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THE PHENOMENON OF ROSACEA-RUSHES (THEORETICAL ASPECTS)

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Abstract. The phenomenon of rosacea-rushes (theoretical aspects). Bocharov V.A., Bocharova V.V., Lebediuk M.M., Sarayreh A.A.S., Kuts L.V. According to the decisions of international scientific forums, the problem of phenomenon of rosacea (acne rosacea), a common dermatosis with numerous unexplained aspects of etiopathogenesis is a promising area of modern medical research. The aim of the study was theoretical substantiation of the essential features of the mechanisms of occurrence, development and clinical manifestations of the first signs of rosacea in women of reproductive age. The use of a systematic analytical methodical approach to assess the data of clinical and laboratory examinations of women with rosacea, conducted in different regions of the world, allowed to establish the originality of such manifestations of dermatosis as the appearance of unexpected rushes to limited areas of the face, accompanied by local redness and local heat areas of the skin differing significantly from similar rushes in other diseases or syndromes (menopause, migraine, etc.). It is established that the peculiarity of the relationship of these clinical characteristics (from English: rush, ruddy, redness, rosacea, reproductive age of women, reaction) allows to indicate the first signs of dermatosis as a phenomenon inherent in this disease Rush-Ruddy-Rosacea-Reproduce-Reaction (abbreviated – «5-R»), the key pathophysiological target of which (as well as the disease as a whole) is a disorder of a set of hierarchically dependent mechanisms of the evolutionarily determined motivational need to ensure reproductive function in women (both at the cellular level and extracellular structures of the ovaries, and at different levels of subcortical formations and centers of the cortex of the cerebral hemispheres). The phenomenon of rosacea rush is closely related to other phenomena of this dermatosis – hypersensitivity of bradykinin receptors, actinic elastosis, development of post erythematous telangiectasia. The prospect of further research on the problem of rosacea is to study the relationship of disorders in the functional systems of molecules of signaling compounds of different classes (hormones, eicosanoids, neuropeptides, kinins, cytokines and others) in the pathogenesis of the disease.

Реферат. Феномен розацеа-приливов (теоретические аспекты). Бочаров В.А., Бочарова В.В., Лебедюк М.М., Сарайрех А.А.С., Куц Л.В. Проблема феноменов розацеа (розовых угрей), распространенного в мире дерматоза с невыясненными многочисленными аспектами этиопатогенеза, согласно решениям международных научных

форумов, является перспективным направлением современных медицинских исследований. Целью работы стало теоретическое обоснование существенных особенностей механизмов возникновения, развития и клинических проявлений первых признаков розацеа у женщин репродуктивного возраста. Использование системного аналитического методологического и методического подхода оценки данных клинических и лабораторных обследований женщин, больных розацеа, проведенных в различных регионах мира, позволило установить первичность такого проявления дерматоза, как появление неожиданного ощущения приливов крови к ограниченным зонам лица, которые сопровождаются локальным покраснением и местным жаром соответствующего участка кожи и существенно отличаются от подобных приливов при других заболеваниях или синдромах (климакс, мигрень и др.). Установлено, что особенность взаимосвязи указанных клинических характеристик (от англ.: *rush* – прилив, *ruddy* – покраснение, *rosacea* – розовые угри, *reproduce* – репродуктивный возраст женщины, *reaction* – реакция) позволяет отметить первые признаки дерматоза, как присущий этому заболеванию феномен (*Rush-Ruddy-Rosacea-Reproduce-Reaction*, сокращенно – «5-R»), ключевой патофизиологической мишенью которого (как и заболевания в целом) является нарушение комплекса иерархически зависимых механизмов реализации эволюционно детерминированной мотивационной потребности обеспечения репродуктивной функции женского организма (как на уровне клеточных и экстрацеллюлярных структур яичников, так и на разных уровнях подкорковых образований и центров коры больших полушарий головного мозга). Феномен розацеа-приливов тесно связан с другими феноменами этого дерматоза – гиперчувствительностью брадикининовых рецепторов, актиническим эластозом, развитием патологических телеангиэктазий. Перспективной дальнейших исследований проблемы розацеа является изучение взаимосвязей нарушений в функциональных системах молекул сигнальных соединений различных классов (гормонов, эйкозаноидов, нейропептидов, кининов, цитокинов и других) в патогенезе заболевания.

To date in international forums among the promising areas of medicine the importance of an analytical approach to solving problems and phenomena characteristic mainly of certain diseases is emphasized, but at the same time being important for a number of other pathological conditions, especially in the early stages of their development [1, 2].

