

Konstantinos Anastassakis

Androgenetic Alopecia From A to Z

Vol.1 Basic Science, Diagnosis, Etiology,
and Related Disorders

 Springer

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and Related Disorders

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The creation of this three-volume work spanned almost 2 decades of my life. During those countless times that I felt exhausted and dispirited, during innumerable smaller or larger setbacks and adversities, I recalled the following poem for inspiration and self-encouragement. Because, in the end, it is not the goal but the journey that should matter. This, often painful, journey rewards with the richest gifts: experience, knowledge, wisdom, and maturity.

*“**Ithaka,**” by C.P. Cavafy (1911)*

*As you set out for Ithaka
wish for a lengthy journey,
full of adventure, full of discovery and enlightenment.
Don't be afraid of Laistrygonians, Cyclops, or angry Poseidon;
you'll never encounter any of those on your path
as long as your consciousness is sharp,
as long as a unique excitement
stirs your spirit and body.
Laistrygonians, Cyclops,
fierce Poseidon you won't encounter any of those
unless you carry them along inside your soul,
unless your soul mounts them in front of you.*

*Wish for a long journey.
May there be plenty summer mornings when,
with what pleasure, what thrill,
you enter first-sighted harbors:
may you stop at Phoenician markets to purchase fine goods,
mother of pearl and coral, amber and ebony,
and all kinds of sensuous and hedonic fragrances,
as many hedonic fragrances and spices as you may gather;
and may you visit many Egyptian cities
to learn and then learn even more from their scholars.*

*Keep Ithaka always in your mind.
Arriving there is your haven.*

But don't you ever rush your journey.

*Better if it lasts for several years,
and you reach the island an old man,
wealthy with all you've earned on your way,
not expecting Ithaka to offer you riches.
Ithaka gave you the fair journey.
Without her you wouldn't have set out.
She has nothing left to offer you.
And if you find her poor, Ithaka hasn't fooled you
Wise and knowledgeable as you have become, so full of experience,
you realize by now what Ithakas mean.*

*This work is dedicated to the best parents in the entire world, my parents!
Efthalia and Konstantinos Anastassakis*

Foreword

Human skin hair, a protein filament that grows from follicles located in the dermis, originates from the common ancestor of mammals. Although already having lost its protection, thermal regulation, and lubrication roles one hundred thousand years ago, hair has great social significance for human beings. According to a population survey of the Department of Economic and Social Affairs of the United Nations, graying and whitening of hair is the most considered age-associated change of the human body; pigmented hair communicates health and youth.

People may spend much time daily to care their hair on the scalp, face, pubic area, and legs. Hair care routine may differ according to individual culture habits and the physical characteristics of the hair. It includes coloring, trimming, shaving, plucking, or completely removing with different techniques. On the other hand, hair color and texture can be a sign of ethnic ancestry. Hairstyle may be an indicator of group membership. Religious groups may follow certain rules regarding hair as part of religious observance. But hair cutting and head shaving has also been used as punishment in the past, especially for women with long hair, but also—in some cases—for men. And in any case, the highly visible differences between male and female body and facial hair are a notable secondary sex characteristic.

All these actions towards hair health and cosmetics take place under the requirement that hair is present where it is supposed to belong. Baldness is not always a sign of age, which may be concealed with a toupee, hat, or cultural adornments. Androgenetic alopecia is a common form of hair loss in both men and women. Hair is lost in well-defined patterns, which differs in men and women. Over time, the hairline in men recedes. Hair also thins near the top of the head, often progressing to partial or complete baldness. In women, the hair becomes thinner all over the head, and the hairline does not recede. Androgenetic alopecia in women rarely leads to total baldness.

Androgenetic alopecia in men and women has been associated with several other medical and lifestyle conditions. A variety of genetic and environmental factors likely play a role in causing androgenetic alopecia. Individuals, who get confronted with early hair loss, often experience a shortage of medical knowledge, effective drugs as well as medical and correcting procedures. Most of the etiologic and risk factors remain unknown. The restoration of this socially important biomaterial with a diameter up to 0.18 mm primarily composed of α -keratin requires significant medical expertise, which is not widely distributed.

Medical expertise is obtained through knowledge and the latter requires the existence of adequate sources. Such sources could widely be found for hair and its science too, but the source that you have in your hands, completely written by a specialist on androgenetic alopecia, Dr. Konstantinos Anastassakis, will overcome your ultimate expectations. With great dedication the author has added to his knowledge a wide literature search to provide current information on hair follicle biology and life and on the secrets of androgenetic alopecia, including its causes and etiologic parameters, comorbidities, drugs and medical treatment, nutrition, lifestyle and dietary supplements, coverage and hair care. At last, the author presents a detailed description of surgical hair restoration techniques and provides an outlook to the future.

