he basks. Like all cold-blooded animals, he depen on nature’s primary radiant energy source, the sun, to get started. But the smooth-surfaced skin th allows him to readily take up heat from his surroundings during the day also causes him to lose it his surroundings during the night. That his body temperature drops during the night is to h advantage, because during these times he doesn't need high-priced fuel (i.e., hard-earned foodstuff to ~~keep warm. The trade-off for his caloric frugality, though, is his nocturnal and early mornin~~ languor.

In contrast to reptiles, the earliest mammals could hunt in the cool night and early morning becau of two major advantages over their cold-blooded neighbors. The first was that they were able generate heat by metabolic processes without direct help from the sun.[4] The second was that, ov eons, their primitive skin sensory filaments had increased in density to form a skin cover that serv as a highly efficient insulator: a fur coat. These two features—warm-bloodedness and insulation enabled them to forage among the nests of their ectothermic neighbors at night and hide from the during the day.[5]

Heat flows from a warmer to a cooler body, as anyone who has ever jogged on a blistering cold da knows, warming in open sunny spots and then cooling again in the shade. In this case, solar he transmits over space directly to us, as it does to the basking turtle. But heat can also transfer fro body to body by direct contact. When you burn yourself eating a straight-out-of-the-oven pizza, f example, you are experiencing the direct spread of heat from the body of the pizza to the body of yo mouth. Heat can also transfer by means of moving currents of water or air, a process referred to convection. For instance, heat transfers by convection when air blowing from a hair dryer picks heat from the heat filament and transfers it to your locks.

In all these examples, heat transfers from a warmer body to our body. But heat can flow in th opposite direction as well, from our warm body to the cold outside. The Coney Island Polar Bear Clu stalwarts celebrate New Year's Day by warming up the frigid waters of the Atlantic Ocean. Movin heat in that direction might be fun for a short while, but after a not-too-long exposure to such col about ten to twenty minutes, vital functions not only slow, they stop.[6]

Active mammalian life depends on a constant body temperature of around 98.6ºF, and skin plays a active role in maintaining it. While skin is not important for heating up the mammalian body, it very important for minimizing heat loss—and this is where hair comes in. Fur efficiently blocks a forms of heat transfer. It does this, first of all, because it grows as a dense array of hairs. Beaver ski for example, has around forty thousand shafts in an area of skin about the size of a fingertip. At th density, fur is virtually an impenetrable barrier; neither wind, water, nor insects can get through. addition, hair itself is a poor thermal conductor—eight thousand times less conductive than coppe Dense hair cover also traps air, and air is an even poorer conductor of heat than hair. As long as ha holds a layer of air over the skin and prevents it from moving (convection), no heat is lost. He cannot transfer through the fur barrier either from the skin surface to the outside or from the outside the skin surface. Fur surface mirrors environmental temperatures, and skin surface, under the fur coa mirrors body core temperature. In an effort to expand that cosseting layer of air and thus enhance th insulating properties of furred skin, hair follicle muscles pull the shafts upward when an anim becomes chilled. This action increases the thickness of the fur coat and the efficacy of the insulatio in all animals—except humans, of course, because we have lost our "fur." So when humans chi although our hairs stand up, giving us "goose flesh," this ancient reflex is really just bluffing, becau our body hairs are neither big enough nor dense enough to maintain the important stationary a insulating air layer.

Befitting its reputation as the fastest land animal, the cheetah can attain speeds as high as sevent one miles per hour, but can only hold that speed for less than a minute before its body temperatu rises and forces it to stop and cool off. This is not to belittle the skills of the cheetah, but rather point out that fur limits its endurance in the unrelenting heat of tropical Africa. Because of fur, th cheetah has only a few means of dissipating body heat: stop running, get into the shade, start pantin lick its paws, or expose its non–fur covered body parts (primarily the paws and ears) to th ~~surrounding air. If the savannah is as hot as or hotter than the cheetah, it will be hard pressed~~ to co itself at all, as heat flows to the cooler body. Thus, in this climate, mammalian adaptive success paradoxically limited by the heat-retaining properties of fur, because fur prevents body heat fro dissipating through it by any heat-transfer mechanism. Such an efficient cover would have prevent the evolution of man.[8]

Scientists have calculated that on a hot and sunny day, fur-covered, upright hominids would hav suffered a heat stroke after about ten to twenty minutes of a nonstop walk; they just couldn’t dissipa heat from their bodies quickly enough.[9] Our human antecedents needed to move around during the da in order to hunt and survive, yet they had to keep their body temperature at 98.6ºF, so they needed better cooling-off mechanism. The problem was complicated by the fact that the human’s efficie evolution was dependent on a huge brain (the largest brain-to-body-size ratio of all animals, in fac and yet brain tissue is exquisitely sensitive to elevated body temperatures: Heat stroke occurs at 104 and brain death at 107ºF. In addition, brain tissue temperature is regulated by core body temperatu and the only way any animal, including a human, can shed excess body core heat is by way of the ski For an evolving hominid, the dense hair cover had to go.[10]

Many ideas have been put forth to explain the loss of hominid body hair. One fanciful notio suggested by Charles Darwin contended that primitive males favored hairless females becau hairlessness is more sexually attractive. According to this argument, sexual selection progressivel led to the hairless state in both males and females.