The relevance of such studies on rosacea (rosacea; pink acne) is due not only to the prevalence of this disease in the world (affects more than 10% of the population, especially women of reproductive age), but also its insufficiently studied etiopathogenesis, which leads to frequent complications after ineffective treatment of patients, significantly impairing their quality of life [9, 11].

In this regard, the aim of the study was to theoretically substantiate the essential features of the mechanisms of occurrence, development and clinical manifestations of the first signs of rosacea in women of reproductive age.

Disclosure of such an aspect as "phenomenality" (from the English – phenomenon, extraordinary) of certain clinical manifestations of rosacea and the mechanisms of their development may have a high level of scientific significance not only for dermatology, but also become a new area of research in those fields of medicine, where such phenomena can also occur, in particular – in endocrinology, angiology, reproductive medicine, psychoneurology, psychology, gerontology and others [7, 12].

New methodological and instructional approaches to solving the set goals and objectives of clarifying the problem can play a significant role in ensuring the reliability of the obtained conclusions. In particular, "phenomenal" refers to the mani-

festations of diseases that differ significantly from those in other pathological conditions, and visible ("with the naked eye") such changes on the skin, clinicians of various specialties widely use in practice in the differential diagnosis of such characteristic ("phenomenal") symptoms of lupus erythematosus, as a form of foci of lesions of the skin in the form of "butterfly", the phenomenon of "apple jelly" in tuberculous lupus, and others. With regard to dermatology, in addition to the above phenomena, a large number of them are recognized in both non-contagious and contagious skin diseases [8]. In this regard, if methodologically correct approach to the collection of medical history in patients with rosacea, one can note a certain "phenomenon" even of the onset of this disease (before the formation of clear clinical manifestations), as well as its further course, which can significantly help clarify mechanisms of rosacea development, and this approach has been recognized in recent years as promising by the world scientific medical community [5].

According to the plan of complex integration research work of Odessa National Medical University and Sumy State University (state registration number 0116U008932) we examined 107 women with rosacea, and anamnesticly it was found that the earliest and mandatory manifestation of the disease was a sudden (often unreasonable) sensation of "flush", which was accompanied by the appearance of redness of a certain local area of facial skin. Already in such "debut" of a dermatosis which at repeated similar attack is designated as "pre-rosacea", initial bases of starting pathological process and its further development can be revealed.

Very precisely the essence of these events (phenomena) is reflected in the English translation:

1) "flush" – rush (about blood); congestion - to infuse (about blood); congest - to overflow (medical term); congested - obstruction (medical term);

2) "redness" – ruddy (ruddy).

Since this reaction (from the English – reaction) is observed in rosacea (rosacea) in women of reproductive age (from the English – reproduce), such a manifestation of rosacea-flushes in this disease can logically be described as the phenomenon of "rush-ruddy- rosacea-reproduce-reaction"(abbreviated – "5-R").

What exactly is the "phenomenality" of such rosacea-flushes, because similar manifestations occur in women with other conditions (syndromes, diseases)? Indeed, at the age of the most frequent manifestations of rosacea in women (40-50 years) hot flushes due to menopause ("menopausal") and/or vegetative-vascular dystonia ("migraine-like") can often occur; but, firstly in menopause there are such signs as a feeling of heat all over the body (and not in local areas of the skin), with "migraine-like hot flushes" they are accompanied by general sweating, changes in heart rate and blood pressure, headache, which are not observed in rosacea. The modern feature of the occurrence of such sudden hot flushes in young women aged 18 to 25 years significantly distinguishes rosacea (pink acne) from acne vulgaris, which are also often observed at this age, but are not accompanied by hot flashes [10].

Constant recurrence of such rosacea-rushes with redness of local areas of facial skin and a feeling of slight local heat (tingling, prickling) almost does not cause patients an uncontrollable desire to scratch these areas, but after changing the stages of transient and persistent erythema, they are necessarily accompanied by development telangiectasis (this, in turn, is sometimes referred to as the phenomenon of "PERT" – posterythema-revealed telangiectasis). In this regard, the methodology of careful analysis of the nature of the definitions of the disease can also be the basis for the interpretation of events, as we have already mentioned the terms of "congest" and "congested" quite accurately indicate the mechanism of formation of these persistent changes in the microcirculatory tract of the skin (telangiectasis). This can be confirmed to some extent by the color of the skin, which at the first flush is referred to as "ruddy" (ruddy), then the process is transformed into livid erythema (from the English – livid-pale), then – in transit (erythema) and in persistent erythema (from the English – persist-persistent), which reflects the stagnant nature of the mechanism of development of changes occurring in the skin.

