Editors
Pierre André • Eckart Haneke
Leonardo Marini • Christopher Rowland Payne

Cosmetic Medicine & Surgery

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Edited by

Pierre André, MD
Paris Université Laser Skin Clinic, Paris, France

Eckart Haneke, MD
Department of Dermatology, University of Bern, Switzerland
Dermatology Practice Dermaticum, Freiburg, Germany
Department of Dermatology, University of Ghent, Belgium
Centro de Dermatologia Epidermis, Porto, Portugal

Leonardo Marini, MD
Skin Doctors' Centre, Trieste, Italy

Christopher Rowland Payne, MBBS, MRCP
The London Clinic, London, UK

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Contributors

Josette André Department of Dermatology, St. Pierre–Brugmann and Children's University Hospitals, Université Libre de Bruxelles, Brussels, Belgium

Pierre André Paris Université Laser Skin Clinic, Paris, France

Raphael André Geneva University, Geneva, Switzerland

Nicolas Bachot Private Practice, Paris, France

Ashraf Badawi Laser Institute, Cairo University, Giza, Egypt; Szeged University, Szeged, Hungary; Laser Consultant, Toronto, Ontario, Canada; and European Society for Laser Dermatology, Strasbourg, France

Anthony V. Benedetto Department of Dermatology, Perelman School of Medicine, University of Pennsylvania; and Dermatologic SurgiCenter, Philadelphia, Pennsylvania

Thierry Besins Department of Plastic Surgery, Clinique St. George, Nice, France

Claire Beylot Department of Dermatology, Bordeaux University, Bordeaux, France

Philippe Blanchemaison Department of Vascular Medicine, University of Paris V, Paris, France

Pierre Bouhanna Hair Transplant Clinic, Paris, France

Geneviève Bourg-Heckly Laboratoire Jean Perrin, Université Pierre et Marie Curie–Paris, Paris, France

Lasse R. Braathen University degli Studi Guglielmo Marconi, Rome, Italy; and Dermatology Bern, Bern, Switzerland

Heike Buntrock Division of Cosmetic Science, Department of Chemistry, University of Hamburg, Hamburg, Germany

Valéria Campos Department of Dermatology, University of Mogi das Cruzes, Mogi das Cruzes, Brazil; and Department of Dermatology and Laser, University of Jundiai, Jundiai, Brazil

Hugues Cartier Centre Médical Saint-Jean, Saint-Jean, France

Tiago Castro Laser Division, Instituto Médico Vilafortuny, Cambrils, Spain

Isabelle Catoni Cabinet de Dermatologie Esthétique et Laser, Neuilly sur Seine, France

Olivier Claude Clinique Nescens Spontini, Paris, France

Julian Conejo-Mir Medical-Surgical Dermatology Department, Virgen del Rocio University Hospital, Sevilla, Spain

Maurice J. Dahdah Dermatology Department, American University of Beirut, Beirut, Lebanon

Karin de Vries Department of Dermatology, Erasmus University Medical Center, Rotterdam, The Netherlands

Henry Delmar Private Practice, Antibes, France

Philippe Deprez Clinica Hera, Empuriabrava, Spain

Christine Dierickx Laser and Skin Clinic, Boom, Belgium

Brian L. Diffey Dermatological Sciences, University of Newcastle, Newcastle, United Kingdom

Javier Dominguez Cruz Medical-Surgical Dermatology Department, Virgen del Rocio University Hospital, Sevilla, Spain

Zoe Diana Draelos Dermatology Consulting Services, PLLC, High Point, North Carolina

Philippe Evenou Private Practice, Paris, France

Jade Frucot Biotechnology Engineer

Claude Garde Centre de Sante de la Femme et du Sein, Paris, France

Alice Garzitto Division of Clinical, Preventive, and Oncologic Dermatology, Department of Surgery and Translational Medicine, Florence University, Florence, Italy

Ilaria Ghersetich Division of Clinical, Preventive, and Oncologic Dermatology, Department of Surgery and Translational Medicine, Florence University, Florence, Italy

David J. Goldberg Department of Dermatology, Icahn School of Medicine at Mt. Sinai Fordham Law School, New York, New York

An E. Goossens Department of Dermatology, Katholieke Universiteit Leuven, Leuven, Belgium

Uliana Gout Private Practice, London, United Kingdom

Tamara Griffiths Manchester Academic Health Science Centre, Dermatology Centre, The University of Manchester, Manchester, United Kingdom

Ewa Guigne Clinique Turin, Paris, France

Shlomit Halachmi Herzelia Dermatology and Laser Center, Herzelia Pituach, Israel

Philippe Hamida-Pisal Society of Mesotherapy of the United Kingdom; and Society of Mesotherapy of South-Africa, London, United Kingdom

Eckart Haneke Department of Dermatology, Inselspital, University of Bern, Bern, Switzerland; Dermatology Clinic Dermaticum, Freiburg, Germany; Centro Dermatology, CUF Porto Instituto, Porto, Portugal; Department of Dermatology, Ghent University, Ghent, Belgium

Trinh Hermanns-Lê Department of Dermatopathology, Liège University Hospital, Liège, Belgium

Philippe Humbert Department of Dermatology, Research and Studies Center on the Integument (CERT), Clinical Investigation Center (CIC BT506), Besançon University Hospital, Besançon, France; University of Franche-Comté, Besançon, France

Argyri Kapellari First Dermatology Department, University of Athens, Athens, Greece

Andreas Katsambas First Dermatology Department, University of Athens, Athens, Greece

Roland Kaufmann Department of Dermatology, Venereology and Allergology, Goethe-University Hospital, Frankfurt, Germany

Gürkan Kaya Department of Dermatology, University Hospital of Geneva, Geneva, Switzerland

Martina Kerscher Division of Cosmetic Science, Department of Chemistry, University of Hamburg, Hamburg, Germany

Philippe Kestemont Clinique Esthetique St. George, Nice, France

Nicolas Kluger Department of Dermatology and Allergology, University of Helsinki; and Helsinki University Hospital, Helsinki, Finland

Oliver Kreyden Dermatology and Venereology FMH, Kreyden Dermatology, Kreyden Hyperhidrosis, Kreyden Aesthetics, Praxis Methininserhof, Muttenz, Switzerland

Max Lafontan Max Lafontan Institute of Metabolic and Cardiovascular Diseases, National Institute of Health and Medical Research (Inserm), France; and Paul Sabatier University, Toulouse, France

Moshe Lapidoth Department of Dermatology, Rabin Medical Center, Petach Tikva, Israel; and Herzelia Dermatology and Laser Center, Herzelia Pituach, Israel

Franck Marie P. Leclère Department of Plastic Surgery, Gustave Roussy, Villejuif, France; and Department of Plastic Surgery and Hand Surgery, Inselspital, Bern University, Bern, Switzerland; and Lille University, Lille, France

Wendy Lewis Wendy Lewis & Co Ltd., New York, New York

Sophie Mac-Mary Skinexigence, Besançon, France

Alessandra Marini Institut für Umweltmedizinische Forschung, Leibniz Research Centre for Environmental Medicine at the Heinrich-Heine-University Düsseldorf, Düsseldorf, Germany

Leonardo Marini The Skin Doctors' Center, Trieste, Italy

Jean-Michel Mazer Centre Laser International de la Peau-Paris, Paris, France

Markus Meissner Department of Dermatology, Venereology and Allergology, Goethe-University Hospital, Frankfurt, Germany

Laurent Meunier Department of Dermatology, Hôpital Carémeau, CHU Nîmes, France; and Institute of Biomolecules Max Mousseron, University of Montpellier I, Montpellier, France

Marie-France Mihout Dermatologist and Psychiatrist, Dermatology Clinic, Hôpital Charles Nicolle, Rouen, France (retired)

Serge Morax Department of Ophthalmic Plastic Reconstructive Surgery, Rothschild Ophthalmic Foundation, Paris, France

Serge Mordon University of Lille, Inserm, CHU Lille, U1189 - ONCO-THAI - Image Assisted Laser Therapy for Oncology, Lille, France

Colin A. Morton Department of Dermatology, Stirling Community Hospital, Stirling, United Kingdom

Martino H.A. Neumann Department of Dermatology, Erasmus University Medical Center, Rotterdam, The Netherlands

Saib Norlazizi PulsarLab Ltd., Brynsiriol Pantlasau, Morriston Swansea, United Kingdom

Alexandre Ostojic Department of Dermatology, CHU Henri Mondor, University of Paris-Est, Creteil, France

Thierry Passeron Department of Dermatology & INSERM U1065, C3M, University Hospital of Nice, Nice, France

Michele Pelletier-Aouizérate European Led Academy; Aesthetic and Dermatology Laser Center, Toulon, France

José J. Pereyra-Rodriguez Medical-Surgical Dermatology Department, Virgen del Rocio University Hospital, Sevilla, Spain

Philippe Petit World Anti-Aging Mesotherapy Society, French and International Society of Mesotherapy, Bordeaux, France

Wolfgang G. Philipp-Dormston Hautzentrum Köln, Cologne, Germany

Gérald E. Piérard Department of Clinical Sciences, Liège University Hospital, Liège, Belgium; and Department of Dermatology, University of Franche-Comté, Besançon, France.

