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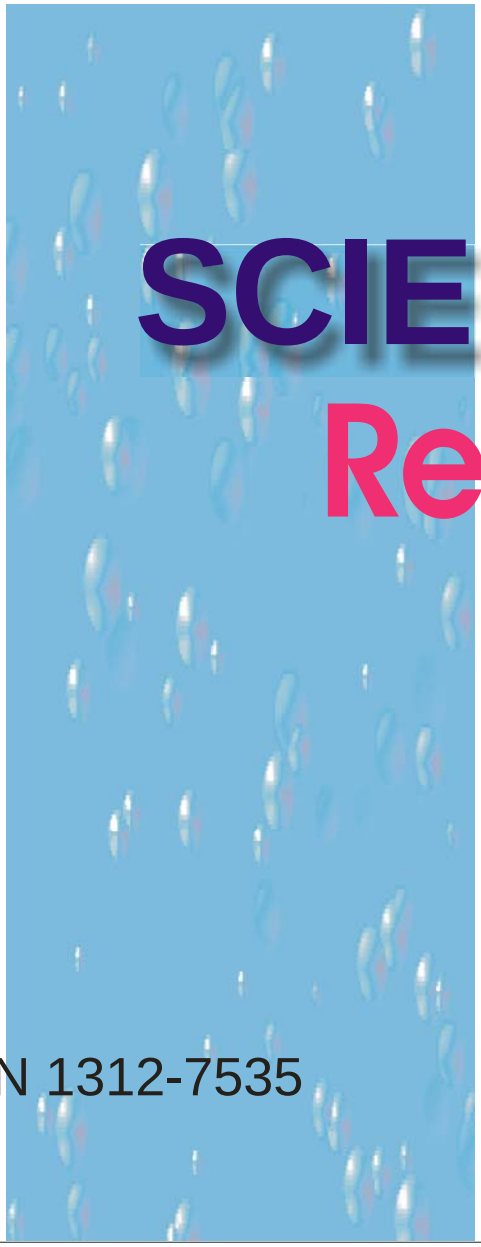

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# WOMEN'S POOL – THE METABOLITES AND HORMONAL MECHANISMS

***Iv. Topouzov***

*South-Western University – Department of Kinesitherapy - Blagoevgrad, Bulgaria*

The mechanisms, controlling lipid storage, lipid mobilization and utilization are interesting. Adipose tissue metabolism varies from one region of the body to another. The fat on ***women's pool*** *(thighs, hips, belly)* is more difficult to be mobilized due to increased α-2-adrenergic receptor activity induced by estrogen and another hormones and enzymes. The obesity of gynoideous type and typical cellulite in women are caused by a number of factors. The increasing adipocytes during growing fat, as well as the retention of liquid during the monthly cycle are becoming a reason for the development of local hypoxy. The hypoxy appears to be a constant irritating factor for these tissues and they make attempts to adapt to it. Than the hypoxy includes the vicious circles which forming the women's pool in girls and its sustainment in women.

**Key words:** women's pool, hypoxy, free radicals.

## Introduction

The two illnesses – Obesity of gynoideous type and Cellulite have a common histological predisposition. They are most commonly found in women effecting prevailingly the thighs, hips and belly (*the women's pool*). They are caused by a number of factors: irrational feeding, genetic predisposition, weak connective tissue, hormonal disbalance, variation of the weight etc. (7, 18, 28). One of the reasons is the insufficient physical activity, which is leading to stagnation of liquids and is a prerequisite for the increasing of the fatty depots in same parts of the body (thighs, buttocks, hips and the transition zone between them). One other mechanism is the monthly cycle during the puberty. A scheme of the hormonal and enzyme mechanisms explaining the puberty development and the menarche in the girls is suggested and their interdependence from the level of the fat tissue is proved. During the puberty in these processes are included very important endocrine and metabolite mechanisms, which control the lipid storage, lipid mobilization and lipid utilization (30, 31). The increasing of estrogens during the puberty leads to an increase in α-2-adrenoreceptors. This increase the lipogenesis and the adipocytes in the gluteofemoral region (women's pool). In the same time, the fat in the women's pool is more difficult to be mobilized due to an increased α-2-adrenergic receptor activity induced by estrogen and another hormones and enzymes. Thus the retention of fats and liquids in girls during the monthly cycle are becoming a reason for the development of local hypoxy. The local hypoxy of the women's pool region appears to be a constant irritating factor for these tissues and they make attempts to adapt to it. This is connected with the vicious circles, related to an increase of adipocytes in the gluteofemoral region in girls, appearance of cellulite in girls and obesity of gynoideous type in women (30, 31, 33).

