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1 Social Impact of Cellulite and Its Impact on Quality of Life

Doris Hexsel, Camile Luisa Hexsel, and Magda B Weber

Introduction

Almost all women have or believe they have cellulite. As it is more common to expose the body in certain cultures and in sunny countries such as Brazil, cellulite is of great concern to many women and also represents a problem of great social impact.

In today's globalized culture, physical well-being, including care taken with appearance, is highly valued. From this perspective, it is very important to evaluate the impact on quality of life (QoL) of such cosmetic problems as cellulite, wrinkles and aging. The fact that these have an impact on the QoL is indirectly shown by the growing interest in the investigation and treatment of these problems, which until recently were considered to be of minor significance. New studies involving QoL will benefit all those who suffer to a greater or lesser degree from these problems, and will be of great value in assessing the need for new scientific research into the treatment of these problems.

Medical treatments traditionally focused on quantitative factors, such as the reduction of morbidity and mortality and the assessment of treatment safety and social markers of health. Qualitative factors, such as patients' perceptions of well-being and capacity to perform activities of daily life were not a primary aim. In recent decades, however, the measurement of patient's quality of life and the evaluation of different treatments have been the focus of growing attention.

Sarwer et al. published a review of the literature that focused on psychological and social-cultural aspects, their relation to physical appearance, and their influence on the decision to undergo cosmetic treatments [1]. Their study revealed that in the 37 different cultures studied, men and women gave greater priority to sexual attraction in the choice of partners than to aspects of personality such as independence, emotional stability and maturity [1]. Dermatological diseases and cosmetic problems significantly affect self-esteem. As the symptoms are visible, the discomfort and psycho-emotional effects are frequently more serious than the physical alterations caused by the disease. Thus, it becomes very important to assess and quantify the emotional and social parameters in these patients, in order to understand the disruption that the problem causes in various daily activities. This will facilitate the follow-up and treatment evaluation, and consequently allow for improvements in the QoL of the patients.

The great importance given to QoL evaluation in clinical investigation and patient care has led to the development of questionnaires designed for the collection of information from the patients on the impact of the disease on their everyday lives. This knowledge allows the medical professional to better observe how the disease affects the patients physically, psychologically, and socially, and facilitates the evaluation of the effects on the lives of the patients.

In the case of cellulite, the reasons that lead the patient to seek treatment are generally social and, sometimes, also emotional. These may include the embarrassment caused by cellulite in

social, affective, and sexual relations as well as the avoidance of normal everyday activities such as visiting a swimming pool or beach, practicing sports or exposing the body during intimacy.

A number of studies have been published that deal with QoL and recognize the value of specific questionnaires for dermatological diseases such as psoriasis, acne, melasma, atopic dermatitis, hyperhidrosis, and alopecia among others [2–9]. These studies have revealed the existence of similar facets related to QoL in patients from various countries [10] and point to the discomfort and the psycho-emotional effect on the patients. However, in general, little research has been done on the psychological, environmental, and social aspects of dermatological diseases. Moreover, to date, no study on the QoL of those afflicted by cellulite has been published.

Patients suffering from skin diseases should not be treated merely for the physical harm caused by the disease [10]. The skin is the most external and apparent organ, and skin contact contributes to the formation and structure of the personality.

Aspects of Cellulite Related to QoL

Cellulite is a clinical and aesthetic condition affecting most women. It may appear in preadolescence, adolescence, or adulthood. With cellulite, the connective tissue and adipose tissue undergo alterations, resulting in blood and lymphatic alterations [11]. Clinically, cellulite is characterized by alterations to the cutaneous surface, especially on the buttocks and thighs, giving the skin an orange peel or mattress appearance [12,13]. Clinically, cellulite is classified into degrees that range from 0 to III according to the clinical characteristics [14]. As well as classifying the cellulite, it is suggested that associated factors such as obesity [measured by the body mass index (BMI)] and degree of flaccidity (classified as light, moderate, or severe) be characterized.

Our clinical experience has shown that cellulite is a problem that has an impact on the QoL of both younger and more mature women, though the impact is greater in younger women. It also seems that cellulite is more frequent nowadays than many years ago.

We report here on a clinical study carried out in 62 female patients, aged between 18 and 45 years (average age 32) with BMIs between 18 and 25 (average 21.8), having various degrees of cellulite on the buttocks and thighs. Over a period of two months, these patients received mechanical treatment in both legs and topical treatment in only one randomly chosen leg. The degree of cellulite in each patient was evaluated before and at the end of the treatment and attributed a classification between 0 and III, according to the clinical appearance of the cellulite. No patients included in this study had a cellulite classification of 0.

