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Management of Androgenetic Alopecia

Mammals have hair, a characteristic as diagnostic as the feathers of birds. Functionally, hair acts as insulation, much like bird feathers. Additional roles of hair include protection from injury, camouflage and sexual or social communication. The color, texture, length and style of hair are highly variable between individuals. As a result, hair significantly contributes to the unique appearance of each human being and therefore affects both our self-image and the way we are perceived by others. Due to this fact, the loss of hair is quite distressing to some individuals and why some may seek methods of hair restoration.

Embryology

Hair follicles start developing between 9 and 12 weeks gestational age. They are derived from the ectodermal and mesodermal layers of the embryo. The ectoderm gives rise to the hair matrix cells and the melanocytes responsible for the pigmentation of hair. Two buds form off of this layer. One bud gives rise to the sebaceous gland and the other bud forms the area of attachment for the erector pili muscle. The erector pili muscle, the hair dermal papilla, the fibrous follicular sheath and feeding blood vessels all arise from the mesoderm. Hair follicle epithelial growth continues down into the mesoderm until the follicle has reached its full size. Once this occurs, matrix cells begin dividing and pushing upward, eventually forming a hair shaft. Hair production can typically be seen by 16 to 20 weeks gestation, forming fine lanugo hair. Some of the lanugo hair will be shed around 32 to 36 weeks and after this time more substantial hair may develop on the scalp, eyebrows and eyelashes.

Anatomy of the Scalp

The scalp is made up of five layers that can be remembered using the mnemonic SCALP. The outermost layer is the skin. The connective tissue layer contains fat, vessels, lymphatics and nerves. The galea aponeurosis is a tendon-like structure to which the frontalis muscle inserts anteriorly and the occipitalis muscle inserts posteriorly.

Loose connective tissue lies between the galea and the pericranium, which is the periosteum of the skull.

The scalp has a rich blood supply derived from both the internal and external carotid systems. Anteriorly, the supratrochlear and supraorbital vessels are found. The superficial temporal and retroauricular vessels supply the lateral scalp. The posterior scalp is supplied by the occipital vessels. Venous drainage mirrors the arterial flow. The emissary veins and the ophthalmic veins are of special anatomic note as they drain intracranially and have the potential to allow spread of infection to this space.

Many surgical procedures on the scalp can be performed using local anesthesia. As a result, it is important to understand the innervation of this area. The supratrochlear and supraorbital branches of the ophthalmic division of the trigeminal nerve innervate the forehead and frontal scalp. The maxillary division, via the zygomaticotemporal branch, supplies the temple region. Sensation of the lateral scalp is provided by the mandibular division's auriculotemporal nerve. The cervical plexus contributes to the great auricular and lesser occipital nerves that innervate the postauricular area. Finally, the occiput and vertex are innervated by the greater occipital nerve. Motor innervation of the frontalis, occipitalis and auricular muscles is provided by the facial nerve.

Anatomy of Hair

Hair is a multilayered structure. The outer root sheath and inner root sheath surround the developing hair shaft. The shaft itself is made up of three layers: an outer cuticle, a bulky middle cortex and an inner medulla. The outer cuticle is made of cells containing dense keratin and serves a protective function. The middle cortex consists of tightly packed spindle shaped cells containing keratin and some pigment. The inner medulla, whose role is unknown, contains cells with cytoplasmic vacuoles that become air-filled as the cells push upward to the epidermis.

An estimated five million hair follicles are on our bodies. Approximately one hundred to one hundred fifty thousand of these are located on the scalp. Transverse sections of the scalp show that hair follicles are organized into follicular units. Each unit contains: one to four terminal hairs, one or two vellus hairs, nine sebaceous glands, nine erector pili muscle insertions and a perifollicular vascular plexus, neural net and connective tissue. These units are arranged in a mosaic pattern and likely function as distinct physiologic entities. The density of hair follicles is approximately 1135/cm² at birth and quickly decreases to 795/cm² by 1 year of age. A gradual decrease is then seen so that 20-30 year olds average 615 follicles/cm², 30-50 year olds average 485/cm² and by age 80-90 average only 435/cm².

Physiology of Hair

Hair growth follows a cyclic pattern consisting of three phases: anagen, catagen, and telogen. Anagen is the active growth phase and its duration varies by anatomic location. In the scalp, anagen generally lasts between 2 and 8 years. Typically, about 90% of hair follicles in an adult are in the anagen phase at any given time. The catagen

phase, which lasts between 2 and 4 weeks, is characterized by separation of the hair shaft from the dermal papilla and migration toward the epidermis. The telogen or resting phase is when hair growth ceases and the follicle attachment weakens until the hair eventually sheds. About 10% of adult hair follicles are in this phase, which lasts 2 to 4 months. Scalp hair growth occurs at a rate of approximately .37-.44mm/day and normal scalp hair loss is 50-100 hairs/day. Alopecia results due to an imbalance between the phases of the hair growth cycle- loss exceeds growth.

