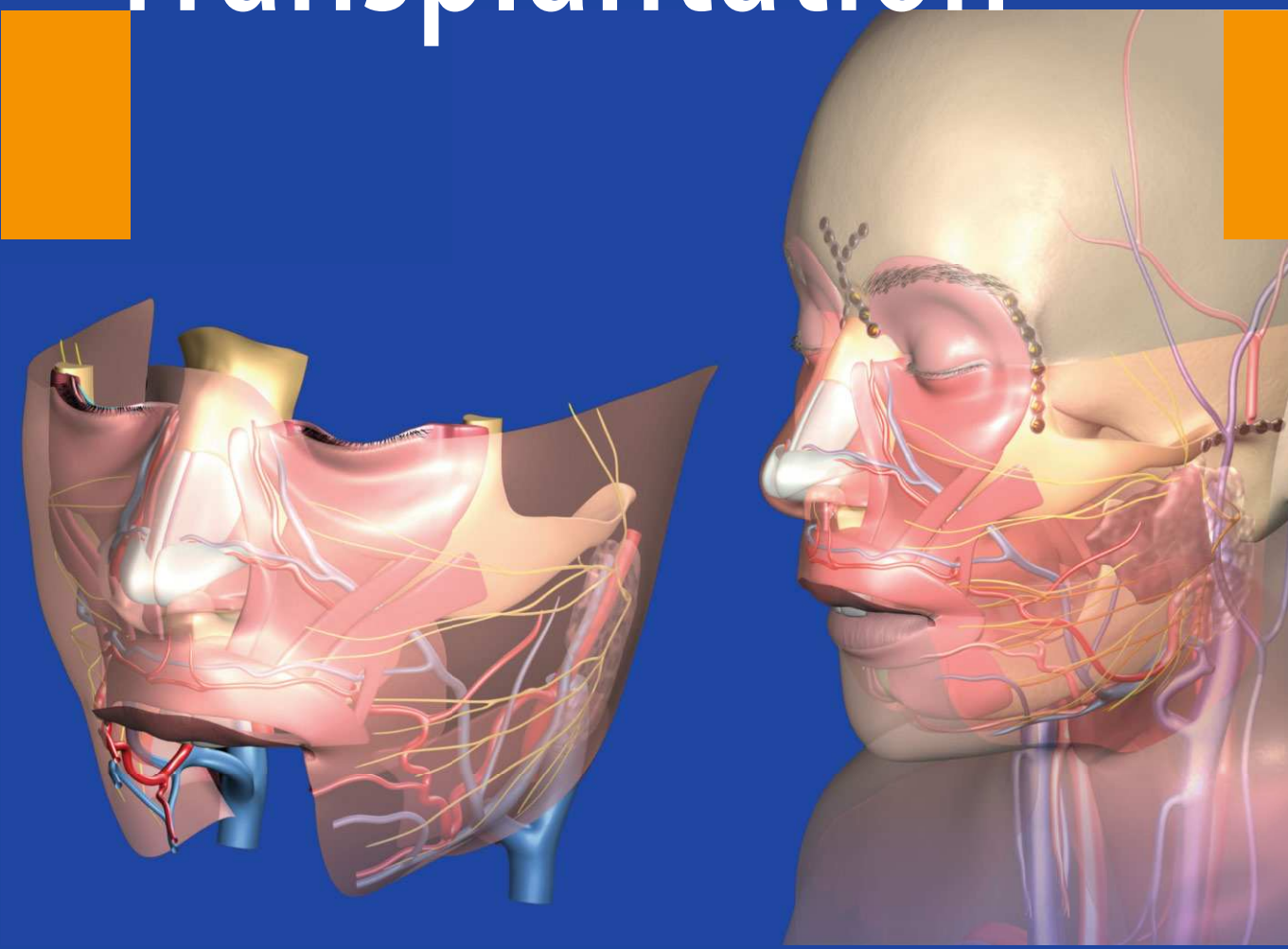
Maria Z. Siemionow
Editor

The Know-How of Face Transplantation



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The Know-How of Face Transplantation

Maria Z. Siemionow
(Editor)

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Editor
Maria Z. Siemionow, M.D., Ph.D., D.Sc
Department of Plastic Surgery
Cleveland Clinic
Cleveland, OH
USA
siemion@ccf.org

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This book is dedicated to all organ donors and their families who are the silent heroes behind medical breakthroughs such as transplantation of the human face.

Preface

It is a great privilege to introduce the book *The Know-How of Face Transplantation* to those who are interested in innovations in plastic and reconstructive surgery as well as innovation in the transplantation field.

The idea to write *The Know-How of Face Transplantation* came early on, even before we had performed the first face transplant in the USA. The preparation process for face transplantation involved experimental studies, cadaver dissections, much legislative work and approval from different organizations including the Institutional Review Board (IRB), organ procurement organizations, coroner's office approvals, as well as approvals from different states' organ procurement organizations.

My intention was to share, with those interested in development of new programs for composite tissue allograft transplantation, our own experience and the experience of others in order to facilitate establishment of reconstructive transplantation programs in other US institutions, as well as in other countries worldwide.

Face transplantation has generated a lot of attention over the last six years, and it started in 2004 with the announcement of Cleveland Clinic granting the world's first IRB approval to proceed with human face transplantation. A lot of ethical, societal, as well as medical debate ensued after this approval was granted. The interest of the media nationally and internationally, as well as patient advocate and other groups, supported this breakthrough concept and procedure; however, many questions were raised regarding ethical issues, medical issues such as the need for lifelong immunosuppression, as well as issues of financial support for this novel procedure.

When I thought about the concept of creating a know-how manual for face transplantation, I did not want the reader to get the impression that this is a recipe which, when followed, will guarantee a 100% success rate. Based on the years of work and preparation and experience in developing the program of face transplantation at Cleveland Clinic, I realized that there are not only surgical and technical issues which need to be shared, but also issues related to experimental studies, anatomical cadaver dissections, ethics, legal approval and legislative issues, as well as societal, financial, and public relations concerns. This was a tremendous undertaking, and I have taken this work very personally due to the fact that a book on a breakthrough procedure which has been performed, for the first time, on only a few patients, brings a great responsibility to the Editor. In order to include the experience of all world experts who have performed face transplantation, I invited all surgeons who had participated, at the time of book production, in face transplantation programs, in their respective countries and institutions. These included Dr. Dubernard and Dr. Devauchelle, from Lyon, France, Dr. Lengele, from Belgium, Dr. Shuzhong, from China, Dr. Lantieri, from Paris, France, Dr. Cavadas, from Valencia, Spain, Dr. Pomahac and Dr. Pribaz, from Boston, as well

as Dr. Butler, from London. I was hoping that all would contribute with a chapter sharing their experience. I also invited experts in transplantation ethics, infectious disease, rehabilitation, transplant immunology, media relation representatives, as well as organ procurement organization experts. I received overwhelming support from most of the centers; however, a few of the institutions' leaders decided to not participate in our educational journey. Therefore, we have included their experience in the review chapters summarizing the world experience with face transplantation.