These patients also answered a non-validated questionnaire created by the authors at the beginning and end of the treatment. This questionnaire evaluated patients' self-esteem and highlighted

changes in the behavior of patients with cellulite such as avoiding wearing tight or small clothing; feeling embarrassed when frequenting swimming pools or at the beach, etc. The impact of cellulite in relation to age group was also evaluated, together with factors that patients believe may influence the cellulite, such as inheritance, diet, and physical activity, as well as the treatment performed and self-perception of the severity of their cellulite. A survey of the answers given to the questions permitted an assessment of:

1. patients' impressions of the problem of cellulite;
2. the everyday situations that result in restrictions or embarrassment for patients with cellulite; and
3. the impact of treatment on patients' QoL.

Some factors, in the opinion of the patient, may influence cellulite. When questioned regarding diet, 65% of patients believed that there is a relationship between cellulite and diet. For 60% of the patients interviewed, a specific diet can help with cellulite. Along the same lines, 90% of patients believed that practicing physical exercise is an efficient treatment for cellulite and may, in isolation, moderately reduce cellulite.

Cellulite was perceived before 20 years of age by 65% of patients. With regard to family inheritance, 80% of patients reported having first- or second-degree relatives with cellulite. Because it is a clinically diagnosed and easily recognizable problem, this information is highly indicative of the presence of positive family cases, bearing in mind that the great majority of patients reported a family member of the first degree, mother or daughter, as having the same problem.

Regarding the restrictions caused by cellulite, when questioned in a generalized way about the degree to which cellulite hampered their lives with the options of "not at all (1)," "a little (2)," "moderately (3)," or "greatly (4)," it was found that 70% of the interviewed patients considered that cellulite hampered their lives greatly. Regarding specific daily situations, it was noted that those suffering from cellulite experience some day-to-day restrictions. Each situation was evaluated by the patient and attributed a value from 1 to 5, in which "1" was given to situations in which having cellulite had no effect, "2" to little effect, "3" to a moderate effect, "4" to a significant effect, and "5" to a very significant effect.

The situations included wearing a bikini and tight clothing, sexual activity, practicing sports, and crossing the legs and sitting, which indicate the great social impact caused by cellulite. Keep in mind that, in all the situations presented and even after treatment, having cellulite influences to a moderate or significant degree the daily lives of the patients. We notice that the treatment, even though it might not be 100% effective for the problem, may modify the behavior of cellulite patients. The results obtained from the studied sample reveal that the presence of cellulite after treatment interferes less in certain activities when the responses from before and after treatment are compared. This reduction is most evident in the item "sexual life" when the total sample is examined: 21.9% of the patients mentioned that cellulite had great or very significant influence on their sexual life before treatment and, although the treatment may not have led to a marked improvement in the cellulite, only 8.3% of the patients gave the same response following treatment. The sitting position, a position that

supposedly makes the cellulite more apparent, reveals that before treatment, 48.9% of the patients interviewed considered the influence very significant, while after treatment this percentage fell to 15.1%. With regard to the embarrassment caused by the presence of cellulite in the practice of sports, the answers both before and after treatment were very similar. The results suggest that, for women, exposing the body during sport is not as embarrassing as in other situations, as for example during sexual relations.

According to Jorge [10], the psychological impact and in interpersonal relations, respectively, is more prejudicial for women than for men. Studies that evaluated patients with dermatosis, carried out in Sweden and Norway, suggest that those at risk of the greatest harm are females who are young and in whom that disease exists over an extended period of time [10]. As cellulite appears basically in women, this condition should be investigated in terms of its impact in QoL.

A study by Harlow et al, that evaluated the impact on quality of life of dermatological diseases during primary attention, noted the differences between men and women in relation to the various forms of constraints caused by the diseases from which they suffered [15]. Ten (10) attributes were evaluated: physical symptoms, feelings, daily routine, clothing, social and leisure, sport and exercise, work and study, personal relations, sexual relations and treatment. Of these, only in the question related to the degree to which the condition affected the practice of sports and exercise was the score given by males higher than that given by women [15]. This shows that the practice of sport may have greater significance in the male group than in the female.

We also checked the impact of treatment on the QoL of patients with cellulite. Each patient attributed a value from 0 to 9, with 0 representing very low self-esteem in relation to the fact of having cellulite, and 9 representing very high self-esteem. The clinical evaluation considered the improvement on the left and right sides, which were treated differently. Even without any improvement in the degree of cellulite noted by the examiner, there was an increase in self-esteem (evaluated from 0 to 9) after treatment. This improvement can be seen in the difference in the percentage of scores found from before and after treatment. This shows that the treatment did have a positive effect on the self-esteem of the patients, indicating that the simple fact of treating the cellulite and caring for themselves, even in the absence of any clinical improvement, influenced the well-being of the patients, who described themselves as better and more confident following the treatment. It may suggest that treatments should be tried, even if there is no cure for this condition.

