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### ANALYSIS OF MODERN METHODS OF ACNE DISEASE AND ITS COMPLICATIONS DIAGNOSTIC AND TREATMENT

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The purpose of the study was to was to outline the main principal ways and schemes of acne and its complications diagnosis and therapy with obvious this complex skin pathology pathophysiological mechanisms understanding. The authors analyzed critically a significant mass of modern scientific foreign literature devoted to main issues of acne clinical manifestations, the features of its diagnostics in children, men and women. The data were cited concerning modern methods of this dermatological pathology treating. Scrupulous attention was attracted to contemporary data analysis on humoral, including immune mechanisms, involved into acne pathogenesis. The review also provides own authors data of clinical observations concerning post-acne complications specifics of diagnosis and treatment. A review of modern literature indicates the need to develop new diagnostic and therapeutic algorithms for acne/post-acne based on individual characteristics of the patient's disease (hormonal background, concomitant pathology, metabolic disorders, lifestyle). Authors conclude about the importance of acne most effective methods of correction of complications use, which would allow to block effectively atrophic post-acne skin damage and achieve the maximum clinical effect in a short period of time.

Key words: acne, postacne, complications, skin scars, pathophysiological mechanisms, diagnostic, treatment.

# М.Е. Запольський, Т.В. Святенко, Д.М. Запольська АНАЛІЗ СУЧАСНИХ МЕТОДІВ ДІАГНОСТИКИ ТА ЛІКУВАННЯ ВУГРОВОЇ ХВОРОБИ ТА ЇЇ УСКЛАДНЕНЬ

Метою дослідження було визначення основних принципових шляхів та схеми діагностики та терапії вугрової хвороби та її ускладнень з очевидним розумінням патофізіологічних механізмів цієї складної шкірної патології. Автори критично проаналізували значний масив сучасної зарубіжної літератури з основних питань клінічних проявів вугрової хвороби, особливостей її діагностики у дитячому віці, у чоловіків та жінок, а також навели дані фахівців із сучасних методів лікування даної дерматологічної патології. Наведено також дані власних клінічних спостережень щодо особливостей діагностики та лікування ускладнень постакне. Огляд сучасної літератури вказує на необхідність розробки нових діагностичних та терапевтичних алгоритмів акне/ постакне з урахуванням індивідуальних особливостей організму хворого (гормональний фон, супутня патологія, метаболічні порушення, спосіб життя та інше). Автори висловлюють важливість визначення найбільш ефективні методи корекції постакне ускладнень, які дозволяють ефективно блокувати атрофічні постакне ушкодження шкіри та в короткий термін досягати максимального клінічного ефекту.

**Ключові слова:** вугрова хвороба (акне), постакне, ускладнення, шкірні рубці, патофізіологічні механізми, діагностика, лікування.

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Acne is a widespread skin pathology associated with the deregulation of sebaceous glands, the disease can affect the most socially active population in the age group from 14 to 25 years (85 % of people) [39]. In recent years, there has been an increase in moderate and severe forms of acne all over the world, which is due to genetic factors, the influence of external factors, features of skin care, and others [9, 11, 27, 28, 36].

Numerous studies aimed at patients with acne quality of life assessing showed their mental state changes – these patients were ill for more than one year. Thus, 56.1 % of respondents showed concomitant anxiety, symptomatic depression or suicidal thoughts associated with acne when analyzing the dermatological quality of life index among 324 patients with acne. 38.4 % among them have symptoms of anxiety, 23.1 % – symptoms of depression, and 12.9 % have suicidal thoughts due to facial rashes. Totally about 96.5 % of respondents have a decrease in quality of life due to acne. Anxiety in acne is the most common symptom, 1.7 times more common than depression, and three times more common than suicidal thoughts. It is noted that 90 % of acne patients have quality of life worsening [7, 10, 14, 24, 36].

The purpose of the study was to outline the main principal ways and schemes of acne and its complications diagnosis and therapy with obvious this complex skin pathology pathophysiological mechanisms understanding.

Kim D. et al. (2024) identified more than 870 studies that were devoted to severe and moderate forms of acne, a total meta-analysis included 24.649 patients, using PubMed, EMBASE and Web of Science resources. Scientists drew attention to the fact that the prevalence of scarring complications after all forms of acne was 47 %, at the same time, high heterogeneity of studies was observed, which raised

doubts about its objectivity. Thus, various risk factors were subject to analysis: location of acne, source of patients, duration of illness, gender, family history, age, region, lifestyle, injuries. In the course of the study, scientists identified several main trigger factors for the formation of acne complications: male gender, family history, duration of the disease [18].

In addition to hormonal deviations, pathogenic and commensal flora, which are present in areas of hypersecretion of sebaceous glands, play an important role in maintaining inflammation and deepening acne. Scientists believe that changes in the hormonal background, nutritional characteristics, genetic determinism significantly affect the nature of microorganisms and their pathogenicity in acne. The combination of unfavorable factors leads to the accumulation of pyogenic flora, increased inflammation and, as a result, increased risks of scar complications in moderate and severe forms of acne [18, 21, 22].

For a better understanding of the features of acne diagnostics and treatment, it is necessary to focus on the pathophysiological mechanisms of this skin pathology. There are four main and interrelated aspects in the pathogenetic mechanisms of acne: an increase in the concentration of androgen hormones, the activity of which is associated with the stimulation of keratinocyte proliferation, sebum production and growth of sebaceous glands; abnormal proliferation of keratinocytes, which contributes to the formation of comedones; a local chronic inflammatory process localized in the hair follicle and, and bacterial colonization of Cutibacterium acnes [15].