Today, most experts believe Darwin’s explanation is too simple. The most convincing recent vie is that humans lost hair in order to protect their uniquely temperature-sensitive brain. It turns out th at the same time primates were growing larger brains—about one to three million years ago—the began to lose their body hair and acquire eccrine (sweat) glands. These events appear to have bee linked. The function of eccrine glands is to control body temperature by liberating sweat, a secretio that is mostly water. A person can sweat as much as several quarts per hour and will continue to swea as long as the heat signal persists, or until the person becomes dehydrated and collapses. The value sweat is based on the physical fact that in order for water to evaporate, or transfer from liquid vapor, it must take up heat—a lot of heat; in fact, five times more heat energy is required fo evaporation than to boil water from room temperature. The trick is to have a lot of exposed bod surface and enough water to cover that surface. Animals intuitively know this cooling property water and they seek ways of exploiting it. One way is by panting, which exposes the multiple bloo vessels lining the moist mouth to evaporative heat loss. Another is by wetting themselves from nearb water sources or by licking saliva over their hairless body parts. The evaporation of water and swe gives an animal the ability to lose heat even if the surrounding environment is hotter than its bod surface. For the furred animal, however, skin surface sweat is of no help because water under fur can evaporate. By the same token, water on fur’s surface will evaporate but it will not remove heat fro the skin surface below the fur. Since sweating over the body is critical to heat dissipation and bra health, a luxuriant fur coat is a hindrance.

Loss of hair had a major impact on the ability of humans to dissipate heat and thus develop an stabilize a large brain, but it may also have had an important social role. Three major characteristi differentiate humans from other primates, such as chimpanzees: hairlessness, walking on two feet, an the family as a social unit. A chimpanzee mother can efficiently forage for herself and her chil because she has two free hands, since the baby is out of the way, clinging securely to the hair on i mother’s back. This could not work for the hairless human. Without hair for the baby to hang fron the naked-ape mother would have to hold the baby in her arms some way or another all the time, th greatly limiting her ability to feed. She needed a babysitter, and any family member would d ~~Professor Shizuyo Sutou of Shujitsu University postulates that the father would have had to~~ play th role if he wanted his progeny to attain reproductive maturity. Father would provide food an protection to mother and child and, *quid pro quo*, mother would provide all the mating opportuniti father might seek. So, by this argument, the loss of hair could also have given rise to the nucle family unit.[11]

With time, the earliest hair follicles evolved into various follicle forms and hair types. The “firs hair follicle was sparse and tiny, its shaft thin, short, and straight. With time, the original spars growth became so dense we named it “fur.” But within the fur and over the body grew many differe kinds of follicles and hair types,[12, 13] and the properties of these unique hairs play an important role the story yet to come.

2

THE WAY THEY GROW

A scalp hair transplanted to the eyebrow continues to grow as it if were still on the scal

On September 10, 2009, British prime minister Gordon Brown issued a posthumous apology behalf of his government to Alan Turing, a mathematician acknowledged today as the father modern computer science. In his proclamation, Brown termed the treatment given by the Britis government to this patriotic scholar as “horrifying “and “utterly unfair.” In March 1952, under t Labouchere Amendment of the Criminal Law, Turing had been found guilty of having had homosexual experience. He was offered the penal alternatives of prison or estrogen injections; chose the latter. Two years later, at the age of forty-one, he was found dead, a half-eaten, cyanid ridden apple beside him. It was a tragic end for a great scientist in his prime—and one who could ha played a major role in the advancement of our understanding of hair. In fact, just months before h arrest, Turing published a paper describing the first credible (and now widely accepted) mechanist model explaining how biological patterning, and thus hair follicle arrangements, might occur in skin.

Biological patterning refers to what an animal or plant looks like and how its parts are organized. is based on the fact that all mature cells and their neighbors know they have an up side, a down side, right side, a left side, an inside, and an outside. The biological question Turing sought to answer wa no small problem in his day or ours: Namely, how do complex animal and plant life-forms take sha when you start out with one very simple cell?

All higher animal life-forms begin when the fusion of a male sex cell (a sperm) and a female s cell (an egg) gives rise to one fertilized cell primed to make a whole new being. That first cell divid many times to form a cluster of cells and, though each cell in the cluster houses the same gene program and looks alike, each eventually assumes a unique shape and function, enabling the group cells to produce one complete baby. Some cells form bones, some liver, some head, and some toe Turing wanted to know how a group of uniform cells could turn into communities of vastly differe cells. How do cells interact with other cells or with the substances in the environment to become finger and not a nose, a brain and not a kidney, a scalp hair and not an eyebrow hair, a blushi princess and not a boasting swain?