The book has 72 contributing authors and 44 chapters which are divided into eight major sub-categories of topics outlined in the following order:

Part I Preclinical Aspects of Face Transplantation

There are 7 chapters in this part which discuss the issues of the face as a functional organ, the face as a sensory organ, and immunological aspects related to face transplantation. In addition, experimental studies in rodents, as well as large animal models including swine and primates, are discussed. Finally, the timeline and preparation for face transplantation in the cadaver model is presented.

Part II Clinical Aspects in Preparation for Face Transplantation

This part includes 8 chapters describing guidelines for technical aspects of face transplantation, anesthesia-related issues in face transplantation, as well as alternative approaches to face transplantation. In addition, ethical concerns, as well as psychological aspects of face transplantation, are thoroughly discussed, and physical therapy and rehabilitation, as well as prosthetic support relevant to face transplantation, are presented.

Part III Monitoring Aspects of Face Transplantation

This part includes 7 chapters and describes the important issues of how to monitor patients after facial transplantation, emphasizing details of immunological monitoring, pathological monitoring, and classification of facial graft rejection. In addition, the issues of brain plasticity, functional EEG, as well as sensory recovery and methods of assessment of cortical plasticity after face transplantation, are discussed.

Part IV Approval Process of Face Transplantation

Here, in 5 chapters, we outline the process of IRB approval, the ethical presentation of patients' informed consent, the legal and regulatory aspects of face donation and transplantation, the issue of death and end of life, as well as organ procurement organizations' approval process.

Part V Societal, Financial, and Public Relations Issues in Face Transplantation

This part summarizes, in 3 chapters, cultural, religious, and philosophical views on face transplantation, a comparative cost analysis of conventional reconstruction versus face transplantation, and finally, media-related aspects, viewed from a public relations perspective, on face transplantation.

Part VI World Experience with Face Transplantation

This part summarizes, in 7 chapters, the global experience with face transplantation: the facial allotransplantation experience in China, Cleveland Clinic's experience, the Spanish team's experience, as well as microsurgical aspects and sensory recovery following face transplantation. In addition, infectious issues related to face transplantation are outlined.

Part VII Future Directions in Face Transplantation

The 6 chapters in this part of the book discuss the military cases relevant to face transplantation, regenerative medicine approaches, the international registry of face transplantation, the aspects of concomitant face and upper extremity transplantation, immunosuppressive protocols for composite tissue transplantation, new cellular therapies, as well as novel aspects of tissue engineering in face transplantation.

Part VIII Current Status of Face Transplantation

This final part of the book summarizes, in one chapter, the technical and functional outcomes of the 13 face transplants performed thus far, between 2005 and 2010, by all institutions worldwide.

I hope that this book will help those who are planning to establish composite tissue allograft programs in their institutions and countries to understand that the approach to a novel procedure requires the cooperative effort of a team of multidisciplinary experts from different fields which are, quite often, far removed from the daily surgical activities of reconstructive surgeons. This book summarizes many of the issues which, as a surgeon, I had not considered when preparing for facial transplantation and which developed during the lengthy process of creating the face transplant program at Cleveland Clinic. I understand, from my interactions with contributing authors, that they have enjoyed the process of writing about a topic as new and undiscovered as face transplantation, a topic on which we do not yet have long-term patient outcomes to report and share.

It has been a privilege to work with so many of the field's experts in putting this book together. I hope that a careful process of preparation for face transplantation, as outlined in this book, will not be underestimated and justifies this procedure as a medical, ethical, and societal breakthrough. The final message which I want to convey is that the technical aspect of face transplantation is only one of many challenges, and the beginning of a fascinating journey of helping patients who have lost their faces, since "You need a face to face the world."

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Contributors

George J. Agich, Ph.D. Department of Philosophy, Social Philosophy and Policy Center, Bowling Green State University, Bowling Green, OH, USA

Selman Altuntas, M.D. Department of Plastic Surgery, Cleveland Clinic, Cleveland, OH, USA

Medhat Askar, M.D., Ph.D. Allogen Laboratories, Transplant Center, Department of Surgery, Cleveland Clinic, Cleveland Clinic Lerner College of Medicine, Case Western Reserve University, Cleveland, OH, USA

Anthony Atala, M.D. Director, Wake Forest Institute for Regenerative Medicine, Wake Forest University School of Medicine, Medical Center Blvd., Winston-Salem, NC, USA

Robin Avery, M.D., FIDSA Department of Infectious Disease, Medicine Institute, Cleveland Clinic, Cleveland, OH, USA

Rolf N. Barth, M.D. Department of Surgery, University of Maryland School of Medicine, Baltimore, MD, USA

Stephen T. Bartlett, M.D. Department of Surgery, University of Maryland Medical Center, Baltimore, MD, USA

Wilma F. Bergfeld, M.D., FAAD Department of Dermatology and Pathology, Cleveland Clinic, Cleveland, OH, USA

Steven Bernard, M.D. Department of Plastic Surgery, Cleveland Clinic, Cleveland, OH, USA

Marino Blanes, M.D., Ph.D. Department of Infectious Diseases, Hospital Universitari La Fe de Valencia, Valencia, Spain

Gordon R. Bowen Lifebanc, Cleveland, OH, USA

Katrina A. Bramstedt, Ph.D. California Transplant Donor Network, Oakland, CA, USA

Grzegorz Brzezicki, M.D. Department of Plastic and Reconstructive Surgery, Cleveland Clinic, Cleveland, OH, USA

Federico Castro, M.D. Department of Plastic and Reconstructive Surgery, Anesthesiology Division, Clínica Cavadas, Valencia, Spain

Pedro C. Cavadas, M.D., Ph.D. Department of Plastic and Reconstructive Surgery, Clínica Cavadas, Valencia, Spain

Linda C. Cendales, M.D. Department of Plastic and Reconstructive Surgery, Division of Transplantation, Vascularized Composite Allotransplantation, Laboratory of Microsurgery, Emory University, Atlanta, GA, USA