I am convinced that this book will satisfy even the most demanding reader and quench the thirst for scientific knowledge and practical guidance on the existing approaches for diagnosis and treatment of androgenetic alopecia in both sexes.

Berlin, Germany
October 2021

Christos C. Zouboulis

Preface

Androgenetic Alopecia and Female Pattern Hair Loss (AGA/FPHL) account for >98% of hair loss cases in males and >70% cases in females, making these conditions probably the most common adult (18–50 years) health disorders besides dental caries!

Surprisingly, AGA/FPHL have been somehow neglected in scientific literature, and no book approaches these all-too-common conditions “holistically,” comprehensively explaining the causative and aggravating factors, dangerous comorbidities, and, most importantly, all treatment options, pharmaceutical, surgical, and adjuvant.

This book is purposefully designed as a complete reference tool for understanding, managing, and efficiently treating AGA/FPHL according to all the latest research and clinical findings. It has been published in three related volumes, each with a specific focus (with intertwined contents), due to the huge amount of relevant, useful information and the vast number of figures, tables, graphs, and clinical photos.

Every aspect of the condition is evaluated, including biology, diagnosis, etiology and related disorders (Vol 1), drug treatment, the intricate effects of nutrition, lifestyle, and food supplements on hair loss (Vol 2), surgical hair restoration, hair care, as well as adjuvant and upcoming treatment options (Vol 3).

Each subject is addressed according to learning and clinical needs, and the presented information is sourced from several thousands of peer-reviewed papers so that readers can rest assured that they will not have to look anywhere else.

The idea for this book occurred to me out of personal interest (as in most major projects in life!) when I started losing my own hair due to AGA at an early age. I tried to find answers on how to save my mane in countless scientific papers and numerous Dermatology/Plastic surgery textbooks. Soon, I realized that a book dedicated to AGA/FPHL that included all the essential information I was constantly discovering in multiple sources was painfully missing. Therefore, out of youthful zeal and with herculean dedication, I decided to review and collect all the relevant and valuable literature findings under one cover. And while this book could be described as “too specialized,” one should consider that it actually offers answers to more than 90% of all hair loss cases in humans.

The initial 891-pages-long Greek edition of this book was published in 2015, included an excess of 7000 citations, and took me more than 8 years of daily hard work, often 16-hour workdays, to complete. Numerous readers approached me and suggested that this work must be translated into English. Even though I could immediately see the logic in their argument, the amount of work required was overwhelming, and it took me more than 2 years to finally jump in the project.

The English edition was extensively updated (more than 9500 citations) and enriched with thousands of pictures from my clinical practice as a certified Hair Restoration Surgeon. Another 4 painstaking years were required, and priceless sacrifices in every domain of my life, fortunately, most not irreparable.

The goal was to bring together all the valuable, up-to-date information on every possible AGA/FPHL-related question and offer it to the interested reader for immediate reference and application.

Collecting all the relevant literature was an extremely laborious task, mainly since many papers date back to the 1960s and only hard copies were available, most of which were personally traced and photocopied by myself. All the material included in the text was selected based on professional/scientific responsibility, ethics, transparency, and, above all, considering the validity of the information provided. Every possible effort has been made to include substantiated, specific, objective, honest, responsible, accurate, balanced, fair, and complete information that the reader can rely on.

The full text of every published, peer-reviewed (or not) paper that can be traced in the literature was individually assessed, and results were evaluated not according to the personal experience or beliefs of the author but according to the established evidence-based evaluation process. Misrepresentation, exaggeration, unjustified emphasis, or oversight of information that could mislead the reader was diligently avoided, focusing on preventing any type of known biases when reviewing the literature (such as selectively collecting citations that support some previous idea or belief of the author, etc.).

One would argue: why go into so much trouble?

Seen from a strictly medical perspective, AGA/FPHL are mild and biologically benign dermatological conditions. However, hair and its appearance have always been associated with youth, virility, strength, and sensuality. Both sexes and affected individuals experience great psycho-emotional stress due to balding, often leading to a severe reduction of quality of life and secondary morbidity.

AGA/FPHL progress unpredictably, their etiology remains uncertain, and the therapeutic options are limited, making it very difficult for patients to accept or adapt.

Accordingly, the “hair loss industry” is worth billions of dollars annually, and a significant proportion of this money funds a section of the industry that preys on the desperate balding individual, who hopes to halt hair loss and regrow hair, advertising untested and mostly ineffective hair loss treatments.

Most balding patients will be initially “fatally” attracted to the fake promises of Internet advertisers, irresponsible and inaccurate advice from friends or casual acquaintances, and charming, yet shameless, charlatans. Unfortunately, most who suffer from AGA/FPHL will first fall victims to one or more of the above, and only a few will seek professional, credible, and responsible diagnosis and direction by the specialist physician.