In 2008, the authors conducted a new clinical trial with the aim to build a specific questionnaire on the QoL for cellulite patients. Fifty patients were included responding to a qualitative survey to evaluate the main spontaneous complaints of patients seen because of cellulite and the effect of cellulite on their quality of life. An open question was asked about the main complaint: *"We are trying to find out how much the fact of having cellulite affects the life of female patients. We would appreciate your cooperation, but your participation is totally voluntary and not compulsory. Could you please describe in what ways having cellulite has affected your life? You may include aspects of your professional and social life, personal relationships, leisure activities,*

Table 1.1 Summarized version of CelluQOL[®] questionnaire

	Not bothered at all	Bothered most of the time	No feelings either way	Bothered most of the time	Bothered all the time
Skin appearance	1	2	3	4	5
Clothing manners	1	2	3	4	5
Feeding habits	1	2	3	4	5
Physical and leisure activities involving exposure of the body in public	1	2	3	4	5
Physical or recreational activities involving the restricted exposure of the body	1	2	3	4	5
Sexual life	1	2	3	4	5
Negative feelings	1	2	3	4	5
Disbelief about results of treatments	1	2	3	4	5

or any other situation. Although we need to know how old you are, no further personal identification is necessary.” The preliminary analysis of the questions answered by the volunteers showed factors and situations which are influenced by the presence of cellulite [16]. These patients mentioned that they usually avoid wearing white colored and beach clothing and prefer to wear black (90%); dislike walking on the beach without wearing beach jackets (56%), this is because they prefer to hide their cellulite; they also feel bothered and constrained by the presence of cellulite (38%); they are afraid about their partners noticing their condition (36%) and also have feelings of low self-esteem (20%). From the preliminary answers, it was possible to establish the main domains that affect the QoL due to the presence of cellulite: clothing choices, leisure habits, physical activities, relationships with partners, personal feelings about themselves, and daily habits [16].

The second part of the same study mentioned above involved 100 patients and aimed to create and validate a new instrument of Quality of Life on Cellulite, called CelluQOL[®]. The authors created two versions of CelluQOL[®], based on the domains revealed in the first part of the study, one complete and the other summarized (Table 1.1). All patients responded to both questionnaires which were compared and validated. The complete data of this study are in process of statistical evaluation and will be published soon. However, the data collected and pre-analyzed from this study suggests that a QoL questionnaire for patients presenting cellulite may be useful in clinical practice [16].

Conclusion

Thorough QoL evaluations will be necessary to evaluate not only the importance given to the problem of “cellulite”, but also the need to develop new treatments for cellulite [17].

It is interesting to note that, even without techniques that can guarantee significant improvement of cellulite in its different degrees, cosmetic patients want alternatives and their emotional improvement is not directly related to the clinical improvement. Care and attention to cosmetic problems can lead to improvement in the emotional state of the patients.

Cellulite has a real impact on the QoL of patients, as it restricts those that suffer from the condition in everyday situations and activities. This causes damage in the psychological area in interpersonal relationships, as also occurs with other conditions that afflict the skin.

Patient complaints should be evaluated objectively regardless of whether defects are visible and pertinent or just imaginary, or even if the patient's concerns seem to be out of proportion with reality. As it is a very sensitive issue, techniques used for esthetic procedures should be improved, and their performance should lead to minimal side effects, faster recovery and greater safety. However, esthetic procedures may not be enough to deal with complaints that may in fact mask fears, anxiety and fantasies, and a full evaluation may be necessary to improve and preserve the doctor-patient relationship.

Finding out what aspects in each domain concern patients and measuring their possible impact may help to make decisions about what type of treatment should be prescribed for any specific patient. Also, the development of instruments to measure the QoL of patients presenting aesthetic complaints is an innovative and challenging area to be studied. The measurement of the aspects in each domain that concern patients may help to make decisions about more effective ways to treat specific patients.

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3 Anatomy of Cellulite and the Interstitial Matrix

Pier Antonio Bacci

Introduction

The understanding of the structure and function of the interstitial (or extracellular) matrix constitutes a relatively recent conceptual revolution. Prof. Francesco Albergati of Milan, student of Prof. Sergio Curri, was the first to study and describe the clinical relevance of this microvascular tissue unit [1]. A brief overview is given here.

Cellulite

The body's silhouette is characterized by a particular localization of the subcutaneous adipose tissue over the osteomuscular structure. The human body is characterized by the presence of rigid fasciae and especially deep muscular fasciae that start from the base of the cranium and continue to the ankles and metatarsus promoting various physiological functions: vascular, neurophysiologic, and orthopedic. Cellulite is a degenerative and evolutionary affect on subcutaneous tissue. The authors describe cellulite from a histomorphologically point of view, defining it as a PEFS: "panniculopatia edematofibrosclerotica (edematofibrosclerotic dermo-lipodermic pathology)" [2].

