# Cellulite

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#### **Core Messages**

- Elements that seem to be involved in cellulite's appearance are: adipocyte hypertrophy, connective tissue abnormalities, fibrous septa, and hormonal influences.
- A new cellulite severity scale (CSS) and classification was recently developed. The CSS considers relevant morphological aspects, such as the number of evident depressions, depth of depressions, aspect of raised areas, grade of laxity, flaccidity or sagging skin, and the previous cellulite scale.
- Diagnosis is mainly clinical although magnetic resonance imaging, laser Doppler flowmetry, thermography, and ultrasound can be used for research purposes.
- A series of treatments can treat or improve the appearance of cellulite, such as topical products, oral supplements, devices (mechanical massage, lasers, light sources, radiofrequency, and other technologies), and surgical procedures (Subcision<sup>®</sup> and liposuction).

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**Fig. 2.1** Common aspect of cellulite depressed lesions on the buttocks

# 2.1 Introduction

Cellulite, also called as edematous fibrosclerotic panniculopathy and local or gynoid lipodystrophy [6], is characterized by irregular relief alterations to the skin surface of the affected areas, giving orange peel, cottage cheese [31], or mattress aspect (Fig. 2.1). It is frequently found on the thighs and buttocks of women. Although cellulite is not a disease, it is considered a noninflammatory phenomenon with alterations in the subcutis.

It is a common clinical condition that usually affects women. It begins in puberty and progresses during the life. Nowadays, some factors involved in the genesis of this condition are better understood [18]. However, there are many other controversial theories that attempt to explain the pathophysiology of cellulite [30].

# 2.2 Prevalence

Approximately 85–90 % of women over 20 years are believed to have some degree of cellulite [31]. It has been described by Goldman [8] as a normal physiological state in postadolescent women, in which the fat storage in the adipose tissue is maximized ensuring adequate caloric availability for pregnancy and lactation [8]. It is highly prevalent in women of all races but seems to be more common in Caucasian females than in Asian females [1]. Ortonne and colleagues distinguished two subpopulations among women with cellulite by characterizing the "orange peel appearance" and the "shadowed surfaces": those of 21–30 years old, presented large but less numerous dimpled surfaces [25].

It is rarely seen in males, except those with androgen deficiency, such as Klinefelter's syndrome, hypogonadism, and post-castration, and in those patients receiving estrogen therapy for prostate cancer [1].

# 2.3 Etiology and Pathophysiology

Cellulite was first described by Alquier and Paviot (1920) as a noninflammatory complex cellular dystrophy of the mesenchymal tissue caused by a disorder of water metabolism. Interstitial liquids would produce a saturation of adjacent tissues in this condition [32].

In 1978, Nürnberger and Müller attributed the appearance of cellulite to two factors: the volume of fat cells and the differences of subcutaneous tissue architecture between men and women [24]. In women, fibrous branches perpendicular to the skin's surface separate voluminous lobules in rectangular sections [34] resulting in the dimpled surface characteristic of cellulite.

Considering theories that have emerged on the etiopathogenesis of cellulite, Terranova et al. [34] identifies the following related causes to cellulite: edema resulting from excessive hydrophilia of the intracellular matrix, microcirculatory alteration, and different anatomical conformation of the subcutaneous tissue in women compared to men [34]. Ortonne and colleagues also propose adipocyte hypertrophy, microcirculation disorders, and venous stasis as important elements linked to the cellulite condition. Besides, they refer connective tissue abnormalities and fibrosis as others important elements [25].

Collagen type I was reported as a major target in cellulite [28]. One of the theories on the etiology of cellulite is based on the collagen breakdown in the dermis [7]. Rossi and Vergnanini [32] relate that estrogen provokes alterations in collagen. In fact, cellulite worsens with pregnancy, menstrual cycle, use of contraceptives, and hormonal replacement. Another estrogen's influence related by those authors is the stimulation of lipoprotein lipase, an enzyme responsible for lipogenesis, process which leads to the fat accumulation [32]. Fat accumulation in the buttocks and thighs is also related to the characteristics of the adipocytes in these areas. They have a great number of  $\alpha$ -adrenergic receptors which are anti-lipolytic and thus responsible for the resistance of adipose tissue mobilization [28], in contrast to visceral and abdominal fat where there is less  $\alpha$ -adrenergic receptors and, for this reason, a better response to lipolysis induced by catecholamines [18]. Skin laxity has also been considered to play an important role in cellulite appearance or worsening [14]. The results of a recent study may corroborate this hypothesis as they suggest the cellulite severity increases with age [16].