Kathy L. Coffman, M.D., FAPM Department of Psychiatry and Psychology, Cleveland Clinic, Cleveland, OH, USA

Joanna Cwykiel, M.Sc. Department of Plastic Surgery, Cleveland Clinic, Cleveland, OH, USA

Jacek B. Cywinski, M.D. Department of General Anesthesiology, Cleveland Clinic Foundation, Anesthesiology Institute, Cleveland, OH, USA

Pamela L. Dixon, MOT, OTR/L Department of Physical Medicine and Rehabilitation, Cleveland Clinic, Cleveland, OH, USA

Risal Djohan, M.D. Department of Plastic Surgery, Cleveland Clinic, Cleveland, OH, USA

Mathieu Domalain, Ph.D. Department of Biomedical Engineering, Cleveland Clinic, Lerner Research Institute, Cleveland, OH, USA

D. John Doyle, M.D., Ph.D. Department of General Anesthesiology, Cleveland Clinic, Cleveland, OH, USA

Bijan Eghtesad, M.D. Department of HPB/Liver Transplant Surgery, Cleveland Clinic, Cleveland, OH, USA

Ann Marie Flores, P.T., Ph.D., CLT Department of Orthopaedics and Rehabilitation, Vanderbilt University School of Nursing, Vanderbilt University Medical Center, Nashville, TN, USA

John J. Fung, M.D., Ph.D. Department of General Surgery, Education Institute, Cleveland Clinic, Cleveland, OH, USA

James R. Gatherwright, M.D. Department of Plastic and Reconstructive Surgery, University Hospitals – Case Medical Center, Cleveland, OH, USA

Bahar Bassiri Gharb, M.D., FEBOPRAS Department of Plastic Surgery, Cleveland Clinic, Cleveland, OH, USA

Alexandra K. Glazier, J.D., M.P.H. New England Organ Bank, Inc, Waltham, MA, USA

Chad R. Gordon, D.O. Division of Plastic and Reconstructive Surgery, Department of Surgery, Massachusetts General Hospital, Boston, MA, USA

Lawrence J. Gottlieb, M.D., FACS Department of Surgery, Section of Plastic and Reconstructive Surgery, The University of Chicago Medical Center, Chicago, IL, USA

Robert G. Hale, D.D.S., COL US Army Dental Corps Craniomaxillofacial Research, U.S. Army Institute of Surgical Research, San Antonio, TX, USA

Charles Heald Community Outreach, LifeBanc, Cleveland, OH, USA

Michael L. Huband, D.D.S. Section of Maxillofacial Prosthetics, Department of Dentistry, Head and Neck Institute, Cleveland Clinic, Cleveland, OH, USA

Helen G. Hui-Chou, M.D. Division of Plastic and Reconstructive Surgery, The Johns Hopkins Hospital/University of Maryland School of Medicine, Baltimore, MD, USA

Javier Ibañez Mata Department of Plastic and Reconstructive Surgery, Clínica Cavadas, Valencia, Spain

Helen G. Hui-Chou, M.D. Division of Plastic and Reconstructive Surgery, The Johns Hopkins Hospital/University of Maryland School of Medicine, Baltimore, MD, USA

Luke S. Jones, B.S. Department of Surgery, University of Maryland School of Medicine, Baltimore, MD, USA

Jean Kanitakis, M.D. Department of Dermatology/Laboratory of Dermatopathology, Edouard Herriot Hospital Group, Lyon, France

Angela Kiska Corporate Communications, Cleveland Clinic, Cleveland, OH, USA

Aleksandra Klimczak, Ph.D. Department of Plastic Surgery, Cleveland Clinic, Cleveland, OH, USA and
Polish Academy of Sciences, Institute of Immunology and Experimental Therapy, Wroclaw, Poland

Yur-Ren Kuo, M.D., Ph.D., FACS Department of Plastic and Reconstructive Surgery, Chang Gung Memorial Hospital – Kaohsiung Medical Center, Kaohsiung, Taiwan

Krzysztof Kusza, M.D., Ph.D., D.Sc. Department of Anaesthesiology and Intensive Therapy, Nicolaus Copernicus University, Collegium Medicum, Poznan University of Medical Sciences, Bydgoszcz, Poland

Luis Landin, M.D. Department of Plastic and Reconstructive Surgery, Clínica Cavadas, Valencia, Spain

Daniel J. Lebovitz, M.D. Department of Pediatric Critical Care, Cleveland Clinic Lerner College of Medicine, Cleveland Clinic Children's Hospital, LifeBanc, Cleveland, OH, USA

Vernon W.-H. Lin, M.D., Ph.D. Department of Physical Medicine and Rehabilitation, Cleveland Clinic, Cleveland, OH, USA

Robert F. Lohman, M.D. Department of Orthopaedic and Plastic Surgery, Cleveland Clinic, Cleveland, OH, USA

Maria Madajka, Ph.D. Department of Plastic Surgery, Cleveland Clinic, Cleveland, OH, USA

Amanda Mendiola, M.D. Department of Surgery, Akron General Medical Center, Akron, OH, USA

Gerhard S. Mundinger, M.D. Division of Plastic and Reconstructive Surgery, Johns Hopkins Hospital/University of Maryland School of Medicine, Baltimore, MD, USA

Can Ozturk, M.D. Department of Dermatology and Plastic Surgery Institute, Cleveland Clinic, Cleveland, OH, USA

Frank Papay, M.D., FACS, FAAP Dermatology and Plastic Surgery Institute, Cleveland Clinic, Cleveland, OH, USA

Palmina Petruzzo, M.D. Department of Transplantation, Edouard Herriot Hospital, Lyon, France

Marc J. Popovich, M.D., FCCM Surgical Intensive Care Unit, Cleveland Clinic, Anesthesiology Institute, Cleveland, OH, USA

Antonio Rampazzo, M.D., FEBOPRAS Department of Plastic Surgery, Cleveland Clinic, Cleveland, OH, USA

Russell R. Reid, M.D., Ph.D. Department of Surgery/Plastic Surgery, University of Chicago, Chicago, IL, USA

Jose Rodrigo, M.D. Department of Plastic and Reconstructive Surgery, Clínica Cavadas, Valencia, Spain

Eduardo D. Rodriguez, M.D., D.D.S. Division of Plastic and Reconstructive Surgery, R Adams Cowley Shock Trauma Center, Johns Hopkins Hospital/ University of Maryland School of Medicine, Baltimore, MD, USA