Claudine Piérard-Franchimont Department of Clinical Sciences, Liège University Liège, Belgium; and Department of Dermatopathology, Liège University Hospital, Liège, Belgium

A. Le Pillouer-Prost Dermatology Center, Le Grand Prado, Marseille, France

Hernán Pinto Aesthetic Specialties & Aging Research Institute (i2e3), Barcelona, Spain

Luiza Pitassi Department of Dermatology, University of Campinas São Paulo, São Paulo, Brazil

Daniela Pulcini Clinique Nescens Spontini, Paris, France

Albert-Adrien Ramelet Department of Dermatology, Inselspital, University of Bern, Bern, Switzerland

Evgeniya Ranneva Clinica Hera, Empuriabrava, Spain

Bertrand Richert Department of Dermatology, Brugmann–St. Pierre and Children's University Hospitals, Université Libre de Bruxelles, Brussels, Belgium

Panagiota Riga First Dermatology Department, University of Athens, Athens, Greece

Christopher M.E. Rowland Payne The London Clinic, London, United Kingdom

Nazanin Saedi Department of Dermatology and Cutaneous Biology, Thomas Jefferson University, Philadelphia, Pennsylvania

Jean-Marie Sainthillier Skinexigence, Besançon, France

Jose Santini Head and Neck Institute of Nice, Nice, France

Christel Scheers Department of Dermatology, Université Libre de Bruxelles, Brussels, Belgium

Klaus Sellheyer Department of Dermatology, Cleveland Clinic Foundation, Cleveland, Ohio

Konstantin Sulamanidze Private Practice, Tbilisi, Georgia

George Sulamanidze Private Practice, Tbilisi, Georgia

Marlen Sulamanidze Private Practice, Tbilisi, Georgia

Rolf-Markus Szeimies Department of Dermatology and Allergology, Klinikum Vest GmbH, Recklinghausen, Germany

Mario A. Trelles Department Plastic Surgery, Instituto Médico Vilafortuny, Cambrils, Spain

Lara Tripo Division of Clinical, Preventive, and Oncologic Dermatology, Department of Surgery and Translational Medicine, Florence University, Florence, Italy

Agneta Troilius Rubin Department of Dermatology, Centre for Laser & Vascular Anomalies, Skåne University Hospital, Jan Waldenströmsgatan, Sweden

Eva Maria Valesky Department of Dermatology, Venereology and Allergology, Goethe-University Hospital, Frankfurt, Germany

Renate R. van den Bos Department of Dermatology, Erasmus University Medical Center, Rotterdam, The Netherlands

Boris Vaynberg Venus Concept Ltd., Yokneam, Israel

Ines Verner Verner Clinic - Aesthetics, Lasers & Dermatology, Kiriat Ono, Israel

Martine Vigan University Hospital Jean Minjoz Besançon, Besançon, France

Krystle Wang The Menkes Clinic & Surgery Center, Mountain View, California

Uwe Wollina Department of Dermatology and Allergology, Hospital Dresden-Friedrichstadt, Academic Teaching Hospital of the Technical University of Dresden, Dresden, Germany

Sabine Zenker Dermatology Surgery Clinic Munich, Munich, Germany

PART I

Fundamental Aspects

What is beauty? A historical excursus through a continuously evolving subjective and objective perception

Eckart Haneke

The striving for beauty is as old as the history of mankind. In earlier days, beauty meant leading a healthy life and begetting offspring. Although the meaning of perception of beauty has changed with time, beauty is still an ideal for an important proportion of the world's population. However, the following questions remain: "What is beauty; can it be defined; is it subjective or objective; are there measurable criteria?"

An old saying claims that "beauty is in the eye of the beholder." The origins of this saying can be traced back to the third century BC in Greece, but its current form appeared in the nineteenth century. The literal meaning is that the perception of beauty is subjective. David Hume in *Essays, Moral, Political, and Literary*, 1742, wrote, "Beauty in things exists merely in the mind which contemplates them" [1]. There are endless more meanings and definitions of beauty, which have varied across time, civilizations, religions, and cultures.

Does personal taste actually and really determine beauty? Is beauty just a matter of taste, what you like, or what pleases you, or does it possess more objective qualities? Thomas Dubay [2] defines beauty in line with science: "The beautiful is that which has unity, harmony, proportion, wholeness, and radiance." Plato described the opposite of beauty as the unpleasantness of seeing a body with one excessively long leg. A disproportionate, asymmetrical person lacks harmony and proportion.

Does beauty have a *moral* component? Persons of great personal beauty should not merely be admired based on their form but also on their substance. Personal beauty extends well beyond possessing physical symmetry. Dubay claims that beauty *is* moral. It is a virtue, an image of goodness as well as an image of proportion. "You can recognize truth by its beauty and simplicity" (Richard Feynman, Nobel laureate in physics). A beautiful performance necessitates honesty, integrity, and no cheating. Even a dishonest person appreciates honesty, but appreciation of morality does not require cultivation of morals. However, just because we can recognize the moral component of beauty does not mean that we are, in fact, beautiful [2]. In ancient Greece, this concept of *kalokagathia*, the ideal of the beautiful and good and the unity of physical beauty and moral value, was developed and became important in the civilization of the Middle Ages [3].

Socrates was said to have asked the sophist Hippias of Elis: "What is beauty?" Hippias replied: "Beauty is a pretty girl, beauty is gold; and beauty is to be rich and respected." Socrates was disappointed and said, "They are beautiful, but you do not know what beauty is!" Socrates' answer was "It is not a question of knowing what is beautiful and what is not, but rather to define beauty and to say what makes beautiful things *beautiful*." His three answers were beauty is that which is appropriate, which is useful, and which is favorable, and he added a fourth definition: beauty is the pleasure that comes from seeing and hearing. What was Hippias' mistake? He did not understand the difference between a beautiful object and beauty as a category.

Is beauty really in the eyes of the beholder? This saying reflects what a certain subject *finds* beautiful, but this is no definition of beauty.

Generations of professionals have repeated this assumption, from fashion tsars to beauticians to cosmetic surgeons and particularly the consumer. In Latin, "*de gustibus non est disputandum*" meant you cannot dispute about taste. What is assumed as beauty has a lot to do with taste. And taste is, of course, extremely subjective and varies from person to person.

How should beauty be defined? In the eye of the beholder? Scientifically? Morally? Why? A popular encyclopedia defines the saying in the way that individuals have different inclinations on what is beautiful and that they have different beauty standards [4].

Socrates' question was not what beautiful is, but what *beauty* is. What makes something or somebody that we call beautiful really beautiful? It is *the beauty behind* it.

The German cosmetics producer Nivea performed a survey all over the world: "What do women believe beauty is?" The answers were very ambiguous. First, the interviewers found out what women *find* beautiful. However, despite all cultural, ethnic, and religious differences, the *archetype of a beautiful woman* is universal: not too tall, and having a symmetrical face, smooth skin, shiny long hair, large eyes, and white teeth. This has been confirmed with facial primes in large cohorts [5,6]. Smooth skin is also a relevant factor for hand attractiveness [7]. The value of *beauty* for the industry is enormous: the overall sales of the beauty industry were $330 billion in 2010 [8].

Studies by researchers from cultural, behavioral, and cognitive sciences confirmed the pattern of a general sense of beauty [9]. Brain researchers found cerebral regions associated with the recognition of beauty [10]. These aesthetic centers start being activated when one recognizes symmetry and order [11]. The brain has neurons exclusively reacting to order. Infants just a few days old look longer at beautiful faces. It takes our brain only 1/7 of a second (150 milliseconds) to distinguish between ugly and beautiful. Attractive face recognition is a fast process [12,13]. Handsome men and beautiful women generally have better chances in professional life. Attractive faces are immediately held to be more trustworthy [14], probably due to a shared brain activity for aesthetic and moral judgments [15]. Persons with a cerebral insult in a certain cortical region lose the ability to recognize

a face while still retaining the ability recognize a person by his or her voice or gait. They can also evaluate whether a face is attractive or not.

Research suggests that we view our loved ones through rose-tinted glasses that overlook the crooked noses, bulging tummies, or other attributes that might put others off. This again is in line with the notion of beauty being an advantage in daily life. Aristotle said: "Beauty is a greater recommendation than any letter of introduction." "The three wishes of every man: to be healthy, to be rich by honest means, and to be beautiful" is ascribed to Plato.

On the other hand, beauty was shown to hinder attention switch [16,17].

We can ask again: What is beauty? Is *beauty* really *in the eyes of the beholder*? Whereas almost everybody believes to know what it is, hardly anybody can define beauty.