# 2.4 Anatomical Considerations

Cellulite is viewed as the result of a combination of the gender-related dimorphism of the hypodermal tissue and mechanobiological effects of tissue tensions inside this tissue, being thus much more prevalent in women than in men [26].

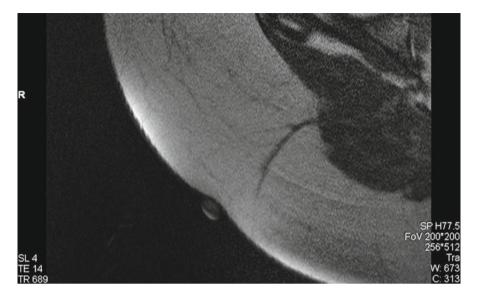


Fig. 2.2 MRI of the subcutaneous septa in cellulite depressed lesion

According to Querleux and colleagues, the results obtained with high-frequency ultrasound confirm an increase in skin thickness in women with cellulite, as well as the presence of deep indentations of adipose tissue into the skin [29]. The standing lobules, called papillae adipose, rise into pits and dells at the surface of the dermis [26].

The bumpy appearance of the skin surface results from the alteration of the network of connective tissue strands normally tethering the dermis to the deeper layers. Some strands are enlarged and fibrosclerotic, whereas other strands become loose. At the latter sites, edema and deposits of proteoglycans may be present in association with alterations in the shape and pattern of distribution of the elastic fibers [26].

The cutaneous alterations found in cellulite are largely due to the subcutaneous fibrous septa present in the dermis and/or in the subcutaneous tissue [14]. In women with cellulite, there are higher percentages of perpendicular fibers in comparison with women (and men) that do not have cellulite [24]. As for the fibers in other directions, women with cellulite have a lower percentage of parallel septa to the skin and higher percentage of angled septa [27]. Corroborating this information, Hexsel and colleagues compared areas of subcutaneous tissue with and without cellulite and have described the presence and characteristics of fibrous septa in the depressed lesions of cellulite (Fig. 2.2). The fibrous septa analyzed were all perpendicular to the skin surface. Furthermore, they were present in 96.7 % of the areas with cellulite depressions, while the percentage to those areas without cellulite was 16.7 % [12]. Under the influence of estrogen, fat is stored in women's buttocks and thighs. The more the fat is stored in predisposed areas, the more apparent is cellulite.

Table 2.1 Cellulite classification according to Nürnberger and Müller

- 0 No alteration to the skin surface
- I The skin of the affected area is smooth while the subject is standing or lying, but the alterations to the skin surface can be seen by pinching the skin or with muscle contraction
- II The orange skin or mattress appearance is evident when standing, without the use of manipulation (skin pinching or muscle contraction)
- III The alterations described in degree or stage II are present together with raised areas and nodules

# 2.5 Classification

The evaluation of the patient's degree of cellulite should be done before starting any treatment. This may interfere in the right choice of the procedure and is useful for follow-up of the results. A previous cellulite classification describes different grades from 0 to 3 and is based on the clinical alterations observed in three situations: with the patient at rest, after the application of the pinch test, or muscular contraction (Table 2.1) [24].

A new cellulite severity scale (CSS) and classification for cellulite was developed by Hexsel and colleagues [13]. This new scale has the purpose of creating an objective method to measure cellulite severity and the effects of different modalities. Five key clinical features of cellulite are evaluated:

A. The number of evident depressions

- B. Depth of depressions
- C. Morphological appearance of the skin surface alterations
- D. Grade of laxity, flaccidity, or sagging skin
- E. The classification scale originally described by Nürnberger and Müller

The severity of each item is graded from 0 to 3, allowing a final sum of scores that range numerically from 1 to 15. Based on the final numeric score, cellulite is classified as mild, moderate, or severe [13].

