

UDC 616.379-008.64-06-089.844:616.13

# **PARTICULARITIES OF WOUND PROCESS DYNAMICS IN PATIENTS WITH PYONECROTIC FORMS OF DIABETIC FOOT SYNDROME, USING COMPLEX APPROACH IN SURGICAL TREATMENT**

**A.V.Proshin**

*Moscow State Medical Stomatology University, mail-net.proshin@yahdex.ru*

Comparative evaluation of drug treatment of diabetic foot syndrome was conducted in patients, who were treated with mechanical methods and ultrasound cavitation for treating the wound, as well as sorbents, in particular Beta-Beta, hygienic certificate №77.72.10.916 P. 05042 dated 25.12.97, prepared with the method of sublimation drying. It was noted that implementation of complex pathogenetical approach in surgical treatment of patients while using proposed medicines influences positively the dynamics of wound process.

**Keywords:** *diabetes mellitus, diabetic foot syndrome, pyonecrotic wounds, wound process*

Проведена сравнительная оценка способов местного медикаментозного лечения ран у больных с гнойно-некротическими формами синдрома диабетической стопы, у которых при лечении раны применяли как механические методы обработки, ультразвуковую кавитацию, так и сорбенты, в частности, пектин-препарат Бэта-Beta, гигиенический сертификат №77.72.10.916 П. 05042.12.97 от 25.12.97, приготавливаемый методом сублимационной сушки. Отмечено, что применение комплексного патогенетического подхода в хирургическом лечении пациентов с использованием предложенных препаратов оказывает позитивное влияние на динамику раневого процесса.

**Ключевые слова:** *сахарный диабет, синдром диабетической стопы, гнойно-некротические раны, раневой процесс*

The problem of treating pus wounds is still the most important in surgery. The frequency of diabetes among the population is still high [1]. Diabetic foot — is one of the most frequent complication of diabetes [2,3]. Every second patient undergoes surgical treatment, most part of which consists of pyonecrotic processes in feet, that are present in 28.6-65.0% of patients with diabetes [3-5]. Detailed and complex examination of patients is necessary for developing science-based approach to treatment, while considering all the pathogenetical parts in development of described pathology. Morphological aspects in treating complicated wounds are still loosely

developed and not clear, and approaches to treating the wounds are often controversial, especially when it comes to the wound process under the diabetes mellitus. Wound healing is a complex process, taking place on different levels (molecular, subcellular, cellular, histological, and organ's), final objective of which is lesion liquidation with maximum rebuilding of anatomical structure while maintaining minimum functional loss [6]. Wound healing proceeds under common rules and principles of tissues' regeneration. The speed of this process as well as its outcome, depend on the degree and the depth of the wound lesion, structural features of the organ, overall organism

condition, treatment methods applied at the moment. There're complex physical and chemical changes taking place in the wound, that leads to acidosis due to accumulation organic and non-organic acids, as a result of inflammatory processes, necrotic changes, tissue dentritis.

Recently the arsenal of medicines used for local treatment of wound has significantly expanded, but, regardless that, the results are still not fully satisfactory, due to high cost and small accessibility of some drugs for the wide administration.

During last years, carbohydrate-containing biopolymers attract more researchers' attention.

These polymers include pectin compounds (frozen greek «pektos» — clotted, frozen), in the base of which there is pectin acid (polygalacturonic acids). Wound ultrasound treatment methods deserve particular attention as well [7].

The objective of this work is comparative evaluation of wound treatment efficiency in patients with pyonecrotic forms of diabetic foot syndrome (DFS), in whom ultrasound cavitation and pectin: Beta-Beta, hygienic certificate # 77.72.10.916, as a sorbent, were administered.

### Data and examination means

We followed up clinical and morphological characteristics of wound process progression in patients with pyonecrotic forms of diabetic foot syndrome, in whom ultrasound cavitation and pectin: Beta-Beta, as a sorbent, were administered. Comparative analysis was conducted in two groups.

Main group consisted of 159 patients with pyonecrotic forms of DFS, in which when treating the wound locally, mechanical methods and ultrasound cavitation, as well as, sorbents, had been administered.

Morphological research was conducted using impression smears and biopsic material for hysto-, cytological and immunocytochemical analysis.