Cellulite is considered as a series of events characterized by interstitial edema, secondary connective tissue fibrosis, and consequent sclerotic evolution. Recent clinical observations demonstrated that if PEFS is a true part of cellulite, it does not represent all the various clinical aspects of cellulite. In fact there are often particular forms of connective and interstitial damage or diffuse syndromes characterized by a lipedema associated with a lymphedema and/or lipodystrophy. Such pathologies are mainly observed on the gluteal muscle and on the lower limbs of women.

Fundamental here is acceptance that cellulite is not a female whim or something considered unsightly, but a real disorder, or rather, different disorders that represent aesthetic pathologies that must be cared for from a medical and cosmetic point of view.

- The cellulite disorder normally is an expression of lipolymphedema, or more precisely a typical expression of mesenchimopathy with microvessel alterations.
- It is, above all, an endocrine-metabolic disorder that may or may not be associated with lipolymphedema, localized adiposity, and lipodystrophy with an alteration of the interstitial matrix and connective tissue. It, therefore, presents various aspects that call for different therapies.
- First and foremost, it displays alterations of the purifying organs that must be controlled and brought back into balance. There are also alterations of the basic regulation of temperature, pH, and the oxidation-reduction systems.
- Such alterations can be discovered with tests to assay free radicals and heavy metals, and by video capillaroscopy. These dismetabolic situations can be corrected through diet (especially protein therapy in two-week cycles), physical activity, and polyvitaminic, alkalizing, and orthomolecular therapy [3–10].

- Cellulite is often also associated with venous lymphatic insufficiency; however, cellulite formation occurs before, not after, the venous disease. It is the cause, not the effect.
- Lipolymphedema and cellulite are the greatest expressions of an alteration of the functionality of the cleansing organs. We also know that unnecessary nongraduated elastic stockings are one of the causes of superficial cellulite due to compression and the slowing of microcirculation [11].

We know that three forms of edema can be associated with cellulite disorder: venous edema, lymphatic edema, and lipedema.

1. What is venous edema?

Venous edema is basically characterized by a release of kinins, toxic substances, and iron that carries calcium with it. It is an edema associated with phlogosis of the tissues and deposition of hemosiderin.

2. What is lymphedema?

Lymphedema is a pathological condition characterized by a state of tumescence of the soft tissues, usually superficial, due to accumulation by stasis of high protein-content lymph caused by primary and/or secondary alterations of the lymphatic vessels. Lymphatic edema is linked to alterations of the lymphatic vessels, and is characterized by free water in the interstices that has bonded with proteins and solutes, forming an edema of lymph with interstitial hyperpressure [12].

3. What is lipedema?

Lipedema is a particular syndrome characterized by subcutaneous deposition of fatty tissue and water, especially in the buttocks and lower limbs, which may or may not be associated with lymphedema and/or lipodystrophy [13,14]. It is an edema characterized by an increase of free water in the interstices; it is not lymph—it is free water and fatty tissue.

Lymphedema

Lymphedema is a chronic and progressive affliction that is very difficult to cure. The aim of treatment is to keep the disease stable in order for the patient to live normally. In this type of pathology, the first component is edema and the second is fibrosis. The increase of protein levels in the tissues contributes to the development of edema and probably causes chronic inflammation and subsequently the fibrosis.

The basic clinical sign of lymphatic problems, either mechanical or dynamic, is a cold and pale swelling, which is initially viscous and later hardens but is not painful in most cases. With the increase in severity of edema, there is an increase in limb volume. At this point, it is not sufficient to hold the limb in an elevated position in order to reduce edema; fibrosis is already present.

Lipedema and Lipolymphedema

Lymphedema is described as a pathology characterized by a tumescent state of soft tissues, usually superficial [15], and is related to an accumulation of lymph with high protein content due to stasis in the interstitial space. It is determined by primary

and/or secondary damage of the transport vessels. In contrast, lipedema is a particular syndrome with a poorly understood etiology characterized by fat and water deposits in the subcutaneous tissue (particularly in lower limbs and gluteal muscle), and associated with lymphedema and/or lipodystrophy.

Lipedema was described for the first time as an accumulation of subcutaneous fat with hard leg edema excepting the feet. In various descriptions [16], the following observation has always been underlined: foot hypothermia with a localized gradient of temperature. Such pathology, often superficially defined as a lymphedema or venous insufficiency or cellulite, is observed in more than 65% of women between the ages of 14 and 35 years, becoming lipodystrophic lipolymphedema after the age of 40. The common characteristics of a lipolymphedema are the absence of venous insufficiency (eventually secondary) and the close relation with the fat tissue metabolism.