One can appreciate hair patterning at various levels. First, there is the arrangement of hair wi respect to other hairs in the neighborhood. At this level, each follicle (and the shaft it makes) appea to demand “breathing” room so that it is comfortably separated from its neighbor. The rows whiskers on the snout of a tiger, dog, or rat are obvious examples; not only are they present in straig lines, but the individual whiskers are predictably and regularly spaced from one another. With prop magnification, one could see that most hairs grow in an array as regular as the streets of midto Manhattan.

The next level of patterning is the way hair falls with respect to the head and the tail. The tips body ~~hair almost always point toward the tail, or at least away from the head. In this position,~~ hairs the coat lie flat as long as the animal faces into the wind. The head-to-tail display of hair is such a inherent part of life experience that one reflexively strokes a dog or cat from head to tail. The moth cat grooms her nursing kittens the same way; if she must clean against the grain to remove a smudg she later flattens the ruffle with a well-placed front-to-back lick. In fact, Swiss mountaineers of t last century took advantage of the natural placement of fur by attaching seal skins to the base of the skis to travel over snowy alpine slopes. They aligned the seal skin so that the skin corresponding to t seal's head was attached to the ski tip: The downhill-pointing hairs of the pelt resisted any back sl on the walk up. For the trip down, they either kept the pelt on for a slow descent or removed it for a unimpeded schuss.

Human belly hair also grows in a characteristic head-to-tail pattern. The strong and curly hair of t lower belly and pubic region of men typically grows in the pattern of a chivalric shield with the pea of the escutcheon pointing, like the symbol of Mars, toward the navel. Pubic hair in women fills t nether regions and forms a discreet horizontal line at the pubis. Above and to the side of these coars hairs in both sexes are fine, short, lightly pigmented hairs that are barely visible.

Finally, hair shafts are patterned differently with respect to one another: long or short, curly straight, thick or thin, dark or light. They differ in character from site to site over the body, bu because the right and left side of mammals are mirror images, there are corresponding doppelgäng hairs on each side. For example, there are hairs on the right upper arm that correspond exactly to hai on the left upper arm. The disparity between hair types may occur abruptly, like a field of tall grass at the edge of a lakefront lawn. Consider the very short, barely visible shafts of the forehead ju before the hedge of short, thick, pigmented eyebrow hairs.

Because of the subtle and not so subtle differences between hairs from region to region, it's logic to assume that there are functional differences. Eyelash hairs are short and rigid, curling away fro the eye surface to minimize particle entry. Underarm and pubic hairs are short and curled, made prevent chafing between skins, fend off insect assault, and transport odors. Beard hairs are coars bushy, and curled, made to protect against trauma, harsh icy winds, and intense light. Different sha structures translate into different services to the skin.

But what determines how hairs are placed and shaped? Turing knew that the way any orga (including the hair follicle) forms and positions itself depends on how its cells grow and move abou But he did not know what makes cells do what they do. To address this question, Turing devise mathematical models that would predict a pattern. In the end, he found that his mathematical mode required three components: receptive cells, special growth factors made by the cells, and gradien formed by the growth factors in the soup surrounding the cells.

That latter term—"gradient"—describes the gradual change in density of something when goi from one place to another. One can think, for example, of the gradient around ice cream eateries. you were to visit my hometown in the middle of summer on a hot Saturday night, you would quick become aware of two wildly popular ice cream parlors located along the main street, both equidista from the town square. One is west of the town square; it sells ice cream in cups with small, dain spoons. The other is east of the town square, and it sells ice cream in cones. Crowds of people buy i cream at each of the parlors. They start licking and slowly walk along the main street to the tov square because that's where the action is. Ice cream–filled containers are in highest number near t individual parlors, but as people walk to the square, the amount of ice cream in the cones or cu decreases. In the town square, all the containers will be empty. You can tell where you are in th downtown area with respect to the two parlors and the town square by considering the density of i cream eaters, the shape of their ice cream containers—cone or cup—and the amount of ice cream le in the individual containers. As long as people continue to buy ice cream and progressively lick whi ~~moving to the square, there will be an ice cream gradient. No GPS needed here. (The critical~~ read will appreciate that we have not accounted for the spoilsport who doesn't want to walk to the tov square or for the glutton who eats his ice cream in one bite or for many other variables that wou disrupt our illustrative gradient.[1])

Now transfer the idea of a gradient back to the developing skin. In the youngest fetus, immatu skin consists of a sheet of identical-looking cells. At a given moment, individual cells in the she start to give off growth factors, which cause neighboring cells to take some sort of action. As th growth factor spreads away from the producing cell, it generates a gradient and, because of th gradient, there will be different neighborhoods—some with little growth factor and some with lot Cells in neighborhoods with lots of growth factor behave one way and cells in a neighborhood wi little growth factor behave a different way. So, by means of growth factor gradients and responsiv cells, Turing's equation predicted patterns—just as we could see pedestrian patterns forming i relation to the ice cream parlors.[2]

Turin saw the patterns, but it took the next generation of researchers—in the mid-20th century— discover what those important pattern-forming growth factors were. But first, scientists had to develo tools that would allow them to grow almost any kind of animal cell in a laboratory flask, to isolate an analyze proteins, to identify the genes stored in DNA and RNA, and to control the expression of gene in living animal models. Using these new tools, scientists from North America, Europe, Japan, an Australia discovered that the growth factors influencing hair follicle placement and formation a small proteins that show several characteristics.