Researchers have found universal biological aspects of beauty, which may be influenced by culture and historical developments [18,19]. In the 1930s, the American mathematician George David Birkhoff proposed a formula to measure beauty [20]:

$$M = \frac{O}{C}$$

where
M is the aesthetic measure
O is the order
C is the complexity

In case of visual arts, order O depends on geometrical relations among identifiable segments of an evaluated object (e.g., curves or planes). Attributes such as symmetry and balance are considered to be relevant for an intense aesthetic perception. Complexity C is "the number of localities our sight will spontaneously rest on." Complexity negatively affects overall aesthetic measure since complex objects tend to deflect an onlooker's contemplation. Order was refined in more detail in a study of ancient Chinese vases [21]:

$$M = \frac{H + V + P + T}{C}$$

where
- H represents the horizontal order, defined by the number of independent relations of ratios 1:1 and 2:1 within pairs of horizontal distances $hi;hj$ between symmetrical characteristic points, $H \leq 4$.
- V stands for the vertical order, defined by the number of independent relations of ratios 1:1 and 2:1 within pairs of adjacent vertical distances $v_i;v_j$ between characteristic points, $V \leq 4$.
- P stands for the proportional order defined by the number of independent relations of ratios 1:1 and 2:1 within pairs of horizontal and adjacent vertical distances $h_i;v_j$ between characteristic points, $P \leq 2$.
- T represents the tangent order and is defined by the number of the following independent relations $T \leq 4$: Perpendicularity of characteristic tangents, parallelism of nonvertical characteristic tangents, verticality of a characteristic tangent at the terminal or inflex points, and intersection of a characteristic tangent or its normal with the vase center are components of a tangent order.

This formula was intended to aesthetically measure nonliving objects. It wonderfully describes a classical violin. One of the marvels of medieval architecture, the Taj Mahal, or the medieval cathedrals, both romanic and gothic, perfectly fit into the extended aesthetic measure. But is it really restricted to nonliving objects? As shown in the worldwide survey, symmetry and proportion are also valued in persons. Classical sculptures stand out by their proportion; distorting one part is immediately recognized as disturbing. A proportionate sculpture activates the insular cortex; a distorted does not.

If beauty of living individuals cannot clearly be defined, can it at least be differentiated from other positive feelings? Aesthetic, attractiveness, and beauty are often used interchangeably. The question is whether this is correct or not. Whereas beauty, to a large extent and for certain objects, can be measured with the mathematical formula, it is an objective category and does not depend on time and fashion, whereas attractiveness is a personal feeling. It is part of social affinity and the basis of individual communication [22]. In intergender relations, sex appeal is part of this attractiveness. No one will deny that some persons are attractive to one and unattractive to another person.

Is there a sense for beauty in nature? In the Middle Ages, there was a golden rectangle, the particularity of which is when a square is removed, another golden rectangle remains. Its sides are $1 : ([1 + \sqrt{5}] / 2)$, which is $1 + \varphi$ with phi being about 1.618.

In nature, the golden angle exists. Mathematically, it is defined as

$$\frac{a+b}{a} = \frac{a}{b}$$

The golden angle is then the angle subtended by the smaller arc of length b. It measures approximately 137.508° [23]. The golden angle plays a significant role in the theory of phyllotaxis. Most notably, the golden angle is the angle separating the florets on a sunflower [24].

The seeds of the sunflower are arranged in spirals. This is governed by nature. The arrangement of the seeds repeats after every 137.5°, the "golden angle." The full circle of 360° is divided in relation to the "golden section."

In the animal kingdom, males are usually the more beautiful because they have to court the female in order to mate and beget offspring. In mankind, females are called the "beautiful gender" and a man's physical beauty is often replaced by his thick wallet. This is a biological fact: wealthy men can better guarantee a good future for the offspring. In couples where the man is rich, the first child is usually his, whereas the next may come from physically more attractive men.

Test series with male faces and hands showed the same ideals for both genders. Whereas in ancient Hellas, a boy was considered to be a beautiful person, this has now changed as we consider women to be more beautiful. The universal standard of a beautiful woman was already mentioned. But there is much more in the mind of both men and women. When seeing a physically good-looking woman, we may consider her a warm and touching beauty that (almost) everybody would like; a "hot" beauty is more seen as a sexually attractive being, whereas a "cold" beauty may be perfect like a classical statue but without personal radiance.

Color is an important part for perceiving beauty. Red apparently has a particular attraction; in many ethnies, red stands for warm, vivid, and stimulating. In eastern slawic and

Yamomi Indian languages, as well as in some Arabic dialects, red and beautiful/good are the same words, or they have the same origins for the word. In some languages, the words for beauty are also synonyms for balance and symmetry.

However, beauty is not only visual. As found out by researchers, palpation of a smooth skin can also arouse the same feelings as seeing a beautiful object. There is no doubt that acoustic beauty exists. In Bach's organ music, one can find harmony and order.

Olfactory beauty is realized with some classic perfumes or the smell of particular fruits. This is closely linked with taste. Gustatory beauty may also exist, for instance, in a delicious meal, even though we do not speak of food or a drink having a "beautiful taste."

CONCLUSION

"Beauty is in the eyes of the beholder" is not correct—what you *find beautiful* is in your eyes or, better, in *your mind*. There is a universal sense of beauty; however, the differentiation between beauty, aesthetics, and attractiveness is somewhat arbitrary.

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Body dysmorphic disorder

Marie-France Mihout

Body dysmorphic disorder (BDD) is a mental disorder in which the affected person is excessively concerned and preoccupied by a perceived defect in his or her physical features. They are convinced of having visible defects, although most of the time these are nonexistent or only of minor importance. The sufferers may complain of several specific features or one single feature of their general appearance. They waste much time in front of the mirror in looking at themselves inquiringly; the pathologic threshold seems to be more than 1 hour per day, causing psychological distress that impairs occupational and/or social functioning, sometimes to the point of severe depression, severe anxiety, the development of other anxiety disorders, social withdrawal or complete social isolation, and more.

Repeated visits to surgeons or dermatologists in an attempt to correct the defect are common; most of the time, the defect is grossly exaggerated.

It is estimated that 1%–2% of the world's population meets all the diagnostic criteria for BDD. The "dysmorphophobia" is a real phobia: a morbid fear, like others' phobias about snakes or spiders; these persons are convinced of having visible defects and are afraid of their appearance and the way other people look at them. To summarize, this is imaginary ugliness.

BDD is defined by the DSM-IV-TR and is assigned to the larger category of somatoform disorders 1994 (Appendix 4) [1], which are disorders characterized by physical complaints that appear to be medical in origin but that cannot be explained in terms of a physical disease, the result of substance abuse, or another mental disorder (normally without delusion, although it can occur).

The disorder can be seen in earlier literature [2], but the earliest known case of BDD in the medical literature was reported by an Italian physician, Enrique Morselli, in 1891; the disorder was not defined as a formal diagnostic category until the introduction of DSM-III-R in 1987. The World Health Organization did not add BDD to the International Classification of Diseases until 1992. The word "dysmorphic" comes from two Greek words that mean "bad" or "ugly" and "shape" or "form"; BDD was previously known as dysmorphobia [3].

EPIDEMIOLOGY

The usual age of onset is late childhood or early adulthood. In 75% of the cases, troubles will persist. The average age of patients diagnosed with the disorder is 17, but the disorder can remain undiagnosed for a long period. In addition, patients are so often ashamed of grooming rituals and other associated behaviors that they may avoid telling their doctor about them. They are more likely to consult an esthetic surgeon or dermatologist [4]. As many as 50% of patients diagnosed with BDD undergo plastic surgery.

The sex ratio seems to be like that of obsessive compulsive disorder (OCD)/BDD and is often misunderstood to affect mostly women, but research shows that it affects men and women equally, unlike the anxiety disorders whose sex ratio is 2:1 female/male. The DSM-IV-TR classification added references to concern about bodybuilding and excessive weight lifting to DSM-IV's description of BDD, in order to cover "muscle dysmorphia," which mainly affects men.

Causes

The causes of BDD fall into many categories.

Neuropsychological Causes

The problem of body image has to be considered all the way from the purely sensory origin of the perception of the body based on the senses to the more abstract concept of a body schema. Furthermore, the patient's own experiments at manipulating the body schema into the perceived body image become a component of the sense of the self.

It is important to point out that the body schema is broadly the same for any human, but body image is particular to each individual, because it is intimately acquainted with the patient's own story [5], representing the total concept, including conscious and unconscious feelings, thoughts, and perceptions that a person has of his or her own body as an object in space independent and apart from other objects. The body image develops during infancy and childhood from exploration of his or her body surface and orifices (sucking, biting, touching) from the development of physical abilities and from play and comparison of the self with others. Body image is strongly influenced by parental attitudes that give the child a perception of certain body parts as good, clean, and attractive or bad, dirty, and repulsive.

Psychoanalytic Approach

The "Skin-Ego" is a psychoanalytic concept by Anzieu, heir to the Freudian ego (it is, strictly speaking, a fantasy—even according to the author, "a huge metaphor" [6]). For Anzieu, the skin supplies the psychic inner mind with constituent perceptions of oneself [8]. He allocates psychic duties to the skin as follows:

Heaving
Containing protective shield
Developing a personality of one's own intersensorial ability and sexual arousal support
Recharging one's libido-registered sensorial and emotional contents—self-destruction (self–nonself)

The concept of one's body image is more a function of the quality of libidinal "cathexis" than of reality. On one hand, there is the real objective anatomy, while on the other hand the

wished-for anatomy. The mother's role is to mold all the things that have been lived through, feelings and so on. In that way, in some cases, when "organ pleasure identification" fails in the early maternal exchanges, the baby's "affects," those that persist in life, become one experience of mental suffering.