Thus, the distinctive features of such manifestations of rosacea as hot rushes ("5-R" – phenomenon), the development of various types of erythema (livid, transient, persistent) and the formation of telangiectasias (PERT-phenomenon) in the characteristics described above are observed mainly in rosacea, but similar manifestations may be in other pathological conditions, which dictates the need to study possible pathophysiological different mechanisms (phenomena) of this dermatosis [5, 7].

With the development of rosacea, especially in its initial stages, there is no complete "set" of the main manifestations of inflammation (rubor, tumor, dolor, calor, functio laesa), and they are manifested to an insufficient extent, so the focus is on pathophysiological moments. These diseases, which are also considered almost as phenomena – hypersensitivity of bradykinin receptors, actinic elastosis, the importance of porphyrins in the harmful effect on the skin of ultraviolet radiation can often occur [6].

It is possible that the category of rosacea phenomena includes the primary localization of the process, namely, the nasolabial fold and adjacent areas of facial skin. This area is influenced by such powerful anatomical regulators as facial muscles and extremely sensitive cranial nerves – trigeminal, facial, pharyngeal, oculomotor, and given the fact that the auricle may be included in this so-called "anatomical pattern" of rosacea, this "set" of nerves is joined by branches of the vagus nerve and the cervical plexus of the spinal cord, which innervate the auricular zones.

Given the importance of the structures of nervous regulation of skin functions, it is possible that it makes sense to draw an analogy of events occurring in rosacea, with the formation of such a psoriatic manifestation as Kebner's phenomenon, which usually develops after external influences. There is no consensus on Kebner's phenomenon about its essence, and more often it is a question of the so-called "isomorphic reaction" without a sufficiently convincing explanation of its essence. In the case of psoriasis, indeed, "psoriasis-like" rashes appear at the sites of itching and injuries (and in vitiligo – "vitiligo-like", in red flat herpes – "lichenoid" specific papules). It is possible that the "phenomenality" of Kebner's symptom does not depend on the disease in which it is revealed, but on the peculiarities of the inflammatory-reparative process in dermatosis, when the "trigger" role of "conductor" of the cell ensemble (forming the histopathological picture of the disease) and the cascade of their numerous regulatory signaling molecules (they form pathophysiological stages of the inseparable inflammatory-reparative process) are sequentially performed

by certain cells: endothelial cells, monocytes/macrophages, basophils/mast cells, leukocytes (neutrophils, lymphocytes, eosino[hils]), and with the activation of the reparative process – and fibroblasts [3]. It is possible that the mechanisms characteristic of the Kebner's phenomenon in other diseases "work" in rosacea, but in this case, most likely, the endogenous mechanism is primary, which plays a very important role in the development of dermatosis.

The "key word" in the problem of the onset of many types of pathological processes lies in its evolutionary expediency (need), and therefore such a mechanism must be so "vital" that it dominates over others and determines the reaction of central mechanisms of response/regulation on a hierarchical principle at their various structural and functional levels in the nervous system (both the most peripheral – receptor, and central and autonomic nervous systems).

If again the above methodological and instructional principles are applied to address this issue, then such a "key word" (determinant, vital need) in women of reproductive age will be the need for "reproduction" – the evolutionary vital need for procreation.

In this case, the unsatisfied motivational need for procreation becomes really dominant, i.e. the first of other needs, it will be aimed at providing such a function as procreation, so modern research suggests that it should be separated to a separate center – "special sexual center of a woman" [4]. In this regard, the Ukrainian term is linguistically successful – "sexual" (Russian – "sex", English – "sex") center or reproductive (reproduce – as indicated in the abbreviation of the proposed phenomenon). These provisions are confirmed by a careful study of the history of women with rosacea (both the disease itself and the history of their lives), which indicate that:

1) in almost all women (of different ages, at which the first signs of rosacea may appear) "sexual" problems are important in one form or another: a) disorders of the ovulatory menstrual cycle; b) the presence of diseases (syndromes), one way or another related to the functioning of the female genitals; c) anamnesticly significant events in the families of parents, during pregnancy and childbirth, etc.; d) actual "sexual" problems;

2) in that part of sick women in whom such problems cannot be established at their initial visit, their further inspections (including modern instrumental and laboratory methods) can specify them.

