Cellulite: A Review of its Anatomy, Physiology and Treatment
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Introduction
Cellulite is a skin alteration often described as an 'orange peel,' 'mattress,' or 'dimpling' appearance on the thighs, buttocks and sometimes lower abdomen and upper parts of the arms of otherwise healthy women. Approximately 85% of post-pubertal women have a form of cellulite (Avram, 2004; Rawlings, 2006). Although rarely observed in males, those men presenting with cellulite are commonly deficient in male hormones (Avram, 2004). The name originated from the French medical literature around 1816 (Scherwitz and Braun-Falco, 1978). The original name, cellulite, implied that it is a disease, however years of study now disprove this disease theory. As a matter of fact, some of the scientific literature refers to this changed skin condition as 'so-called cellulite, an invented disease' (Nurnberger and Muller, 1978). This article will present a comprehensive review of cellulite research, answer several pressing questions and discuss purported treatments.

What is Cellulite?
To better understand what cellulite is a review of skin microanatomy is needed. The outermost layer of skin is referred to as the epidermis. Immediately under this is the dermis (also called the corium), which is richly filled with hair follicles, sweat glands, blood vessels, nerve receptors and connective tissue. The next layer of tissue is the first of two layers of subcutaneous (which means beneath the skin) fat (Rawlings, 2006). It is in this first region of subcutaneous fat (called the areolar layer with fat cell chambers [or lobules] that are arranged vertically in females) where the prevailing evidence-based understanding of cellulite is described (Wanner and Avram, 2008; Rawlings, 2006; Avram, 2004). According to this scientific explanation, cellulite is caused by small protrusions of fat (called papillae adiposae) into the dermis. This structural alteration of subcutaneous fat protruding (or herniating) into the dermis gives skin the 'bumpy' appearance referred to as cellulite (Sadick and Magro, 2007). This theory has been confirmed using magnetic resonance imaging (Querleux et al., 2002), sonography (high-frequency sound waves to construct an image) (Rosenbaum et al., 1998), and skin biopsy (Nurnberger and Muller 1978). A second, similar theory adds that cellulite is a result of a laxity (or weakening) in the connective tissue bands in the dermis that allows for the fat protrusions to occur (Pierard, Nizet, and Pierard-Franchimont, 2000).

Why is Cellulite Rarely Observed in Males?
Rosenbaum and colleagues (1998) and Nurnberger and Muller (1978) explain that men and women have a different connective tissue organizational structure at the first layer of subcutaneous fat. With females, the adipose tissue is contained in chamber-like structures that favor the expansion of adipose tissue into the dermis. Contrariwise, men have a network of criss-crossing connective tissue architecture, forming smaller polygonal units which allow for subcutaneous fat deposits to expand laterally and internally, but with little or no protrusion (if any) into the dermis. As well, men have thicker epidermis and dermis tissue layers in the thighs and buttocks than females (Wanner and Avram, 2008; Nurnberger and Muller 1978).

When do the Gender Differences in Subcutaneous Fat Cell Organization Occur?
According to Nurnberger and Muller (1978) who examined male and female fetuses, up to 7 or 8 months of fetal development there is no recognizable difference in subcutaneous tissue. During the end of the 3rd semester of fetal development the gender structure differences become to be apparent and manifest themselves at birth. Variations in hormones between genders largely explain this skin structure deviation. It has been shown that men who are born deficient in male hormones will often have a subcutaneous fat cell appearance similar to females (Wanner and Avram, 2008).

What is the Connective Tissue in the Dermis?
The connective tissue in the dermis provides the framework, insulation and stability of the dermis layer below the epidermis. It offers a necessary insulation and stability between the various organelles, permitting...
their proficient function, without inhibition to adjacent structures. It's composed primarily of collagen (an inelastic tissue with great tensile strength), ground substance (consists mainly of water whose major role is to provide a route for diffusion transport between tissues), and elastic tissue (which gives the skin it's ability to extend and return to normal constituency).

What are the Proposed Treatments for Cellulite?

The following is an orderly review of surgical options, injectable interventions, noninvasive devices, thermal treatments, topical ointments, herbals, lasers and shock wave treatments that have all been used in the treatment of cellulite. It is important to note that many of the cellulite treatment studies have been completed with relatively small sample sizes and generally do not follow up with their participants for extended periods of time. Also, some of the methods used to analyze patient results are often based more on human observation rather than on scientific assessment. Lastly, it is difficult to rule out external factors such as change in diet and exercise when interpreting the results of some studies.

Liposuction

Liposuction is a contentious intervention for the treatment of cellulite. Although there are subjective reports that it has improved the appearance, others have noted that it actually worsens the dimpled skin appearance (Van Vliet, 2005; Avram, 2004). Thus, Van Vliet and Avram do not recommend liposuction as a cellulite treatment.