Neurobiological Causes

In neurological and embryological development, brain and skin are formed very early in the development of the embryo from the ectoderm.

Research indicates that patients diagnosed with BDD have serotonin levels that are lower than normal. Serotonin is a neurotransmitter (a chemical produced by the brain that aids in transmitting nerve impulses across the junctions between nerve cells). Low serotonin levels are associated with depression and other mood disorders.

Psychosocial Causes

Another important factor in the development of BDD is the influence of the mass media in developed countries, particularly the role of advertising in spreading images of physically "perfect men and women." Impressionable children and adolescents absorb the message that anything short of physical perfection is unacceptable. They may then develop distorted perceptions of their own faces and bodies [7].

Body Dysmorphic Disorder Has a High Rate of Comorbidity

The prevalence of BDD in psychiatry has been calculated to be about 13%, although some doctors think that it is underdiagnosed because it coexists so often with other psychiatric disorders [8], which means that people diagnosed with the disorders are highly likely to have been diagnosed with another psychiatric disorder [9,10].

Most other commonly associated psychiatric disorders are

- Major depression (about 29% of patients with BDD eventually try to commit suicide)
- OCDs and trichotillomania
- Social phobia
- Drug addiction
- Psychiatric hospitalization (the prevalence is 13%)
- Anorexia nervosa
- Olfactory reference syndrome

And there are many esthetic consequences:

- Incorrectly performed surgery (when disappointed, the patient's condition can become worse)
- Medical nomadism to find a practitioner who will agree to their requests
- Frequent requests for repeated or unnecessary procedures, with discontent with the result

BDD must be evaluated for severity in advance of any treatment [7,11].

Detection

BDD Modification of the Yale Brown Obsessive Compulsive Scale

The *Yale Brown Obsessive Compulsive Scale Modified for BDDs* is a 12-item semistructured clinician-rated instrument designed to rate the severity of BDD [9]. Its purpose is to produce a quick and reliable evaluation of the severity of the illness and to evaluate the threshold of the patient's consciousness of the illness in order to give the appropriate treatment. For each item, the clinician circles the number identifying the response that best characterizes the patient during the previous week.

The scale is a tool for diagnosis to rate the severity of the condition and to give a prognosis for its evolution; it can also be repeated in the course of treatment to reevaluate the severity and prognosis of the condition.

Clinical Aspects

Looking questioningly at the mirror is a compulsive and repetitive activity, reported in 80% of patients. This is a kind of ritualistic behavior performed to manage anxiety, and that takes up excessive amounts of the patient's time; patients are typically upset if someone or something interferes with or interrupts their ritual.

Camouflaging the "problem" feature or body part with makeup, hats, or clothing appears to be the single most common symptom among patients with BDD. (It is reported in 94% of patients [12].)

Treatment

Patients with BDD have in about 40% of cases good self-insight, 20% low self-insight, and 40% bad or no self-insight.

How can the clinician help them? These patients have an incorrect "insight." They are vulnerable because they believe that others are always right. How can they get close to beauty when they think they do not possess it?

Beauty should be fully understood, all things considered, as an emotional reaction. Beauty often easily emerges from ordinary relationships with the others and the world.

These patients need to learn again to live serenely with their body, and one has to make them admit that it is their self-representation that is called into question and not reality. They need to learn to use time and hope.

Primary aims in the consultation are as follows:

- Recognize the patient's suffering.
- Do not discuss the reality of the defect.
- Recognize the strength of the patient's anxious preoccupations.
- Engage with the patient and determine with him or her which treatment could improve the condition.
- Wait for any correction to take place.
- See if the demand for change to their appearance continues.

The standard course of treatment of BDD is a combination of medication and psychotherapy.

In some individuals, the clinician must ensure that the somatic preoccupation is not part of another psychiatric disorder such as anorexia nervosa or gender identity disorder.

When the trouble is severe and there is an "unshakeable conviction" (delusion), the main work will be to bring patients round to consulting a psychiatrist, which can sometimes be very difficult. Unshakeable convictions may reveal borderline or even psychotic personality.

In the case of associated depression, the physician has to be careful about underrating the effect of bad mood, sleep, appetite, tiredness, and so on.

The medications most frequently prescribed for patients with BDD are most commonly the selective serotonin reuptake inhibitors (SSRIs [11]):

- *Fluoxetine* and *sertraline* can reduce sleep.
- *Paroxetine* reduces anxiety.

In fact, it is the relatively high rate of positive responses to SSRIs among BDDs that has led to the hypothesis that disorder has a neurobiological component related to serotonin levels in the body. An associated finding is that patients with BDD require higher dosages of SSRI medications than patients who are being treated for depression with the drugs, which would also explain why OCDs are associated.

The use of neuroleptic drugs in patients with borderline psychosis is disappointing and very ineffective.

The most effective approach to psychotherapy with BDD is cognitive behavioral restructuring.

Cognitive-oriented therapy that challenges inaccurate self-perceptions is more effective than purely supportive approaches. Techniques to stop thoughts and encourage relaxation also work well with BDD patients when they are combined with cognitive restructuring [12].

Some doctors recommend couples therapy or family therapy in order to involve the patient's parents, spouse, or partner in his or her treatment. This approach may be particularly helpful if family members are critical of the patient's looks or are reinforcing his or her unrealistic body image.

In complementary therapies, yoga has helped some persons with BDD acquire more realistic perceptions of their bodies and to replace obsessions about external appearance with new respect for their body's inner structure and functioning.

PROGNOSIS

The prognosis of BDD is considered good for patients receiving appropriate treatment. On the other hand, researchers do not know enough about the lifetime course of BDD to be able to offer detailed statistics.

PREVENTION

Parents, teachers, primary health-care professionals, and other adults who work with young people can point and discuss the pitfalls of trying to look "perfect." In addition, parents or the other adults can educate themselves about BDD and its symptoms and pay attention to any warning signs in their children's dress or behavior.

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Pathophysiology of skin aging

Laurent Meunier

INTRODUCTION

Skin aging is a complex process determined by genetic factors (intrinsic aging) and cumulative exposure to external factors such as ultraviolet radiation (UVR), smoking, and particle pollution (extrinsic aging) [1–4]. The fine wrinkles and reduced elasticity, which characterize intrinsically aged skin, are exaggerated in photoaged skin, where exposure to UVR is associated with the development of both deep wrinkles and a marked loss of elasticity. Photoaging, like chronological aging, is a cumulative process that depends primarily on the degree of sun exposure and skin pigment. Individuals who have outdoor lifestyles, live in sunny climates, and are lightly pigmented will experience the greatest degree of photoaging [5].

STRUCTURAL AND FUNCTIONAL CHANGES

Major structural and functional changes occur in the dermal extracellular matrix (ECM) where fibrillar collagens, elastic fibers, and proteoglycans are required to confer tensile strength, resilience, and hydration, respectively. The extreme longevity of these biomolecules, compared with intracellular proteins, promotes the accumulation of damage over time, which in turn impacts on their ability to mediate tissue homeostasis [1]. Skin function is mediated primarily by the structure of the epidermal and dermal layers. The two layers are joined by the dermal–epidermal junction (DEJ) in which basal epidermal keratinocytes are secured to a type IV collagen-rich basement membrane (BM) by hemidesmosomes, and the dermis is anchored by collagen VII fibrils and fibrillin-rich microfibril bundles. The disruption of BM at the DEJ in sun-exposed skin may be induced by increased levels of BM-damaging enzymes, such as plasmin and matrix metalloproteinases (MMPs). The impairment of BM structure may be associated with functional changes of epidermal cells and dermal cells and consequently facilitates aging processes by damaging dermal ECM and inducing abnormal keratinocyte responses [6]. Collagens I and III are the most abundant proteins in the dermis and are preferentially distributed in the papillary and deep reticular dermis. Collagen VII is localized to perpendicularly oriented anchoring fibrils that play a key role in securing the dermis to the DEJ. Elastic fibers are composed of multiple components, including cross-linked elastin, fibrillin-rich microfibrils, microfibril-associated glycoproteins, fibulins, and latent transforming growth factor (TGF)-binding proteins. Many ECM proteins are glycoproteins, which have undergone posttranslational modification with numerous oligosaccharides. In contrast, proteoglycans are glycoproteins, in which at least one of the oligosaccharide side chains is a glycosaminoglycan (GAG). Glycoproteins and proteoglycans are distributed throughout the dermis where they play a key role in maintaining skin hydration [1].

In intrinsically aged skin, there is evidence not only for the degradation of fibrous ECM components, including elastin, oxytalan fibers, and collagens I, III, and IV, but also for the loss of the oligosaccharide fraction, which in turn impacts on the ability of skin to retain bound water. Reduced production of type I procollagen is a prominent feature of chronologically aged human skin. Recent findings indicate that downregulation of the TGF-β/Smad/connective tissue growth factor axis likely mediates reduced type I procollagen expression in aged human skin [7].