Many women would like to selectively lose fat from a specific area of the body. The thighs and buttock area seem to be the area of most frequent concern for women. This desire

for cosmetic change has been the basis for much popular and professional writing. The structure of subcutaneous adipose tissue accounts for the development of the *peau d'orange* appearance. Fibrous connective tissue septae surround groups of fat cells and attach to the underside of dermis. As fat cells enlarge, these septae are stretched and pull down on the overlying skin [10]. The result of this process is an indentation or dimpling of the skin over the thigh and buttock area in women to which N. Ronsard (21) has given the name *cellulite*.

The aim of this study is to present the importance of the adipose tissue, monthly cycle, local hypoxy and oxidative processes and their connections as mechanisms forming the women's pool.

**Lipolysis**

Adipose tissue metabolism varies from one region of the body to another. The authors demonstrated that fat was absorbed more slowly in the femoral region in women losing weight after the jeuno-ileal bypass operation for server obesity (14, 26). These observation suggested regional differences in the lipolytic processes that might respond to the local application of lipolytic agents. More detailed studies on the nature of lipolysis describes the symptomatic and anatomic pathology of cellulite in some detail, and urges that deterioration of the microvasculature leads to fatty accumulations, rather than vice versa (5).

The lipolytic process has been described in great detail in the past 20 years. Lipolysis, the process of hydrolyzing triacilglycerol into glycerol and fatty acids, is mediated by the enzyme Hormone sensitive lipase (HSL). HSL is active in the phosphorylated form. This activation is produced by proteinkinase-A wich is activated by cyclic AMP. Membrane-bound adenylate cyclase can be inhibited or stimulated by the action of inhibitory or stimulatory GTP binding proteins (Gs-proteins) acting on adenylate cyclase **(**10, 11).

A number of hormones react with cell surface receptors on the adipocyte to influence lipolysis. Stimulation of the β-adrenergic receptors stimulated the Gs-proteins which activates adenylate cyclase which, in turn, activates cyclic AMP. The α-2-adrenergic receptor and the adenosine receptor, on the other hand, stimulate GTP inhibitory binding proteins (Gi - proteins) which inhibit adenylate-cyclase and thus inhibit the lipolytic process. The relative number of β- and α-2-adrenergic receptors on the surface of the fat cells determine the lipolytic balance of those cells (2, 3, 15).

Hormones can have long-term effects on the lipolytic processes by influencing the number of α-2- and β-receptors on the fat cell. Thus by controlling lipolysis, hormones can determine body fat distribution. Women, through the effect of estrogen, have more α-2-receptors on the fat cells of their hips and thighs. This gives a higher lipolytic threshold and causes concentration of fat in the area in women (1, 2, 20).

The adipocytes have 3 different types of receptors in its outer membrane, a β- adrenergic receptors, an α-2-adrenergic receptors and proteinkinase (pkC)- receptors:

**β-receptors**: These receptors block or inhibit phosphodiesterase production, leading to increased levels of cyclic-AMP which are known to trigger lipolysis. A β-receptor stimulator or activator Isoproternol (β-agonist), inhibit phosphodiesterase increase cyclic AMP and the lipolysis. Lipolysis involves processes such as the breaking-down of triglicerides into small-molecule fatty acids which can be internally metabolized like the adipocyte, or excreted, resulting in elimination of the fat from the cell (10).