An extremely important role is assigned to the study of the level of individual hypothalamic, adrenal and pituitary hormones in severe forms of acne. A number of scientists continue to study signaling pathways affecting androgen biosynthesis; the results of the study showed an important role in regulating the activity of sebocytes in the expression and function of androgen receptors, as well as in the post-translational regulation of excess androgens in areas of inflammation in acne. These disorders are most actively manifested in low acne-related syndromes, for example, polycystic ovary syndrome and congenital hypoplasia of the adrenal glands. Scientists have proven that the level of androgens not only affects the activity of acne, but also, in general, the functional quality of the skin of the face, its homeostasis, and the microbial landscape. The work proves the effectiveness of some hormones (antiandrogens, estradiol), even when used locally, to restore the microbiome and sebum secretion in patients with acne [44, 45].

Insulin-like growth factor (IGF) is another important regulatory peptide that affects sebaceous gland differentiation and activity. The interaction between insulin, IGF, androgen synthesis, p53 signaling pathways, according to Tingting Hu et al. (2021), is crucial in the pathogenesis of acne [42].

Changes in insulin secretion in response to high glucose concentrations increase significantly during puberty and adolescence, while insulin sensitivity decreases significantly. These changes are of utmost importance because insulin can reverse the androgen axis, which is necessary at this stage of puberty.

Insulin acts on the liver, where it suppresses the production of sex hormone-binding globulin [1]. Furthermore, hyperinsulinemia can promote acne by two mechanisms: first, it suppresses the liver production of IGF-binding protein-1 and IGF-binding protein -3 and increases androgen synthesis; second, it activates the phosphatidylinositol 3-kinase/Akt pathway, which reduces the expression of FOX O1 (Forkhead box O1) protein at the nuclear level [25, 38].

Both testosterone and dihydrotestosterone exert androgen receptor-dependent genomic effects. The mechanisms of the activation of androgen transport pathways continue to be studied, but it can already be stated that they are influenced by both dietary factors and environmental factors and genetic determinism. Regulation is aimed at the functionality and activity of the sebocyte, the excessive stimulation of which leads to the development of severe forms of acne [42].

It was established that progesterone (PG) increasing in women during the luteal phase of the menstrual cycle increases the sensitivity of receptors to dehydroepiandrosterone and stimulates the activity of sebocytes. At the same time, the limit values of the PG level capable of causing acne activation are purely individual (permissible fluctuation in the range of 6.99–56.6 nmol/l). Women who suffer from polycystic ovaries and have problems with cyclic maturation processes of the follicle and corpus luteum are most prone to severe acne. However, the wide range of physiological fluctuations of PG, depending on the phase of the cycle and individual characteristics of the body, do not allow using its level as the main prognostic criterion for acne. Testosterone, dehydroepiandrosterone, cortisol, and sex hormone-binding globulin are among the most significant markers of the endocrine system that affect the course of acne. Undoubtedly, the main sex hormone involved in the regulation of sebaceous glands is testosterone [10, 26, 42].

It must be remembered that the level of free testosterone in most patients with acne remains within the normal range with a tenfold increase in the conversion of testosterone to dihydrotestosterone (DHT). In the cytoplasm of sebocytes there are enzymes  $3/17~\beta$ -hydroxygenase and 5L-reductase, which affect the metabolism of testosterone. It is known that  $\beta$ -hydroxygenases are involved in the transformation of adrenal androgens, and 5L-reductase stimulates the transformation of free gonadal testosterone into DHT. Further, dihydrotestosterone binds to receptors of sebocytes and stimulates the destruction of sebaceous cells, thereby increasing sebum secretion [32, 41, 46].

To this day, questions about the regulation of the secretory activity of the sebaceous glands by hormones other than testosterone, including prolactin and insulin, remain open. It is known that stress hormones: adrenaline, cortisol, prolactin significantly affect the human body, especially the female body, during stress. It was outlined that acne in women is often associated with hyperandrogenism, stress and metabolic disorders. According to the results of the study, about 75 % of women indicated a premenstrual outbreak of acne, as well as a significant influence on the course of acne stress, a humid environment and frequent use of cosmetics. 33 women suffering from acne were examined, after ultrasound diagnosis of the pelvic organs, it was established that 14 (45 %) of them suffered from polycystic ovaries, and 2 patients were found to have single cysts larger than 5 cm. According to the results of the analysis of biochemical markers of insulin resistance (glucose, insulin, glycated hemoglobin, NOMA index) deviations from the norm of at least one marker were found in 97 % of patients. Insulin resistance is considered an inflammatory symptom complex and is closely related to acne. In the course of the study, the author analyzed a number of additional manifestations of hyperandrogenism in patients with acne, the main of which were hirsutism, adrogenic hair loss, acanthosis nigricans, and acrochordons [7, 14].

Of particular interest were studies that confirmed the theory of vitamin D levels influence on acne manifestation. The identification of vitamin D receptors in human sebocytes, the ability to modulate the secretion of lipids and anti-inflammatory cytokines indicates the connection of this vitamin with the severity of acne. A number of studies also indicate the ability of vitamin D to inhibit Th17 differentiation and, accordingly, the level of the pro-inflammatory cytokine IL17. Vitamin D is also associated with the level of skin colonization by Propionibacterium acnes (Cutibacterium acnes) [9, 21, 36, 40].

Bertolani M. et al. (2021) identified IGF-1 as one of the important seboregulatory components that plays a key role in maintaining inflammation in acne [4]. Scientists believe that all common acne treatments used in modern clinical practice combine to increase the expression of the p53 protein, which attenuates IGF-1 signaling and regulates the processes of proliferation and apoptosis.