In this regard, it may be important that has been established in recent studies [5]:

1) the ovaries "produce" not only "purely" sex hormones (androgens and estrogens), but also

"asexual" hormones ("hormones", such as prostaglandins), which are the strongest vasomodulators and can primarily provoke a reaction of the hemodynamic centers of the main brain at different levels, which is manifested not only in the form of hot flushes (central levels), but also redness of the skin (peripheral level);

2) in addition to "steroid" hormones, various ovarian cells can produce "non-steroid" metabolites (such as prostaglandins), as well as neuropeptides – which at a very high rate (the first of other signaling molecules) can "work" for providing them with the necessary numerous functions (mediators, transmitters, modulators, etc.), including in the key "effector" structural target of the skin in rosacea – Merkel cell complex-nerve terminal, keratinocytes, and possibly – sebocytes or their stem precursors; it is no less important that the "effector localization" of the first clinical manifestations of rosacea-flushes (nasolabial fold) is not accidental, because it is in this place that there is a set of conditions for the "triggering" of the above-mentioned "pathophysiological phenomena" such as actinic elastosis (and the role of porphyrins), hypersensitivity of bradykinin receptors of the cutaneous neurovascular microcirculatory complex.

It is possible that in rosacea the so-called "PERT" phenomenon develops as a result of a complex of mechanisms associated with the functioning of the endothelial cell and its extracellular matrix.

The peculiarity of the above-mentioned phenomenon "5-R" may depend on the paroxysm (suddenness) of the vasoactive peptides entering the bloodstream from both the ovarian and skin structures.

The fact that the "nociceptive reactions" in patients are not pain and intense itching, and subjective feelings of another modality (feelings of local "heat", "fever", and sometimes – "tingling", "tingling sensation all over the body", "tightened skin", etc.), can also be explained by the change of producer cells and the corresponding biologically active compounds during the penetration of such cells into the lesion of the skin during the development of neurogenic, vascular and other components of inflammation.

Dilation of blood vessels (both in the microcirculatory tract of the skin and in the centers of the brain) is replaced by periods of their narrowing (vegetative-vascular dystonia), which can further affect the change in permeability of skin vessels, edematous infiltration of the walls of arterioles, followed by complication of blood flow in them, the opening of arteriovenous shunts and blood stasis in the venules.

It is possible that in addition to such a characteristic of regulatory systems of homeostasis as "hierarchy", in the problem of rosacea development both age unevenness of their development and decrement play a role, which depends on both genetically programmed processes (primarily), and on external factors that determine the level of functional reserves of the body; it is by puberty that their formation is finally completed, and in old age the mechanisms of their support are exhausted.

The reaction of the organism (of all or separate structures) to the stimulus of sensory value develops in the form of a reflex with the subsequent formation of reflex arcs that provide a reflex act. Polysynaptic arcs are formed by a chain of neurons with the formation of nerve "centers" (clusters of neurons) to regulate individual functions, which are "complex" functional associations, consisting, in turn, of "simple" centers capable to "connect" structures of the central nervous system necessary for the implementation of the reflex act.

The fact that clinically patients with rosacea in the case of the development of hot flushes clearly indicate their localization and the corresponding sensations (fever, heat, etc.) in certain areas of the facial skin, due to the peculiarities of this area and the fact that each area transmits signals to certain areas of this "hierarchical chain of management", including for the cortical part of the cerebral hemispheres, and in this regard it can be assumed that this accuracy of indication of changes in the skin by the patients is due to the organization of communication, in which the spatial location of neurons in the central nervous system, which is associated with certain receptors (or structures), allows you to reflect (the so-called "reflected sensitivity" of neurons of cortical structures) implementation of a special representation of functions (not accidentally in the known "homunculus" of the face takes a large "representation"). Among the many properties of the nerve centers, one of them is important, such as "comparability", because in response to changes on the facial skin, various of them gradually "adjust" in a certain rhythm (common to them). It is the involvement of several centers is necessary for the regulation of such complex reflex acts that are observed in rosacea patients in "rushes", with each of the centers, performing their reflexes, interacts with other principles (coordination, inhibition, irradiation, concentration, summation, etc.) to achieve the final result. In this case, one of the centers can become "dominant", and it can "be attracted to others, and this is more likely to occur when high (dominant) excitability creates humoral influences (including pathogenetically significant for

rosacea – a substance P, opioids, pro-staglandins, bradykinin, sex hormones, etc.).