Elliott H. Rose, M.D. Division of Plastic and Reconstructive Surgery, The Mount Sinai Medical Center, New York, NY, USA

Eileen M. Sheil Corporate Communications, Cleveland Clinic, Cleveland, OH, USA

Steven T. Shipley, DVM, DACLAM Veterinary Medicine, Comparative Medicine Program, University of Maryland School of Medicine, Baltimore, MD, USA

Maria Z. Siemionow, M.D., Ph.D., D.Sc. Department of Plastic Surgery, Cleveland Clinic, Cleveland, OH, USA

Vlodek Siemionow, Ph.D. Department of Plastic Surgery, Lerner Research Institute, Cleveland Clinic, Cleveland, OH, USA

Angela Sirigu, Ph.D. Center for Cognitive Neuroscience, CNRS, Bron, France

Erhan Sonmez, M.D., Ph.D. Department of Plastic and Reconstructive Surgery, Hacettepe University Hospital, Ankara, Turkey

Jason S. Stratton, M.D. Department of Pathology, Cleveland Clinic, Cleveland, OH, USA

Alessandro Thione, M.D., Ph.D. Department of Plastic and Reconstructive Surgery, Clínica Cavadas, Valencia, Spain

Claudia D. Vargas Department of Neurobiology, Institute of Biophysics Carlos Chagas Filho, Rio de Janeiro, Brazil

Tracy Wheeler Corporate Communications, Cleveland Clinic, Cleveland, OH, USA

Tsung-Lin Yang, M.D., Ph.D. Department of Otolaryngology, National Taiwan University Hospital, Taipei, Taiwan

James J. Yoo, M.D., Ph.D. Wake Forest University School of Medicine, Wake Forest Institute for Regenerative Medicine, Winston-Salem, NC, USA

Jose Maria Zarzalejos Andes, M.D. Department of Internal Medicine, Infectious Disease Unit, Hospital Universitario Gran Canaria Dr. Negrín, Las Palmas de Gran Canaria, Spain

Xiaoming Zhang, Ph.D. Medical Research Service, Louis Stokes Cleveland VA Medical Center, Cleveland, OH, USA

Fatih Zor, M.D. Department of Plastic Reconstructive and Aesthetic Surgery, Gulhane Military Medical Academy, Ankara, Turkey

Part I

Preclinical Aspects of Face Transplantation

Face as an Organ: The Functional Anatomy of the Face

1

Maria Z. Siemionow and Erhan Sonmez

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Abstract The role of the face in the daily interactions of a person through its expression of feelings, beauty, and identity is pertaining to life. Thus, severe facial trauma and disfigurement stemming from burns, tumor resection, and congenital and acquired malformation have deleterious effects on a person's life and expose a person to the stigmata of being different.

Face transplantation in humans, which has been performed worldwide, has raised the question of whether the face is just a "tissue" or if it is an "organ." This issue has been approached from different perspectives by different societies, agencies, and communities. We have summarized the anatomic, physiologic, and aesthetic functions of the human face in this chapter, and we propose that the face should be accepted as an organ. Additionally, face transplantation should be considered as an organ transplantation that enhances the quality of life to a degree comparable to that of solid organ transplantations.

1.1 Introduction

The face plays a central role in the daily interactions of a person through its expression of feelings, beauty, and identity. Consequently, severe facial trauma and disfigurement stemming from burns, tumor resection, and congenital and acquired malformation have deleterious effects on a person's life and expose a person to the stigmata of being different.[1,2] All of these conditions are difficult if not impossible to accurately reconstruct with autologous tissues despite the great advances in reconstructive surgery. The body contains no tissues possessing the texture, pliability, and complexity of the face. Therefore, the only option for restoring facial features in severely

M.Z. Siemionow (✉)
Department of Plastic Surgery, Cleveland Clinic, Cleveland, OH, USA
e-mail: siemiom@ccf.org

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disfigured patients remains transplantation of face from a human donor.[2] The concept of facial transplantation has become a reality with a total of ten cases worldwide at the time of this report since the first case that was reported from Lyon, France in 2005.[3,4]

Solid organ transplantations are essential for the continuation of life and have saved the lives of millions of people since the first kidney transplant, which was performed by Nobel laureate Joseph Murray of Brigham Women's Hospital in December 1954.[5] However, composite tissue allografts such as face, larynx, or hand, although certainly improving the life quality, are not essential for patient's survival. The risk of lifelong immunosuppression in patients receiving transplants which do not have a direct impact on their survival is the focus of debates regarding the use of composite tissue allotransplantation in daily practice. Although there has been a great improvement in quality and specificity of immunosuppressive drugs, their side effects are still of major concern.[2] Consequently, face transplantations in humans have raised the question of whether the face is just a "tissue" or an "organ." This issue has been approached from different perspectives by different societies, agencies, and communities. We have described the anatomic, physiologic, and aesthetic functions of the human face in this chapter.

1.2 Is the Face an "Organ" or a "Tissue"?

Based on the definitions of standard medical and general dictionaries, an "organ" (from Greek "organon," via Latin organum, "tool, implement") is a differentiated structure comprising tissues that perform a specialized function in an organism. On the other hand, "tissue" (ultimately from the Latin "texere," "to weave") is defined as an aggregate of similar cells, along with their intercellular substances, which comprise the materials that build structures in an organism.[6] Consequently, an organ comprises tissues from the conventional anatomic view. We want to examine this view from the perspective of the face and therefore want to raise the question of whether the face can be regarded as an organ that performs one or more specific functions or is it simply an aggregation of tissue with no discernible specific functions.

1.3 Anatomic and Physiologic Composition of the Face

The anatomic composition of face can be described starting from its most superficial to its deeper structures:

1.3.1 Skin

Based on our cadaver studies, we have confirmed that the surface area of the skin of the total face is 1,192 cm^2 with the scalp, and 675 cm^2 without the scalp.[7-10] It is composed of 3 functional layers: epidermis, dermis, and subcutis. Blood vessels and epidermal appendages such as hairs and glands are found in these layers[11] (Fig. 1.1).