**α-2-receptors**: These receptors increase level of phosphodiesterase, reduce the level of cyclic AMP and reducing lipolysis. Thus, α-2 inhibition is desirable. α-2-inhibitors are Yohimbine, Gincko biloba etc. (15, 34).

**Protein-kinase receptors**: Protein kinase-C (pkC) also increase phosphodiesterase and reduce cyclic AMP-level and inhibiting lipolysis. Thus inhibition of the pkC- receptors is desirable. Xanthine, Caffeine and Theophilline inhibit pkC-receptors (16).

**Local hypoxy and oxidative processes**

The increasing adipocites during growing fat, as well as the retention of liquid during the monthly cycle are becoming a reason for the development of local hypoxy. The hypoxy appears to be a constant irritating factor for these tissues and they make attempts to adapt to it. The process is lasting for a long time, sometimes during the whole life. Many other normal mechanisms are effected by it, like the oxygenasis, local hormones (Leucotriens, Thromboxan – A2 ), NO, prostaglandines (PGE, PGI-2) etc. (17, 23, 24). The accumulated not thoroughly oxidated products stimulate the oxidative modification of Low density cholesterol (LDL- C), the result of which is ox-LDL-C. They oxidate and in the blood appear lipoprekises and $H_2O_2$. A part of the metabolites are stimulating the fibroblasts, which is leading to growth of the connective tissue. It fatness the *tela subcutanea* of the fats particles and embarrasses the metabolism and circulation. The lower activity of the oxygenasis promotes the delaying of the speed of the oxidating phosphoriling and for the lower activity of Glutathion peroxidasis (GPX). The accumulated reactive metabolites ($H_2O_2$, HO• etc.) are leading to degradation of the hialuronous acid and of the collagen in the hypoderma – morphological changes (7, 19).

On principle, during the normal physiological reactions in the cells and tissues of the organism are acting harmful oxidative processes, which produce as a result oxygen free radicals /OFR/. It is considered that for one year in the organism of a middle-aged man there are generated about 2-3 kg only from the superoxide radical. When there is hypoxy, stress or intensive physical overloading, this quantity grows significantly.

During the reduction of electrons from the oxygen molecule is generated a Superoxide anion radical /$\bullet O_2^-$/, a Hydroxil radical /HO•/ and a Hydrogen peroxide /$H_2O_2$/. All of them, together with the other familiar OFR are damaging the cellular membranes, the cells and tissues, with which they come into contact. Their harmful action is not only on the place of their generation, but reaches the neighboring tissues as well (19).

This is very characteristic in conditions of local hypoxy, where the possibility for neutralizing the metabolites is lower due to the lower activity of the oxygenases. This slows down the speed of the oxidative phosphoriling and as its result the resynthesis of ATP. The concentration of NADP is changing, and it affects the interrelation between the restoring and oxidated glutation /GSH : GSSG/. The disturbed restoration of GSH is reflecting negatively to the activity of the glutathion peroxidasis, which makes harmless the generated during the neutralization of the superoxide anion radical hydrogen precis. There is a possibility for accumulation of $H_2O_2$.