Lipolymphedema is a syndrome of unknown etiology, characterized with fat deposition in the subcutaneous tissue and associated with orthostatic and recurrent edema in the legs and gluteal muscle that induces the impression of an increased volume in the limbs. Lipedema always begins in the legs, excluding the ankle and foot, which makes it different from lipolymphedema. It can be related to weight increase but is often independent of it. It is often related to familial factors. The characteristic of this extremely frequent disease is that edema always succeeds fat deposition. The latter is subsequent to endocrinometabolic disorder of the interstitial matrix and is not accompanied with obesity.

The edema here is not caused by structural changes of venolymphatic vessels, but by the modified ratio of the distance from the adiposity and connective structure with a loss of support. It is an edema that worsens with walking and standing, in contrast to phlebolympedema. Another difference from lymphedema is its softness and the possibility of its making a skin fold that is not obstructed by the viscosity. Thus it is different from lipolymphedema, phlebolympedema, Barraquer-Simmond disease (characterized by upper body thinness), and Dercum syndrome; the latter, which is clinically similar, has an etiology related to toxicities of the autonomous nervous system linked to an intestinal dysbiosis.

Dercum Syndrome

The word "lipodystrophy" means a pathology characterized by structural and functional damage of adipose tissue. Lipodystrophy can be associated with some form of lipolymphedema, the more typical being Dercum lipodystrophy or painful lipodystrophy. Women are affected early with recurrent lipedema. Typically painful fat nodules are often preceded by the appearance of lipedema and are often associated with asthenia, neuropsychic and adynamical troubles (depression or anxiety), and intestinal dysbiosis. Limb pain is different from the pain of lipolymphedema or from superficial hypoxia, where pain is induced by pinching the subcutaneous tissue and is associated with tissue viscosity due to interstitial hyperpressure of toxic lymph.

Pathogenesis of the Dercum syndrome is not endocrine or metabolic (as in recurrent lipedema), but from nerve damage of the neurovegetative—either the hypothalamic or the peripheral—system. Interstitial inflammation phenomena have been demonstrated to be related to the nervous network linked to the adipose tissue in the environment of the extracellular matrix.

In this context, bacteria from intestinal origin have also been found. This disease is certainly attributable to a suffering of interstitial mesenchyma with exaltation of the lipogenesis (slowdown of the microcirculatory flux and damage of the α -2-fibers) due to the damage to the peripheral neurovegetative regulatory system.

"Big Leg"

For Robert Stemmer [16], famous French phlebologist and memorable president of the International Union of Phlebology, "big leg" means a lower limb in which volume increase is measurable and palpable. A total or partial big leg can be observed, but there are also different kinds of big leg such as venous, post-phlebitis syndrome, posttraumatic, angiodysplastic, lymphatic, adipose, or cellulitic big leg. The main characteristic of big leg is edema—systemic, lymphatic, venous, or interstitial edema. Considering that lymphatics run in the interstitial subcutaneous tissue, it is easy to assume that the increase of lymphatic edema or of adipose tissue could induce a lymph slowdown. We know that there is a neoangiogenesis, stimulated by collagen production, obtained after adipocyte rupture. Such collagen production also stimulates fibrinogenesis and vascular formation. The difference between localized adiposity and lipodystrophy or angiolipodystrophy is this: Localized adiposity means physiological or pathological accumulation of fat tissue in determined body areas, without a dystrophic process. Lipodystrophy means a pathologic affection of both supporting tissue and subcutaneous adipose tissue, characterized by various circulatory and metabolic damages. For this type of pathology, we now essentially use liposculpture.

Interstitial Matrix

These cells represent the functional units of all living organisms by virtue of their specific structural organization. They possess complicated biochemical and molecular systems, complexly organized and highly sophisticated. Such systems not only guarantee the survival of the cell, but they also (above all) allow numerous fundamental activities to take place for the biological life of the cell. This affirmation could appear banal at first: In reality the cell and its functional organization represent an extraordinary example of "natural functionality," as the natures of both are able not only to organize the constitutive elements of the tissues but also to predispose them, in the functional sense, to their precise and mutable adaptation in answer to the different biological changes that happen every second in the living organism.

An example of the importance of such sophisticated mechanisms is that some cellular passages are open only to sodium but not to potassium ions, while others are open only to glucose but not to amino acids. The protein in the transport membrane functions as a real "organ" to a degree that allows, through specific sites of recognition, the selective entry of substances into cells, determined by some precise passages. The ionic transport has extreme importance in biology. Perfect operation of the ionic pumps is vital for cellular life. The ionic movement through the membrane is also at the base of the production of adenosine triphosphate (ATP) in all cells, and particularly for the nervous system [17].

The ionic concentrations in the intra- and extracellular environments are shown in Fig. 3.1 [18].

