

## A Cytologic Study of Wound Process Dynamics in Purulent Soft Tissue Diseases with the Use of Programmed Rehabilitation Technologies

Vladimir A. Sergeev<sup>1\*</sup>, Alexander A. Glukhov<sup>2</sup>, Alexander S. Sorokin<sup>3</sup>

<sup>1\*</sup>Voronezh N.N. Burdenko State Medical University, Voronezh, Russia.

Orel State University named after I.S. Turgenev, Medical Institute, Orel, Russia. E-mail: sergeevdoc60@yandex.ru

<sup>2</sup>Voronezh N.N. Burdenko State Medical University, Voronezh, Russia.

<sup>3</sup>Plekhanov Russian University of Economics, Moscow, Russia.

### ABSTRACT

**Purpose of research:** to study cytological features of healing processes in patients with soft tissue phlegmons using programmed rehabilitation technologies.

**Methods:** The study involved 167 patients with purulent phlegmon of soft tissues at various locations. Patients were randomised in two groups. Conventional postoperative local treatment was provided to patients from the control group ( $n=79$ ). In the intervention group ( $n=88$ ), after surgical debridement the wound tube drainages were used, withdrawn through separate incisions; the wound was blindly sutured. Post-surgical period included programmed rehabilitation procedures carried out using the AMP-01 device. The dynamics of reparative processes in purulent wounds was evaluated according to the cytologic pattern of the material taken employing surface or needle biopsy method.

**Results:** A higher speed of cell-mediated responses in purulent wounds is noted in the intervention group of patients. By the 9<sup>th</sup> day after surgery, the cytologic pattern corresponded to the regenerative type of cytograms. Noteworthy were statistically significant more rapid decrease in the number of degenerative forms of neutrophils and positive redistribution of banded and segmented neutrophils together with high values of regeneration and degeneration index ( $p<0.001$ ), indicating that the reversal of inflammatory process speeds up. In earlier periods, a statistically significant occurrence of macrophages and cells of young connective tissue as fibrocytes, fibroblasts, fibrous fibers ( $p<0.001$ ) was also observed, what demonstrated active regeneration processes in the wound. Low intensity of cell-mediated responses in the wound, prolonged inflammation phase, long-lasting regeneration phase, and later onset of scar reorganisation phase were found in the control group. With that, by the 9<sup>th</sup> day of post-surgical period, the cytologic pattern in the control group corresponded to the inflammatory type of cytograms.

**Conclusion:** The conducted cytologic study has proved the effectiveness of using programmed rehabilitation technologies, which facilitate shortening of inflammation phase and acceleration of reparative processes in suppurative foci of soft tissue phlegmons.

### KEYWORDS

Purulent Inflammatory Diseases of Soft Tissues, Phlegmon of Soft Tissues, Programmed Rehabilitation Technologies, Cytologic Study, Reparative Process.

### Introduction

Purulent inflammatory diseases of soft tissues represent one of the most important and complex problems of modern surgery [1,2,3]. It is related not only to a wide spread of surgical infection, but to challenges in diagnosing it, variable and persistent clinical course, complex treatment, and unpredictable prognosis.

Patients with acute purulent inflammatory diseases of soft tissues amount to nearly 40% of the total number of all surgical inpatients and outpatients [4,5]. According to the national U.S. statistics, each year emergency departments receive more than 3 million people with skin and soft tissue infections, more than 500,000 of them are hospitalized, and costs for their treatment exceed US\$ 10 bln. [6,7]. From the data of the Department of Health Monitoring, Analysis, and Strategic Development of the Ministry of Health of the Russian Federation, in 2018, 1018694 surgeries were performed in surgical hospitals of the country for purulent diseases of skin and subcutaneous tissue, what amounted to 10.2% of surgeries in total, and mortality among inpatients with purulent diseases has increased over the last years and amounted to 1.92% in 2018 [8].

In recent years, fundamental scientific research studies in molecular and cellular biology have made it possible to more fully understand the key mechanisms of wound healing. It has been proved that healing process with any injury is genetically determined, formed during ontogenesis and phylogenesis, an inflammation phase occurs always first, then giving way to scar regeneration and the phase of scar reorganisation and epithelization [5,9,10,11]. Here is

the essence of the biological law of healing with the same pathogenesis for any wound process irrespective of a wound nature, origin, and location.