Wound ultrasound treatment of main group patients was conducted with ultrasound device «Sonoca-180» of «Söring» company (img.1). Comparison group (control) consisted of 163 patients with pyonecrotic forms of DFS, who, after receiving surgical d-bridement of wound, underwent its local treatment with unctures on water soluble base — Levomekol, dioxidin.



Img.1. Wound ultrasound cavitation device — «Sonoca-180», of Söring company

Ultrasound — mechanical oscillation of elastic medium with a frequency higher than 16 kHz, having definite energy and spreading in a form of alternate compressions and expansions. This phenomenon is also characterized by the following physical processes: «microexplosions», forming of sound waves, local temperature peaks, that stimulate sound-chemical reactions in the exposed area. When applying ultrasound to heterogeneous media, small- and medium-scale currents, or turbulations, are formed, that speed up diffusion, dissolving, and dispersion processes. Thus, cavitation processes that form on waveguide end, lead to destruction and deletion of fibrin deposits on the boarder of 2 media. Exposed normal tissue is not affected.

Wound ultrasound treatment was conducted according to the principles of treating inflammatory processes as well as with regards to its stages. The choice of power parameters, the time of exposure, intermediate solution was done strictly individually, and it depended on the wound type, the time of its existence, inflammation type, patient's individual sensitivity. As a process solution 0.02% chlorhexidine water solution was used. Ultrasound treatment would begin with small power, with its gradual increase, paying attention to the pain sense modality of the patient. The medium speed of processing is 1 sq.cm/min, while all wound surface was exposed to ultrasound.

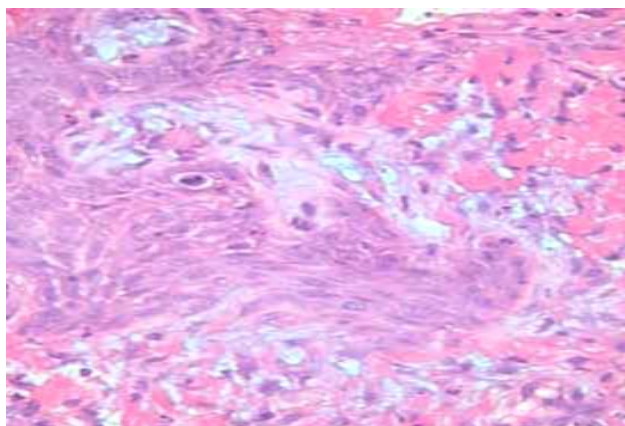
After wound ultrasound cavitation, pectin - Beta-Beta drug (pulvis of red table beet, «Bordeau» cultivar, hygienic certificate # 77.72.10.916 P. 05042 dated 25.12.97, obtained by cryodesiccation method) was administered as a sorbent in local treatment of pus wounds. Beta-beta medicine an ultrasound cavitation were administered in phases I-II of wound process under following method: after applying 3% solution of hydrogen peroxide to the wound surface, ablation with 1% chlorhexidine solution, would ultrasound cavitation with antiseptic solution would be performed. Later, after airing, we would apply thing layer of medication in pulvis form. Depending on intensity of exudative-histological reaction, the wound would be covered with drape, sterile dry, or moistened with 10% NaCl solution; then fixed with dressing. Procedure would be repeated once-twice daily. Effectiveness evaluation of medication would be conducted on the following basis: wound visual examination; decreasing duration of its detersion; granulation tissue formation; decrease of the wound defect area; forming of marginal epithelialization; cytological examination, wound bacteriological characteristics, the duration of patient's stay in hospital (bed-day).

Initial specimen sampling was made on the time of initial surgical d-bridement, and the final one — on 15-20<sup>th</sup> day of treatment.

### Results and discussion

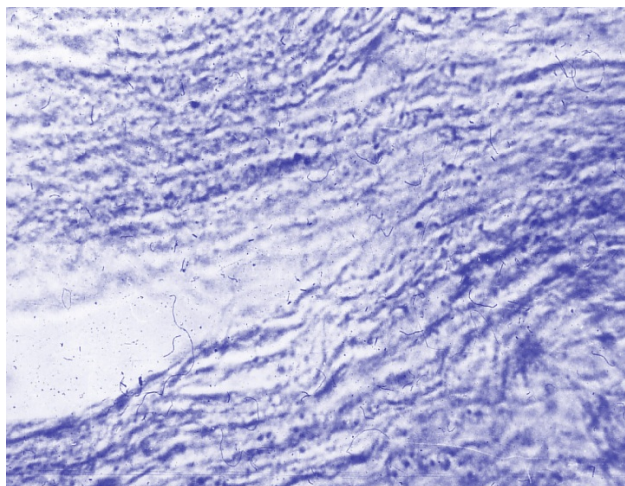
The implementation of ultrasound cavitation method led to evacuation of fibrin, as well as necrotic tissues and exudations, from wound hardly accessible areas, with minimum traumatization of sound tissue. Faster termination of inflammation phase would occur, and then — transition of wound process inflammatory phase — to reparative one. This was characterized by

onset of rich granulations in the wound, as well as decrease of its area, insular and marginal epithelialization (Img.2).