The hair on the face is composed of hair shaft, root, and a shaft bulb at the base of the hair, similar to the hair all over the body. Root of the hair ends in the hair bulb, that lies in a sac-like pit in the skin called hair follicle. Hair follicles are lined with cells that synthesize the proteins needed for the growth of the hair. The oily coating of the hair shaft is secreted by a sebaceous gland which is associated with this follicle.[12]

Keratinocytes, fibroblasts, melonocytes, Langerhans cells, and the Merkel Cells are the five types of cells that make up the skin. Subcutis layer is composed of fat cells and the endothelial cells, and the superficial

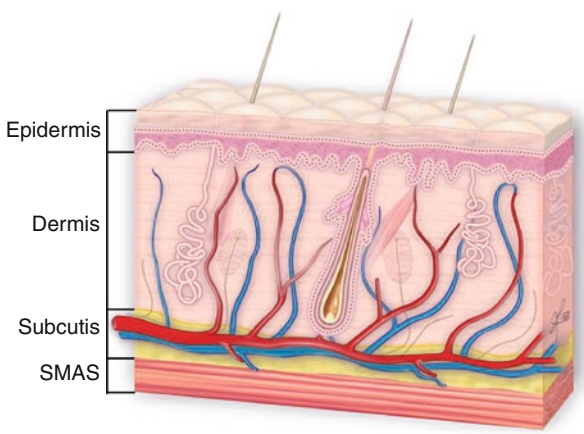

Fig. 1.1 Cross section of the skin (From Siemionow and Sonmez[2])

musculoaponeurotic system of the face is composed of striated muscle cells.[11]

The dermis (or Corium) is the layer of skin beneath the epidermis that contains appendages from the epidermis, such as hair follicles and sweat glands. The dermis is structurally divided into two areas: the "papillary region" is a superficial area adjacent to the epidermis which contains loose collagenous and elastic fibers, together with fibroblasts, mast cells, and macrophages. The deeper and thicker layer of the dermis is the "reticular region" which consists of dense, coarse bundles of collagenous fibers.[12]

The subcutis is the layer just beneath the dermis and is also known as the subcutaneous layer. It consists of a network of collagen, a layer of fatty areolar tissue that overlies the more densely structured fibrous fascia. The subcutaneous tissue serves as a "shock absorber" and insulation of heat of the body. Eccrine and apocrine glands are the sweat glands found all over the body, but eccrine glands predominate the skin of the face. They are particularly concentrated in the forehead skin.[11]

Sebaceous glands (halocrine glands) are found over the entire surface of the body except the palm, soles, and the dorsum of the feet. They are particularly concentrated in the skin of the face and scalp. The glands produce and secrete sebum which is a group of complex oils. The function of sebum is to lubricate and protect the skin against trauma and keep the moisture.[12]

The next deeper layer is called the superficial musculoaponeurotic system. This sheet is well developed in the scalp and face and includes the occipitofrontalis muscle, the tempoparietal fascia, the orbicularis oculi muscle, occipitofrontalis muscle, zygomatic muscles, levator labii superioris muscle, temporal branches of the facial nerve, superficial temporal vessels, and the auriculotemporal nerve. The superficial muscles of the face and their functions are summarized in Table 1.1 (Fig. 1.2).

The eyelids are composed of skin, subcutaneous tissue, orbicularis oculi muscle, submusculoareolar tissue, the fibrous layer consisting of the tarsus and the orbital septum, lid retractors of the upper and lower eyelids, retroseptal fat pads, and the conjunctiva from most superficial to the deeper consequently. The lids move through the action of the orbicularis oculi muscle and of the levator of the upper lid. The borders of the eyelids are lubricated by an oily secretion (called sebum) of the meibomian glands.[13]

The nose is composed of cartilaginous anterior portion and a bony posterior and superior portion. The

Table 1.1 Functions and innervations of the superficial muscles of the face

Superficial muscles of the face	Function	Innervation ("n" refers to nerve)
Frontalis	Pulls the eye brows	Temporal branch of facial n.
Auricularis posterior	May move the ears	Temporal branch of facial n.
Auricularis anterior	May move the ears	Temporal branch of facial n.
Auricularis superior	May move the ears	Temporal branch of facial n.
Orbicularis oculi	Squints the eyes	Temporal and Zygomatic branch of facial n.
Pyramidalis	Lowers glabella	Temporal branch of facial n.
Zygomaticus major	Pulls lip corners upward	Zygomatic and Buccal branch of facial n.
Zygomaticus minor	Pulls lip corners downward	Buccal branch of facial n.
Levator labii superioris	Pulls the upper lip upward	Buccal branch of facial n.
Levator labii superioris alaque nasi	Wrinkles nose	Buccal branch of facial n.
Levator anguli oris	Elevates lateral part of the lips	Zygomatic and Buccal branch of facial n.
Orbicularis oris	Purses the lips	Buccal and Mandibular branch of facial n.
Risorius	Retracts lip corners	Buccal branch of facial n.
Mentalis	Elevates the lower lip and skin	Mandibular branch of facial n.
Depressor anguli oris	Pulls the corners of the mouth down	Buccal and Mandibular branch of facial n.
Depressor labii inferioris	Pulls the lower lip down	Mandibular branch of facial n.
Platysma	Pulls the corners of the mouth down	Cervical branch of facial n.
Nasalis	Compresses the nostrils	Buccal branch of facial n.
Compressor naris	Constricts the nostrils	Buccal branch of facial n.
Depressor naris	Flares the alar parts of the nose	Buccal branch of facial n.

From Siemionow and Sonmez[2]

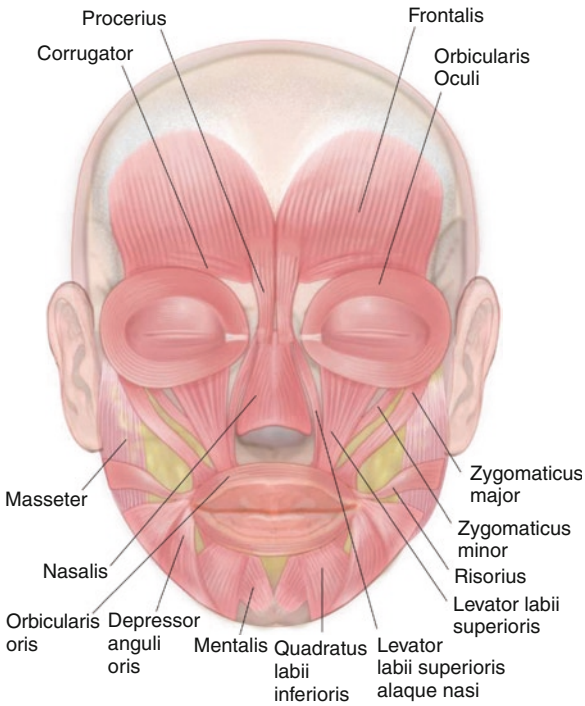

Fig. 1.2 Superficial muscles of the face (From Siemionow and Sonmez[2])

cartilaginous portion of the nose is made up of a paired set of cartilages which includes the greater alar (lower lateral), septal, lateral nasal (upper lateral), and lesser sesamoid cartilages. Paired nasal bones and the nasal processes of the maxillary and frontal bones form the bony framework of the nose. Posterosuperiorly, the bony nasal septum is composed of the perpendicular plate of the ethmoid.[2,14]