As is known, the large concentration of Na^+ outside of the cell is compensated by the concentration of Cl^- while the strong

Component	Intracellular (nM)	Extracellular (nM)
Na ⁺	5–15	145
K ⁺	140	5
Mg ²⁺ (cytosol)	0.5	1–2
Ca ²⁺ (cytosol)	1/100000	1–2
H ⁺	7 x 1/100000	4 x 1/100000
Cl ⁻	5–15	110
Fixed anions	Tall	0

Figure 3.1 The ionic concentrations in the intra- and extracellular environments.

concentration of K⁺ is counterbalanced by a series of negative intracellular ions. For example, this narrow joining ensures the activity of the pump only when there are proper ions to transport, so that there is no wastage of ATP (Fig. 3.2).

Every cell, as a separate living cellular mechanism, has the vital necessity “to feel” its environment and “to interact” with it, to be able to survive dispatching its vital functions.

We could say that every cell necessarily has to have a “social life,” and it therefore must develop “senses” that allow it to communicate with other cells and with the whole extracellular environment, or rather with the “extracellular matrix.”

In a multicellular organism, cells have to coordinate their behavior in many different ways, exactly as happens in a community of human beings; here, in fact, communication is constant and fervent: Nearby individuals are spoken to and discussions are held with them; public announcements are transferred to whole populations; urgent messages are delivered from near or far to precise individuals; and precise alarms are sounded when dangers or threats draw near. What would seem difficult to humans is in reality even more difficult (but not impossible) for the individual constituents of our body, firmly created to be gathered in “organs” and “apparatuses” developing precise and defined functions.

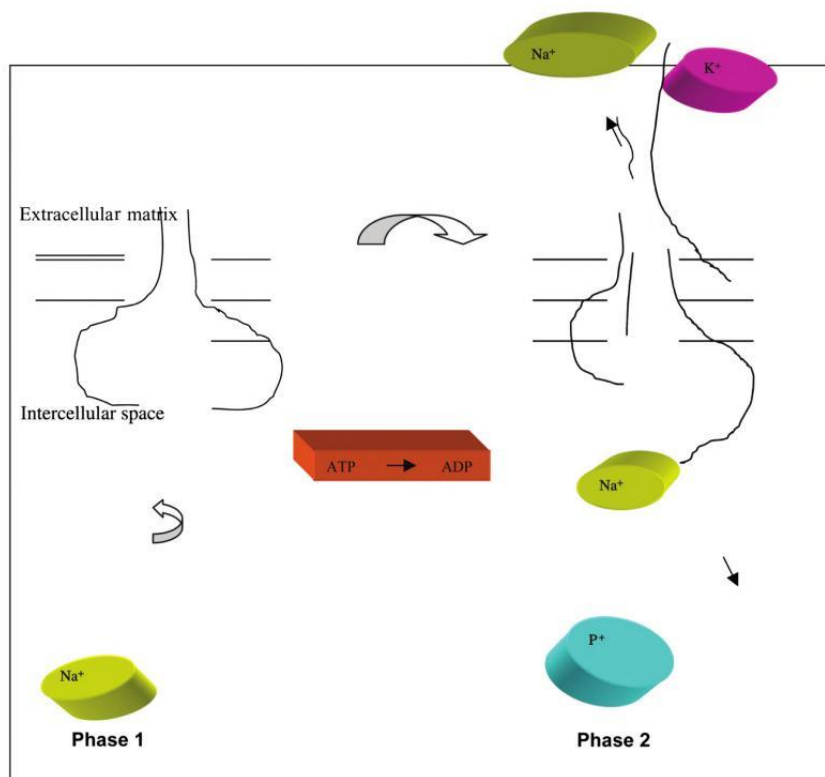


Figure 3.2 The ionic pumps.

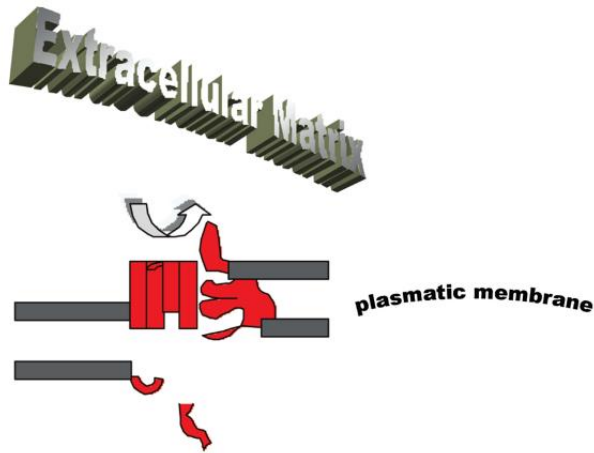


Figure 3.3 Schematic representation of a G protein coupled receptor. The receptors that tie the protein molecules (signal protein) ask for a site at the extracellular matrix level, formed by the polypeptidical substance identified on the figure. Smaller molecules (signal protein), such as adrenaline, ask for a small extracellular site.