Img.2. Microspecimen. Epidermis formation. Multilayered flat epithelium stratum intussusception. Mitosis is clearly seen in the epithelium stratum. Hematoxylin & eosin.  $\times 400$

Such direction of wound process is also explained by the fact that during cavitation increase in regional hemodynamics occurs. The increase of curve oscillation amplitude as well as index of microcirculation, by average of 0.2, was marked. It also was stated that after already 1-2 cavitation sessions the level of wound bacterial contamination would dramatically decrease, by average from  $10^{11}$ - $10^8$  to  $10^3$ - $10^5$  colonies (Img.3). It is explained both by direct bactericidal effect of ultrasound, and deep infiltration of process solution.

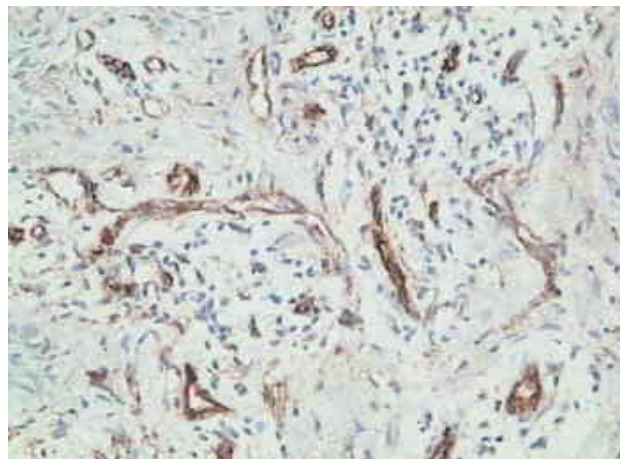


Img.3. Microphotography. single bacteria adsorbed and phagocytized by leukocytes can be observed. Gram-Weigert stain.  $\times 200$

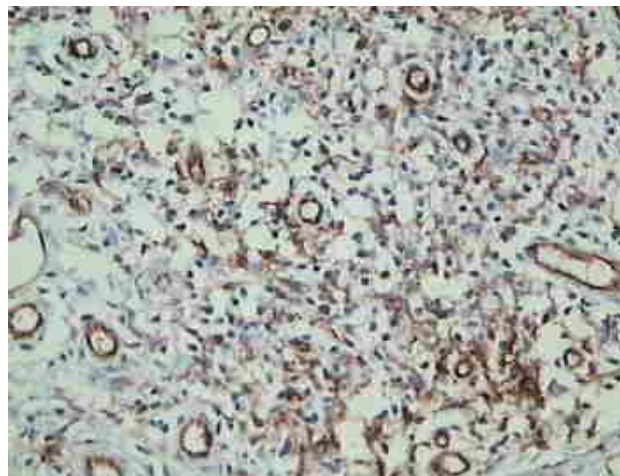
After wound ultrasound cavitation, pectin (Beta-Beta) was used as a sorbent in septic wound local treatment.

By the 7<sup>th</sup> day of treatment essential differences in the wound process dynamics were already marked in the main and comparison group. It manifested in 115

patients (72.3%) of main group by accelerated transition from, 1<sup>st</sup> phase of wound healing into second. Clinical picture corresponded to as of wound purification from necrotic tissue with formation of active granulation tissue and the presence of vertical vessels in it, reduction of perifocal inflammation. The wound flow obtained serous characteristics, the normalization of microcirculatory derangements occurred as well. The results of morphological analysis would confirm clinical findings and demonstrate the cases of small vessels' neoplasm, with evident proliferation of endothelial cells (Img.4-5), which in their turn are the inducers of regeneration processes.