The researchers analyzed the effect of various treatments, including topical ones, on body mass index and IGF-1 levels. A total of 36 patients were examined (15 women and 11 men). It was found that the highest level of IGF-1 was observed among patients with the most severe forms of acne. Increased sebum secretion is one of the main factors in the worsening of acne, according to scientists, this mechanism is regulated not only by testosterone, but also by insulin-like growth factor-1, which is also activated during puberty. In the course of the study, scientists show the mechanisms of lipogenesis activation with further influence on the metabolism of androgens. In addition, IGF-1 activates transport pathways regulating protein synthesis and glucose transport, which can also indirectly affect the course of acne. It was interesting that the long-term use of isotretinoin (when reaching a course dose of 120 mg/kg of body weight) contributed to a decrease in the level of IGF-1 and this led to a decrease in inflammation and an acceleration of the regression of pustules/other elements of acne. However, scientists claim that the IGF-1 level does not decrease against the background of treatment, and the risk of acne exacerbation remains in most cases [6, 9, 32].

A number of scientists associate the development or exacerbation of acne with a disturbance of the intestinal microflora. A large number of commensal microorganisms are constantly in the intestines, they include: actinomycetes, bifidobacteria, butyricococci, lactobacilli, all of them stimulate phagocytic activity at various levels of gastrointestinal digestion. However, adverse factors of the external environment, nutritional features, and the use of antibiotics lead to a change in the intestinal flora with the dominance of Proteus. According to the authors, it is proteins that stimulate the development of acne in some people. In the study, scientists used MR analysis with two samples to assess the level of connection between acne and intestinal flora, and managed to prove that at least seven commensal intestinal microorganisms (Allisonella, Bacteroides, Candidatus soleaferrea, Eubacterium coprostanoligenes group, Fusicatenibacter, Lactobacillus) have a positive effect on the course of acne and can be used as therapeutic agents to displace more aggressive, pathogenic intestinal flora such as Protea [5, 11, 28].

Interesting studies were devoted to the mechanisms of sebocyte maturation and skin lipid synthesis processes. Scientists studied the unique system of differentiation and death of sebocytes, it turned out that the holocrine secretion of the sebaceous glands is affected by the inflammatory reaction of tissues, the metabolic transmission of signals through the spinal ganglia is indirectly enhanced, with subsequent selective regulation of receptors. According to scientists, autophagy, which occurs during inflammation, provides energy generation for the biosynthesis of proteins of new cell structures. The composition of sebum regulates inflammatory processes and the level of Propionibacterium acnes colonization; in fact, there are much more sebocyte regulation mechanisms than sex hormones, neuropeptides, endogenous opioids and environmental factors play an important role here. It is important to remember that the Western diet (milk and hyperglycemic foods) can affect serum IGF1 levels, thus contributing to the development of acne [7, 14].

This type of diet increases glycemic load levels, insulin, IGF1, and leucine production; in turn, increased levels of these factors decrease FOX O1 activity, thereby losing the ability to inhibit androgen receptors and mTORC-1 (nutrient-responsive mammalian target of rapamycin complex) activity. Moreover,

these factors also stimulate basal keratinocytes to release interleukin-1 (IL-1) and other cytokeratins, which leads to hyperproliferation with hyperkeratinization of the follicle wall, which is a precursor to comedone formation [2, 3].

Hypotheses about the influence of diet on acne pathogenesis are supported by the observation of a low incidence of acne in people who adhere to a paleolithic diet – consisting of minimally processed foods, vegetables, low carbohydrates, and no dairy products or their derivatives [3, 25]. In addition, these diets contain high levels of omega-3 and omega-6 polyunsaturated fatty acids (PUFAs), which are important mediators of inflammation and have a positive effect on acne [8, 17].

Low intake of vegetables and fruits has also been shown to worsen acne. In contrast, the Mediterranean diet — rich in vegetables, fruits, antioxidants, unsaturated fatty acids, and low glycemic index foods — has a protective effect against the development of this condition [23, 34].

Among the modern, promising methods of postacne treatment, combined therapeutic strategies, including carbon laser and plasma therapy (PRP), are being considered today. A number of studies have shown high efficiency in the elimination of post-acne atrophic scars after the specified therapy, the best results were obtained after 3 sessions of laser therapy with plasma therapy. The authors note that the use of PRP significantly increased the level of hyaluronic acid (HA) in the skin, even the introduction of ready-made stabilized hyaluronic acid did not contribute to a higher concentration of HA in the areas of post-acne lesions. The effectiveness of treatment was evaluated based on the results of clinical observation and Goodman's quantitative and qualitative classification system. In addition, the scientists conducted a histological study, which showed better results regarding the concentration of HA in areas of atrophy precisely when autoplasm was introduced, and not with ready-made stabilized hyaluronic acid. Scientists have also drawn attention to a number of other post-acne complications (dyschromia, enlarged skin pores, increased skin density), which did not resolve (or were resolved insufficiently) after the treatment. [12, 13, 37, 45].

Drugs containing HA were shown help to reduce the inflammatory reaction expression and also have osteoplastic activity [19, 20].

A significant contribution to the study of acne and its complications was made by the well-known Australian scientist Jack Goodman, who actually systematized the clinical relationship between the severity of acne and the subsequent development of post-acne complications. The scientist drew attention to the fact that scar changes in certain forms of acne have a number of features, can be predicted and require early treatment.

The author notes that grade 1 scars with flat red, white, or brown spots are best treated with topical therapy, fractionated and pigmented or vascular-specific laser, and occasionally pigment transfer techniques. Moderate grade 2 scarring, seen mostly in the mirror, is now the territory of non-ablative fractionated and non-fractionated lasers, as well as skin-rolling techniques. Grade 3 scars visible at a distance but extensible are best managed with traditional resurfacing techniques or with fractional non-ablative or ablative devices, sometimes including preparatory surgical procedures. Grade 4 scars, where the scars are the strongest and do not stretch, are most in need of a combined approach [31, 36].