In the hierarchy of the centers of the brain structures, a special place belongs to a reticular formation (from the Latin *rete* – a net) – a net of neurons of the brainstem, forming the end of nuclei, as well as a number of nuclear formations of the thalamus, among the numerous functions of which are the regulation of hemodynamics (in Therefore, numbers are in separate zones). This is essentially important for understanding the nature of clinical manifestations on the skin in the case of rosacea, since the integration function of the proper stem part of the reticular formation is not accompanied with "specific" sensations - it apparently "protects" the cerebral cortex from excess signal information to perform the latter more important, first priority ("lifesaving") function (in rosacea – reproductive). This "non-conscious" by the cerebral cortex part of the signal information nonetheless acts on it. In cases when subjective feelings are "realized" (in rosacea-rushes), both stem and the thalamic part of the reticular formation in sensory systems of the body participate, including the "skin analyzer", capable of evaluating separate "undertows" of sensations, including those above-mentioned: fever, heat, etc. (and this is a complex chain of relationships from peripheral receptors of different skin structures to the neurons of the cerebral cortex). The principle of the structure and functioning of the "sensory" skin system is not different from other systems. Beginning with receptors later, bodies of ascending afferent neurons in different divisions of the central nervous system form nuclear (!) accumulation (at least three) in the spinal cord or in the trunk, thalamus and cerebral cortex. The most important thing is that at the level of the cerebral cortex the skin sensory system refers to the number of the most significant for the whole organism.

CONCLUSIONS

In female, patients with rosacea (pink acne), the first signs of the disease in the form of sudden flushes accompanied by local redness and fever sensation on the face occurring in reproductive age, significantly different from similar flushes during climacterium, migraine and other diseases and syndromes, which allows them to be considered as a separate phenomenon "Rush-Ruddy-Rosacea-Reproduce-Reaction" (shortened – "5-R"). The prospect of further research is to establish correlative relationship of this clinical phenomenon with pathophysiological phenomena (hypersensitivity of bradykinin receptors, active elastosis) typical for this disease, as well as mechanisms

that provide vital evolutionarily deterministic reproductive function of the female body.

Conflict of interest. The authors declare no conflict of interest.

REFERENCES

1. Dashko MO, Syzon OO. [The role of chronic stress, reactive and personal anxiety and some neuro-endocrine, metabolic and immunological disorders in the pathogenesis of acne]. *Ukrainskyi zhurnal dermatologii, venerologiyi, kosmetologii*. 2019;2(73):7-17. Ukrainian. doi: <https://doi.org/10.30978/UJDVK2019-2-7>
2. Kolyadenko KV, Tkachyshyna KS. [28th Congress of the European Academy of Dermatology and Venereology]. *Ukrayinskyi zhurnal dermatologii, venerologii, kosmetologii*. 2019;4(75):107-8. Ukrainian doi: <https://doi.org/10.30978/UJDVK2019-4-107>
3. Shirzad M, Hamedi J, Motevaseli E, Modarressi MH. Anti-elastase and anti-collagenase potential of Lactobacilli exopolysaccharides on human fibroblast. *Artif. Cells Nanomed. Biotechnol*. 2018;46(1):27:1-11. doi: <https://doi.org/10.1080/21691401.2018.1443274>
4. Bocharov VA. Role in the development of rosacea special female genital center: Part I. *Dermatovenerology and Cosmetology*. 2020;1(4):18-35. doi: [https://doi.org/10.26886/2523-6946.1\(4\)2020.2](https://doi.org/10.26886/2523-6946.1(4)2020.2)
5. Bocharov VV. Steroid hormone dysregulatory of rosacea: Part I *Dermatovenerology and Cosmetology*. 2020;1(4):3-17. doi: [https://doi.org/10.26886/2523-6946.1\(4\)2020.1](https://doi.org/10.26886/2523-6946.1(4)2020.1)
6. Diehl C. Peptides in cosmeceuticals. *Ukrainian Journal of Dermatology, Venereology, Cosmetology*. 2019;1(72):28-35. doi: <https://doi.org/10.30978/UJDVK2019-1-28>
7. Fiedler F, Stangl GI, Fiedler E, Taube K-M. Acne and Nutrition: A Systematic Review. *Acta Derm. Venereol*. 2017;97(1):7-9. doi: <https://doi.org/10.2340/00015555-2450>
8. Habif Thomas P. *Clinical Dermatology: A Color Guide to Diagnosis and Therapy*. Sixth edition. St. Louis. Missouri: Elsevier; 2016.
9. Hofmann MA, Lehmann P. Physical modalities for the treatment of rosacea. *J. Dtsch. Dermatol. Ges*. 2016;14(6):38-43. doi: <https://doi.org/10.1111/ddg.13144>
10. Lynn DD, Umari T, Dunnick CA, Dellavalle RP. The epidemiology of acne vulgaris in late adolescence. *Adolesc. Health Med. Ther*. 2016;7:13-25. doi: <https://doi.org/10.2147/AHMT.S55832>
11. Barbara MR, Sewon K, Ana LC. Rosacea: Epidemiology, Pathogenesis, and Treatment. *Dermato-Endocrinology*. 2017;9(1):e1361574. doi: <https://doi.org/10.1080/19381980.2017.1361574>
12. Grossi E, Cazzaniga S, Crotti S, et al. The constellation of dietary factors in adolescent acne: a semantic connectivity map approach. *J. Eur. Acad. Dermatol. Venereol*. 2016;30(1):96-100. doi: <https://doi.org/10.1111/jdv.12878>