The lips are the soft, protruding, and movable parts of the face. The lower lip is usually somewhat larger than the upper one. The skin of the lips is very thin compared to the skin of the face and lacks sweat glands and sebaceous glands. The number of the melanocytes in the lip skin is very low, and because of this, the blood vessels appear through the skin of the lips and make the red coloring.[2]

The parotid gland, which is the largest of the major salivary glands, is located in the posterolateral side of the face, and in front of the external ear along the posterior border of the ramus of the mandible. It secretes saliva through Stensen's Duct into the oral cavity to facilitate mastication and swallowing. The paired submandibular glands (submaxillary glands) are located below the mandible on each sides of the jaw.[2]

In some parts of the face, the anatomic layers are condensed, forming the "retaining ligaments" which serve to anchor the skin of the face to the underlying bony structures. The zygomatic ligament is located in the cheek, anterior and superior to the parotid gland and posteroinferior to the malar eminence. The mandibular ligament is located on the jaw line and forms the anterior border of the jowl. The other two ligaments, the platysma-cutaneous and platysma-auricular ligaments, are aponeurotic condensations attaching the platysma to the underlying dermis. All of these ligaments support the facial structures and skin against gravitational pull.[15,16]

1.3.2 Vascularization of the Face

The arterial supply of the face relies on the terminal branches of the external carotid and internal carotid arteries. The superficial temporal artery and the internal maxillary artery supply the upper third and the deeper structures of the face, and the facial arteries supply the central and lower parts of the face. The ophthalmic artery, a collateral branch of the internal carotid artery, supplies the medial upper face and the periorbital area.

Most of the veins in the face run parallel to their corresponding arteries. These veins lack valves and therefore allow bidirectional blood flow. Because of this, wound infections of the perioral area and the upper lip have the potential to gain access to the cavernous sinus. Venous drainage of the face relies on the external, internal, and anterior jugular veins, which drain the superficial temporal vein; facial vein; and inferior labial and chin veins consequently[8,9,17] (Fig. 1.3).

1.3.3 Innervation of the Face

Innervation of the face is divided as sensory and motor. Sensory innervation to the face (and the rest of the head) is supplied by the sensory component of the trigeminal nerve (fifth Cranial Nerve). The trigeminal nerve divides into three major divisions which supply three major areas of the face.[3,10,17]

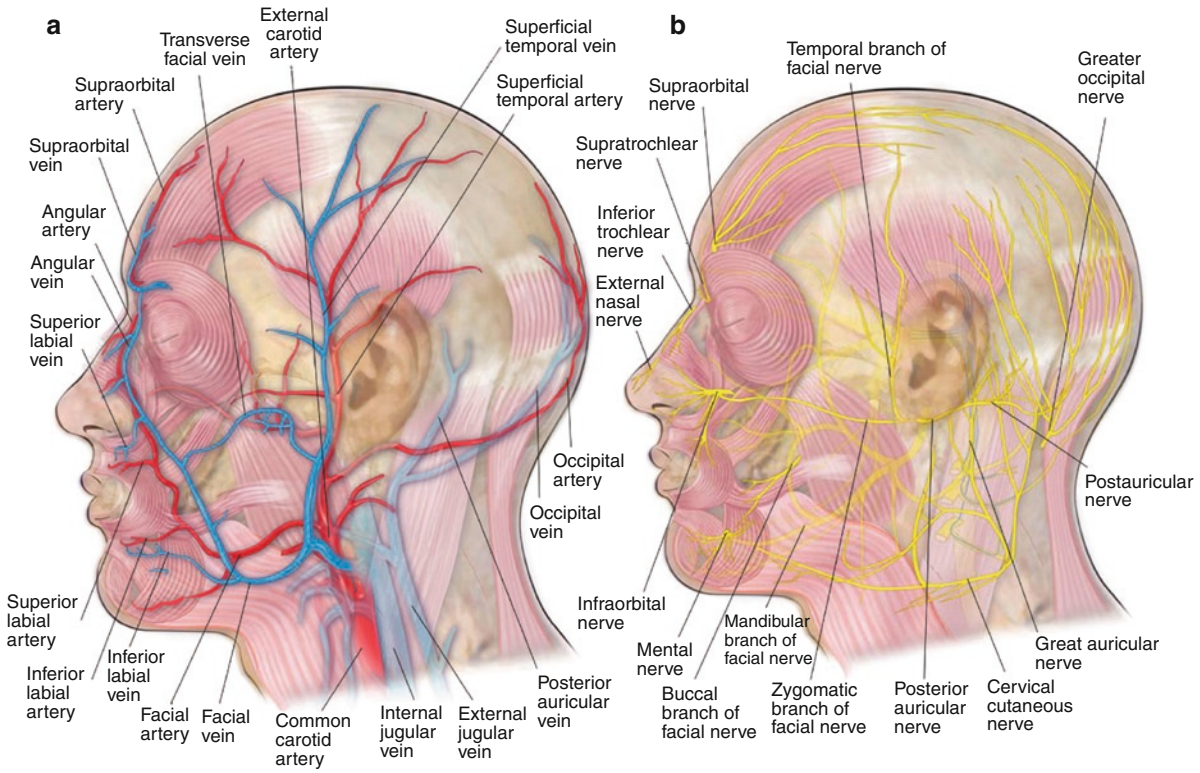

Fig. 1.3 Arteries, veins (**a**), and nerves (**b**) of the face (From Siemionow and Sonmez[2])

The ophthalmic division supplies the mucosa at the frontal sinus, the skin and conjunctiva, and skin over the forehead and scalp posterior to the region of the region of the lambdoid suture via the supraorbital branch. The maxillary division supplies the skin of the lower eyelid, cheek, nose, upper lip, and possibly the conjunctiva and skin over the maxilla via infraorbital branch. The mandibular division supplies the lower jaw, the lower lip, and the chin via mental branch.