Androgenetic Alopecia

Alopecia is the loss of hair from skin areas where it is normally present. There are many different types of alopecia which are attributed to the underlying cause. Hair loss is a common problem for both men and women. The most common form of hair loss is androgenetic alopecia, also known as male pattern baldness. Androgenetic alopecia is characterized by a pattern of hair loss typically affecting the bitemporal and frontal hairline first, followed by diffuse thinning of hair over the vertex. This pattern of hair loss is described by Norwood's classification of male pattern alopecia. As this process progresses, the bald patch over the vertex gradually joins the receding frontal hairline, eventually leaving behind a horseshoe-shaped band of hair on the parietal and occipital scalp. Another pattern described by Norwood is an anterior to posterior progression known as a type A variant. Androgenetic alopecia is caused by a gradual miniaturization of hair follicles with each successive hair cycle. The dermal papilla is most likely the target for these androgen-induced changes. As the follicle becomes smaller, the hair becomes finer and less pigmented. Also, the time of each cycle spent in anagen becomes shorter while the telogen phase becomes longer. The ratio of time spent in anagen compared to telogen reduces from 12:1 to 5:1. Time in anagen is the primary determinate of hair length, so as this time shortens, so does the length of hair. In addition, the latency between shedding and the next anagen phase becomes longer, reducing the number of hairs present on the scalp at any given time.

Androgenetic alopecia occurs in genetically predisposed individuals as long as they have adequate levels of circulating androgens. Androgenetic alopecia is transmitted in an autosomal dominant pattern, but there is variable penetrance. Approximately 33% of people with a positive family history of androgenetic alopecia will be affected. Thirty percent of white men have androgenetic alopecia by age 30 and 50% are affected by age 50.

Circulating androgens have different effects on hair depending on location. Vellus prepubertal pubic, axillary, chest and beard hair follicles are stimulated to grow into terminal hairs. The same hormones have the opposite effect on hair follicles in the scalp. The reason for this site-specific action is not clear. The main circulating androgen in men is testosterone, while in women dehydroepiandrosterone sulfate, androstenediol sulfate and 4-androstenedione are the most abundant androgens. The enzyme 5-alpha reductase, which has two forms—type 1 and 2—present in the scalp, converts testosterone or the adrenal androgens to dihydrotestosterone. Dihydrotestosterone binds to androgen receptors five times more effectively than the parent molecules. It is unknown whether individual follicle susceptibility to androgen induced involution is

related to increased numbers of androgen receptors, increased local production of dihydrotestosterone or increased levels of circulating androgens.

Medical Therapy

Many patients, particularly those in the early stages of hair loss, will prefer to try medical therapy prior to considering surgical intervention. There are two aims with medical management: one is to increase hair coverage of the scalp and two is to prevent further hair thinning and/or hair loss. Currently there are two FDA approved drugs available in the United States for the treatment of androgenetic alopecia: minoxidil and finasteride.

Minoxidil was initially introduced as an antihypertensive whose mechanism of action is opening of potassium channels and vasodilatation. The occurrence of hypertrichosis as a side effect of this medication led to investigation for its use in androgenetic alopecia. Although the mechanism of action is unknown, topical minoxidil has been demonstrated to both stop the progression of balding and reverse some of the changes in the hair follicle induced by androgenetic alopecia. Specifically, vellus hairs develop into terminal hairs, miniaturized hair follicles revert to their normal morphology and the number of hair follicles in the anagen phase increases. Topical minoxidil is available in 2% and 5% formulations. The efficacy of both of these solutions has been demonstrated in several large, placebo-controlled studies. Individual response to the drug is variable. Results of minoxidil use are noticeable only after several weeks of use and application must be continued in order to retain the effects. Side effects are minimal and primarily include local effects such as scalp dryness, itching or scaling.

Finasteride was initially introduced as a treatment for benign prostatic hypertrophy. Finasteride specifically inhibits the action of the enzyme 5-alpha reductase type 2, thereby blocking the conversion of testosterone to dihydrotestosterone and reducing circulating levels of dihydrotestosterone by as much as 60%. Lowering hormone levels likely slows or stops the process of androgen-induced miniaturization of hair follicles. Finasteride in doses of 1mg per day has been shown to effectively treat androgenetic alopecia in three blinded, placebo-controlled, randomized studies. Improvement in scalp hair counts and on self and expert assessments of hair growth has been demonstrated. Like minoxidil, results are seen only after several months of therapy and are rapidly reversed upon discontinuing the drug. Finasteride does not act directly on the androgen receptor and therefore does not interfere with the normal activity of testosterone. Side effects are similar to those seen with placebo except a 1.8% reported incidence of decreased libido.