First, the growth factors never act alone: They always act as a well-coordinated team. If the factors were athletes, they would look more like soccer players—dribbling upfield, passing, receivin kicking—than like solitary long-distance runners. Accordingly, as players have designated position such as fullback, center, and forward, each growth factor plays a special role: Some stimulate cells t stick to one another in order to form follicle foundations, others stimulate cells to form hair shaft and others stimulate cells to curl or color hair shafts. No one factor brings about all these chang alone; it takes a team.

Second, the growth factors can either swim from cell to cell or else remain on their cell of orig and figuratively shake hands with a neighbor cell without leaving home. However they get there, th growth factors will attach to the receptor on the outside surface of the cell. Once the growth fact binds to the receptor, the receptor shuttles a signal from the outside cell membrane to the nucleus. Th nucleus ponders a response and—*boom*—it generates the signal for the cell to act, and the cell do something, like changing shape.

The third characteristic is that growth factors come in the form of both activists and obstructionist that is, some factors stimulate the process and others prevent it. Scientists have found that hair follic formation is ultimately under the control of inhibitory growth factors; these obstructionist facto usually act by blocking the action of another growth factor. For an inhibitor to turn on a process counterintuitive until you recognize that the inhibitor is inhibiting the inhibitor of the activator; other words, once the inhibitor of the activator is neutralized, the system "blasts off." If, for exampl a delivery man (an activator) is trying to transport a package to you, but a hoodlum (an inhibito stops him, no package will be delivered. However, if a police officer (an inhibitor to the hoodlum) able to apprehend the hoodlum, your package will arrive. Of course, the hoodlum himself could b helped or hindered by other members of his gang or he could be blocked by members of a rival gan likewise, the police officer could be assisted by other police or blocked by red tape. So, if multip actors play a role in package delivery, as this fanciful example suggests, a large number of decision would have to be made in order for you to get your package. Because there are many such go and n go steps in hair follicle formation, the system is under tight and scrupulous control. Without th ~~multilayers of regulatory signals, cells might form hair follicles in a higgledy-piggledy array~~ witho regard to neighboring cells or might even form hair follicles in a site where they are not needed—c worse, grow into a cancer.

Hair follicle formation begins in all mammals within the immature epidermis. But in order to grov a hair follicle needs help from the dermis, which provides structural support, blood supply, an important growth factors. A vigorous and voluble cross-talk starts between the epidermis and derm early in the process. The conversation between the compartments goes something like this:

“Hey, Derm,” says the epidermis. “I am now sending you positive hair follicle growth factors. A the point of highest concentration, set up the foundation for a hair follicle.”

The dermal cells respond by sending back to the epithelium a missive in the form of another grow factor, saying: “Okay, Ep. I’m sending you back a growth factor telling you I’m ready. But in order t move the project along, send down another signal telling some dermal cells to gather under the sp where the new follicle should form.”

“Sure thing,” the epidermis responds. “Here it comes, but, Derm, you’ve got to start making bloo vessels, because those rapidly growing hair follicles will need plenty of food.”

And so this two-way *tête-à-tête* goes on and on stimulating, restraining, molding, and balancing. A long as the follicle is developing, and even after the follicle is fully formed, the epidermal and derm cross-talk continues and must continue for the lifetime of the hair follicle.

If you were to look at the epidermis of a human fetus while hair follicles are forming, at first you see a pattern of spots due to epidermal thickenings: the epidermal cells at the point of new follic formation swell with expectant pride. Rather quickly, these epidermal cells grow into a small nubbi and the nubbin grows into a finger, which extends into the underlying dermis. In time, at its deepe portion, the finger embraces a small piece of dermis, now called the dermal papilla, and then th finger matures into a full follicle with its characteristic embedded concentric cylinders: a sebaceou gland, a muscle, and, finally, the egressing shaft.

Although all mammals form hair follicles essentially the same way, different mammals comple their first hair follicles at different times. Some mammals form their first hair coat in the wom while others form it just after birth. Cows, horses, and dogs are born with a full coat of hair, wherea mice, rats, and opossum are born hairless. In humans, the first body hairs appear during the secon trimester of pregnancy but at birth the hair—except for that on the scalp and eyebrows—may b barely noticeable. Eventually there will be about one hundred thousand hair follicles on the scalp an between three and five million over the body. Humans don’t normally develop additional hair follicle over a lifetime; even worse, as men and women age, the number of follicles over the body decreases.