Cellulite can be either classified in primary or secondary cellulite. In the primary cellulite there are no causal factors involved, such as previous trauma. In the secondary cellulite, the alterations are due to other factors, such as surgical trauma, mainly from liposuction, injections that cause lipoatrophy, or subcutaneous fibrosis from previous inflammatory or infectious process [14].

#### 2.6 Diagnosis

It is important to ask the patient about medical history and regarding the age at which cellulite appeared, as well as prior occurrence of trauma, liposuction or injections on the affected area, presence of chronic vascular or associated hormonal disorders, and use of any medication that may contribute to the increase in the deposit of fat in the affected area. Diagnosis of the cellulite is done mainly on clinical basis during the physical examination with the patient in the standing position. Cellulite normally occurs in areas with fat accumulation, such as buttocks, thighs, flanks, abdomen, and upper legs [14, 30]. The characteristic appearance of cellulite is the presence of depressions on the cutaneous surface, surrounded or not by elevations. The depressions can be deep or superficial, single or multiple. The lesions are essentially asymptomatic; nevertheless, sensation of heaviness and pain may occur in the affected areas in advanced degrees of cellulite, probably as a result of nervous terminal compression or inflammatory reactions [14].

For the initial evaluation, it is also important to make an anthropometrical examination, which consists of measuring weight, height, and calculating the body mass index. It is a good method also to evaluate obesity [32], a condition that is associated with the worst degree of cellulite.

Digital photographs should be taken at the initial evaluation and after treatment and should follow the same standardized light patterns, position, and camera settings [17].

Rarely, complementary exams may be indicated for some cases or for research purposes. Ultrasound can be used to study the thickness and the quality of the connective tissue and the edematous component of cellulite [2]. Ultrasound imaging of the skin affected by cellulite at this stage reveals thinning of the dermis with subcutaneous fat pushing upward, which translates into the rumpled skin known as cellulite [7].

Laser Doppler flowmetry (LDF) is an optical technique used to evaluate skin microcirculation which provides information on blood flow and erythema. The radiation is reflected by the skin and converted to electrical signal, which is proportional to the flux of erythrocytes of the blood flow. Hence, it consists in a reliable method to estimate cutaneous microcirculation [2].

Thermography is an effective technique to evaluate the local skin temperature. It is based on the detection of infrared radiation emitted by skin. Areas affected by cellulite present less local skin blood flow, presenting thus lower temperature [2].

Magnetic resonance imaging (MRI) allows to visualize changes in skin architecture caused by cellulite – pointing out clearly in the images the skin fat layers beneath the dermis and down to the level of muscles – as well as to quantify herniations of adipose tissue into the dermis. It is a good method to evaluate cellulite in clinical trials [2] and also to determine anatomical features of cellulite [12].

# 2.7 Treatments

Many different treatments have been proposed to treat the cellulite. Weight loss is frequently employed as well as skin massage and a variety of topical agents. Mechanical devices, surgical procedures, and oral supplements can also be recommended [31]. Aerobic exercise is capable to burn fat deposits and to improve the body contour.

# 2.7.1 Manual Lymphatic Drainage

It is performed through compressions over specific lymphatic system sites intending to improve lymphatic flow by removing lymph from tissues. There are four different techniques for manual lymphatic drainage [22]: stationary circles technique, pump technique, scoop technique, and rotary technique.

#### 2.7.2 Topical Treatment

Topical agents are often used by women to treat cellulite. Normally, they are recommended to treat mild-to-moderate cellulite and as an adjuvant treatment for severe cellulite.

Topical anticellulite preparations may be divided in four major groups according to the mechanism of action of its compounds. Active substances used in topical treatments for cellulite act by increasing the microcirculation flow, reducing lipogenesis and promoting lipolysis, restoring the normal structure of dermis and subcutaneous tissue, and preventing free radical formation or scavenge free radicals. Such products normally come in the form of creams, lotions, and gels. These products, which act in both the health and beauty of the skin, have been recently defined as cosmeceuticals and comprise a category placed between cosmetics and pharmaceuticals [11].