To solve the problems of predicting the course of reparative processes, that underlie structural and functional restoration of altered tissues, becomes increasingly important in recent times. Hence, of relevance is an interest in developing both new treatment strategies and methods for assessment of the dynamics in healing of wound defects [12-15].

To quickly obtain the objective data on the course of reparative processes in the wounds of various origin, the use of cytologic method remains pertinent [5,16,17,18,19]. A cytologic study enables characterisation of different types of the wound process course, and adequate assessment of the effectiveness of provided treatment [5,20,21]. 6 cytologic pattern types according to V.F. Kamaev (1954) are distinguished, that correspond to different stages of wound process: degenerative necrotic type, degenerative inflammatory type, inflammatory type, inflammatory regenerative type, regenerative inflammatory type, regenerative type [5,22]. To fully evaluate the wound healing pattern, a regeneration and degeneration index (RDI) is computed by the formula [23]. Less than 1 value of RDI is indicative of a pronounced inflammatory process in the wound. If the value of this indicator becomes equal to more than 1, it implies the transition of the wound process to the regeneration phase.

Assessment of reparative response in the wound based on cytologic verification constitutes an objective method for examining the specifics of the wound process course, which enables optimisation of the disease management.

**Purpose:** to study the results from a cytologic study of healing processes in purulent soft tissue diseases using programmed rehabilitation technologies.

## Material and Methods

Over the period from 2011 to 2019, 167 patients with purulent soft tissue phlegmons at various locations were under the authors' supervision. The research study inclusion criteria are as follows: more than 18 years age of patients, extremity or neck soft tissue phlegmon, voluntary informed consent available. The research study exclusion criteria are: extensive skin defects within surgical debridement area, signs of anaerobic infection, pregnancy, diabetes mellitus and oncological pathology, functional abnormality of circulation organs, and type III respiratory failure.

Patients involved in the study were randomised in two groups according to the postoperative techniques for rehabilitation of suppurative focuses. Control group included 79 patients: 44 men, 35 women. Following surgical debridement, patients were given typical local treatment utilising iodophor solutions, polyethylene glycol-based ointments. Intervention group included 88 patients: 46 men and 42 women. After surgical debridement, the wound tube drainages were used, withdrawn through separate incisions; then the wound was blindly sutured. Drainages were connected to the AMP-01 original device (patent for invention No. 2539165 dated 27.11.2014), used to carry out programmed postoperative rehabilitation procedures. A customised program was installed on the device control unit for irrigation, antiseptic aspiration, and continuous vacuum cyclical processes, implemented autonomously. Programmed rehabilitation procedures, alternated with 1-hour vacuuming, were performed every 3 hours. The specified level of vacuum in purulent cavity (60-80 mm Hg) was maintained using a built-in pressure sensor. The method was applied during the first 5-6 days of treatment, with active aspiration performed afterwards. Sutures were removed on the 7-9<sup>th</sup> day. Baseline therapy was identical in both groups of patients.

To evaluate the parameters by study groups, mean values ( $M$ ) and mean square deviation ( $M \pm \sigma$ ), median ( $Me$ ), first and third quartiles ( $Q_1$ ,  $Q_3$ ) were utilised. Mean age of patients from intervention group ( $M \pm \sigma$ ) was  $59 \pm 13$  years;  $Me = 56$ , from control group –  $60 \pm 11$  years;  $Me = 59$ . Gender- and age-wise distribution of patients with soft tissue phlegmons from study groups is given in Table 1.

**Table 1.** Gender- and age-wise distribution of patients from study groups

Indicator	Intervention group (n=88)	Control group (n=79)	p-value of significance of differences between groups
Mean age $M \pm \sigma$	$59 \pm 13$	$60 \pm 11$	0.857*
Gender	men (n, %)	46 (52.3%)	0.845**
	women (n, %)	42 (47.7%)	

Note: \* t-criterion for independent samples

\*\* Fischer's exact test

Thus, there are no statistically significant differences between the study groups in age and gender, what allowed inferring about homogeneity of groups.

The distribution of patients with soft tissue phlegmons in the study groups, determined according to phlegmon location, is given in Table 2.