During the enzyme detoxication of •O2 $^-$with the participation of superoxidismutasis (SOD), is formed the intermediate product $H_2O_2$, the neutralization of which is taking place on the following two ways: through catalasis (CAT) and through glutathion peroxidasis (GPX). The insufficient activity of GPX could become a reason for the accumulation of $H_2O_2$, which is leading to a tissue acidosis. The huge amount of $H_2O_2$ and the availability of Fe2+ generate a lot of hydroxil radicals (HO•). This is the most potent oxidant know, has an extremley short half-life, reacting at the site of its formation through its ability to attack most biological molecules resulting in the propagation of OFR chain reactions. Due to the lower possibilities of the hypoxical tissues of detoxication, in the hipoderma are accumulated other OFR, as well as products of the precis oxidation of the lipids, including conugates of dien, manol dialdehide, etc. (6, 22, 35). Their accumulation causes a degradation of the hialironic acid and the collagen, damaging of the cells through peroxidation of the polinotsaturated fat

acids and destruction of the permeability of the cells membranes and the structural elements. It is even possible to be got to acidosis with the additional after-effects for the tissue.

**The vicious circles**

The accumulating metabolites gradually organize and form cellulite formations in the hipoderma – *cellulite*. This is connected with the **1-st vicious circle** *cellulite – obesity – cellulite:* Cellulite - Local hypoxy with peroxidation – Disturbed permeability of the cellular membranes – Entrance of Ca++ ions in the cells – Activation of the phosphoinozitid–specific phospholipase-C – Stimulation of the phosphoinozitides – Activation of the proteinkinases – Desensitisation of the β-receptors – Embarrassed lipolyse – Accumulation of triglicerides – gynoideous type Obesity – Local hypoxy and Cellulite. Thus, distributed fat metabolism leads to subcutaneous fat retention which encroaches on the microvascullariture, displacing and constricting it leading to poor microcirculation which in turn reduces the blood flow to the dermis and epidermis. The deteriorated skin caused by the poor blood flow leads to retention of liquid. Together these phenomena create the visible sings of cellulite.

The increased lipogenesis is leading to local (gynoideous) density, which includes the **2-nd vicious circle** *obesity – cellulite – obesity* **:** Increased lipogenesis – Enlargement of adipocites (obesity) – Higher interssue pressure – Worsened draining – Retention of liquids and metabolites – Growth of connective tissue (cellulite) – Local hypoxy – Enzyme degradation – Embarrassed lipolyse – Gynoideous type of obesity. Than the hypoxy includes the vicious circles which forming the women's pool in girls and its sustainment in women.

It was demonstrate that the peripheral vasoconstriction response to sympathetic activation is reduced in obese women. The decrease in cutaneous vasoconstriction is consistent with a decrease in sympathetic activation. The influence of age and the duration of obesity are also important determinants of the lower vasoconstrictive response (35). There are and other mechanisms interfering as well. Due to its less significance for the survival of the organism in comparison with the internal organs, the brain and the muscles, the hipoderma, and the whole skin too have adopted to catch the harmful metabolites, when they are a huge amount and to store them as in a depot, thus protecting the vitally-important organs and systems.

In order to prevent its vitally important organs and systems from the progressively increasing harmful products, the human organism acts according to the Law for common biological adaptation, by storing them and gradually organizing them in its hypoderma. There are formed cellulite nodules, new morphological structures which worsen the common state and outside look of the skin**.** ***Nature sacrifices esthetics for the save of the survival of the organism.***

**Conclusion**

The present study was designed the hypothesis of oxidative processes in organism and its relevance for the genesis of typical cellulite and obesity of gynoideous type in women. The close interaction between these two illnesses of the women's pool has been discussed. It should be apparent that this complex body's area and much is still to be learned.

The obesity of gynoideous type and typical cellulite, this blatant manifestation of unsightly symptoms frequently produces negative psychological effects upon the afflicted women. They lead to undesirable behavioral changes such as poor eating habits and lack of exercise which in milder form, may have initiated the disturbances in fat metabolism in the first place. Thus the indicated *cellulite-obesity circles* feeds upon themselves.

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***Address for correspondence:***
Prof. Ivan Topouzov, MD, PhD, DSc
k. Lulin, bl. 333-b, ap. 17
tel: 00359-2-827-92-82
GSM: 0887 / 713-905
E-mail: ivan_topouzov@yahoo.com
*http:// cellulite.hit.bg*