In severely photoaged skin, there is a loss of not only fibrillar collagens (I and III) throughout the dermis but also the loss of collagen VII anchoring fibrils at the DEJ. In contrast, dermal GAG content, in particular hyaluronic acid (HA) and the chondroitin sulphate–containing GAGs, is increased and redistributed to colocalize with the elastic fiber network [1]. HA is an abundant component of skin ECM matrix, where it plays many roles such as hydration and architectural support. Downregulation of HA during photoaging may be due to regulation of hyaluronidase activity induced by UVB exposure [8]. During the early stages of photoaging, both fibrillin-1 and fibulin-5 are lost from the microfibrillar apparatus (oxytalan fibers) at the DEJ. In severely photoaged skin, however, the reticular dermis is characterized by the distribution of abundant, apparently disorganized elastic fiber proteins including tropoelastin, fibrillin-1, fibulin-2 and fibulin-5, and latent TGF-beta binding protein-1 (LTBP-1) [1].

In contrast to intracellular proteins, whose half-lives are measured in hours or days, many ECM proteins have half-lives that are measured in years. This remarkable longevity is thought to predispose them to the risk of molecular aging. In addition, elastin synthesis and deposition is predominantly confined to fetal and early postnatal skin. Thus, elastic fiber proteins are required to function for many years and may be at risk of accumulating damage.

Although the fundamental mechanisms in the pathogenesis of aged skin are still poorly understood, a growing body of evidence points toward the involvement of multiple pathways.

BIOLOGICAL PROCESS OF SKIN AGING

Recent data indicate that the most important biologic processes involved in skin aging are alterations in DNA repair and stability, mitochondrial function, cell cycle and apoptosis, ECM, lipid synthesis, ubiquitin-induced proteolysis, and cellular metabolism. Among others, a major factor that has been implicated in the initiation of aging is the physiologic decline of hormones occurring with age [9].

Matrix Metalloproteinases

Most studies of photoaging have focused on the upregulation and activation of ECM-degrading MMPs [10]. Elevated MMPs in photodamaged dermis can be divided into following groups: collagenases, MMP-1; gelatinases, MMP-2; stromelysins, MMP-3, MMP-9, and MMP-11; membrane-associated, MMP-17 and the recently identified MMP-27 [1].

Among the 18 MMPs expressed in human skin, 7 are significantly elevated in a photodamaged forearm, compared with sun-protected underarm skin, and all MMPs that are elevated in photodamaged skin, except MMP-3, are primarily expressed in the dermis [11].

MMP-1, MMP-3, and MMP-9 are primary UV-inducible collagenolytic enzymes, and MMP-1 is the major protease capable of initiating degradation of native fibrillar collagens in human skin *in vivo* [10,12]. Epidermal keratinocytes are the major cellular source of UV-induced MMPs. However, dermal cells may also play a role in epidermal production of MMPs by release of growth factors or cytokines, which in turn modulate MMP production by epidermal keratinocytes [10]. Interstitial collagenase (MMP-1) initiates the degradation of type I and III fibrillar collagens, and then further degradation is followed by MMP-3 (stromelysin-1) and MMP-9 (gelatinase B) action.

Increased expression of MMP-1 and reduced production of type I collagen by dermal fibroblasts are prominent features of aged human skin. MMP-1-mediated fragmentation of dermal collagen fibrils alters the function of dermal fibroblasts and may be a key driver of age-related decline of skin function [13–16]. With aging, collagen fragmentation reduces fibroblast-ECM binding and mechanical forces, resulting in fibroblast shrinkage and reduced collagen production. Injection of dermal filler, cross-linked HA, into the skin of individuals over 70 years of age stimulates fibroblasts to produce type I collagen and results in an increase in mechanical forces, which also stimulates fibroblast proliferation, expands vasculature, and increases epidermal thickness [17]. *In vitro* collagen fragmentation recreates many of the abnormalities seen in photodamage *in vivo* [11]. These data indicate that fragmentation of the collagenous ECM in photodamaged dermis alters collagen homeostasis by influencing the function of dermal fibroblasts and indicate that fibroblasts in aged human skin retain their capacity for functional activation, which is restored by enhancing structural support of the ECM. Mechanisms by which ECM microenvironment in photodamaged human skin control fibroblast function are not well understood. Fragmented collagen in photodamaged skin may impair integrin signaling events and induce transcription factors such as activator protein-1 (AP-1), which contributes to elevated MMPs and loss of type I collagen expression [11]. Indeed, activated AP-1 binds to the promoter region of the procollagen gene to inhibit its transcription and also activates the MMP gene enzymes that degrade collagen. The matricellular protein cysteine-rich protein 61 (CCN1), a member of the CCN family, is elevated in replicative senescent dermal fibroblasts and in dermal fibroblasts from UV-exposed skin. This protein may mediate MMP-1-induced alterations of collagen fibrils and may promote cutaneous aging and collagen loss via induction of IL-1beta, inhibition of type I collagen production, and upregulation of MMP-1 [18,19].

Aberrant remodelling of the elastic fiber system is likely to have profound cellular and biochemical effects. In particular, elastin fragments appear to exert an influence on the immune system, upregulate elastase expression, and promote apoptosis. Elastin and fibrillin peptides may induce the expression of several MMPs that have the potential to degrade most major dermal ECM. The fibrillin microfibril may also be degraded by direct UV exposure, and the results of this damage may impact not only the mechanical but also the biochemical functions of the tissue by activating lymphocytes, inducing the expression of proteases, and profoundly influencing TGF-β signalling [1]. Among all four known tissue inhibitor of metalloproteinases (TIMP) genes (TIMP-1, TIMP-2, TIMP-3, and TIMP-4) that are expressed in human dermis, none is preferentially expressed in sun-exposed skin. However, overexpression of TIMP-1 in a human skin xenograft photodamage model resulted in significant inhibition of ECM degradation, as well as suppression of decreased skin elasticity and roughness [20].

Reactive Oxygen Species, Mitochondrial DNA, and Telomere Shortening

Mitochondrial DNA (mtDNA) damage, increased reactive oxygen species (ROS) production, and telomere shortening are thought to play a role in the intrinsic aging process. In contrast, the mechanisms leading to photoaging of the skin are caused mainly by the repetitive adsorption of UVR, which can upregulate the expression of ECM proteases via AP-1 signalling. In addition, UVR can directly damage cutaneous biomolecules, which are rich in chromophores, and may induce the production of ROS, which in turn can act on both cells and matrix components. Free radical damage on the skin by chronic ROS and UV stress plays a major role in photoaging. After UV exposure, ROS trigger the release of proinflammatory cytokines and growth factors (AP-1 and NF-kB), which upregulate key MMPs such as MMP-1, MMP-3, MMP-8, and MMP-9. These proteases degrade the collagen and elastin fibers of the ECM. MMP-1 expression is associated with the presence of mtDNA common deletion, and UV-induced ROS have been shown to decrease TGF-β expression, which decreases collagen production and enhances elastin production. Hence, ROS degrade the structural integrity of skin by way of altering the collagen and elastin components of the ECM.

Mutations of mtDNA such as the 4977 base-pair large-scale deletion, also called common deletion, are increased in photoaged skin, and these mutations seem to represent long-term *in vivo* biomarkers for actinic damage in the human skin [21]. Gradual depletion of mtDNA in human skin fibroblast causes a gene expression profile, which is reminiscent of that observed in photoaged skin [22].

The mitochondrial–free radical theory of aging proposes that aging is caused by damage to macromolecules by mitochondrial ROS that may induce mutations in mtDNA, which in turn leads through a vicious circle to further ROS generation. Elevated ROS levels can cause cumulative damage to various cellular molecules, like proteins, lipids, and nucleic acids, and contribute to a decrease in physiological functions with age. Alternatively, ROS may be associated with aging because they play a role in mediating a stress response to age-dependent damage [23]. Anyway, the extent of age-related mitochondrial dysfunction may vary between different tissues and the mitochondrial oxidative stress theory of aging, and its role for human aging remains to be fully understood.

The accumulation of altered proteins within cells, which is one of the most common symptoms of aging, may be due to decreased elimination of oxidized proteins. The ubiquitin–proteasome pathway is implicated in the degradation of oxidized

proteins [24–26] and plays a major role in signal transduction associated with stress and aging [27–29]. In most cases, proteasome activity was reported to decrease with aging, and functional interplay has been described between mitochondrial and proteasome activity in skin aging [30].

Telomeres are specialized DNA structures at the chromosome ends that undergo progressive shortening unless they are elongated by a ribonucleoprotein named telomerase. In somatic cells lacking telomerase, gradual telomere loss and ultimate senescence are inevitable, and consistent with this model, there is a strong association between cell immortalization and persistent telomerase expression. Progressive telomere loss may be responsible for p53 activation and progerin production during cellular senescence [31]. Furthermore, telomerase reactivation reverses tissue degeneration in aged telomerase-deficient mice [32].

Recent data suggest that photoaging may be at least in part a process of damage-accelerated intrinsic aging [33]. Indeed, progerin accumulation, which has been described not only in Hutchinson–Gilford progeria syndrome but also during normal intrinsic aging, may be accelerated by UVA-induced ROS [34].

Although intrinsic aging is accompanied by a decline in DNA repair activities attributed to both base excision repair and nucleotide excision repair [35], chronic sun exposure also induced changes in DNA repair activities [36]. These defects could be partly responsible for nuclear and mitochondrial genomic defects in senescent cells.