**Table 2.** Nosology-related distribution of patients from study groups

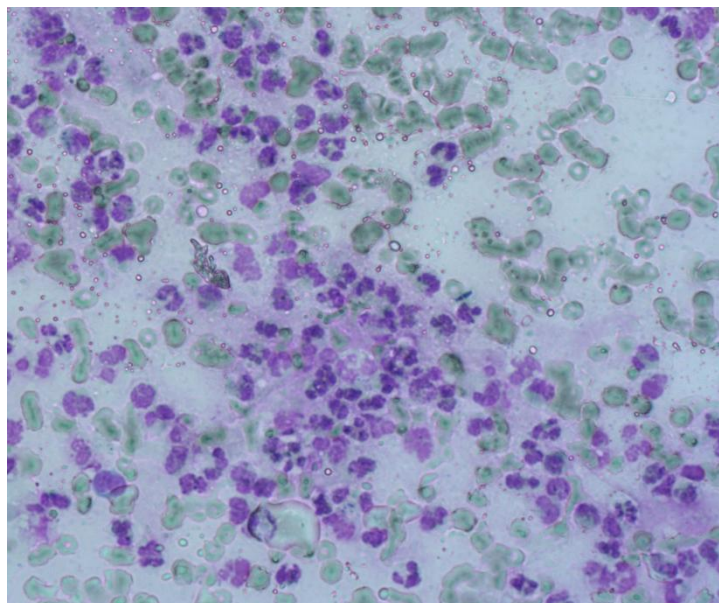
Nosological entity	Intervention group		Control group		Total
	<i>n</i>	%	<i>n</i>	%	
Hand phlegmon	7	7.95	6	7.6	13
Forearm phlegmon	23	26.1	20	25.3	43
Shoulder phlegmon	7	7.95	8	10.1	15
Foot phlegmon	10	11.4	11	13.9	21
Lower leg phlegmon	26	29.5	19	24.1	45
Thigh phlegmon	9	10.2	9	11.4	18
Neck phlegmon	6	6.8	6	7.6	12
Total	88	100	79	100	167

Note: percentages are given as applied to the number of patients in the study groups.

No dependence of nosology-related patients' distribution and the type of group was found ( $\chi^2$ -Pearson criterion  $p=0.953$ ). Thus, intervention and control groups constitute the parts of a single general population.

To evaluate healing of suppurative foci, a cytologic research method has been employed in our study. A surface biopsy procedure according to Pokrovskaya M.P. and Makarov M.S (1942) as modified by Kamaev M.F. (1954) has been applied. In control group, the material was sampled by gently scraping the wound surface layer with a special spreader or a surgical scalpel handle. The obtained material was applied on the glass, fixed, and stained according to the May-Grunwald-Romanowski-Giemsa stain method. In the intervention study group, cellular tissue elements were sampled using "needle biopsy" method (Kaem R.I., Karlov V.A., 1977; Sergel' O.S., Goncharova Z.N., 1990). 4-5 smears were taken sequentially from one and the same wound segment. Cytologic examination of smears from the surface of wounds was made during the 1<sup>st</sup> day and further on the 3, 5, 7, 9<sup>th</sup> day. Smears were examined using a microscope with photographic lens  $\times 63$ , formed elements were therewith counted, and a mean value for 10 fields of view was derived. The obtained value was expressed as a percentage per 100 counted cells. A light microscope Axio A1 (Zeiss, Germany) with a set of accessories was utilised. Photographs were captured with AxioCam 105 color camera (Zeiss, Germany) using ZEN 2 blue edition software (Zeiss, Germany), calibrated employing stage-micrometer for transmitted light (SMT) with 0.005 mm sensitivity.

At the time of randomisation, patients with soft tissue phlegmons from both study groups had a cytologic pattern inherent in the degenerative necrotic type of cell-mediated response. Degenerate neutrophils (DN) predominated (64.5 $\pm$ 9.2%) among cell elements, with very few intact leucocytes. Regeneration and degeneration index (RDI) was well below 1 (0.2 $\pm$ 0.1). Mostly extracellular microflora was abundant; however, intracellular microflora could be sometimes found in the state of incomplete or degenerate phagocytosis. Accumulation of necrotic masses and amorphous gelatinous intermediate substance were seen in specimens. Figure 1 presents a fragment of Pap smear from the wound surface in patients with soft tissue phlegmons at the moment of randomisation on the 1<sup>st</sup> day of examination.