In addition to cicatricial changes, the complications of acne include postacne erythema (PAE), which can persist for a long time and is accompanied by moderate subjective phenomena in the form of tingling, burning, itching. According to scientists, there are still no effective methods of treating post-acne erythema and dyschromia. Mohamed E.M. et al. (2021) suggested using a laser beam with a wavelength of 577 nm to treat this complication, which was usually used to remove vascular skin changes (hemangiomas, telangiectasias, angiopapillomas) [26]. There were 21 patients under observation who underwent three sessions of laser irradiation with an energy load of 12-15 J/cm², the time between procedures was 30 days. primary outcome measures such as erythema index, melanogenesis index, overall improvement, and patient questionnaires were assessed. According to the obtained data, all patients had improvement already after the first session of laser irradiation with a wavelength of 577Nm [26].

According to the authors, this method can be considered as an effective adjuvant treatment for PAE and early erythematous atrophic scars. In addition to the most popular CO<sub>2</sub> (carbon) laser interventions, there are also neodymium laser techniques that show good effects not only in the treatment of post-acne erythema, but also erythematous atrophic scars [7, 14, 18, 42].

Scientists pay special attention to the fact that patients' quality of life is affected not only by pustular and cystic elements but also by post-acne complications in the form of hypertrophic and atrophic scars. Thoughts about the formed atrophic and hypertrophic scars irreversibility lead to frequent depressive states, especially in adolescents. Several observational studies on acne cicatricial complications indicate the depression interrelation with the main epidemiological factors of these complications, their results have discrepancies, and the approaches to diagnosis and analysis of the results themselves are quite variable [36].

Teder-Laving M et al. (2024) believe that it's important to determine the main etiopathogenetic links of the disease and the possibility to influence on them for the correct choice of therapeutic strategies in acne treatment. Not only follicular hyperkeratosis, the sebaceous glands excess secretion formation, the

Propionibacterium acnes reproduction and inflammation are of great importance in acne pathogenesis, but also genetic factors [41]. An autosomal dominant type of this disease inheritance is assumed but genetic studies have not provided definite evidences [43]. Nevertheless, close relatives, as a rule, suffered from a similar disease in patients with acne in the family history [33].

36 subjects (94.5 % Fitzpatrick type IV-V) with severe acne/post-acne complications were included in a double-blind randomized study. The patients' faces were divided into two halves for two different therapeutic strategies, one of which was Jessner peeling, the other – salicylic acid. The authors noted the lack of evidence base regarding the chemical peelings efficacy as well as the possible risk of adverse reactions during the procedure. Statistical analysis in observation groups was performed using SPSS v22.0. Significance was set at p=0.05. According to the results, 76.4 % of patients who received Jessner peeling were satisfied with the effect after the procedures, among respondents who received treatment with salicylic acid satisfactory results were 86.7 %. Although the difference in different types of peels use was not significant the authors note the greater salicylic acid efficacy in acne moderate and severe forms treatment. Post-inflammatory hyperpigmentation observed in only one patient who received Jasner peel was indicated as the significant adverse reaction [16].

Sánchez-Pellicer P. et al. (2022) analyzed the existing methods of acne treating and the possibility of issuing therapeutic strategies expanding taking into account acne pathogenetic mechanisms peculiarities [22]. Special attention was attracted to seboregulation mechanisms investigation and to adipocytes' destruction as the result of certain endogenous factors influence (i.e. hormones, proinflammatory cytokines, concomitant pathology, etc.). The scientists considers the ability of commensal flora to form biofilms as the main risks and failures in acne treatment which significantly reduce the efficacy of a number of antibacterial and antiseptic agents. The biofilms presence can also be due to excessive use of systemic antibiotics in the past. The author considers dietary disorders to be another important aspect in acne treatment – especially the use of excessive amounts of carbohydrates and animal fats. The first one stimulates the growth of pathogenic and commensal flora, the latter increase the skin oiliness. Therefore, authors suppose that future therapeutic strategies should combine not only a seboregulating effect but antibacterial and antiseptic effects also. They believe the skin microbiome of affected areas restoration to be quite important [35].

The studies devoted to acne pathogenetic markers level investigation are of especial interest. 60 patients with moderate to severe acne vulgaris (according to the Global Acne Classification System) were observed only 35 among them had post-acne scars. The quantitative latex agglutination method with turbidimetry was used to estimate blood serum C-reactive protein (CRP) concentration while the hepcidin concentration in serum was estimated using a commercially available double-antibody sandwich enzymelinked immunosorbent assay (ELISA) kit. The study revealed that patients with post-acne had significantly lower serum hepcidin levels (p<0.001) and significantly higher CRP levels (p<0.05) compared with the same biochemical indexes in healthy individuals. Scientists concluded that CRP and hepcidin can be considered as prognostic markers for post-acne complications development [27, 29].

Post-inflammatory hyperpigmentation is considered to be a rather undesirable acne complication. Scientists performed new topical retinoid, trifaroten, efficacy analysis which revealed that this retinoid drug provided not only seborrheic and anticomedonic properties but also demonstrated depigmentation result. This was a double-blind analysis of two observational groups with patients with active acne and post-acne manifestations aged from 13 till 35 years. Trifaroten 50 (μg/g cream) significantly improved the end-result in ODS scores from baseline compared to vehicle (–1.6 vs –1.1, p=0.03) at week 12, but the investigated indexes were comparable between groups at week 24 (primary endpoint). Trifaroten had a better reduction in PAHPI score at week 24 (–18.9% vs –11.3% vehicle, p<0.01). Adverse events were more common in the vehicle group compared to trifarotene (30.2% vs 16.7%, correspondently). The researchers concluded that trifarotene is effective across all skin phototypes, provides post-acne hyperpigmentation faster improvement but is more effective when used together with skin moisturizer [32, 36, 40].