Dutasteride is another drug that acts on the enzyme 5-alpha reductase and is currently used for the treatment of benign prostatic hypertrophy. The difference between finasteride and dutasteride is that dutasteride acts on both the type 1 and type 2 5-alpha reductase. Dutasteride has not been approved by the FDA for use in treatment of alopecia.

Patient Evaluation for Surgery

It has been well established by several studies that hair loss can have a profound negative psychosocial impact on individuals suffering from the condition. Balding men report feeling less attractive and are dissatisfied with their body image. This negative self-image considerably affects quality of life. Additionally, negative social stereotypes are applied to individuals with hair loss. They tend to be perceived as older, weaker and less attractive than individuals without hair loss. Given these negative effects of hair loss, it is understandable why so many people seek treatment for the condition.

Hair replacement surgeries are cosmetic procedures. As with any cosmetic surgery, appropriate patient selection for these treatments is paramount to a successful outcome. These patients must have realistic expectations for improvement of their hairline. Adequate counseling regarding what can and cannot be accomplished for each individual is an absolute necessity. Self-motivated patients are most likely to complete the full course of replacement therapy, which may include two or more surgeries. Since the course may be long before the end result is achieved, patients must be willing to live through some inconveniences.

It is important to emphasize that the hair replacement techniques available today do not result in new hair growth, but instead involve redistribution of remaining hair. In order to be a candidate for these procedures, a patient must have adequate donor hair available.

Age is not a contraindication for hair replacement surgery. In fact, the ideal patient may well be older individuals, in whom a well established pattern of hair loss is present. It is more difficult to determine the pattern of hair loss that a younger patient will undergo, thus affecting the end result and potentially creating a disappointing result. As a result, patients under the age of twenty-five should initially be treated conservatively. Also in older patients, gray or salt-and-pepper hair may actually provide better coverage of the balding scalp.

Surgical Therapy

The types of surgery for alopecia fall into three basic categories—scalp reduction, scalp rotation flaps, and hair transplantation.

Scalp Reduction

Reduction of the balding area of the scalp can be accomplished using several techniques. First, serial excision of non-hair-bearing scalp can be performed. This process was originally described in 1978 by Unger and Unger. They described multiple distinct patterns of scalp reduction including the sagittal midline ellipse, “Y” pattern, lateral patterns (including “S”, “J” and “C” shape excisions), “U” pattern and miscellaneous patterns including the “T”, “I”, transverse ellipse and crescent ellipse. The pattern of excision must be individualized to each patient taking into account the shape of the bald area and the availability of donor scalp. This technique has enjoyed widespread

use, primarily because of ease of performance and reliability of results. After the pattern of excision has been determined, the bald scalp is excised down to but not through the pericranium, followed by wide undermining of remaining scalp and primary closure of the wound in two layers—the galea and skin.

A potential complication of this technique is excessive scalp excision. This results in excessive tension on the wound closure. As a result, necrosis of tissue and widening of scar may occur. The challenge is finding just the right amount of tension to enhance stretching and expansion of scalp flaps without creating excessive tension.

One of the major problems with scalp reduction is the phenomenon of “stretch-back.” Stretch-back is the tendency for the bald scalp to expand after each reduction. The amount of stretch-back is dependent upon the elastic properties of the scalp and varies between 10 and 50% of the reduction. Most of this re-expansion occurs within two months of surgery. Scalp extenders, anchoring galeal flaps and the “Nordstrom suture” have been developed to reduce stretch-back.

Frechet introduced scalp extenders in 1993. The extender itself consists of a 1mm thick sheet of silastic with two opposing rows of titanium hooks. The silastic has the ability to stretch up to 200% and demonstrates memory with a tendency to return to its natural shape. After scalp reduction is performed, this apparatus is attached to the deep surface of the galea parallel to and 1-2cm lateral to the wound margin on one scalp flap. It is then stretched and attached to the opposite flap at a predetermined distance from the wound margin. The wound is closed in layers and the extender left in place for 4-6 weeks. The tendency of the extender to return to its original size places continuous tension upon the lateral scalp toward the incision line, which effectively produces a negative stretch-back or shrinking of the bald area. When the extender is removed at a second stage, more lateral hair-bearing scalp is available so that further scalp reduction can be performed. This technique asserts the benefit of maximizing the area of scalp that can be excised while minimizing the number of procedures needed and the time to achieve similar results.