**Fig. 1.** Cytogram fragment of smear from the wound surface in patients with soft tissue phlegmons on the 1<sup>st</sup> day. Degenerative-modified polymorphonuclear leukocytes predominate, mostly extracellular microflora is abundant; accumulation of necrotic masses and amorphous gelatinous intermediate substance are seen. Romanowski-Giemsa stain. Photographic lens  $\times 40$

Cell composition of Pap smears in patients with soft tissue phlegmons in study groups at the moment of randomisation is presented in Table 3.

**Table 3.** Cell composition of Pap smears in patients with soft tissue phlegmons in study groups at the time of randomisation, in % per 100 cells

Types of cells	Intervention group		Control group		p-value of t-criterion	p-value of the Mann-Whitney test
	M $\pm\sigma$ , in % per 100 cells	Me[Q1;Q3]	M $\pm\sigma$ , in % per 100 cells	Me[Q1;Q3]		
BN	1.8 $\pm$ 0.2	1.82 [1.77;1.87]	1.7 $\pm$ 0.2	1.74 [1.64;1.81]	0.682	536,500
SNN	15.2 $\pm$ 0.6	15.19 [15.07;15.32]	16.2 $\pm$ 0.4	16.16 [16.07;16.25]	0.647	502,500
DN	64.5 $\pm$ 9.2	65.89 [63.65;68.13]	62.2 $\pm$ 6.2	68.84 [67.57;70.09]	0.022	414,000
RDI	0.2 $\pm$ 0.1	0.18 [0.16;0.21]	0.2 $\pm$ 0.1	0.18 [0.16;0.21]	0.976	558,000
L	0.4 $\pm$ 0.2	0.39 [0.35;0.43]	0.2 $\pm$ 0.1	0.17 [0.15;0.19]	0.000	69,000

Note: BN - banded neutrophils, SNN - segmentonuclear neutrophils, DN - degenerate neutrophils, RDI - regeneration and degeneration index, L - lymphocytes.

Most parameters of statistical assessment of Pap smear cell composition on the first observation day in both study groups had similar values ( $p > 0.05$ ), what allowed inferring about homogeneity of groups. However, DN and L indices were not proved to be statistically homogeneous, what can be accounted for a small size of sampling. On the whole, it is not essential and has not any effect on achieving adequate results of the research study.

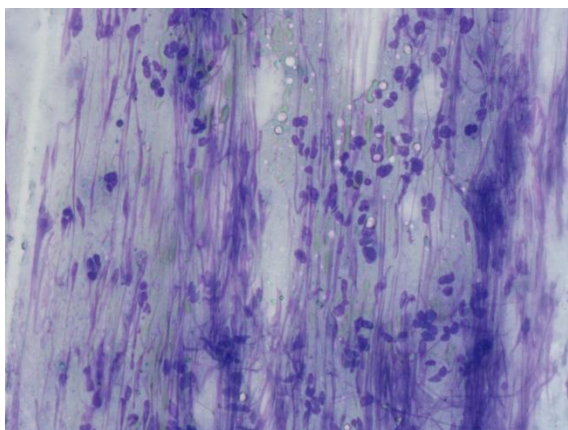
The work has been carried out as a simple randomised comparative controlled study in parallel groups. SPSS Statistics 25 (IBM) software was used to statistically process the obtained data. To examine interrelationship between quality-related attributes, contingency tables were compiled, and  $\chi^2$ -Pearson criterion or Fischer's exact test were computed. If interrelationship between quality-related attributes exists, parts of attributes were further compared using z-criterion of equal parts. A significance of differences between groups by quantity-related attributes was estimated applying parametric t-criterion of Student and non-parametric Mann-Whitney criterion for independent groups. For dependent groups, a parametric t-criterion for dependent samples and non-parametric Wilcoxon signed-rank test were used. A variance analysis with repeated measurements, specifying a factor of time and group, was employed to

evaluate changes in the dynamics of quantity-related attributes. The results of variance analysis with repeated measurements were used to verify the following hypotheses: whether the change in indices over time is significant, whether there is a difference between groups, and whether the statistically significant interaction between factors of time and group exists. The last hypothesis allowed the difference in a time-wise change in controllable indices depending on the group to be proved. The differences with less than 0.05 probability and a two-tailed critical area were considered statistically significant.