СПИСОК ЛІТЕРАТУРИ

1. Дашко М. О., Сизон О. О. Роль хронічного стресу, реактивної та особистісної тривожності і деяких нейроендокринних, метаболічних та імунологічних порушень у патогенезі акне. *Укр. журнал дерматології, венерології, косметології*. 2019. Т. 73, № 2. С. 7-17. DOI: <https://doi.org/10.30978/UJDVK2019-2-7>
2. Коляденко К. В., Ткачишина К. С. 28й конгрес Європейської академії дерматології та венерології. *Укр. журнал дерматології, венерології, косметології*. 2019. Т. 75, № 4. С. 107-108. DOI: <https://doi.org/10.30978/UJDVK2019-4-107>
3. Anti-elastase and anti-collagenase potential of Lactobacilli exopolysaccharides on human fibroblast / M. Shirzad et al. *Artif. Cells Nanomed. Biotech*. 2018. Vol. 27. P. 1-11. DOI: <https://doi.org/10.1080/21691401.2018.1443274>
4. Bocharov V. A. Role in the development of rosacea special female genital center: Part I. *Dermatovenerology and Cosmetology*. 2020. Vol. 4, No. 1. P. 18-35. DOI: [https://doi.org/10.26886/2523-6946.1\(4\)2020.2](https://doi.org/10.26886/2523-6946.1(4)2020.2)
5. Bocharova V. V. Steroid hormone dysregulatory of rosacea: Part I *Dermatovenerology and Cosmetology*. 2020. Vol. 4, No. 1. P. 3-17. DOI: [https://doi.org/10.26886/2523-6946.1\(4\)2020.1](https://doi.org/10.26886/2523-6946.1(4)2020.1)
6. Diehl C. Peptides in cosmeceuticals. *Укр. журнал дерматології, венерології, косметології*. 2019. Т. 72, No. 1. С. 28-35. DOI: <https://doi.org/10.30978/UJDVK2019-1-28>
7. Fiedler F., Stangl G. I., Fiedler E., Taube K. M. Acne and Nutrition: A Systematic Review. *Acta Dermatol. Venereol*. 2017. Vol. 97, No. 1. P. 7-9. DOI: <https://doi.org/10.2340/00015555-2450>
8. Habif Thomas P. *Clinical Dermatology: A Color Guide to Diagnosis and Therapy*. 6 ed. St. Louis. Missouri: Elsevier, 2016. 1008 p.
9. Hofmann M. A., Lehmann P. Physical modalities for the treatment of rosacea. *J. Dtsch. Dermatol. Ges*. 2016. Vol. 14, Suppl. 6. P. 38-43. DOI: <https://doi.org/10.1111/ddg.13144>
10. Lynn D. D., Umari T., Dunnick C. A., Dellavalle R. P. The epidemiology of acne vulgaris in late



adolescence. *Adolesc. Health Med. Ther.* 2016. Vol. 7. P. 13-25. DOI: <https://doi.org/10.2147/AHMT.S55832>

11. Rainer Barbara M., Kang Sewon, Chien Anna L. Rosacea: Epidemiology, Pathogenesis, and Treatment. *Dermato-Endocrinology.* 2017. Vol. 9, No. 1. e1361574.
DOI: <https://doi.org/10.1080/19381980.2017.1361574>

12. The constellation of dietary factors in adolescent acne: a semantic connectivity map approach / E. Grossi et al. *J. Eur. Acad. Dermatol. Venereol.* 2016. Vol. 30, No. 1. P. 96-100.
DOI: <https://doi.org/10.1111/jdv.12878>

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