Paschalidou E. et al. (2024) draw attention to differences in medical products perception by females including those for acne treatment [30]. Scientists attracted attention to the fact that there is not enough research that could explain the females' organism number of medical products perception peculiarities. So, the sensitivity to acne therapy in women is significantly higher but important that number of negative reactions in women also increases, this can be explained by more sensitive skin.

Gender recognition revealed significantly higher overall adverse reaction rates for all treatments in women (1.8 times for conventional systemic agents [57.30/100 PY vs 31.69/100 PY] and 2.0 times for biologic agents [27.36/100 PY vs 13.9/100 PY], p<0.0001) as well as higher drug discontinuation rates for most conventional systemic treatments. Thus, the researchers concluded that women are associated with significantly higher rates of adverse reactions and drug discontinuation rates. This outlines the need for additional studies related to gender-specific acne treatment and the specificities of female hormones levels [28, 32].

128 patients (main group -83, control group -45) were under our observation for moderate and severe forms of acne and pos-tacne complications. We monitored the formation of post-acne complications.

When analyzing patients with destructive skin changes, the following groups of post-acne complications were identified: post-traumatic pigmentation, scar lesions (keloid, atrophic and hypertrophic scar), stagnant hyperemia, couperosis (Table 1).

Analysis of post-acne complications of the main and comparative groups

Control group Group of observation Clinical forms Men (n=40)Women (n=43) Men (n=40) Post-traumatic pigmentation 35 (27.3 %) 41 (32 %) 19 (14.8 %) 17 (13.2 %) 4 (3.1 %) 1 (0.78 %) 3 (2.3 %) 2 (1.56 %) Keloid Atrophic scar 34 (26.5 %) 37 (28.9 %) 19 (14.8 %) 16 (12.5 %) 5 (3.9 %) Hypertrophic scar 2 (1.56 %) 4 (3.1 %) 2 (1.56 %) Congestive hyperemia 39 (30.4 %) 40 (31.25 %) 21 (16.4 %) 19 (14.8 %) Cooperosis in places of dissolved elements 8 (6.2 %) 11 (8.58 %) 8 (6.2 %) 11(8.5 %)

Based on the above analysis of post-acne complications, the main ones were post-traumatic pigmentation, found in 35 (27.3 %) men and 41 (32 %) women in the main group. In the comparison group, post-traumatic pigmentation was recorded in 19 men (14.8 %) and 17 (13.2 %) women. Characteristic features of post-traumatic post-acne pigmentation were erythema, couperosis in the places of resolved elements, pigmentary changes in the color of the skin.

Atrophic scars were recorded in 34 (26.5 %) men and 37 (28.9 %) women in the main group. In the comparison group, atrophic scars were found in 19 men (14.8 %) and 16 (12.5 %) women. Atrophic scars are characterized by their location below the level of the surrounding skin, thin, flat, with transparent vessels, they do not smooth out when the skin is stretched.

The following types of atrophic scars were found in patients who were under supervision (Table 2): V-shaped (Ice-pick), M-shaped (rolling) and U-shaped (Boxcar).

## Characteristics of atrophic scars during postacne

Table 2

Table 1

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Groups of patients	Types of scars registered		
	V-shaped (Ice-pick)	M-shaped (rolling)	U-shaped (Boxcar)
Main group:			
Men (n 40)	21 (16.4 %)	14 (10.9 %)	8 (6.25 %)
Women (n 43)	25 (19.5 %)	9 (7.03 %)	5 (3.9 %)
Control group:			
Men (n 23)	12 (9.3 %)	8 (6.25 %)	3 (2.3 %)
Women (n 22)	14 (10.9 %)	6 (4.6 %)	4 (3.1 %)

V-shaped atrophic scars were found in 21 (16.4 %) men and 25 (19.5 %) women in the main group. In the comparison group, there were 12 (9.3 %) men and 14 (10.9 %) women. Characteristic features of V-shaped scars were: deep skin defects, sunken zones, diameter up to 3 mm, lesion reached the level of dermis and hypodermis, clear succession of scar edges. The surface opening of the scars was wider than the inner part of the scar, forming a V-shaped shape. When the skin was stretched, the scars did not smooth out.

M-shaped atrophic scars were found in 14 (10.9 %) men and 9 (7.03 %) women in the main group. In the comparison group, there were 8 (6.25 %) men and 6 (4.6 %) women. Features of M-shaped atrophic scars were the retraction of visually unchanged skin due to tissue fusion at the level of the dermis and hypodermis, the width of the scars reached up to 5 mm.

U-shaped atrophic scars were found in 8 (6.25 %) men and 5 (3.9 %) women in the main group. In the comparison group, there were 3 (2.3 %) men and 4 (3.1 %) women. Characterized by rounded, clear vertical edges, the surface part of U-shaped scars is wider than that of V-shaped ones, and does not have a narrowing to the base of the scar. Both deep and superficial scars were observed.

Hypertrophic scars were recorded in 5 (3.9 %) men and 2 (1.56 %) women in the main group. In the comparison group, hypertrophic scars were found in 4 (3.1 %) men and 2 (1.56 %) women. Hypertrophic scars are characterized by a dense nodule protruding above the skin level, with a bluish color, the growth of the scar was observed in the first months, while some patients complained of paresthesia. Scars rose up to 4 mm or more above the level of the surrounding skin. Against the background of treatment, from 4-6 months, the inflammatory reaction faded, growth stopped, a weakening of the vascular pattern, a change in skin color was observed. Flattening and smoothing of the scar occurred, but elevation above the surrounding tissues was partially preserved. Patients noted positive dynamics during 12-18 months of therapy.