Neutrophils and Mast Cells

Neutrophils, which infiltrate sunburned skin, are capable of degrading elastic fibers and collagen fibers, and neutrophil-derived proteolytic enzymes are probably important players in the pathophysiology of photoaging [37,38]. The number of mast cells in sun-exposed skin is higher than in nonexposed skin, and UV exposure leads to increased mast cell numbers and tryptase expression in human skin [39]. The activation of mast cells by UV irradiation may participate in wrinkle formation, ECM proteins modification, and inflammation in UV-exposed skin. Indeed, the mast cell stabilizer ketotifen prevents wrinkle formation in mice chronically exposed to UV irradiation [40].

Aging and Genomic Analysis

Molecular mechanisms involved in aging or photoaging are still poorly understood at the level of global gene expression. Transcriptome analysis of sun-exposed skin suggests that disruption of cutaneous homeostasis and downregulation of skin metabolism may play important roles in the process of photoaging [41]. A recent genome-wide association study in middle-aged Caucasian women pointed out a putative role of STXBP5L and FBX040 genes in facial photoaging [42]. Genetic variations of melanocortin-1 receptor (MC1R) seem to be important determinants for severe photoaging [43], and constitutive activity of the wild-type MC1R in keratinocytes may reduce UVA-induced oxidative stress [44].

Infrared and Visible Radiations

At least 50% of the total energy that is being emitted by the sun and that reaches human skin is in the infrared (IR) range. In addition, within the IR range, IRA rays (770–1400 nm), which represent one-third of the total solar energy, are capable of penetrating human skin and directly affecting cells located in the epidermis, dermis, and subcutis. More than 65% of IRA reaches the dermis, and there is now increasing evidence that IRA, similar to UVB or UVA, significantly contributes to photoaging of human skin [45,46]. Recent work demonstrates that IR and heat exposure each induces cutaneous angiogenesis and inflammatory cellular infiltration, disrupts the dermal ECM by inducing MMPs, and alters dermal structural proteins [47]. The recent analysis of IRA-induced transcriptome in primary human skin fibroblasts identifies IRA as an environmental factor with relevance for skin homeostasis and photoaging [48]. Repetitive IRA irradiation produces significant wrinkle formation in hairless mice [49]. Exposure of human skin fibroblasts *in vitro* [50] and human skin *in vivo* [51] to physiologically relevant doses of IRA causes an increase in MMP-1 without a concomitant upregulation of TIMP-1 expression. IRA exposure also reduces type 1 collagen expression, possibly by reducing the production of procollagen-1-stimulating TGF-β1, TGF-β-2, and TGF-β-3 expression in human skin [52].

The underlying mechanisms responsible for UVB-, UVA-, and IRA-induced MMP-1 expression markedly differ. The major chromophores for UVB appear to be nuclear DNA and cytoplasmic-free tryptophan, whereas the UVA stress response is controlled by the lipid composition of specialized membrane microdomains (rafts) [53]. IRA radiation is strongest absorbed by mitochondria, and the earliest biological event following IRA irradiation of human skin fibroblasts is an increase in mitochondrial production of ROS [54]. Such ROS activate mitogen-activated protein kinase (MAPK) and cause increased transcriptional expression of MMP-1 in the nucleus [55]. IRA exposure induces similar biological effects to UV radiation, but the underlying mechanisms are substantially different since the cellular response to IRA irradiation mostly involves the mitochondrial electron transport chain. Mitochondrial ROS production due to UVA and IRA may trigger retrograde signalling pathways that alter gene expression in fibroblasts in a way that disturbs collagen metabolism and induces neovascularization and that may also be responsible for other features of photoaged skin, for example, the development of an inflammatory infiltrate (dermatoheliosis) [55,56]. Thus, effective sun protection may require specific strategies to prevent IRA-induced skin damage, and mitochondrial-targeted antioxidants may be used to protect human skin against IRA radiation–induced damage [57].

Other portions of the solar spectrum aside from UV, particularly visible light, may also contribute to signs of premature photoaging in skin. Indeed, irradiation of human skin with visible light induces production of ROS, proinflammatory cytokines, and MMP-1 expression [58,59].

REJUVENATION STRATEGIES

Reversing age-related changes remains a major challenge and requires different strategies. Vitamin A treatment reduces MMP expression and stimulates collagen synthesis in naturally aged, sun-protected skin, as it does in photoaged skin [60]. Retinoids may be able to repair intrinsically aged skin as well as photoaged skin by inhibiting the UV-induced induction of c-Jun protein thereby preventing increased MMPs [61,62]. Retinoids influence both the collagenous and elastic dermal matrices. These derivatives of vitamin A may induce the deposition of newly synthesized collagens (I and III) and fibrillin-rich microfibrils in the superficial papillary dermis.

Blockade of MMPs may represent one strategy for preventing UV-initiated photodamage. Peroxisome proliferator–activated receptor (PPAR) δ is a ligand-inducible transcription factor that modulates multiple biological functions pertaining to skin homeostasis. PPARδ-mediated inhibition of MMP-1 secretion prevents some effects of photoaging. Ligand-activated PPARδ confers resistance to UVB-induced cellular senescence by upregulating phosphatase and tensin homolog (PTEN) and thereby modulating PI3K/Akt/Rac1 signalling to reduce ROS generation in keratinocytes [63]. They also attenuate the UVB-induced secretion of MMP-1 by inhibiting ROS generation, in a process mediated by the JNK/MKP-7 signalling pathway [64]. The PPARalpha/gamma activator 5,7-dimethoxyflavone (5,7-DMF) strongly decreases MMP expression, production, and activity. In addition, 5,7-DMF significantly increases PPARalpha/gamma activation and catalase expression, thereby downregulating UVB-induced ROS production, ROS-induced MAPK signalling, and downstream transcription factors [65].

Estrogens play a key role in aging skin. Prevention of skin aging by estrogen/progesterone replacement therapy is effective if administered early after menopause and influences intrinsically aged skin only [66]. A selective estrogen receptor b (ERb) agonist may play a role in preventing the aging process, and estradiol treatment increases the amount of dermal hyaluronan and versican V2 by inducing the release of epidermal growth factor [67].

Heat exposure might exert biological effects on human skin, but the possible role of heat in photoaging is currently controversial [45]. HSP70 inducers could prove beneficial for the prevention of UV-induced wrinkle formation. Indeed, recent data demonstrated that UV-induced skin elasticity and degeneration of ECM as well as wrinkle formation could be suppressed in hairless mice that were concomitantly subjected to a mild heat treatment [68].

Light-emitting diode (LED) at 660 nm may be a safe and effective collagen-enhancement strategy. Indeed, LED therapy has the potential to reverse collagen downregulation and MMP-1 upregulation [69]. This could explain the improvements in skin appearance observed in LED-treated individuals. Broadband light (BBL), also known as intense pulse light, is a commonly available treatment to rejuvenate the skin. Recent data demonstrate that BBL treatment promotes the gene expression pattern of young skin [70]. The precise mechanisms by which BBL alters gene expression are currently not well understood. BBL may influence pathways controlled by NF-kB, whose blockade in aged murine skin is known to restore the gene expression program and phenotypes of young skin [71] and whose accumulation is associated with a reduced type I collagen expression in human skin fibroblasts [72].

Photoprotection is essential for preventing UV-induced premature skin aging, and *in vivo* studies have indicated that the regular application of sunscreen may diminish UV-induced epidermal and dermal changes [73]. Recent data indicate that regular sunscreen use retards skin aging in healthy, middle-aged men and women [74].

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Clinical signs of aging

Claire Beylot

INTRODUCTION

As life expectancy has increased significantly in industrialized countries, retaining one's youthful appearance has become more and more sought after. Skin and facial aging, which is visible to all, may be a particularly traumatic experience with repercussions in personal life and social relations. Everybody would like to look and stay young for his own well-being, respect for his family and his circle of friends, and also for business needs. Consequently, the correction of facial aging has become the main reason why people look for solutions in cosmetic dermatology and surgery. At a time when self-image and quality of life are becoming increasingly important, this demand, which is especially expressed by women and also by more and more men, should not be thought of a frivolous search for lost youth. In recent years, great progress has been made in the treatment of facial aging, and it is now quite possible to delay and correct aging and even to obtain a more youthful appearance.

To provide the most suitable treatment for each patient, one must analyze how a face has aged. The examination is not limited to skin aging but also involves the underlying structures, facial muscles, fat, and even bones. A similar approach should be taken in the extrafacial areas, especially the neck, back of hands, and forearms, which patients also often would like to see improve.

These components of facial and extrafacial aging are described and evaluated in this chapter, which discusses skin aging extensively, because the other topics are also dealt with in the chapters concerning botulinum toxin, fillers, and surgery. The pathophysiological mechanisms involved are briefly referred to because another author discusses these in detail.

SKIN AGING [1,2]

The skin of people of the same age may vary greatly depending on their genetic profile and their environment with intrinsic (chronological aging and menopause-induced aging) and environmental factors (photoaging and smoking-related aging). A person's phototype is genetic, but the degree of photodamage depends very much on his or her phototype.