Img.4. Microphotography. Considerable number of new-formed vessels. Immunoperoxidase method with antibodies to the marker of endothelial cells — antigen CD31.  $\times 400$

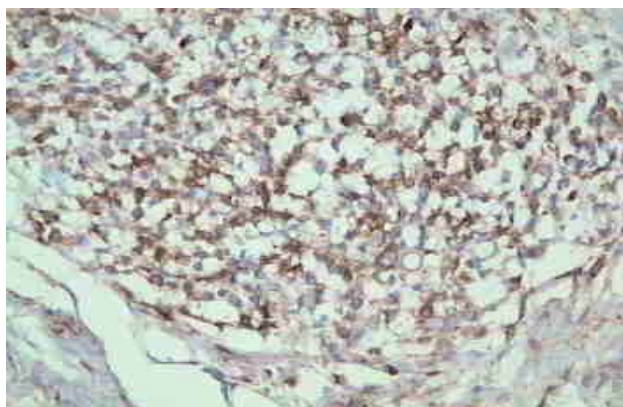


Img.5. Microphotography. Evident cases of angiogenesis with endothelial proliferation. Immunoperoxidase method with antibodies to the marker of endothelial cells — antigen CD31.  $\times 400$

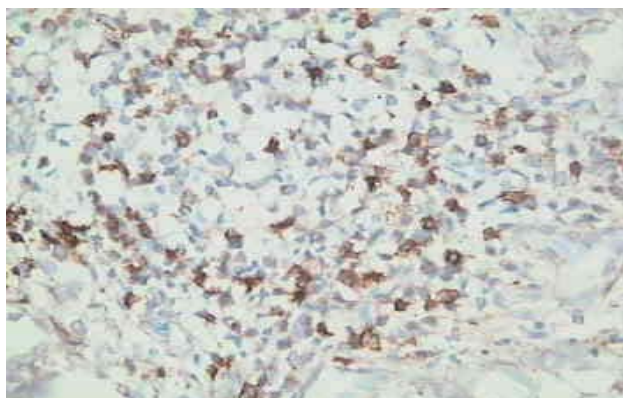
Active endotheliocytes correlated with the increase in number of wound macrophages. It is known that macrophages are able to extract angiogenesis inducers, that stimulate endotheliocytes' proliferation [8,9]. Macrophages are the cells that take fundamental positions in realization of functions of both specific defense — immune system (interaction with T and B lym-



phocytes), and non-specific defense (phagocytosis), as well as play an important role in inflammation and regeneration reactions [10]. The increase of macrophage quantity occurred simultaneously with the increase of their functional activity, which is proven by their ultra-structural organization: developed Golgi complex, granular ER, considerable number of lysosomes. More often than in comparison group patients, contacts between macrophages and fibroblasts would be defined. The quantity of more mature fibroblasts with dilated granular ER cisterns, that were surrounded by mature collagen fibers, also increased. More favorable course of wound healing process of main group patients give evidence in favor of T-lymphocyte-helpers' prevalence in granulation wound (Img.6) and moderate presence of T-lymphocyte-suppressors (Img.7).

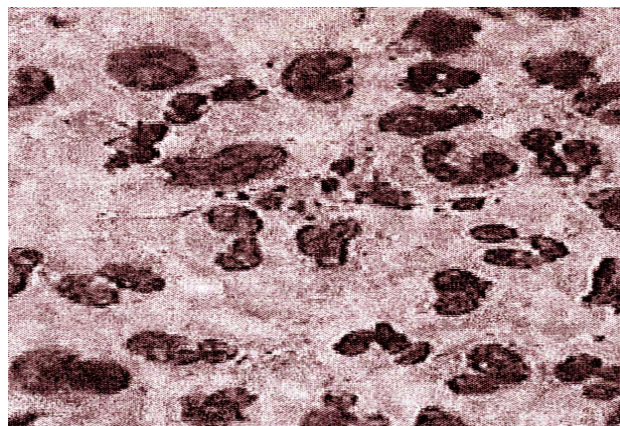


Img.6. Microphotography. Large number of T-helpers (CD4+) in granulation tissue and in 2nd phase of wound process (211-356 cells in field of view with microscope magnification  $\times 400$ ). Immunoperoxidase method with CD4 antibodies.  $\times 400$



Img.7. Moderate number of T-suppressors and killers (CD8+) in granulation tissue, second phase of wound process (126-198 cells in the field of view with microscope magnification  $\times 400$ ). Immunoperoxidase method with CD8 antibodies.  $\times 400$

Cytological picture was characterized by the prevalence of neutrophilic leukocytes with normal nucleus and cytoplasm structure, as well as completed phagocytosis in them (Img.8). The number of destroyed neutrophils after initial d-bridement with ultrasound and Beta-Beta product decreased from 78% to 11%.