Anecdotal observation from pediatricians reveals that kids show different scalp hair grow patterns. Some babies are born with long hair that continues to grow, some shed their birth hair after few months and grow new hair immediately, and still others are born bald and don’t start to grow ha until they are a few months old. In many infants, the first hairs float like a gossamer over the scal Not heavy enough to drop onto the scalp surface, the fibers point straight up and, in the proper ligh form a resplendent, fleeting, once-in-a-lifetime, newborn nimbus.

We now understand a great deal more about hair placement, patterning, and growth than Turing di but there are still aspects we do not yet understand. For instance, once a hair follicle acquires its ov identity, it is no longer dependent on any growth factor gradient surrounding it. So when a surgeo transplants a scalp follicle into the eyebrow region, the scalp follicle will continue to grow a scalplil hair shaft—long and straight. We are not entirely sure why this happens, but surgeons use th property to great advantage in treating hair loss, a topic we will return to.

Clinical studies indicate that the underlying brain appears to affect hair follicle placement in th scalp. One example, the hair whorl (commonly known as a cowlick) is a vortexlike placement of ha at ~~the top and back of the scalp. Hairs making up the whorl can rotate clockwise, counterclockwise~~, a combination of both. Clinicians find that the hair whorl direction in a cowlick, which is a hair- ar skin-related feature, reflects left- or right- handedness, a brain feature. In a sampling of five hundre adult North Americans, Amar Klar of the National Cancer Institute[3] found that more than 90 perce of right-handed people had a clockwise whorl, while non-right-handed persons (either left-handed ambidextrous) had neither clockwise nor counterclockwise associations. Underscoring t implications of hair patterns, Professor Bernd Weber and his colleagues at the University of Bonn reported that subjects with a clockwise hair-whorl orientation had a strong association with left-bra language dominance while subjects with a counterclockwise hair-whorl had no such association. Th associations of whorl patterns and handedness are not unique to humans. Right-lateralized hors (defined based on preference of the individual horse for galloping, jumping, or dressage movemen on the right rein) display significantly more clockwise facial hair whorls.[5] Scalp whorls may also fla underlying pathology. Multiple hair whorls, for example, occur twice as often on the scalp of mental stunted children compared to controls;[6] moreover, children with multiple or intersecting whorls sho a higher probability of having underlying brain malformations.[7]

These are fascinating correlations, even if we don’t yet fully understand how this brain–hair follic patterning comes about. Embryologists have suggested that the association may reflect the fact that the very early embryo, skin and brain cells share a common antecedent tissue that divides to produc brain and skin. In any case, the observation evokes the evolutionary concept described in chapter that the hair follicle evolved from, and is related to, a sensory or neural-like structure.[8]

What we do know is that, once formed, the hair follicle starts producing a shaft and undergoes unique growth cycle. The story of that cycle depends on a very special cell. Finding that cell require yet another generation of scientists.

3

A MYSTERIOUS CYCLE AND A UNIQUE CELL

Cells making up the hair follicle are among the most rapidly dividing cells in the body.

In the late 1980s, George Cotsarelis—a hard-driven, no-nonsense, and appropriately baldi academic—made a discovery that would redirect the course of hair biology research for decades come. From his course work at the University of Pennsylvania Medical School, Cotsarelis had learne that hair grows out of skin from a fingerlike collection of cells called a follicle and that a follicle mu regrow in order to produce a new hair. But regrowth of any living tissue requires stem cells—cel with the dual ability to regenerate themselves as well as to give rise to specialized cells. Experts in t field recognized that new hair growth requires the participation of these cells, but they didn't kno where in the follicle they rest. Confident that those very special cells would enable him and his fello researchers to clone hair follicles and consequently provide new hair for balding people, Cotsarelis s out to find and isolate them. It would take him fifteen years.

During the 19th and early 20th centuries, medical investigators first embarked on the enormous ta of describing the cellular composition and organization of all normal and diseased tissues—t genome project of their day. They used light microscopes and stains, tools simple but powerf enough to discriminate between different types of tissues, cells, and cellular components. Taking th approach, a small group of British and European researchers, including Francis W. Dry, Ludwi Auber, and William T. Astbury in England, and Felix Pinkus in Germany, chose to study the hai follicle. With so little detailed information available at that time on any organ or tissue, why in t world did these scientists decide to focus on the tiny hair follicle? Human motivation doesn't chang money. Because sheep farmers and wool merchants hoped to improve both the quantity and quality their product, they set up research foundations: the Wool Industries Research Association in Englan Deutsches Wollforschungsinstitut in Germany, and the Commonwealth Scientific and Industri Research Organization in Australia. These institutions provided laboratory support for anatomist pathologists, biologists, and physical chemists to conduct hair research that would make the wo industries more profitable. The discoveries made by these investigators became the bedrock of wh we know about hair today.