Intrinsic Factors

Chronological Aging

Clinical Aspects The signs of chronological aging are difficult to perceive on the face owing to the superposition of photoaging. It is more obvious on unexposed areas of the body, with thinning, puckering, and drying of the skin resembling clothing that is too large (Figure 4.1).

The skin is pallid and the moles progressively disappear with aging as a result of a decrease in the melanocyte count. The wrinkles are fine, crumpled, and almost parallel to each other owing to the atrophy of the skin. These are obvious on the forearms or on the dorsal face of the wrists; they are also visible on the face and the neck. On prints, there is a decrease in the lines and all run in the same direction especially on the dorsal face of the wrists.

Itching is frequent in chronological aging due to dryness of the skin, and it is worsened by inadequate hygiene such as too hot water and/or prolonged baths or showers, too much use of detergent soaps, and consumption of multiple oral drugs [3].

This atrophic skin is fragile and wound healing takes longer.

The hair and the nails are also affected by chronological aging. Scalp hair goes gray and then white, thins out, and grows more slowly. The growth of the nails is slowed down. Whereas the fingernails become fragile and brittle with more longitudinal ridges, the toenails become thicker and difficult to cut with frequent onychomycosis of the big toes.

At the histological level, the following occurs (Figure 4.2a through d):

- Epidermal thinning with a decrease in living Malpighi cells and an increase in dead corneocytes. The number of melanocytes decreases by 10% with each decade.
- Flattening and weakness of the dermoepidermal junction, which is a very complex structure. In aging, the number of each component decreases: integrins of hemidesmosomes, laminin of the lamina lucida, type IV collagen of the lamina densa, type VII collagen of the anchoring fibrils, and fine elastic fibers.
- Disappearance of the thin oxytalan and elaunin elastic network of the papillary dermis, which is a marker of chronological aging. This and the weakness of the dermoepidermal junction explain the decrease in dermoepidermal adhesion.
- Loss of dermal density, with a decrease in all components: collagen, elastic fibers, hyaluronic acid of the extracellular matrix, and sebaceous and sudoral secretions. The loss of dermal density is responsible for vessel dilatation and fragility.

Chronological aging mechanisms are complex and some of them are similar to those of photoaging:

- Genetically determined biological clock, with shortening of the telomeres at every cellular division, leading to replicative senescence with apoptosis or cellular transformation
- Aging-related cellular damage, with 50% decrease in turnover from the age of 20 to 70, less synthesis, and more destruction of collagen

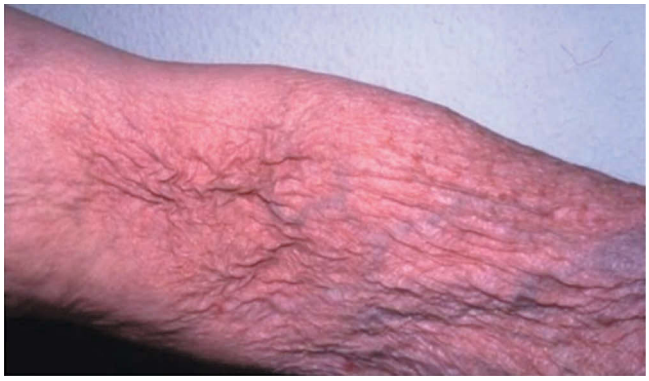


Figure 4.1 Chronological aging. Thinning, puckering, and drying of the skin resembling clothing that is too large.

Menopause-Induced Skin Aging [4]

Signs of Estrogenic Deficiency Menopause-induced aging resembles chronological skin aging. It is due to estrogenic deficiency and sudden skin aging occurs in women who do not take hormonal replacement treatment. The skin fades and becomes thinner and dry with fine wrinkles, especially on the face where there are more estrogen receptors. This skin atrophy is primarily related to a decrease in collagen dermis that is thought to be between 1% and 2% per year. This decrease is correlated with osteoporosis. Climacteric flushing with sweating is sometimes dramatic and embarrassing in early menopause and impacts the quality of life, although it decreases in the postmenopause phase. There are other signs such as palmoplantar keratoderma *climactericum*. Estrogen deficiency also changes the vulvar mucous membrane, which becomes atrophic and dry, leading to pruritus and dyspareunia.

Signs of Relative Hyperandrogenism Hyperandrogenism often occurs owing to a dramatic decrease in ovarian hormones, estradiol and progesterone, whereas the level of androgens decreases to a lesser extent. Cutaneous signs of virilization occur, such as hirsutism and alopecia. These are often mild but deeply affect women since they see it as a visible loss of their femininity.

- Menopausal and postmenopausal alopecia mostly affects the top of the head, making it difficult to adopt any hairstyle, but it spares the thin front hairline. The anagenic phase becomes shorter, leading to depletion of the hair, which becomes thinner like vellus hair. This androgen-dependent process is progressive, frequently beginning many years before the menopause and increasing thereafter.
- Postmenopausal frontal fibrosing alopecia is quite different. An inflammatory lymphocytic lichenoid infiltrate impairs the upper portion of the hair follicle, leading to a symmetrical regression of the frontal and temporal hairline with partial or total loss of the eyebrows. The implication of menopause and androgens has not yet fully been established, but some improvement has been reported with hormonal treatment such as hormonal replacement or antiandrogenic treatment.

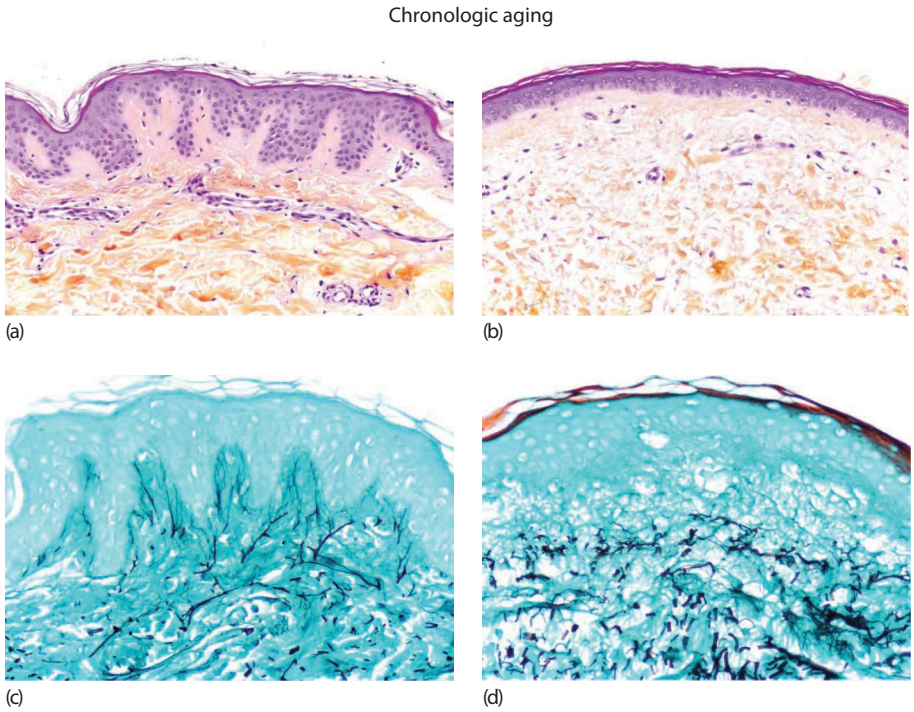


Figure 4.2 From (a) young to (b) old: epidermal thinning, flattening of dermo-epidermal junction, loss of density of dermis with decrease of all its components, especially collagen. From (c) young to (d) old, in papillary dermis, the thin elastic network disappears.

General and Psychiatric Diseases

These diseases, especially depression, accelerate chronological aging.

Environmental Factors [5]

Photoaging [1]

The implication of sun exposure in skin aging was first pointed out by Unna and Dubreuilh in the late nineteenth century. Thereafter, Kligman and Kligman proposed the term of "photoaging" in order to distinguish this process clinically and at the histological level of intrinsic chronological aging, and there have been numerous studies about the very complex mechanisms involved.

In photoaging, genetic factors (phototype) with more severe aging in fair skin and environmental factors (cumulative sun exposure) are closely related and differently combined, explaining the wide variability in appearance between individuals. However, there are also ethnic differences. In fair-skinned Caucasian types, the skin is severely atrophic with multiple telangiectasia and premalignant lesions such as actinic keratosis, whereas in dark-skinned persons, deep wrinkles and furrows occur. In Asians, there are more pigmentary spots but fewer wrinkles [5].

Level of Penetration of UVA and UVB in the Skin and Histological Outcome (Figure 4.3) UVB (290–320 nm), which penetrates the epidermis, and UVA (320–400 nm), which goes deeper into the superficial dermis, are the main causes of photoaging. However, infrared light (740–1400 nm), which reaches as far as the hypodermis, can play a role in this aging process. These levels of penetration of UVA and UVB explain why histologically the changes in photoaging are mainly localized in the upper part of the skin. The main alteration is actinic elastosis. The accumulation of abnormal thick and fragmented elastic fibers in the papillary dermis associated with the decrease in collagen is responsible for the alteration of the biomechanical properties of the skin, loss of elasticity, textural changes, laxity, and wrinkles. Changes also occur in the epidermis, with thinning, excessive, and irregular dispersion of melanin, which is responsible for solar lentigo and cellular atypia, leading to actinic keratosis with a risk of evolution to cancer.