Keloid postacne scars were recorded in 4 (3.1%) men and 1 (0.78%) woman in the main group. In the comparison group, keloid scars were found in 3 men (2.3%) and 2 (1.56%) women. Characteristic features of keloid scars were spontaneous growth after resolved inflammatory elements, progress of scar growth, inflammatory reaction, spread to intact surrounding tissues, growth and hyperemia of the scar

lasted from 3 to 8 months after healing. Keloid scars were characterized by a dense consistency, a bright vascular pattern, telangiectasia, a spherical or dome-shaped shape with a smooth surface. Patients complained of itching, periodic soreness in the area of scar formation.

Keloid and hypertrophic scars were most often formed on the skin of the upper and middle third of the back, scapular region, back of the neck, sternum and shoulders, less often on the skin of the face in the area of the angle of the lower jaw.

Congestive hyperemia was noted in 39 (30.4 %) men and 40 (31.25 %) women in the main group. In the comparison group, stagnant hyperemia was detected in 21 men (16.4 %) and 19 (14.8 %) women. Atrophic scars were recorded in 34 (26.5 %) men and 37 (28.9 %) women in the main group. In the comparison group, atrophic scars were found in 19 men (14.8 %) and 16 (12.5 %) women.

#### **Conclusions**

- 1. A review of modern literature indicates the need to develop new diagnostic and therapeutic algorithms for acne/post-acne based on individual characteristics of the patient's disease (hormonal background, concomitant pathology, metabolic disorders, lifestyle). Among the modern variety of therapeutic and hardware technologies, it is important to apply the most effective methods of correction of complications, which would allow to effectively block atrophic post-acne skin damage and achieve the maximum clinical effect in a short period of time.
- 2. Our analysis of post-acne complications indicates a high frequency of post-traumatic pigmentation found in 35 (27.3 %) men and 41 (32 %) women of the main group, as well as in 19 men (14.8 %) and 17 (13.2 %) women. comparison group. The most frequent variants of atrophic complications were V-shaped atrophic scars, found in 21 (16.4 %) men and 25 (19.5 %) women in the main group, in the comparison group in 12 (9.3 %) men and 14 (10.9 %) of women.
- 3. The Woodman scale remains a rather attractive criterion for assessing complications, which achieves not only an assessment of the depth of atrophic/hypertrophic changes in the skin, but also predicts the speed of skin recovery after aesthetic interventions.

#### References

- 1. Akasheh RT, Ankireddy A, Gabel K, Ezpeleta M, Lin S, Tamatam CM et al. Effect of Time-Restricted Eating on Circulating Levels of IGF1 and Its Binding Proteins in Obesity: An Exploratory Analysis of a Randomized Controlled Trial. Nutrients. 2024; 16(20): 3476. doi: 10.3390/nu16203476.
- 2. Akdağ N, Atli E, Zhuri D, Sezgi Ner Güler H, Gürsel Ürün Y. A Study of FoxO1, mTOR, miR-21, miR-29b, and miR-98 Expression Levels Regarding Metabolic Syndrome in Acne Vulgaris Patients. Cureus. 2024; 16(3): 56562. doi: 10.7759/cureus.56562.
- 3. Alia E, Feng H. Rosacea pathogenesis, common triggers, and dietary role: The cause, the trigger, and the positive effects of different foods. Clin Dermatol. 2022; 40(2): 122-127. doi: 10.1016/j.clindermatol.2021.10.004.
- 4. Bertolani M, Rodighiero E, Saleri R, Pedrazzi G, Bertoli S, Leone A et al. The influence of Mediterranean diet in acne pathogenesis and the correlation with insulin-like growth factor-1 serum levels: Implications and results. Dermatol Reports. 2021; 14(1): 9143. doi: 10.4081/dr.2022.9143.
- 5. Bronnec V, Eilers H, Jahns AC, Omer H, Alexeyev OA. Propionibacterium (Cutibacterium) granulosum Extracellular DNase BmdE Targeting Propionibacterium (Cutibacterium) acnes Biofilm Matrix, a Novel Inter-Species Competition Mechanism. Front Cell Infect Microbiol. 2022; 11: 809792. doi: 10.3389/fcimb.2021.809792.
- 6. Callender VD, Baldwin H, Cook-Bolden FE, Alexis AF, Stein Gold L, Guenin E. Effects of Topical Retinoids on Acne and Post-inflammatory Hyperpigmentation in Patients with Skin of Color: A Clinical Review and Implications for Practice. Am J Clin Dermatol. 2022; 23(1): 69-81. doi: 10.1007/s40257-021-00643-2.
- 7. Chen J, Wan Y, Lin Y, Jiang H. Fractional Carbon Dioxide Laser or Erbium: Yttrium-Aluminum-Garnet Laser Assisted by Topical Application/Intradermal Injection of Platelet-Rich Plasma for Postacne Scars. Plast Reconstr Surg. 2021; 148(6): 915-927. doi: 10.1097/PRS.00000000000008513.
- 8. Cheng T, Yu D, Liu B, Qiu X, Tang Q, Li G et al. Oily fish reduces the risk of acne by lowering fasting insulin levels: A Mendelian randomization study. Food Sci Nutr. 2024; 12(6): 3964-3972. doi: 10.1002/fsn3.4054.
- 9. Eichenfield L, Kwong P, Lee S, Krovchuk D, Arekapudi K, Hebert A. Advances in the topical treatment of facial and trunk acne in adolescents: A pooled analysis of the safety and efficacy of 0.005% trifarotene cream phase 3. J Drugs Dermatol. 2022; 21(6): 582-586. doi: 10.36849/JDD.6778
- 10. Eichenfield LF, Hebert AA, Gold LS, Cartwright M, Moro L, Han J et al. Long-Term Safety and Efficacy of Twice-Daily Topical Clascoterone Cream 1% in Patients Greater Than or Equal to 12 Years of Age With Acne Vulgaris. J Drugs Dermatol. 2023; 22(8): 810-816. doi: 10.36849/jdd.7592.
- 11. Feng Chen, Xueqing Hu, Kun Dong Consistency changes of potential lipid markers in acne patients of different ages and their role in acne pathogenesis. J Cosmet Dermatol. 2021; 20(7): 2031-2035. doi: 10.1111/jocd.14009
- 12. Feng Y, Li J, Mo X, Ju Q. Macrophages in acne vulgaris: mediating phagocytosis, inflammation, scar formation, and therapeutic implications. Front Immunol. 2024; 15: 1355455. doi: 10.3389/fimmu.2024.1355455.
- 13. Firlej E, Kowalska W, Szymaszek K, Roliński J, Bartosińska J. The Role of Skin Immune System in Acne. J Clin Med. 2022; 11(6): 1579. doi: 10.3390/jcm11061579.
- 14. Gaumond SI, Abdin R, Yaghi M, Mahmoud RH, Rodriguez M, Eber AE et al. Platelet-rich plasma as an adjuvant therapy to fractional ablative carbon dioxide lasers for cutaneous repair: a complementary treatment for atrophic acne scarring. Lasers Med Sci. 2024; 39(1): 254. doi: 10.1007/s10103-024-04192-y.
- 15. González-Mondragón EA, Ganoza-Granados LDC, Toledo-Bahena ME, Valencia-Herrera AM, Duarte-Abdala MR, Camargo-Sánchez KA et al. Acne and diet: a review of pathogenic mechanisms. Bol Med Hosp Infant Mex. 2022; 79(2): 83-90. doi: 10.24875/BMHIM.21000088.