First, these scientists established that the follicle is a layered structure. Like a Russian doll or t sleeves of a collapsible telescope, the follicle consists of three embedded cell cylinders, each tucke into one slightly larger, with the central-most cylinder making up the hair shaft itself. They als discovered that the complex nature of the hair follicle extends beyond its intricate layering. Under t microscope, the whole shape and size of follicles changed predictively and repetitively over time;

short, hair follicles grow in cycles.

~~Today, we recognize that growth cycles are hardwired into all forms of life, be they single~~-celle amoebas or multicelled mice. Even cells isolated from human skin and farmed in a laboratory sho cyclic changes. After all, life-forms evolve, grow, and flourish in a milieu of cycles set by the spin ar orbit of the earth and the pull of the moon. Moreover, since mammalian embryos grow in the uteru adjacent to the largest blood vessels of the body, they rock to the cadence of their mother's pulse fro the moment of conception. However, while all living beings demonstrate rhythms, such as sleep wake-sleep, very few show the dramatic changes in form and activity of the hair follicle.

Actually, people in the Stone Age were acquainted with the cyclic nature of hair development we before the sophisticated wool and hair scientists of the 19th century. The indigenous people of Nor America, for example, understood that in late autumn, the beaver's coat displays optim characteristics for clothing, because at this time the animal's fur is thickest and best suited to resi the ice, snow, cutting winds, and freezing waters of the Canadian winters. They had observed not on that fur growth is denser in autumn than spring, but also that no hair growth occurs during the depth winter or the height of summer. They knew that for the best furs, they had to collect skins fro beavers trapped during the cold months.

For most furred animals, hair growth starts and stops in relation to the position of the earth in i course around the sun. This solar connection means that, throughout the year, each body hair grov and sheds at the same time as its neighbor; in other words, body hairs of furred animals grow unison, synchronously. At any one moment, hair follicles in animals ranging from beavers to lap ca are either growing, resting, or shedding. In late spring, when you coddle your cat and find gobs of f balls on your sweater—much more than you see other times of the year—you are experiencing th period when most of the follicles are in the shedding phase.

Human scalp hair follicles differ in this respect. They cycle, but they are, for the most par oblivious to celestial events. They produce hair for a period ranging from two to six years, and the stop growing, apparently independent of all external or internal rhythms. So, while one shaft on yo head may be growing, another may be shedding, and a third anchored and resting.

In 1926 at the University of Leeds, Professor Francis W. Dry, a skilled light microscopist, set out t describe the structure of hair follicles over the course of the cycle.[1] He found that although no ne follicles arise during adult life, over time they change shape in fundamental and predictable ways. H likened these changes to the cyclic phases of the moon and gave them names.

"Anagen" is the name he gave to those follicles forming a new shaft. During this phase, the follic projects into the deep skin, and the cells in its lowest portion divide at a blistering pace. As new formed cells add to its base, the shaft moves toward and beyond the surface, about one half inch p month; the more time a follicle spends adding new cells to its base—that is, the more time it spends the anagen phase—the longer the shaft becomes. Since scalp follicles remain in anagen for a period two to six years, uncut human scalp hair may grow from one to three feet in length before sheddin Other hairs on different parts of the body are shorter because their anagen phase is not as long; eyelas hair, for example, grows only thirty days, and the resultant fiber is less than a half inch.[2]

As long as cells in the follicle base divide rapidly, the shaft will grow outward; however, when th shaft gets to a certain genetically determined length, the hair follicle stops producing hair shaft cell the hair shaft stops moving outward, and the bottom of the follicle shrinks upward. Dry called th follicle-shrinkage phase "catagen." At this time, the follicle shortens because the cells making up i lower half shrivel up like raisins and disappear. What's fascinating about this shrinkage phase is th the lower follicle cells disappear in such a way that the follicle base withdraws in a bottom-to-to direction; the top of the follicle, however, does not change during the whole cycle, even as the sha stops growing. By means of this life cycle, the hair follicle moves down and up, over and over, like yo-yo, throughout a person's lifetime. As long as a person lives, his or her hair follicles will cycle i this way.[3]

Currently, scientists who study hair believe that very specific molecular signals tell the hair follic when to start growing and when to stop growing and enter catagen. If we knew what those signa were, we would be able to turn hair growth off or on at will. Although we know little about thes molecular keys, one study suggested a lead. Professor Gail Martin directs a laboratory at th University of California, San Francisco, that investigates the role of growth factors in mouse bra development.[4] In order to test the importance of any one factor, she and her team use genetic tools t generate mice lacking that factor. When the team removed one factor—fibroblast growth factor five- from all the cells in a group of mice, they discovered that the mice were perfectly healthy and had n nerve problems at all, but had very long coat hairs. In fact, these mice resembled angora animals suc as angora guinea pigs, rabbits, goats, and cats, all of which have long, fine body hairs. When the studied the hair cycle phases of these mice, they found the mice had an abnormally long anagen phas that long anagen phase produced abnormally long hair shafts. When these scientists looked f fibroblast growth factor five in other angora animals, they found much less than in normal-haire breeds. (A later study showed that a decrease of this factor in human hair follicles also results in ver long hairs.[5]) Professor Martin and her colleagues concluded that this factor acts like an anagen bra regulating hair-shaft length. Currently, hair researchers are trying to find out how that factor work and if it can be used to treat hair disorders.