The methylxanthines are commonly added in cellulite products. The most used are caffeine, aminophylline, and theophylline, and they are used because of their proposed effect on adipocyte lipolysis via inhibition of phosphodiesterase and increasing cyclic adenosine monophosphate (AMP) [11, 31].

Many herbal extracts are used in slimming products such as verbena, green tea, lemon, and kola nut. The results would be an improvement of the peripheral microcirculation and to facilitate lymphatic drainage [11, 31]. The use of retinoids is shown to be efficient. It increases the dermal content and architecture of collagen and dermoepidermal proteins together with anchoring and elastic fibrils [11, 31].

The clinical efficacy of many active ingredients is limited owing to their inability to penetrate the corneal stratum barrier. For this reason, some topical formulations include skin enhancers, which are substances capable of augmenting cutaneous penetration of the active ingredients [15]. Vitamins, such as ascorbic acid and vitamin E, may work as antioxidants, protecting dermal and subcutaneous cell membranes from free radical toxicity [11].

#### 2.7.3 Oral Treatment

Formulations taken orally also have to reach and act in the target site. Distante and colleagues have proved that plant extracts such as grape (*Vitis vinifera*), *Ginkgo biloba*, Asiatic centella, melilotus (*Melilotus officinalis*), and fucus (*Fucus vesiculosus*) contained in orally administered medication show good bioavailability and are effective in improving all clinical signs and symptoms associated to cellulite [6]. The extract of fucus has an important effect on peripheral fat tissue. Results of a study testing the effect in vitro of wild yam root (*Dioscorea opposita*), cocoa bean (*Theobroma cacao*), horse chestnut tree seed (*Aesculus hippocastanum*),

horse chestnut tree bark (*A. hippocastanum*), and tomato (*Solanum ycopersicum*) in adipocytes suggest that those plant extracts have the potential to modulate glycerol release from the adipocytes, stimulating the reduction of fat content in adipose tissue [4].

#### 2.7.4 Endermologie<sup>®</sup>

It is a French-designed method of deep massage approved also by the United States Food and Drug Administration (FDA) to diminish the appearance of cellulite. During the massage, suction is used to pull the skin into a handheld machine where the skin is compressed and rolled to increase blood and lymphatic flow and to modify the underlying connective tissue [30].

One side effect related to this type of treatment is the possible increase of cutaneous laxity. Besides that, it is not recommended to pregnant women and to people that present with hypertension, diabetes, circulatory disabilities, or excessive skin flaccidity conditions.

### 2.7.5 Radiofrequency

Radiofrequency (RF) efficiency for different aesthetic and dermatological applications is due to the use of thermal energy, which contracts loose, lax skin through collagen denaturalization. When the collagen is heated, the bonds that are sensitive to heat begin to break and originate a disorganized gel rather than the previous organized crystalline structure. Collagen contraction occurs when the tension of residual crossed intermolecular unions stabilizes to heat. The amount of the tissue contraction depends on various factors, including the highest reached temperature, the RF exposure time, and the mechanical stress applied to the tissue during the heating process [27]. Pino and colleagues [27] have demonstrated that the effect of RF over the connective tissue was evident in the ultrasound images where a visible compression of the entire thickness of the dermis to the muscle could be appreciated but with better results on the thigh. Radiofrequency is indicated for treating cellulite mainly caused or influenced by skin laxity.

#### 2.7.6 Lasers and Lights and Combinations

TriActive<sup>™</sup> (Cynosure, Westford, MA, USA) is an FDA-approved device which combines a localized cooling, six diode lasers, and mechanical massage [1]. The low temperature reduces edema, the laser favors blood and lymphatic flow, and the mechanical massage increases local drainage.