To transmit a message “person to person,” we can write it on paper, then repeat it by voice, sending it in the form of “sensorial” impulses, for example by telephone. This sensorial impulse will come to another individual that will turn it into nervous impulses.

In the various phases of this simple communicative run, the same message is represented with different forms of signals: The real critical points of the transmission meet when information is converted from one form into another. This process of conversion is known as “translation of the signal.”

Cells come into contact with the complicated extracellular world through their surface, constituted by lipid and protein molecules composing the plasma membrane. Additionally, they come into contact with the specific areas of these molecules that are found, because of their steric and biochemical encumbrance and their conformation, in the extracellular environment, forming intimate and complex biochemical-functional relationships with the extracellular matrix. Thanks to the continuous activity of this real interface of cellular contact, the cells are able to recognize other cells, near or distant, as real functional entities of a similar subject, or as structures extraneous to them; to send and to continually receive chemical and physical signals; and to stick to other cells or other substances present in the interstitial spaces of the extracellular matrix. For example, cellular receptors have great importance, especially the receptors that tie the molecular protein conducting the signal to the extracellular matrix, where the union happens with the membrane (Fig. 3.3).

The cellular membranes are responsible for the internal organization of cells as well as for interaction with external stimuli and for “structural integrity.” The plasma membrane prevents a mixing of cellular contents with extracellular molecules and acts as the first element of “contact” between the cells and the extracellular environment. The composition and the maintenance of this structure is essential for the generation and regulation of different functional signals and biochemicals, both in the normal and in the pathologic cells [19,20].

The extracellular matrix is represented by a complex structural entity that surrounds, nourishes, and furnishes support to all the cells. The extracellular matrix is generally described as being composed of three biomolecular classes of substances:

1. structural proteins (collagens and elastin)
2. specialized proteins (fibrillates, fibronectin, laminin, etc.)

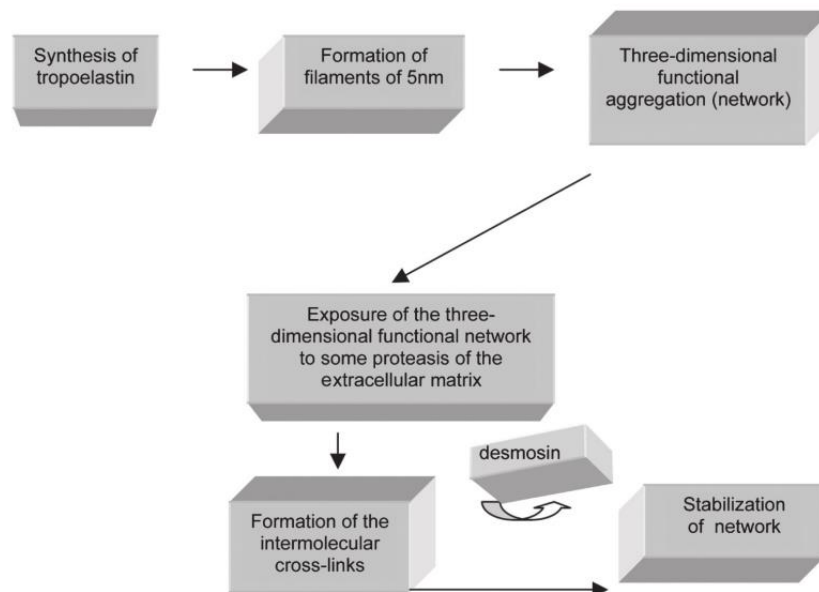


Figure 3.4 Interpretative scheme of the formation of the elastin from the tropoelastin.

3. proteoglycans (composed of a “core” of protein with long chains of two saccharides of glycosaminoglycan forming, in such a way, complexes of high molecular weight that represent a cardinal part of the extracellular matrix)

The connective system has great importance in the interstitial matrix. Many trials could be represented by the scheme in Fig. 3.4, reported to be the interpretative scheme of the formation of elastin by tropoelastin.

Therefore, it appears fundamental to begin to consider cellular homeostasis, both in a molecular and in an anatomic-functional biological sense, as a complex interaction of mechanisms and reactions that can begin and also evolve from the outside of the cell in the extracellular matrix [21]. The cellular matrix, the fundamental substance for life, is found as a rule as a solution. Some alterations can make it vary into a gel. These variations play a role in physical, chemical, and metabolic changes, among which are the alterations typical of cellulite [22]. In the dermal site and in the superficial subcutaneous site, we can have an activation of “metalloproteases-2” directly connected with the evolution of lymphedema, lipolymphedema, and mesenchymopathies [23–28].