Raposo, et al described the use of anchoring galeal flaps in 1998. In this technique, scalp excision is performed routinely but on one side of the incision the galea is not excised. Instead, three rectangular segments of galea are left in continuity with the scalp flap. These are then sutured to the undersurface of the opposing flap, drawing the wound together. The incision line is then closed in the usual fashion of two layers. The benefit of the use of galeal flaps was found to be a reduction in stretch-back of 80-88% at one month after surgery.

The “Nordstrom suture” is the most recently described technique to reduce stretch-back. It is a suture of silicone polymer that is 2mm in diameter and attached to a heavy cutting needle and is capable of stretching to 400% of its original length. After scalp reduction is performed, the suture is introduced through the galea and tied on itself. The galea is then reapproximated using a running, buried, mattress suture, taking 1-2cm bites of galea. The Nordstrom suture induces a shrinking of the remaining bald area that has been shown to be three times greater than that seen with scalp extenders. It also has

the advantage of being capable of placing stretch in different directions simultaneously. Another benefit is the ability to remove the suture without a second operation.

Tissue expanders are very useful in the treatment of alopecia. Placement of these devices increases the total surface area of hair-bearing scalp available to cover balding areas. The number of hair follicles is not increased, rather the skin between follicles is expanded, providing a more even distribution hair density. The expander is placed in the avascular layer between the galea and the pericranium. The overlying galea protects the feeding vessels of the scalp that run in the subcutaneous layer. This allows higher filling pressures than are tolerated elsewhere. Various sizes and shapes of expanders are available and are selected depending upon the area of alopecia to be covered and the donor scalp available. Most devices utilize a remote injection port. The location of incisions for expander placement warrants some consideration so that the end result yields hidden scars. One option is to place the incision in an area planned for future excision. Another option would be to place the incision along one side of a planned scalp flap. Incisions must be distant enough from the expander to minimize the risk of extrusion but close enough to facilitate accurate placement of the device. Typically, at the time of placement, the expander is injected with sufficient saline to obliterate the dead space created by scalp elevation. Most authors recommend waiting 1-2 weeks to begin filling the device. Injections are then performed once or twice a week by the physician. The amount tolerated will vary between individuals, but is limited by tissue blanching that would indicate compromise of blood supply. This process typically takes 6-10 weeks before adequate expansion is achieved. The advantages of tissue expansion are increased area of hair-bearing scalp available for coverage. Disadvantages include the cosmetic deformity imparted by the inflated expander, frequent office visits for injection and discomfort associated with inflation. Even if results are achieved more quickly than with other methods, patients must be highly motivated and understand the significant time commitment of this process.

Scalp Rotation Flaps

The use of scalp advancement or rotation flaps has the advantage providing immediate coverage of alopecic areas with dense hair-bearing tissue. Types of scalp flaps include the lateral scalp flap, the temporoparietal occipital (TPO) or Juri flap, the preauricular flap and free scalp flaps. Of these, the most widely utilized is the TPO flap, which was initially described by Juri in 1975 and has further been revised by Fleming and Mayer. Due to the vast array of scalp rotation flaps, they will not be addressed in this paper.

Hair Transplantation

The method of using small full-thickness autografts of hair-bearing skin to correct alopecia was first described by Okura, a Japanese dermatologist, in 1939. His work went essentially unrecognized and the credit for introducing this technique is often given to Orentreich who published his experience in 1959. The technique has evolved substantially since that time. The modern day pioneer of this technique is Dr. Bobby Limmer. Hair transplantation is currently the most common cosmetic procedure

performed in men.

The original technique described by Okura and Orentreich was that of punch grafting. This method utilizes small, typically 4-5mm, sharp, round punch trephines to harvest hair-bearing tissue, most often from the parietal and occipital scalp. Grafts typically contain 10-20 hairs per punch depending on hair density of the donor site. Similar punch trephines are utilized to create recipient sites in the balding areas. The recipient punch is 0.25-1.0mm smaller than the donor punch to allow for expected graft shrinkage after harvest. Important aspects of this technique are proper spacing of the punches so as to not compromise blood supply to the remaining scalp, directing the recipient punches to allow for hair growth in a natural direction, and appropriate timing of subsequent sessions. It is not unusual for four or more sessions to be necessary to achieve an optimal result. Most surgeons would advocate waiting a minimum of 6 weeks between surgeries, others time subsequent procedures based on growth from previous grafting so that hair distribution can be visualized and the remaining spaces filled in with new grafts.