VelaShape<sup>™</sup> (Syneron Medical Ltd., Yokneam Illit, Israel) is a system based on the application of an infrared light to the skin combined to RF energies and vacuum suction pulses [35]. The IR and RF act synergically, promoting heating in the target

tissue, collagen remodeling, and improvement of the adipose tissue metabolic rate. The negative pressure vacuum massage improves circulation and also allows the treatment of both the superficial and deep dermal layers [3]. A recent study has showed the effects of this device on the reduction of cellulite severity and body circumference measures in the buttocks [17].

SmoothShapes<sup>™</sup> (Cynosure, Westford, MA, USA) is also approved by FDA and combines 915-nm laser and 615-nm light to mechanical massage. It stimulates metabolism, reducing edema and thus improving the skin appearance. Another relevant effect is over collagen, remodeling the fiber and consequently improving skin appearance. Studies [19, 20] have demonstrated both the safety and efficacy of this device in subjects treated over a 4–6-week period.

## 2.7.7 Liposuction

Liposuction involves the removal of local adipose tissue deposits to achieve a grater aesthetic body contour. It requires general or local tumescent anesthesia and the use of a small tip suction cannula to remove fat from the selected areas, without altering other skin tissues. Liposuction may decrease the appearance of cellulite because it reduces the local fat volume, and it may also disrupt the fibrous bands that cause the dimpling appearance of the skin surface [30]. Despite that, alterations of the cutaneous surface may result from liposuction being caused by subcutaneous fibrosis. They usually appear late, from 3 months to 1 year after surgery, and may be slight, moderate, or severe [14].

#### 2.7.8 Mesotherapy

Mesotherapy was developed in France, where it is well known and frequently used. It comprises injections of very small doses of solutions – composed by some active substances – into the skin at 2–6 mm depths. Its objective is to inject the medication directly on the affected site. These substances present vascular and lipolytic action [5, 23]. Although the design of injectables is more detailed, among other cautions, extreme care should be taken to ensure the sterility of the formulation.

#### 2.7.9 Subcision<sup>®</sup>

Subcision<sup>®</sup> was developed as a treatment for cellulite by Dr. Hexsel and Dr. Mazzuco [9]. It is a surgical technique that does not require incisions and leave no scars. A needle is introduced into the skin, and it is used to cut the fibrous septa responsible for the depressed lesions of cellulite [10].

In this book you will find a specific chapter about Subcision<sup>®</sup>, in which further information and explanation will be provided.

#### 2.7.10 Carboxytherapy

Carboxytherapy is the therapeutic use of carbon dioxide  $(CO_2)$  in its gaseous state, either by transcutaneous or subcutaneous injections. It seems to increase vascular tone and produces active microcirculatory vasodilatation due to the action of  $CO_2$  on arteriole smooth muscle cells. By improving capillary blood flow, it reduces stasis and contributes to the restoration of microvascular tissue unit exchanges [21].

## 2.8 Prognosis

Cellulite is worsened by age, skin laxity, and weight gain. One of the causes that exacerbate cellulite seems to be the repeated cyclical collagenase production during women's life, in which more and more dermal collagen is destroyed. If the amount of collagen destroyed is enough to weaken the reticular and papillary dermis, it will allow subcutaneous dermis to herniate among the structural fibrous septa found in female fat. If higher amount of subcutaneous fat is present, there will be a more pronounced herniation [12].

The skin laxity, a condition which is also related to the aging process, worsens the cellulite.

Weight gain may also worsen this condition. Weight loss has been suggested as a strategy to reduce cellulite by decreasing the dermal papillae adipose herniation, but it may not affect the underlying connective tissue network [33].

#### Conclusion

Cellulite is a very common condition which has been more studied in past few decades. Many morphological and physiological aspects have been described, but the precise cellulite's etiology has not been established yet. Many factors are involved in cellulite, such as adipocyte hypertrophy, microcirculation disorders and venous stasis, and connective tissue abnormalities and fibrosis. Recently, hormonal influences in collagen are being mentioned as a relevant cause for cellulite. Skin laxity has also been regarded as another relevant contributor to worsen cellulite, especially in older women. Besides the far known treatments such as diet, exercises, and lymphatic drainage, several other treatments have been developed lately presenting successful results. Devices, such as laser, lights and radiofrequency, are being used to treat this condition as well.

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