Subcision

Subcision is a method in which a needle is inserted into the dermis (after injection of a local anesthesia) of the cellulite site. The needle serves to alter the connective tissue structure to purportedly improve the cellulite appearance. Adverse side effects include pain, bruising for 3-6 months, and skin pigmentation alterations (for 2-10 months) (Van Vliet, 2005). No objective scientific assessment data is available with this technique (Van Vliet).

Injectables

Phosphatidylcholine, which is a major component of biological membranes, is one proposed injectable intervention for cellulite. The injection of biological agents into the subcutaneous tissue is done in order to promote local lipolysis (i.e., fat cell shrinkage from the breakdown of fat), and hopefully improve the appearance of cellulite. No current scientific evidence is available to prove the effectiveness of these injections in treating cellulite (Van Vliet, 2005).

Mesotherapy is a European therapy that was originally developed for pain relief for certain skin inflammatory conditions (Rotunda and Kolodney, 2006). It involves a series of microinjections into the tissue layer just beneath the skin. Mesotherapy is now also being employed as a cosmetic treatment for fat reduction and cellulite reduction using injectable medications and homeopathic substances (such as vitamins, minerals, amino acids and enzymes) into a cellulite site in the body. The ingredient most consistently used in mesotherapy is phosphatidylcholine (Alster and Tanzi, 2005). Although data does exist that mesotherapy does induce lipolysis and slight improve the appearance of cellulite (Caruso et al., 2007), Goldberg, Fazeli, and Berlin (2007) note that due to the lack of a precise treatment protocol and the risk of adverse effects (including swelling, infection and irregular contours) the use of this therapy is discouraged. Alster and Tanzi note that mesotherapy was banned by the Brazilian National Agency of Health in 2003 due to its undesirable effects.

Endermologie

Endermologie is a suction massage technique developed in France. This type of electrically powered device has two rollers components. Users often wear nylon stockings to decrease the amount of friction while the skin is draw into the machine (with a low-pressure vacuum) and kneaded by the two revolving rollers. Treatments range from 10 to 45 minutes of rolling the skin of the hips, thighs, legs, buttocks and stomach. Claims are that endermologie improves fat tissue architecture, lymphatic drainage and capillary circulation. Research on the mechanobiology (the science that integrates mechanics, molecular biology and genetics) of the skin shows that deep mechanical massage will induce changes in the dermis connective tissue (Silver, Siperko, and Seehra, 2003). However, in review of the published research on endermologie, which is minimal, this device does not show meaningful efficacy in the treatment of cellulite (Avram, 2004; Van
Massage
Massage and tissue manipulation techniques are employed to enhance the removal of accumulated fluid in the dermis area. These techniques do not remove the cellulite, but may have a temporary effect in reducing the amount of 'dimpling' appearance. Similar to endermologie, deep massage may induce alterations in dermis connective tissue (Silver, Siperko, and Seehra 2003). However, massage appears to offer only short-term minor skin changes, probably more related to the removal of excess fluid (Rawlings, 2009).

Thermotherapy
Thermotherapy is a heat application technique that promotes blood flow and vasodilation. Van Vliet (2005) notes that no studies demonstrate any effectiveness with this treatment and it may actually aggravate the cellulite appearance.

Topical Ointments
The role of topical treatments in cellulite removal is divisive (See Side Bar 2 for all ingredients included in cellulite creams). An initial challenge of any topical cream is that it must be able to penetrate the skin and dermis to reach the target fat tissue before being absorbed by the tissue. Although numerous topically applied creams are advertised as cellulite diminishing creams, there is minimal data substantiating any of them. The majority of these creams function to promote lipolysis of fat. Methylxanthines (e.g., caffeine, aminophylline, and theophylline) are agents that stimulate lipolysis. In the review by Wanner and Avram (2006) the authors note that the research with methylxanthines shows modest decrease in thigh circumference and/or subcutaneous fat thickness, but no reduction of cellulite.

Some topical cellulite creams use retinoids. Retinoids are similar in chemical structure to Vitamin A, a well-known anti-aging ingredient in many facial creams. Retinoids, like Vitamin A, have been found to increase the denseness of the epidermis to facial skin when applied for years. The hypothesis of retinoid treatment in cellulite site areas is to promote dermis thickness. Some research suggests modest improvements in cellulite appearance with retinoid creams over a treatment period of 6 months (Kligman, Pagnoni, and Stoudemayer, 1999). Yet other randomized, placebo-controlled research with retinol in the treatment of cellulite shows no responsiveness in cellulite appearance (Pierard-Franchimont, Pierard, Henry, Vroome, and Cauwenbergh, 2000). Alster and Tanz (2005) observe that the downside of topical treatments is their inability to appreciably penetrate skin in order to render more than a superficial tissue effect. However, new studies show that iontophoresis may enhance the transport of some of these creams across the skin (Akomeah, Martin and Brown, 2009), therefore enhancing the creams efficacy. Iontophoresis is a skin permeation enhancement strategy that delivers a charged substance across the epidermis using an electrical current (which helps to drive other molecules across the membrane). Akomeah and colleagues suggest this 'electroperturbation' of the epidermis technique may serve as a potential approach to enhance delivery of topical cellulite creams.