All muscles of facial expression (plus platysma in the neck, the small muscles around the ear and the scalp muscles) are innervated by the facial nerve (seventh cranial nerve) via four branches. The temporal branch supplies the facial muscles superior to the zygomatic arc including the forehead muscles and the orbicularis oculi. The zygomatic branch innervates the muscles in the zygomatic, orbital, and infraorbital regions. The buccal branch supplies the buccinators and the muscles of the upper lip. The mandibular branch supplies the muscles of the lower lip and chin. The muscles of mastication are supplied by the mandibular division of the trigeminal nerve[3,4,10,17] (Fig. 1.3).

Sympathetic innervation of the face arises from the postganglionic cell bodies in the superior cervical ganglion that is located opposite the second and third cervical vertebra. Sympathetic preganglionic neurons that control the salivary glands are located in T1–T4 levels of the spinal cord. Stimulation of the sympathetic fibers leads to vasoconstriction of the vessels in the glands and cutaneous arteries of the face.[18]

Parasympathetic nerves are distributed to blood vessels in salivary glands and vessels of the nasal mucosa of the face. The major target of cranial parasympathetic pathways is the secretory glands associated with the secretion of tear (eye), saliva (mouth), and mucosa (nose). Stimulation of the parasympathetic system leads to vasodilatation and consequently secretion of watery fluid. Parasympathetic paraganglionic neurons that control the submaxillary and sublingual glands are located in the salivary nucleus (Cranial Nerve VII). Postganglionic fibers arise from postganglionic cell bodies in the submaxillary ganglion and course with the facial and trigeminal nerves to reach the glands. Parasympathetic preganglionic neurons

that control the parotid glands are located in the inferior salivatory nucleus (Cranial Nerve IX), and its stimulation leads to secretion from the parotid gland via concomitant vasodilatation.[18]

1.4 Functions of the Face

Facial features arise from the subtle arrangement of many diverse tissues. The face is not simply a mask, but a functional, dynamic, and aesthetic organ. Functions of the face can be grouped as physiologic, expressive, and aesthetic functions. It also plays an important role in a person's identity.[2,19]

1.4.1 Physiologic Functions of the Face

The skin of the face serves as an anatomic barrier between the internal and external environment, providing bodily defense. The skin of the face is also a sensory organ containing a variety of nerve endings that react to warmth, cold, pressure, vibration, and tissue injury. The skin of the face regulates heat and controls evaporation, as is the case with the skin on other parts of the body, primarily through vasodilatation and vasoconstriction of the cutaneous blood vessels.[11]

The hair in the nose, ears, and around the eyes protects these sensitive areas from the infiltration of dust and other small particles. Eyebrows and eyelashes protect the eyes by decreasing the amount of light and particles that can enter the eyes.

Eyelids protect the ocular globes from mechanical injury and help to provide essential moisture for the conjunctiva and cornea.[20]

The nose warms and moisturizes the inspired air, removes bacteria and particulate debris, and conserves heat and moisture from expired air. It has an area of specialized cells which are responsible for the sense of smelling. The sense of smell plays a major role in the flavor of foods, and it is common for individuals who lose their sense of smell to report that food loses its taste although the food has only lost its aroma, but the taste (sweet, salty, sour, bitter) remains intact.

Nasal breathing (as opposed to mouth breathing) permits optimal pulmonary function.[21]

1.4.2 Expressive Function of the Face

The face is an organ of emotion apart from its physiologic functions. As an expressive organ, the face provides an effective and communicative presence to others. We constantly read facial expressions to understand what others are feeling. We can understand the happiness, anger, pain, sorrow, sadness, or even madness from the expressions on the face. Conscious and unconscious facial expressions are crucial in our encounters with others. We constantly perform a stream of facial movements when we communicate in person. We can say that approximately two thirds of our communication with others takes place via the nonverbal channels of the face.[22]

Consequently, the face can be accepted as the most powerful instrument of nonverbal communication, allowing us to express our thoughts and feelings and to decode the thoughts and feelings of others.[23]

There are numerous reports about the difficulties experienced by the people who are unable to use their faces to communicate effectively, whether through the absence of expression, or miscommunication resulting from altered expressions.[22-25]

1.4.3 Aesthetic Function of the Face

The face plays a critical role in physical attractiveness. It is perhaps the most important human art object. Attractive facial features in women may include a narrow facial shape; narrow, thin eyelids; and a slightly wider distance between the eyes; large eyes; a prominent zygomatic arc; thin eyebrows; a small nose; small chin; small jaw bones; and full lips. Male attractiveness includes prominent chin bones, large jaws, a prominent chin, thin lips, and thick eyebrows.[26]

A great deal of research has shown the robust effects of facial attractiveness on interpersonal perception. It has been observed that facially attractive people have social advantages. For instance, they are occupationally more successful, more popular, more assertive, and have more self-confidence. Social and developmental physiologists have proved that facial attractiveness produces a halo effect causing people to ascribe many positive qualities and characteristics to attractive persons.[27,28]

On the contrary, facial deformities from trauma, congenital disabilities, and post-surgical scars are perceived as dysfunctional and produce significant adverse consequences for the physiological and social functioning of affected persons. Functional facial deformities have been variously described as only those that impair respiration, eating, hearing, or speech; however, it has been documented in the literature that facial scars and cutaneous deformities can have a significant negative impact on social functionality.[25,29-32] Consequently, facial reconstructive goals include not only restoration of orifices for adequate respiration, vision, and alimentation, but also reestablishment of improved surface or contours meant to transform a deformity to an acceptable range of normal appearance. At that time "beauty" is not the goal, but rather the goal is to eliminate the negative stigma that arises from a facial configuration that lies outside of the range of normal.[33]

In a recent study, the authors confirmed that in the population, people do place a high value on a normal facial appearance that is delineated as distinct from a beautiful appearance, and normal appearance is accepted as an important function of the human face by the people. The subjects in that study ranked the face as "the most important body part to restore after an injury," followed by the hand, leg, arm, knee, and breast.[33]

1.4.4 Role of the Face in the Formation of Identity

The face plays a central role in the perception and formation of identity. Human beings recognize each other by first looking at the face. Our face develops from childhood into adulthood, then into middle age, and finally into senior years. Yet it retains features that were already prominent in childhood. Face help us understand who we are and where we come from with markers of genetic inheritance over many generations, providing evidence of parentage, ancestry, and racial identity.[34] These persisting features contribute to the relatively unchanging expression of the face and define its physiognomy. Disruption to one's facial appearance, particularly the inability to recognize oneself, represents the disruption of the body image and may constitute a major life crisis.[22,35]

The formation of identity function of the face cannot be totally transferred from donor to recipient without the transfer of all the underlying bony structures. The shape of the face is closely related to the shape of the underlying bones, a subject that has engendered debate with regard to facial identity transfer.[36]

1.5 Conclusion

Based on the functional anatomy of the face that is summarized in this chapter, we propose that the face should be accepted as an organ. Additionally, face transplantation should be considered as an organ transplantation that enhances the quality of life to a degree comparable to that of solid organ transplantations. The aim of this chapter is to emphasize multiple vital functions of face and to make awareness that without these functions, quality of life of severely disfigured patients is jeopardized.