UVB is responsible for epidermal changes, particularly precancerous and cancerous lesions, while UVA exposure leads to aging, especially actinic elastosis. However, the effects are complex, and recent publications demonstrate that UVA also plays an important role in the genesis of cutaneous cancers.

Photoaging Depending on Localization Photoaging is usually predominant on the face, but the skin of the neck, low neck, forearms, and legs are also involved and even the whole body in fanatics of sun-tanning and bed or cabin tanning. Sometimes, there is a dramatic contrast between sun-exposed skin, where the photoaging is severe, and unexposed skin, which appears much younger (Figure 4.4).

On the Face

Aspect and Texture of the Skin On the face, the skin is often thickened owing to solar elastosis and yellowy or gray yellow (Figure 4.5a), with follicular dilated orifices resembling lemon peel. However, the skin sometimes becomes thin particularly in fair persons.

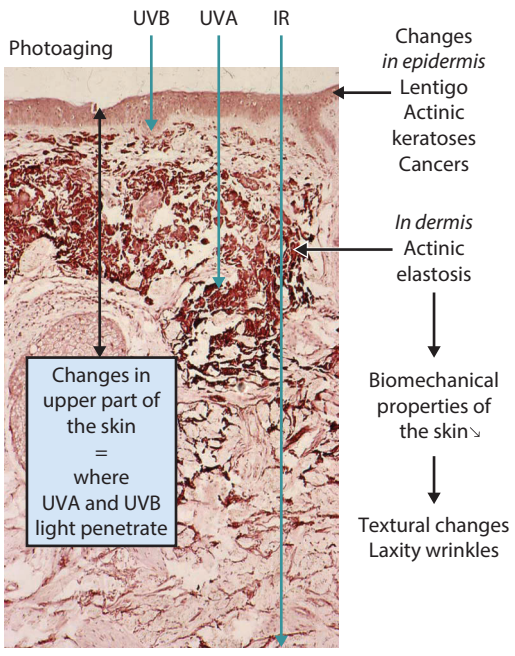


Figure 4.3 The levels of penetration of UVA and UVBA explain why histologically the changes in photoaging are mainly localized in the upper part of the skin.

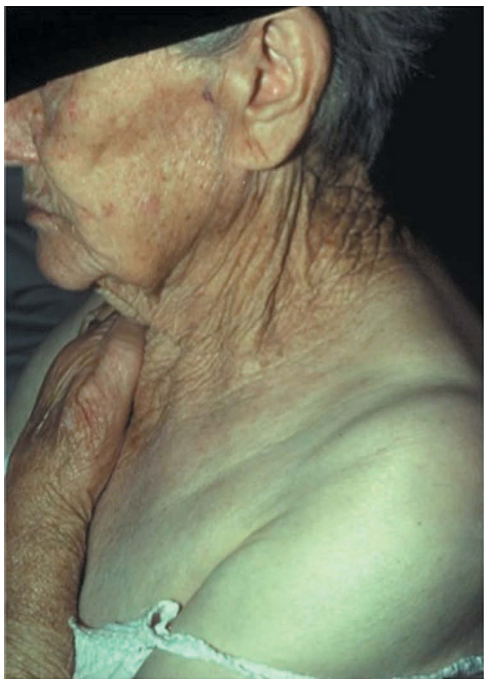
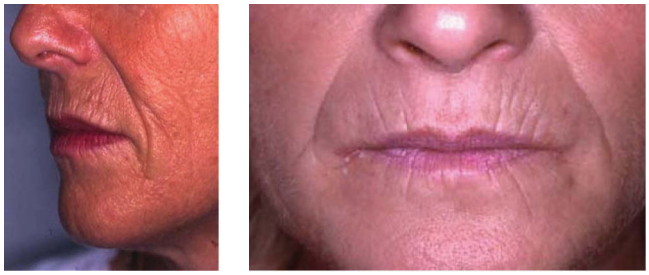


Figure 4.4 There is a dramatic contrast between sun-exposed skin, where the photoaging is severe, and unexposed skin, which appears much younger.



(a) (b)

Figure 4.5 (a) Solar elastosis, with thickened and yellowy skin. Heliodermic wrinkles of the upper lip ("sun pleated wrinkles"). (b) Dynamic "bar code" wrinkles are deeper and oblique, because they are perpendicular to the direction of contraction of the *orbicularis oris* muscle.

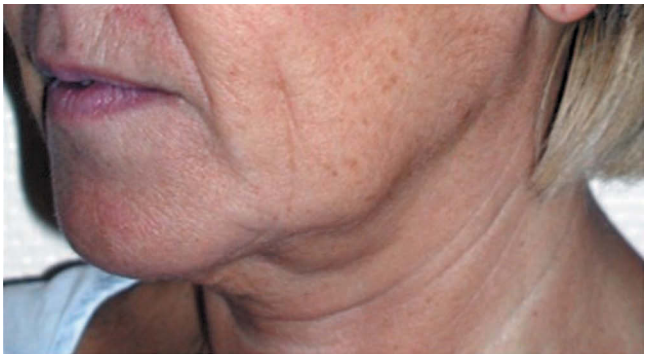


Figure 4.6 Transversal lines of the neck are gravitational wrinkles due to skin and fat ptosis.

Textural changes also occur leading to progressive alteration of the biomechanical properties of the skin. The gradual loss of skin elasticity and its flaccidity, combined with fat ptosis, leads to sagging, with lowering of the eyebrows, upper eye skin excess (dermatochalasis), accentuation of the nasolabial folds, flabby cheeks, and loss of the oval shape of the face.

However, in the patient's opinion, wrinkles are the most noticeable sign of aging.

There are different kinds of wrinkles and it is important to distinguish them because the treatment is not the same [6,7]:

- Elastotic creases (heliodermic wrinkles), which become progressively permanent, develop on sun-exposed areas such as the upper lip (Figure 4.5a). The latter is more exposed than the lower lip because its surface is not quite vertical but slightly oriented upward. The cheeks and nape of the neck are also involved. In these areas, the solar elastosis is hypertrophic, compact, overcompensating the collagen atrophy in volume, and forming a cobblestone sequestrated material making the skin more rigid.
- Dynamic wrinkles due to the underlying muscles and always oriented in a stereotypic pattern perpendicular to the direction of muscular contraction especially in the upper third of the face the glabellar lines, giving the patient an anxious and severe look, forehead lines, crow feet wrinkles, or a perioral area (Figures 4.5b and 4.14a through c). In forehead lines, the role of the thickening and shortening of the retinacula cutis fastening the wrinkle bottom in depth has been demonstrated [8].
- Crumpling wrinkles that are fine and almost parallel to each other are due more to chronological aging and to the atrophy of the skin than to actinic elastosis. They are obvious on the forearms and the dorsal face of wrists but may be visible on the face and the neck.
- Gravitational folds are not really wrinkles, because they are due to tissue ptosis and to fat more than to the skin, with an accumulation above especially in the nasolabial area, the mobile fat of the cheek knocking against the fixed area of the superior lip, thereby hollowing out a deep furrow (Figure 4.17). The same is true for the transversal lines of the neck (Figure 4.6). The main histological change is a loosely and elongated fibrous network in the hypodermis related to gravitational forces followed by a similar elongation of the dermis. When these are mild, fillers can correct such gravitational folds, but lifting is needed if these defects are severe.

Permanent vertical frontal wrinkles and vertical wrinkles of the mid cheek, also known as "pillow wrinkles," are due to the pressure constraints during sleep. They impact aging skin and weaken the underlying structures. Their mechanism of formation is therefore similar to that of gravitational wrinkles.

However, this classification remains artificial, because photoaging with its textural alterations plays an important role even in dynamic wrinkles. Indeed, such dynamic wrinkles are absent in young people, because their skin has biomechanical properties, especially elasticity, allowing muscular movements to occur without the development of permanent wrinkles.

In some localizations such as the upper lip, one must distinguish between heliodermic wrinkles and dynamic wrinkles because the treatment is not the same. The first, i.e., "sun-pleated wrinkles" (Figure 4.5a), are vertical and superficial in a very elastotic skin and require laser treatment or deep peel. The latter, which are sometimes known as "bar code" wrinkles (Figure 4.5b), are deeper and oblique, because they are perpendicular to the direction of contraction of the *orbicularis oris* muscle and are more visible when the patient blows or whistles. These dynamic wrinkles require botulinum toxin. Frequently, however, these two mechanisms are associated and a combined treatment is needed.

Other changes related to photoaging and elastosis are as follows:

- Favre and Racouchot syndrome (*elastosis nodularis cystica et comedonica*) (Figure 4.7): In very elastotic sun-exposed areas such as orbitomalar or laterofrontal eminences and even on bald scalp or the nape of the neck, comedones, sebaceous cysts, and nodules without inflammation may occur. Sebaceous secretions are not increased. The mechanism is simply a sebaceous build-up in distended follicles in flabby skin. These aspects are more frequent and occur earlier in smokers.