The overall goal of this 3-volume series is to offer the physician a complete “toolbox” to deal with any question on every possible aspect of AGA/FPHL using evidence-based data and according to ethical standards. This book offers every plausible scientific “ammunition” to the physician to treat successfully and safely balding patients, debunk myths and lies concerning hair loss, and keep patients safe, happy, and ...hairly.

Hopefully, the professional readers will use this massive amount of fully updated, peer-reviewed, and relevant information to educate their patients, to keep them sailing in safe, evidence-based waters, and away from commercially advertised “snake oils,” and even manufactured “pay-per-page” popular literature that supports several world-famous hair loss products.

The material in this book can indeed be a “beacon of knowledge” for physicians and help them debunk the pseudo-myth of the “incurable” nature of AGA/FPHL that dooms patients to unnecessary progressive hair loss (and distress).

It can also help physicians keep patients away from the perilous waters of pseudo-scientific “online discussions” and the catastrophic decisions often made by the desperate balding patients after getting “self-educated” on hair loss forums and social media.

My ambition is that the physician, and their patients, will realize that with the right strategy more than 90% of patients with AGA/FPHL can safely maintain their hair for even decades after being diagnosed with AGA/FPHL.

A final comment on choosing to adopt a distinctly idiosyncratic style: the text contains expressions that might surprise the reader on several occasions. This more genuine approach might include imperfections but, in the writer's idea, will make reading the text a livelier

experience, without diminishing its clarity or negatively impacting contents or methodology. Indeed, one might argue, endeavoring to hide one's inevitable flaws is as pointless as trying to borrow someone else's more elegant nose in having one's portrait taken. Fortunately, editors did not object too much to this stylistic choice, and I hope the readers will not, either.

Athens, Greece

Konstantinos Anastassakis

Acknowledgments

Words of acknowledgment are far from sufficient to express my gratitude to my parents. This task would not have been possible without their unabated support, unconditional love, understanding, faith, and patience. They have always been there for me through every endeavor, in ways I cannot even fathom. I aspire to match their strength, ethos, integrity, kindness, caring, and love for my future family. I hope they are as proud of me as I am of them.

The guidance of my brother, Ioannis Anastasakis, has also been decisive. As an international author himself, he inspired me with the proper mindset for this huge work. In his own words, “If you don’t think big, no one else will do it for you.” Thank you, my brother.

With great respect and thankfulness, I would like to acknowledge my deepest gratitude to Prof. Christos Zouboulis, Prof. Antonella Tosti, and Dr. William Rassman for sacrificing their valuable time to review the text of the individual volume they foreworded and for honoring me with their warm words.

Furthermore, I would like to acknowledge Panagiotis Itsios for his creativity, patience, and professionalism in designing all the unique figures and charts in this work. His elegant, clear, and comprehensive illustrations animate the text and aid the reader to apprehend concepts better.

The names of the dozens of contributors who supported me in numerous ways during the creation of the earlier (2014) single-volume version of this book are extensively addressed in the relevant section of that book.

I would like to express my sincere thanks and deep appreciation to my editor, Juliette Ruth Kleemann, for her patience, assistance, support, and guidance to make this project a reality. She generously offered me her valuable time and know-how on every occasion, and she went above and beyond to make my “dream project” an actual book. Any author benefiting from her work is fortunate beyond belief.

Finally, I would like to recognize all my hair loss patients over the years, especially the difficult ones, who have challenged me and herewith taught me the most about hair loss and its successful management than any academic authority. All this work is for you, actually! I hope it will make a difference in your life.

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Part I

The Hair Follicle Biology and Life

Diagnosis of Androgenetic Alopecia

Shedding, thinning, hypertrichosis, and hirsutism are all too frequent in Clinical Dermatology, and diagnosing hair follicles disorders is one of the oldest known medical practices. Nevertheless, one truth still stands: the critical point for the successful management of patients with any disorder of the pilosebaceous unit is a correct diagnosis.

The hardest part in diagnosing any disorder that manifests with hair loss (shedding, thinning, or both) lies in distinguishing between an actual disorder and a “hair loss condition”, which the patient describes but is hard or impossible to confirm clinically or by laboratory work. It is common in daily clinical practice to have patients reporting no less than massive hair shedding or “severely thinner hair, lately” that the physician cannot confirm by the physical findings since many of these patients still have a full head of hair and their lab work is excellent.