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The Face as a Sensory Organ

2

Maria Z. Siemionow, Bahar Bassiri Gharb, and Antonio Rampazzo

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Abstract The human face is a highly specialized organ which receives sensory information from the environment and transmits it to the cortex. The advent of facial transplantation has recently shown that excellent reconstruction of disfiguring defects can be achieved; thus, the expectations are now focused on functional recovery of the transplant. So far, restoration of the facial sensation has not received the same attention as the recovery of motor function. We describe the current knowledge of the sensory pathways of the human face and their respective functions, the available methods of sensory assessment, and the data on normal sensation. The topographical sensory anatomy of facial subunits is summarized, the trigemino-facial connections are illustrated, and the implications of these anatomical variations on facial allotransplantation are emphasized.

2.1 Introduction

Since 2005, 11 reports on face transplantation have confirmed that this procedure is technically and immunologically feasible. The goal of reconstructing severely disfiguring facial defects by coverage with similar tissues coming from human donors has been achieved. This opened the discussion on the best approach to achieve functional recovery of the transplanted face with restoration of fine facial movements and sensation. These two determinants of optimal functional recovery were restored differently for documented cases of face transplantation. In three patients, the facial nerve was repaired either directly (two patients)[1] or with interpositional nerve grafts (one patient),[2-4] whereas the sensory nerves were satisfactorily repaired only in one case.[1] These differences in the reconstructive approaches

M.Z. Siemionow (✉)
Department of Plastic Surgery, Cleveland Clinic, Cleveland, OH, USA
e-mail: siemiom@ccf.org

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to motor and sensory nerve repairs were mainly dictated by the extent of facial trauma before transplantation.

One of the fundamental functions of the human face is the ability to receive multimodal sensory information from the environment and to convey it to the cerebral cortex for integration and processing. The presence of normal sensation is important not only for the discrimination of touch, temperature, and pain, but also for initiation of vigilant or defense reactions. The presence of labial sensation helps in avoiding drooling while eating or drinking.[5] Stretching of the perioral skin contributes to the precise articulation in speech.[6] Interestingly, cutaneous stimulation increases the intensity of estimates of the olfactory system.[7] It has also been reported that facial skin cooling decreases the heart rate and increases blood pressure.[8] Finally, normal sensory pathways allow to draw pleasure and satisfaction when exposed to external stimuli.[9] It is clear that restoration of the above functions is expected and essential for the optimal outcomes following face transplantation.

To learn more about the importance of the face as a sensory organ, the aim of this chapter is to illustrate the complexity of the sensory pathways of the face and their specific functions, to review current methods of assessment of facial sensation, and to summarize the available data on normal sensation. Finally, the topographical sensory anatomy of facial subunits is summarized and the implications of sensory–motor communications on the mechanism of recovery of facial sensation after trauma and face allotransplantation are discussed.

2.2 Facial Skin Receptors and Their Function

Over 17,000 corpuscles have been reported in the human face, which contribute to several sensory functions.[10] For the discrimination of touch, four different types of receptors have been described in the hairy skin of the face and include Ruffini corpuscles, Meissner corpuscles, Merkel cell disks, and hair receptors (Fig. 2.1).

Ruffini corpuscles are especially sensitive to skin stretch, consist of axon terminals and surrounding Schwann cells that envelop tightly bundles of collagen fibrils and are associated with vellus hairs. They are innervated by the superficial portion of the dermal neural network.

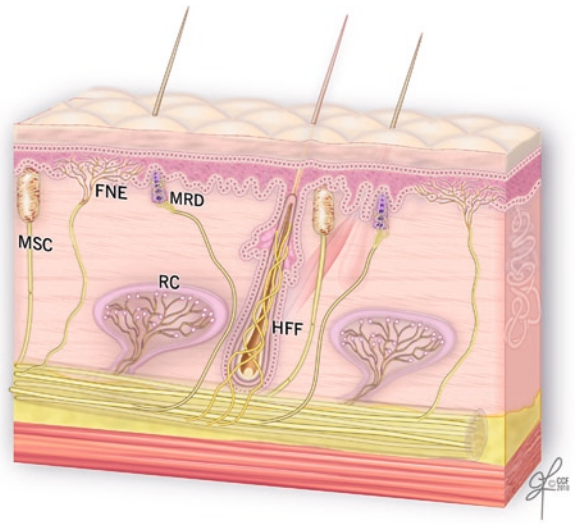

Fig. 2.1 The receptors of the human facial skin. *MSC* meissner corpuscle, *FNE* free nerve endings, *MRD* merkel disk, *RC* ruffini corpuscle, *HFF* hair follicle fiber (Reprinted with permission, Cleveland Clinic Center for Medical Art & Photography © 2010. All Rights Reserved)

Meissner corpuscles are more sensitive to stroking and fluttering of the skin and are localized in the dermal papillae. They are globular fluid-filled structures enclosing a stack of flattened epithelial cells. The terminal axons are entwined between the various layers of the corpuscles.

The *Merkel disk receptors* are formed by a small epithelial cell surrounding the nerve endings. Merkel receptors detect pressure applied on the skin and discriminate texture of objects. Two different types of Merkel cells have been described in facial skin.[11] The first type is localized in the dermis, on the external root sheath collar; it is not associated with nerve terminals and it is undifferentiated. The Merkel cells localized in the basal layer of the epidermis are associated with nerve terminals and have different granules within a single cell. An endocrine function has been attributed to them via regulation of the autonomic nerves.[12]

Interestingly, the *Pacini corpuscles*, which are well described in the fingertips and the palm of the hand where they are responsible for detection of vibrations, are absent in the skin of the human face.[12-14]

Hair follicle fibers work in a similar way to Meissner corpuscles, displaying a lower threshold for light stroking. They form a palisade of lanceolate terminals, which abut the external root sheath of the vellus hair in