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4 Definition, Clinical Aspects, Classifications, and Diagnostic Techniques

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Definition

Cellulite is a very common topographical alteration [1,2] in which the skin acquires an orange peel, mattress or cottage cheese appearance (Fig. 4.1) [3,4]. There are many theories to explain the physiopathology of this condition. The majority of the theories involve modifications that occur to the adipose tissue and microcirculation, resulting from blood and lymphatic disturbances, causing fibrosclerosis of the connective tissue [2]. It is generally considered a non-inflammatory, degenerative phenomenon that provokes alterations to the hypodermis [5] producing irregular undulations on the skin overlying affected areas.

Cellulite results from many complex events that involve the epidermis, dermis and subcutaneous tissue [1]. Cellulite can be divided into four stages:

1. alterations to the precapillary arteriolar sphincter, leading to changes in vascular permeability and capillarectasia resulting in pericapillary and interadipository transudation, leading to edema;
2. edema, provoking metabolic changes that result in hyperplasia and hypertrophy of the reticular network, leading to the formation of pericapillary and interadipository transudation, leading to edema;
3. organization of collagen fibers around groups of adipocytes forming micronodules; and
4. union of the micronodules to form the macronodules that cause sclerosis [6].

Anatomically, the cutaneous alterations found in cellulite are largely due to fibrosis of the connective tissues present in the dermis and/or in the subcutaneous tissue [7]. The connective tissue of the reticular dermis is connected to the deep fascia (SMAS), by means of the interlobular trabeculas (fibrous septa). Subcutaneous fat lobes are separated from one to another by these thin, usually rigid strands of connective tissue, which cross the fatty layers and connect the dermis to the underlying fascia. These septa stabilize the subcutis and divide the fat [8]. The shortening of these septum due to fibrosis provokes retraction at the insertion points of the trabeculas [9], causing the depressions that are characteristic of cellulite.

Nürnberg and Müller studied the anatomy and histology of fat and the connective tissue structure of the subcutaneous tissue in cellulite patients. They demonstrated the anatomical basis of the characteristic mattress aspect of cellulite and pointed out important differences in the organization of the subcutaneous between genders [10,11]. They also showed that in women the fibrous septa are usually orientated perpendicularly in relation to cutaneous surface, while in men they have a crisscross pattern [11]. Several studies have shown that the fat is divided into lobes, and in women these are larger and more rectangular when compared with those in men [4,11–15]. These anatomical

and histological findings explain the greater frequency of cellulite in women.

Nomenclature

In France in 1920, Alquier and Paviot described cellulite as an unaesthetic condition [6,16]. In the same decade, Lagueze described cellulite as a disease of the hypodermis, characterized by interstitial edema and an increase in subcutaneous fat [17].

Initially Curri denominated cellulite as nodular liposclerosis [6,18] and, later, adopted the term “cellulitic dermohypodermosis” [19]. In 1958, Merlen defined cellulite as a histoangiopathy [20] and, in 1978, Benazzi and Curri, after a histopathological study, suggested the term “sclerotic-fibrous-edematous panniculopathy” [21,22]. Nurberguer and Müller used the name panniculosis of the dermis [16,23] to describe cellulite from the histopathological viewpoint. Bacci and Leibaschoff suggest the terms cellulitic hypodermosis [16].

In recent years, the term “gynoid lipodystrophy” (GLD) has been mentioned in some studies [2,9,24]. The terms hydrolipodystrophy or herniation of the fat with hypodermic tension bands are also used to describe cellulite [25,26].

The presence of the suffix “ite” in a medical term indicates inflammation, therefore, the term cellulite is more appropriately used to designate inflammation and/or infection of the subcutaneous tissue [27]. However, the term cellulite has become very popular, and its use has been consecrated [20,28], being accepted throughout the world. Other synonyms often used for cellulite are listed in Table 4.1.

Clinical Aspects

Although it is found in all age groups and in both sexes [10,29,30], cellulite occurs mainly in women [6,31], especially after puberty [32] and in obese people, being considered a normal manifestation of obesity by Burton and Cunliffe [12,29].

There is evidence to suggest that estrogen is the most probably involved element in the initial dysfunction, aggravation and persistence of cellulite [1,20,33]. The greater incidence of cellulite in females, post puberty onset, the worsening of the condition in relation to some conditions, such as pregnancy, menstrual cycle, use of contraceptives and hormonal replacement, are cited to support this hypothesis [1].

Cellulite normally manifests itself in areas of greatest fat accumulation, such as the buttocks, thighs [29] (Fig. 4.2), flanks, abdomen [6,29] and upper legs [26,29,32].

The lesions are essentially asymptomatic. However, in severe cases of cellulite, symptoms such as a sensation of weight and pain are reported by patients in the affected areas [10,20,29]. Some authors believe these probably occur as a result of compression of the nervous terminals or the presence of inflammatory reactions [16,19].