- 16. How KN, Lim PY, Wan Ahmad Kammal WSL, Shamsudin N. Efficacy and safety of Jessner's solution peel in comparison with salicylic acid 30% peel in the management of patients with acne vulgaris and postacne hyperpigmentation with skin of color: a randomized, double-blinded, split-face, controlled trial. Int J Dermatol. 2020; 59(7): 804-812. doi: 10.1111/jjd.14948.
- 17. Kim HJ, Kim YH. Exploring Acne Treatments: From Pathophysiological Mechanisms to Emerging Therapies. Int J Mol Sci. 2024; 25(10): 5302. doi: 10.3390/ijms25105302.
- 18. Kim DH, Yoon JY, Lee JH, Suh DH. Alterations in epidermal stem cells within the pilosebaceous unit in atrophic acne scars. Australas J Dermatol. 2024; 65(4): 311-318. doi: 10.1111/ajd.14224.]
- 19. Larkina SA, Seletskaya AV, Makarenko OA, Vastyanov RS. Rat skin inflammation markers change in response to calcium hydroxyapatite and hyaluronic acid administration. Journal of Education, Health and Sport. 2021; 11(8): 510-519. doi: 10.12775/JEHS.2021.11.08.057
- 20. Larkina SA, Seletska OV, Makarenko OA, Vastyanov RS, Badiuk NS. Study of osteoplastic and anti-inflammatory efficiency of drugs containing calcium hydroxyapatite and hyaluronic acid. PharmacologyOnLine. 2021; 3: P. 958-967.
- 21. Lee HG, Kim CJ. Classic and backdoor pathways of androgen biosynthesis in human sexual development. Ann Pediatr Endocrinol Metab. 2022; 27(2): 83-89. doi: 10.6065/apem.2244124.062.
- 22. Li J, Duan F, Kuang J. Meta-analysis of fractional radiofrequency treatment for acne and/or acne scars. J Cosmet Dermatol. 2022; 21(12): 6754-6766. doi: 10.1111/jocd.15348.
- 23. Liu YT, Wang YW, Tu C, Ren JW, Huo J, Nan XJ et al. Recommendations for managing adult acne and adolescent acne based on an epidemiological study conducted in China. Sci Rep. 2024; 14(1): 16327. doi: 10.1038/s41598-024-67215-2.
- 24. Ly S, Kamal K, Manjaly P, Barbieri JS, Mostaghimi A. Treatment of Acne Vulgaris During Pregnancy and Lactation: A Narrative Review. Dermatol Ther (Heidelb). 2023; 13(1): 115-130. doi: 10.1007/s13555-022-00854-3.
- 25. Meixiong J, Ricco C, Vasavda C, Ho BK. Diet and acne: A systematic review. JAAD Int. 2022; 7: 95-112. doi: 10.1016/j.jdin.2022.02.012.
- 26. Mohamed EM, Tawfik KM, Elsayed IB, Bölke E, Gerber PA. 577-nm high-power optically pumped semiconductor laser is safe and effective in the treatment of inflammatory acne: a prospective, single-center, split-face comparative study. Eur J Med Res. 2021; 26(1): 103. doi: 10.1186/s40001-021-00573-z.
- 27. Mohsin N, Hernandez LE, Martin MR, Does AV, Nouri K. Acne treatment review and future perspectives. Dermatol Ther. 2022; 35(9): 15719. doi: 10.1111/dth.15719.
- 28. Najafi-Taher R, Kohnelu AJ, Farsani VE, Rayeni NM, Mohimi HR, Ehsani A. et al. Topical tea tree oil nanoemulsion gel containing adapalene versus marketed adapalene gel in patients with acne vulgaris: a randomized clinical trial. Arch Dermatol Res. 2022; 314(7): 673-679. doi: 10.1007/s00403-021-02267-2
- 29. Pala E, Bayraktar M. Relationships Between Disease Severity and the C-reactive Protein/Albumin Ratio and Various Hematological Parameters in Patients With Acne Vulgaris. Cureus. 2023; 15(8): 44089. doi: 10.7759/cureus.44089.
- 30. Paschalidou E, Katsaras G, Papoulakis T, Kalloniati E, Kavvadas D, Karachrysafi S et al. The Effect of Isotretinoin on Insulin Resistance and Serum Adiponectin Levels in Acne Vulgaris Patients: A Systematic Review and Meta-Analysis. Clin Pract. 2024; 14(3): 1021-1037. doi: 10.3390/clinpract14030081.