The catagen phase is short, lasting just a few days. At its end, the follicle enters a resting phas which Professor Dry called "telogen," during which there is no cell growth, no cell division, and n shaft growth. In this phase, follicle length is the shortest, shaft length is longest, and shaft anchorag is strongest. That the resting phase can last from weeks to months is advantageous for furred anima living in cold habitats because, during the winter, protein-rich foods necessary for new sha production may be limited. This resting phase finally ends when an anagen-stimulating growth fact signal arrives.

The fourth phase of the hair growth cycle is the phase of shedding, called "exogen." In this phas hair-shaft mooring loosens and the shaft falls out. Because the hairless state is not viable for mo mammals in the wild, there must be a delicate synchronization between shedding and new hair growt Normally, exogen does not occur before a new hair shaft grows out. Studies suggest that sheddin results when a battery of enzymes loosen the attachments holding the shaft in place. The rate of ha loss in humans is steady, with about fifty to one hundred scalp hairs falling out each day. Control o the shedding phase is important because most of us don't care whether our hair is growing or restin but when we sense we are shedding more hair than usual, we push the panic button.

Biologists have asked why hair follicles go through the bother of cycling. After all, except for th uterus (whose inner lining forms and sheds each month in a healthy menstruating woman), no oth mature adult human organs cycle, form, cast off, and re-form. There must be an important surviv reason for an organ to cycle, because building an organ and discarding it is expensive—costly in tern of the processes and resources needed both to build it up and tear it down. Three plausib explanations have been suggested. The first is based on the recognition that hair shafts wear dow even after such gentle handling as combing, shafts suffer structural damage. The second is that ha shedding provides animals a means of cleansing their coat, of exchanging a soiled cover for one fre of dirt and vermin. The third explanation is that, through shedding, animals can adapt their fur coat the changing habitat, such as when Minnesota weasels replace their sparse, brown summer coat for dense, white winter coat. But why do humans shed hair? The simplest answer is that the cycle is pa and parcel of hair growth itself—a remnant, or hand-me-down, of our distant past.

An abnormal hair cycle may have medical consequences. Following pregnancy, a woman may sta ~~shedding large quantities of scalp hair. That’s because during pregnancy—when blood hormone~~ necessary for development of a fetus are at high levels—the anagen phase is longer, and shedding delayed, resulting in longer hair shafts and denser hair growth. After childbirth, when hormone leve return to normal, an unusually large number of hair follicles on the mother’s scalp stop growing ar enter the resting phase. Once a three-month resting phase is over, the hair shafts shed—in much larg quantities than most women have ever experienced. Happily, in this case, by the time the old shaf shed, new hair fibers, though still rather short, have appeared.

Having recently given birth is a completely normal reason for any woman to undergo abunda shedding. But abnormal hair shedding may also occur as a result of other stressful life events, such after general surgery, severe trauma, bereavement, divorce, and job loss. (We will revisit th phenomenon in the next chapter.) The fact that one can pinpoint a previous stressful event after thre months (at the end of anagen, the follicle rests three months before shedding) reflects the remarkab consistency of the follicle’s inherent clock.[6]

The hair cycle is also altered during cancer therapy. Once the diagnosis of breast cancer, fo example, is established, the patient and her doctor choose from a number of different treatme options. In many cases the possible side effects may influence or even dictate the patient’s ultima treatment choice. During chemotherapy, the patient takes a cocktail of toxic drugs that kills all rapid growing cells, both healthy and cancerous. The most actively dividing cells in the body are found the bone marrow, intestine, and hair follicle base, and complaints of the patient receivin chemotherapy reflect injury to these tissues. She is weak and susceptible to infection because sh lacks red blood and immune cells; she has abdominal cramps and diarrhea because of widesprea injury to her gastrointestinal epithelial cell lining, and, most conspicuously, she has extensive ha loss because of damage to the rapidly growing cells in the lower hair follicle.

Using modern chemotherapy, we are not yet able to selectively destroy rapidly dividing cancer cel without injuring, at the same time, rapidly dividing normal cells. The hair follicle cycle is importa to this discussion because telogen hair follicles, which house few dividing cells, are in fact resistant chemotherapy:[7] They lack rapidly growing cells, the target of chemotherapy. The problem is that mo scalp hair follicles are in the anagen phase and stay in anagen for years. Theoretically, if you coul place hair follicles in the telogen phase during chemotherapy, you would minimize hair loss. We ju don’t know how to do that yet.