Vallis was the first to describe strip grafting in 1964. This technique involves a free composite graft of hair-bearing scalp. It is most commonly utilized to enhance the appearance of a spotty or thin frontal hairline. The length of the graft is limited only by the donor tissue available and the amount of frontal hairline to be covered. The width of the graft is the limiting factor in graft survival. In previously unoperated frontal scalp, a graft up to 8mm wide can take without difficulty. The graft is harvested by creating two parallel, horizontal incisions in the donor scalp, down to the level of the galea. It is elevated in this plane and the donor site closed. The recipient site is incised along the anterior border of the existing hairline. In this case, the fascia is incised to allow some relaxation of the recipient site and accommodate the graft. The graft is inset so that the hair follicles are angled anteriorly to mimic the natural direction of hair growth. The graft is then sewn in place. Typically strip grafting is performed in two stages composed of one side of the hairline followed by the other side.

Follicular-unit transplantation is probably the most widely used hair grafting method today. In this technique, large numbers of minigrafts (3-4 hairs per graft) and micrografts (1-2 hairs per graft) are utilized to cover significant areas of balding scalp. The technique involves harvesting a strip of hair 1 cm wide from the occipital scalp. After injection of local anesthesia, the donor site is marked and the subcutaneous tissue infiltrated with tumescent solution. This simplifies the harvesting process by separating the donor tissue from the underlying fascia and improving hemostasis. It also aids graft dissection by separating the hair follicles from each other. After the donor strip is harvested, the site is closed in one layer without undermining. Graft dissection proceeds on a separate table using a stereomicroscope. The donor tissue is first cut into 2mm segments, aligning all incisions in the direction of follicle growth. Then, a #10 blade is used to further dissect the segments into micrografts and minigrafts, taking care to preserve natural groupings of hair follicles. This step can be expedited by having multiple technicians working at the same time. The grafts are kept moist in Ringer's lactate or saline and cool while the recipient area is prepared. Again, a tumescent solution is infiltrated into the recipient scalp. Since the frontal hairline is the most critical

for achieving a satisfactory result, graft insertion begins here and priority is given to obtaining optimal density in this area prior to proceeding to the crown and vertex regions. Slits are created in the recipient scalp using an eleven blade or needles of various gauges. As the surgeon partially removes the scalpel or needle, an assistant inserts a graft using jeweler's forceps. During the first pass, the slits are placed 4-5mm apart. A second and third pass over the same area may be performed to obtain the desired density. The direction of grafted hair growth can be controlled by changing the angle of the scalpel when creating the slits. This is particularly important along the frontal hairline where the direction of growth should be angled 45-60 degrees anteriorly. If there are residual native hairs in the region being grafted, the slits should be placed parallel to the existing hairs. Some surgeons advocate dressing placement, while some use no dressing. Patients are then instructed to shampoo daily on post-op day one so crusts are removed. Patients have clinic follow-up scheduled for one week post-op.

Complications

The goal hair replacement is to restore a natural appearance of the hair to the individual patient's satisfaction. Poor outcomes or patient dissatisfaction often occur as a result of an unnatural appearance. The good news is that many corrective techniques have been developed to improve upon undesirable outcomes. For the patient who wishes complete reversal of hair transplantation, graft removal can be performed. The grafts are excised with a punch trephine and the defects closed primarily. Often, this needs to be done over several stages so that excessive tension is avoided on the punch closures. To reposition poorly placed grafts, the same method of punch removal of grafts can be utilized, but the excised hair is then retransplanted in the appropriate location. Correction of rows of large punch grafts can be revised by reducing the size of the original grafts and placing smaller grafts in the intervening spaces. Excessively thin transplanted hair or an unnaturally abrupt thick frontal hairline can be improved with additional grafting. This will be dependent upon adequate remaining donor hair. To soften the frontal hairline, placement of several layers of irregularly spaced minigrafts or micrografts can be very effective. Unsightly donor site or scalp reduction scars may be improved with scar revision techniques. For any revision procedure, appropriate preoperative counseling cannot be overemphasized. A good outcome and a satisfied patient will be dependent not only on choosing the right method of correction and meticulous performance of surgery, but also on honest communication with the patient about what should be expected from the surgery.

Conclusion

The correction of alopecia can be performed using multiple approaches, including both medical and surgical options. The currently favored surgical technique in hair replacement is follicular unit transplantation. This technique continues to be perfected upon and has a foundation that has been formed by many of the earlier developed techniques. As more experience is gained by physicians performing these procedures, it is likely that patient satisfaction will increase, potentially also increasing the number of patients seeking these treatments.

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