- 31. Pavlačková J, Pecháčková H, Egner P, Mokrejš P, Gál R, Janalíková M. The Effect of Cosmetic Treatment and Gel Laser Therapy on the Improvement of Comedogenic Skin Type. Gels. 2023; 9(5): 370. doi: 10.3390/gels9050370.
- 32. de Pessemier B, Grine L, Debaere M, Maes A, Paetzold B, Callewaert C. Gut-Skin Axis: Current Knowledge of the Interrelationship between Microbial Dysbiosis and Skin Conditions. Microorganisms. 2021; 9(2): 353. doi: 10.3390/microorganisms9020353.
- 33. Ražnatović Đurović M, Janković J, Đurović M, Spirić J, Janković S. Adolescents' beliefs and perceptions of acne vulgaris: A cross-sectional study in Montenegrin schoolchildren. PLoS One. 2021; 16(6): 0253421. doi: 10.1371/journal.pone.0253421
- 34. Ryguła I, Pikiewicz W, Kaminiów K. Impact of Diet and Nutrition in Patients with Acne Vulgaris. Nutrients. 2024; 16(10): 1476. doi: 10.3390/nu16101476.
- 35. Sánchez-Pellicer P, Navarro-Moratalla L, Núñez-Delegido E, Ruzafa-Costas B, Agüera-Santos J, Navarro-López V. Acne, Microbiome, and Probiotics: The Gut-Skin Axis. Microorganisms. 2022; 10(7): 1303. doi: 10.3390/microorganisms10071303.
- 36. Shah N, Shukla R, Chaudhari P, Patil S, Patil A, Nadkarni N. et al. Prevalence of acne vulgaris and its clinico-epidemiological pattern in adult patients: results of a prospective, observational study. J Cosmet Dermatol. 2021; 20(11): 3672-3678. doi: 10.1111/jocd.14040
- 37. Sitaniya S, Subramani D, Jadhav A, Sharma YK, Deora MS, Gupta A. Quality-of-life of people with keloids and its correlation with clinical severity and demographic profiles Wound Repair Regen. 2022; 30(3): 409-416. doi: 10.1111/wrr.13015.
- 38. Taha S, Shakhshir M, Zyoud SH. Acne Vulgaris and adherence to the mediterranean diet among university students: a case-control study. J Health Popul Nutr. 2024; 43(1): 41. doi: 10.1186/s41043-024-00535-1.
- 39. Tan J., Beissert S., Cook-Bolden F, Chavda R, Harper J, Hebert A. et al. Impact of facial atrophic acne scarring on quality of life: a multi-country population survey. Am J Clin Dermatol. 2022; 23(1): 115-123. doi: 10.1007/s40257-021-00628-1.
- 40. Tan J, Chavda R, Baldwin H, Dreno B. Management of Acne Vulgaris With Trifarotene. J Cutan Med Surg. 2023; 27(4): 368-374. doi: 10.1177/12034754231163542.
- 41. Teder-Laving M, Kals M, Reigo A, Ehin R, Objärtel T, Vaht M et al. Genome-wide meta-analysis identifies novel loci conferring risk of acne vulgaris. Eur J Hum Genet. 2024; 32(9): 1136-1143. doi: 10.1038/s41431-023-01326-8.
- 42. Tingting Hu, Ziyu W, Qiang J, Wen CC. Sexualhormone und Akne: Aktueller Stand. J Dtsch Dermatol Ges. 2021; 19(4): 509-516. doi: 10.1111/ddg.14426\_g.
- 43. Vasam M, Korutla S, Bohara RA. Acne vulgaris: A review of the pathophysiology, treatment, and recent nanotechnology based advances. Biochem Biophys Rep. 2023; 36: 101578. doi: 0.1016/j.bbrep.2023.101578.
- 44. de Vries F, Driessen R, Tjin E, Westenberg A, Vehof H, van de Kerkhof P. The association between acne care provision and quality of life: A cross-sectional survey. Health Sci Rep. 2022; 5(2): 487. doi: 10.1002/hsr2.487.
- 45. Xie W, Zhang C, Wang T, Wang J, Fu F. Effects of natural products on skin inflammation caused by abnormal hormones secreted by the adrenal gland. Front Pharmacol. 2023; 14: 1156271. doi: 10.3389/fphar.2023.1156271.]
- 46. Zhu Z, Zhong X, Luo Z, Liu M, Zhang H, Zheng H et al. Global, regional and national burdens of acne vulgaris in adolescents and young adults aged 10-24 years from 1990 to 2021: a trend analysis. Br J Dermatol. 2025; 192(2): 228-237. doi: 10.1093/bjd/ljae352.

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