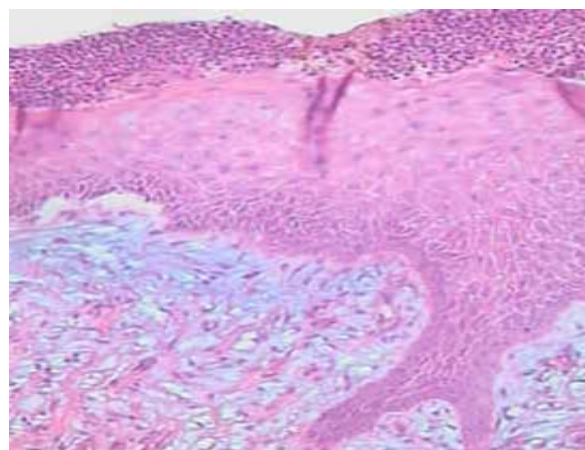


Img.8. Microspecimen. The prevalence of neutrophilic leukocytes with normal nucleus and cytoplasm structure. Romanovskiy-Guimza stain,  $\times 400$

In impression smears of 28 patients (45.9%) the absence of microflora, and its considerable suppression in smears of 24 patients (39.3%) were noted, this allows to classify the drug as of mixed antiseptic group. It is noted that Beta-Beta has manifesting adsorptive, hygroscopic, and proteolytic properties, which facilitates wound cleansing from septic exudate and detritus.

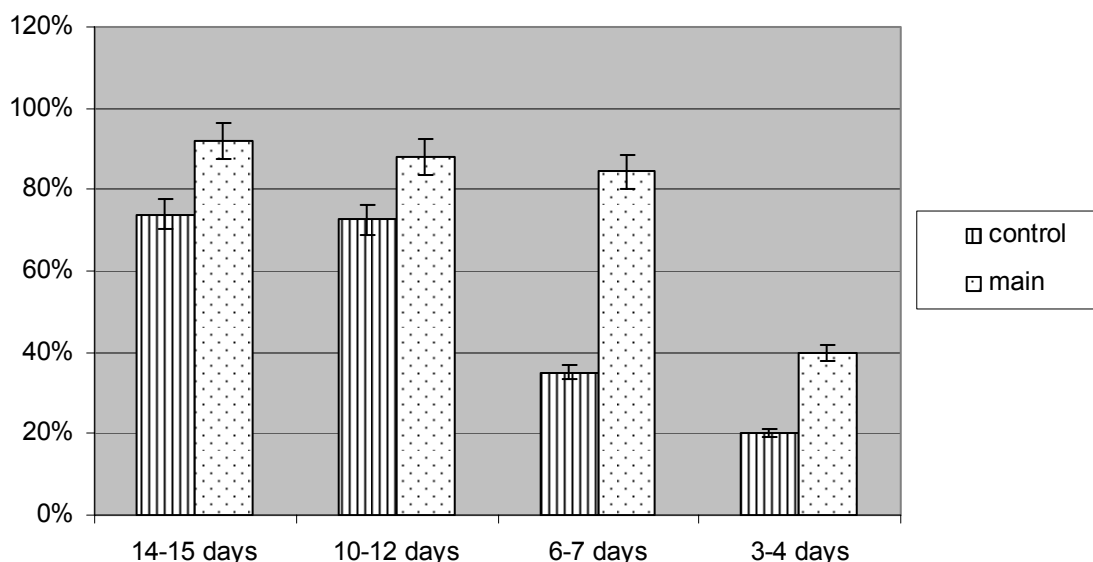
Wound cleansing was accompanied by activation of regenerative processes, as well as granulation and epithelium formation, which indicated the restoration of damaged epithelial-mesenchymal bonds (parenchymal-stromal interactions).

By the 15<sup>th</sup> day of treatment the differences in wound process in observed groups kept increasing. The patients of main group had faster completion of the wound process' second stage, as well as the onset of insular and marginal epithelization. Morphological finding of histology specimens correlated with clinical dynamics of wound process. The clear presentation of epithelial tissue formation appeared on specimens (Img.9).