Once patients are off the anticancer drugs, all affected follicles undergo a well-deserved rest, ar then reenter anagen to form a new shaft. However, the important hair follicle dividing cells have bee destroyed, so how does the woebegone hair follicle reenter another cycle? This is where hair follic stem cells come to the rescue.

In the years following World War II, Ludwig Auber obtained his PhD from the University c Edinburgh and joined the Wool Industries Research Association (now the British Textile Technolog Group, Ltd), where he initiated a series of microscopic studies of the sheep hair follicle. Among mar other fundamental observations, he documented that virtually all the rapidly growing cells of the ha follicle are located in a circumscribed region in the deepest portion. Other scientists in Nor America, Europe, Asia, and Australia confirmed Auber’s observations and concluded that since mo of the dividing cells are tucked into the lowest part of the follicle, the stem cells responsible for ha follicle cycling must be there as well.

This was the accepted wisdom until almost fifty years later, when George Cotsarelis challenged th convention. Cotsarelis knew that stem cells in other systems are very slow-growing reserve cells th have the unique ability to divide and form two daughter cells: One becomes a stem cell, like its parer and the other becomes a cell that can form into one or more adult tissues, such as the hair follicle, i sebaceous gland, and the adjacent epidermis.[8]

~~Cotsarelis understood that if he could tag (in this case, the tag was a cell dye) all hair follicle cel~~ at one time and then examine them weeks later, only the cells dividing at the slowest rate (that is, th stem cells) would retain the tag. This approach is based on the observation that when cells grow, the divide into equal halves, diluting the tag carried by the parent cell to one half in each of the daught cells. Consider a teenager tippling her parents' vodka and then surreptitiously refilling the bottle wi water each time the bottle reached half empty. By the sixth refill, the alcohol content would be belo 1 percent, and no one—including her parents—would recognize the contents as anything even close vodka; in fact, it would be more like pure water. The same dilution occurs for rapidly dividing cells the deep follicle: As each cell divides at a rate of about twice per day, the dye tag becomes so dilute that by one week it is undetectable. On the other hand, cells that divide slowly, like stem cells, reta some of the initial tag even after a long period of time.

Using this approach, Cotsarelis carefully scrutinized the skin and its hair follicles for dye-retainin cells weeks after the skin cells had been tagged. Initially, he searched where his teachers told him look—where all the action was, at the bottom of the follicle. But no tagged cells were there. On when he moved his sights above the deep follicle—to the upper permanent portion of the hair follic —did he discover his quarry. He found tagged cells clustered higher up in the anagen-phase follicle, the point where the muscle of the hair follicle inserts. He reported to the scientific community th stem cells are located in the follicle mid-portion, a region referred to as the "bulge," not in its base The finding indicated that stem cells responsible for re-forming a new follicle after chemothera actually live in the mid-follicle, far away from the actively growing cells in the follicle base.

You might then assume that if you had a stem cell, all you would have to do is implant it anywher in the skin and—*voilà!*—a new hair follicle would form with its stately shaft. But that's not wh happens. Despite many attempts, when a pure population of these cells was placed into skin, no ne hair follicles appeared. These experiments suggested that a second cell was needed to complete th task.

The story of that second cell takes us back across the Atlantic to the Firth of Tay, Scotland, wher Professor Roy Oliver, an uprooted Englishman, had set up a laboratory at the University of Dundee study the formation of organs, such as the tooth, liver, feather, and hair. At the time, during the 1960 embryologists knew that the creation of most organs requires an interaction between two tissues: th epidermis and the dermis. Throughout the process of organ formation, these two tissues sit very clo to each other and communicate, a conversation we listened to in the last chapter.

As wool scientists had previously found that hair follicles contain both epidermal and derm portions, Oliver assumed these two tissues must play an important role in new hair follicle formatio He therefore chose to study the hair follicle as a model system for analyzing the dermal component organ formation. In early studies, he found that if he removed the dermal papilla, a dense collection dermal cells at the follicle base, hair growth stopped; when he transplanted it back, hair grow resumed. Moreover, in some eye-popping studies, when he and colleagues implanted a dermal papil under the epidermis of rat skin, they found that the papilla had the embryonic power to induce ha follicles even in epidermis where none had existed before.[10]

To analyze how the dermal papilla works, Oliver assigned his then-graduate student Colin Jahoda the project. Jahoda first established techniques for isolating dermal papillae from hair follicles, ar then for growing dermal papilla cells in the laboratory. Eventually this team demonstrated that cel making up the dermal papilla can be propagated in the laboratory, and when the cells were injecte back into the skin of a living mouse or rat, they had the power to induce new hair follicle formation By means of multiple experiments, the Dundee group showed that the process of hair growth requir

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