Herbals
The basis of most of the herbal treatments is to enhance the microcirculation in the dermis area and to promote lipolysis of subcutaneous fat (Rawlings, 2006). It is interesting to note that research has shown a slight decrease in thigh girth with herbal treatments but a return to normal when the application ceases (Rawlings).

Lasers
Within the past few years, researchers have begun testing lasers, also referred to as radiofrequency energy as a treatment for cellulite. Radiofrequency current is defined as a high-frequency electric current in the 0.3 to 100 MHz range (del Pino et al., 2006). It produces a thermal effect (light heat) on living tissue and is currently used in surgery for various dermatological applications. As a cellulite intervention, the application of radiofrequency current is being tested to observe if it can cause weakening dermis connective tissue in the hips, thighs and buttocks to 'tighten' up. The heating process of the current causes the collagen proteins in this connective tissue to denaturalize (changes occurring in the structure of proteins) and then 'tighten' as they regain their structural integrity, as if it were like a wound healing. It is also theorized that this treatment increases local blood flow and fat metabolism at the site (Sadick and Muholldan, 2004). In the del Pino et al. study, twenty-six healthy female patients (ages 18 to 50) with cellulite received 2 treatment sessions (15 days apart) of unipolar radiofrequency. Appropriate energy was set and the treatment was delivered in 3 passes of
30 seconds each. Evaluation of the thickness of the subcutaneous tissue on buttocks and thighs took place before the first treatment, second treatment, and 15 days following the second treatment with a real-time scanning image ultrasound. The treatment resulted in visually (and with ultrasound imagery) observable decreases in cellulite appearance that were observed six months following the treatment. Goldberg, Fazeli, and Berlin (2008) also employed radiofrequency treatments (6 treatments every other week) and noted that immediately post-treatment and 6 months after the treatments that there were noticeable decreases in cellulite appearance. Side effects of this radiofrequency treatment are minimal (little blisters), but the long-term effects are unknown at this time. Other researchers have reported similar cellulite appearance reducing results, and minimal side effects, with radiofrequency treatments (Fink et al., 2006; Nootheti et al., 2006; Sadick and Magro, 2007). This pioneering technology looks promising for the treatment of cellulite.

Shock Wave Therapy
Shock wave therapy is an energy pressure pulse of large amplitude followed by some small wave components (Angehnhn, Kuhn, and Voss, 2007). High-energy shock waves are used therapeutically for the treatment of kidney and urethral stones. The application of low-energy shock wave therapy on biological tissue is very recent. It is non-invasive, side effect free and delivered in brief treatments. There is a loud audible sound with this treatment that may be irritating to some. Angehrn, Kuhn and Voss treated the thighs of 21 females (ages 20 to 60 years) with shock wave therapy twice a week for 6 weeks. Results (via visual analysis and ultrasound measurement) showed a diminished appearance in cellulite in most subjects. The authors hypothesize that shock wave therapy promotes a 'remodeling' of the collagen proteins in the connective tissue in the dermis. However, the authors continue that more research is needed in this area to determine the appropriate regimes and equipment parameters that work most effectively for cellulite reduction.

What Are Some Realistic Cellulite Guidelines to Give to Clients? Five Take-Away Messages from the Research
1) It is important to educate clients that research distinctly shows that cellulite is a unique and distinctive layer of subcutaneous body fat that is common to females (Querleux et al., 2002).
2) Improving diet and exercise is an excellent way start improving cellulite appearance (Avram, 2004). It has been shown that females who lose weight have less cellulite appearance (Sadick and Magro, 2007). So, a caloric-restricted diet plan combined with a comprehensive exercise (aerobic exercise and resistance training) program to reduce some of the underlying body fat should be implemented. Histological (microscopic structure of tissue) research shows that the fat cells do retract slightly from the dermis with weight loss (Rawlings, 2006).
3) Subcutaneous fat is layered on top of muscle. Therefore if the muscles in the hips, thighs and buttocks are weak and flaccid it will contribute to the 'uneven' view of the skin surface (Rossi and Vergnanini, 2000). Therefore, educate clients that a meaningful benefit of resistance training is definitely for minimizing the appearance of cellulite.
4) Encourage your clients NOT to invest their hopes and monies in liposuction, subcision, injectables, skin kneading and manipulation techniques, thermotherapy, topical ointments, and herbals for cellulite management.
5) The new frontier in the treatment of cellulite appears to be with laser therapy (Avram, 2004) and potentially with low-energy shock wave therapy (Angehnnhrn, Kuhn and Voss, 2007). Laser therapy is non-invasive, has little side effects, and shows great promise for appreciably reducing the appearance of cellulite.