Img.9. Intussusception of multilayer flat epithelium strata — epidermis formation. Deeper — granulation tissue with plethoric neogenic vessels, active large fibroblasts, moderately evident leucocytic and lympho-macrophageal infiltration. Hematoxylin & eosin stain

The evaluation of the microbiological research results shown drastic decrease of wound contamination (average in  $10^2$ ). It allowed to perform the connection of wound margins and plastic closing of wound defect.



Img.10. Comparative characteristics of wound healing process and terms of wound cleansing (in days) in main and compared (control) groups of patients

The wound process in control group that received traditional treatment was essentially different from that in main group: the tendency towards trophic ulcer cleansing was observed in 39 (61.9%) only on 10<sup>th</sup>-12<sup>th</sup> day, and granulation tissue formed no sooner than on 14<sup>th</sup> day (Img.10)

Thus, the administration of ultrasound cavitation and Beta-Beta sorbent in patients when treating wounds with septic-necrotic forms of DFS, (simultaneously with complex, pathogenetic treatment) in 1<sup>st</sup> and 2<sup>nd</sup> phase of wound process, shows positive effect, proved by clinical, morphological, and immunocytochemical findings.

### Conclusions

1. The administration of ultrasound cavitation using device «Sonoca-180» in complex treatment of patients with complicated forms of DFS is proved to be effective addition to existing means of wound treatment.

2. Ultrasound treatment allows (twice as) faster sanation of wounds, decreasing of microbial contamination, optimization of wound process, and accelerate regeneration processes (1.8×) in necrotic suppurative forms of DFS.

3. Administration of ultrasound cavitation and sorbent — Beta-Beta preparation, allows to strengthen angiogenesis and reconstruct damaged microcirculation, increase macrophageal reaction, fibroblasts' proliferation, granulation tissue maturation, remodeling, and proliferation, as well as decrease onset of inflammatory reaction.

4. The research results allow to consider the necessity of using clinical morphology (biopsy specimens, impression smears) as control and effectiveness criteria and thus decrease the length of stay in hospital.

5. Optimized tactics of wound local treatment in necrotic suppurative forms of DFS allow to prepare patients for plastic surgery in short terms and thus decrease the time of hospital stay.

1. Greenhalgh D.G. Wound healing and diabetes mellitus // J. Clin. Plast.Surg. 2003. Vol.30. №1. P.37-45.
2. Gostishyev V.K., Afanasyev A.N. The standards of medical and preventive measures in patients with diabetic osteoarthropathy and purulo-necrotic lesions of feet // Conference on «Standarts of diagnostics and treatment in contaminated surgery», collection of articles. Moscow. 325 2001. P.107-112.
3. Briskin B.S., Dibirov M.D., Hamitov F.F., Proshin A.V., Yakobshvili Y.I. Purulo-necrotic complications of Diabetic Foot Syndrome and its representation in ICD-10 and insurance medicine standarts // Surgery. 2007. №1. P.49-55.
4. Svetukhin A.M. Surgical Approaches in treatment tactics for purulo-necrotic forms of diabetic foot / A.M.Svetukhin, A.B.Zemlyanoi // Modern aspects of diagnostics, treatment, and prevention of lower ligaments' involvement in diabetic patients. M., 1996. P.177-183.
5. Dedov I.I., Anfitzirov M.B., Galstyan G.R. Tokmakmakova A.Y. Diabetic Foot Syndrome. Clinics, Diagnostics, treatment, and prevention. M., 1998. 150 p.
6. Серов В.В., Пауков В.С. Воспаление. М.: Медицина, 1995. (5) 640 с.
7. Chaplinskiy V.V. Ultrasound treatment of septic wounds // Surgery. 1982. ©6. P.75-78.
8. Leibovich S.J., Polverini P.J., Fong T.W. Production of angiogenic activity by human monocytes requires an L-arginine/nitric oxide-synthase-dependent effector mechanism // Proc. Nat. Acad. Sci. USA. 1994. Vol.91. P.4190-4194.
9. Leibovich S.J., Ross R. The role of the macrophages in wound repair. A study with hydrocortisone and antimacrophage serum // Amer. J Path. 1975. Vol.78. P.71-101.
10. Kaufman O.Y., Shechter A.B. Macrophages/Inflammation (edited by Serov V.V., Paukov V.S.). M.: Medicine, 1995. P.115-136.