The explanation for this frequent phenomenon lies in the limitations of human visual perception: in order for the physician (or the patient himself) to be able to actually detect the hair as “thinner” by the naked eye, that patient will need to have already lost no less than to 50% of the hair mass in that area! (see Vol. 3, Chap. 99). That loss in “hair mass” can come either as shedding (hair falling from the scalp), as thinning (reduction in the average hair diameter), or, most frequently, both these processes simultaneously. The sad result is that when the doctor can finally see with his/her own eyes that the patient is actually “thinning”, it is usually already too late to reverse the condition and restore all lost hair fully.

So, considering the limitations of our senses, the physician must be thorough and careful when examining patients reporting hair loss. Diagnosing a patient with hair loss requires a full medical history, a family history of hair loss, a detailed physical examination of the scalp skin, examination of the quantitative and qualitative characteristics of hairs, and a physical examination of the skin and hair in other areas of the body.

Scalp and hair examination is performed with methods sensitive enough to detect and identify even hair shaft abnormalities. The clinician will have to determine quantitative and qualitative values, such as follicular density, hair density, physical hair characteristics, hair diameter, the ratio of anagen/telogen hair follicles, the hair’s growth rate, etc. All the data the physician collects during the diagnostic steps provides essential information for identifying the underlying condition and choosing the appropriate treatment.

Indeed, all these might sound as hard and plenty of work. However, it is much easier than one would expect.

The updated diagnostic algorithm for AGA and FPHL (S1 guideline) diagnosis is largely simplified and can be easily used in daily clinical routine while the patient himself can file the diagnostic evaluation form. A biochemical or an extensive endocrinological workup is neces-

sary only in rare cases, while semi-invasive (pull test) or invasive (scalp biopsy) tests are to be avoided altogether unless absolutely necessary.

Today, with newer, cost-effective, yet extremely precise diagnostic tools, such as the magnifying

video-dermatoscope, the physician can offer patients an accurate, evidence-based diagnosis of AGA and FPHL on an early enough stage to halt the progression of the condition and regrow the largest percentage of the lost hair.

Causes and Etiologic Parameters of AGA/FPHL

Baldness has been a cosmetic problem for humans since antiquity. Hippocrates, the ancient Greek physician who is considered the “father” of modern Medicine, was the first to make a correct observation concerning Androgenetic Alopecia (AGA). Paradoxically, Hippocrates himself was the most typical example of extensive AGA. The wreath of permanent hair encircling the back and sides of the head is still today referred to as the “Hippocratic wreath”.

AGA and Female Pattern Hair Loss (FPHL), the female counterpart of AGA, are -by a huge margin- the most prevalent causes of hair loss in all human races: no less than 98% of men with any type of hair loss suffer from AGA and probably >70% of women with hair loss suffer from FPHL. Also, severity and frequency in the population increase with advancing age but with differing frequencies among races. Despite the high prevalence of hair loss in both sexes, the question of why so many otherwise healthy men and women lose their hair while others do not remains unanswered.

Hair always had a highly symbolic value, and hair decoration as a means of social communication and projection of social identity and position. It determines appearance, it is an essential component of identity and self-image, and it advertises health and mating fitness. Accordingly, societal attitudes towards male balding vary between indifference and negativity, even though male hair loss patients suffer emotionally in excess. In balding females, things are much worse. Considering that hair's significance to women is imbued with cultural and personal symbolisms related to gender identity, femininity, sexuality, attractiveness, and personality, hair loss can be psychologically devastating in FPHL patients.

Since “stakes are high” for both sexes, efforts to explain and treat AGA/FPHL date back to ancient times. Hippocrates was the first to report that eunuchs failed to become bald, and he argued that hair was nurtured by a “mysterious secretion which in libidinous men is dissipated too rapidly.” Baldness was thought to be the price for sexual excess! To his defense, the role of testosterone was first recognized by James Hamilton, an American anatomist just in the early 1940's. Ever since, there has not been too much progress, and the exact pathophysiology of AGA remains unclear even today. Considering AGA, we have managed to scientifically support and document theories on two essential parameters, namely androgens and heredity. Unfortunately, these do not seem to explain the whole picture, especially for FPHL, which does not even seem to require androgens.

Admittedly, there are still significant gaps in our understanding of the etiology of AGA and FPHL. It seems that the biological, genetic, and molecular details of AGA/FPHL remain a puzzle that we still have not put the pieces together and, to make things even more challenging, there are missing pieces to discover. We have not discovered the exact molecular mechanisms that cause hair follicles to miniaturize and shed on specific areas of the scalp, while neighboring follicles, just a few centimeters away, remain unaffected.

In the following chapters, all those parameters that have been reported to be involved in the pathophysiology of AGA/FPHL will be extensively discussed. The information offered will allow the physician to understand the complicated nature of these entirely benign -yet psychologically overwhelming- condi-

tions. With this updated knowledge, the physician can offer convincing explanations, evidence-based answers and help patients stay away from pseudo-scientific myths and ineffective management strategies.