Side Bar 1. Ten Primary Questions and Answers About Cellulite
1) Why is it rare to see cellulite in pre-puberty stages of growth? Rossi and Vergnanini (2000) propose that hormones play a predisposing role in the pathophysiology of cellulite after puberty. The authors note that oesetron (female steroid sex hormones that are secreted by the ovary) may aggravate the physiological changes causing cellulite. Oestrogen also stimulates lipoprotein lipase, the main enzyme responsible for splitting lipoproteins found in chylomycrons (particles that transport dietary lipids from the intestines to other locations in the body) and very low-density lipoproteins into fatty acids for storage in fat deposits in the body.
2) Do slender women also have cellulite?
Yes, Rosenbaum and colleagues (1998) explain that cellulite is often present in slender women, however the researchers continue that it is exacerbated with weight gain.

3) Why does cellulite seem to get worse with age?
The dermis reaches its maximal thickness at the age of 30 years (Nurnberger and Muller, 1978). It steadily diminishes in thickness and structural integrity thereafter (Nurnberger and Muller, 1978). Secondly, the connective tissue in the dermis starts to get looser, due to the aging process of the collagen and elastic fibers. This allows for more adipose cells to protrude into the dermis area, accentuating the cellulite appearance (Nurnberger and Muller, 1978). In addition, an increased deposition of subcutaneous body fat, due to overeating and inactivity, may contribute.

4) Is cellulite present in women of all races?
Yes, Avram (2004) notes that cellulite is present in females of all races. However, he highlights that it is more prevalent in Caucasian females as compared to Asian females.

5) Why is cellulite more prevalent in the thighs and buttocks of females?
It is well established that women generally have a higher percentage of body fat than men. For instance, the average percent body fat values for adult men and women (18 to 34 years) are 13% for men and 28% for women (Heyward, 2006). The thighs and buttocks of women tend to store more of this body fat. This type of fat deposition is characteristically termed gynoid, or pear shape. del Pino et al. (2006) also note that there are five times more adipocytes (fat cells) in the thighs, hips and buttocks of women then in other sites of their body.

6) Is there any truth to the proposition that cellulite is caused by damaged blood vessels?
There is no supporting evidence that cellulite is caused by damaged blood vessels. In addition, no evidence exists that cellulite is a result of a weakening of capillaries or a decreased circulation in the subcutaneous area.

7) Is cellulite related to any lymphatic disorder?
Some non-scientific sources have suggested that cellulite is a lymphatic disease, yet there is no scientific support for this contention. However, limitations to fluid movement and drainage (as seen with inflammatory skin conditions) may contribute to the appearance of cellulite.

8) When a person gains subcutaneous fat is it in the areolar layer?
There is a second layer of fat, beneath the areolar layer, called the lamella layer. The fat cells are arranged horizontally in this second region and when a person gains subcutaneous fat this is the primary area that typically enlarges (Rawlings, 2006).

9) Is cellulite hereditary?
Yes, Rossi and Vergnanini (2000) and del Pino et al. (2006) state that there is a clear genetic predisposition for cellulite to develop. This inherent tendency will affect the fat distribution and deposition.

10) Will smoking worsen the appearance of cellulite?
Yes, cigarette smoke has been shown to weaken the formation of collagen, the chief structural protein of connective tissue (Fink et al., 2006). Therefore, weakened connective tissue may allow for easier protrusion of fat into the dermis.

Side Bar 2: What are the Ingredients of Cellulite Creams?
Sainio, Rantane, and Kanerva (2000) examined the ingredients of 32 cellulite cream products. A total of 267 difference substances were found with most cellulite creams having an average of 22 ingredients. Botanicals (substances from a fruit) and emollients (moisturizing cream) are the chief ingredients in all the products. The most common active agent is caffeine as it is a stimulatory agent for lipolysis. All cellulite creams also contain some type of fragrance. The authors note that one fourth of the substances in cellulite creams have been shown to cause an allergy. Therefore the risk of unpleasant effects should always be known.

References:


Querleux, B., Cornillon, C., Jolivet, O., and Bittoun, J. (2002). Anatomy and physiology of subcutaneous adipose tissue by in vivo magnetic resonance imaging and spectroscopy: relationships with sex and presence of cellulite Skin Research and Technology 8: 118-124.


Bios:
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