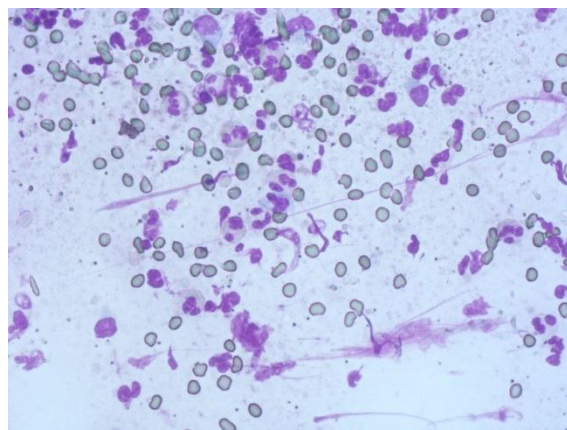
## Results

A cytologic pattern of smears in intervention group on the 5<sup>th</sup> day after randomisation corresponded to inflammatory or inflammatory regenerative type of cell-mediated response. A statistically significant decrease in the number of degenerate neutrophils (DN) ( $16.7 \pm 2.2\%$ ), an increase in the number of intact neutrophils: segmentonuclear (SNN) ( $41.6 \pm 3.8\%$ ) and banded neutrophils (BN) ( $-6.2 \pm 0.8\%$ ) ( $p < 0.001$ ) were seen. A statistically significant increase in regeneration and degeneration index (RDI) ( $-2.9 \pm 0.4$ ) ( $p < 0.001$ ) was noted. Plasma cells, histiocytes appeared. A statistically significant increase in the number of active macrophages ( $-4.6 \pm 0.6\%$ ), lymphocytes ( $-5.8 \pm 0.6\%$ ), fibroblasts ( $-4.2 \pm 0.5\%$ ) ( $p < 0.001$ ) was observed. Groups of young connective tissue cells in the form of fibrocytes, fibroblasts, fibrous fibers were found. Little microflora in the phase of complete phagocytosis was identified.

On the 5<sup>th</sup> day of treatment, in control group a cytologic pattern in smears was characterised by a neutrophil response: the number of intact neutrophils increased: SNN ( $42.6 \pm 3.8\%$ ), BN ( $-6.2 \pm 0.8\%$ ). The number of degenerate forms decreased:  $56.7 \pm 2.2\%$ . RDI was close to  $1:0.9 \pm 0.2$ . Extracellular and intracellular microflora was found, however, with more frequent cases of complete phagocytosis. The number of young neutrophils increased; poorly differentiated mononuclear cells appeared. Single actively phagocytizing leucocytes, macrophages, lymphocytes were encountered in the cellular component of the wound wall. Granulation tissue elements were occasional. A cytologic pattern corresponded to inflammatory type of cell-mediated response. Figures 2 and 3 present the fragments of Pap smears from the wound surface on the 5<sup>th</sup> day in study groups.



**Fig.2.** Cytogram fragment of smear from the wound surface on the 5<sup>th</sup> day, intervention group. Fibrocytes, fibroblasts, fibrous fibers were found among neutrophils and polyblasts. Romanowski-Giemsa stain. Photographical lens  $\times 40$



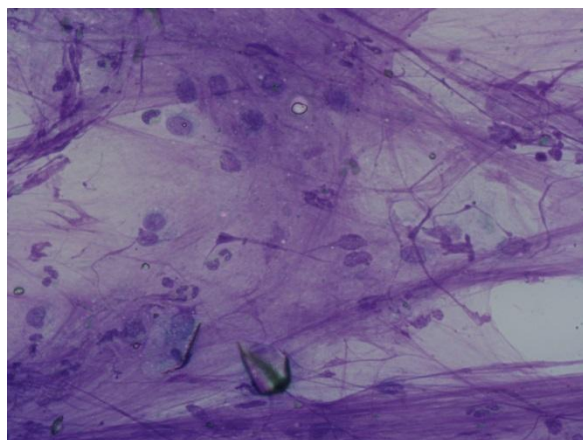
**Fig.3.** Cytogram fragment of smear from the wound surface on the 5<sup>th</sup> day, control group. Sporadically active phagocytizing leucocytes, macrophages, lymphocytes are seen. Granulation tissue elements are occasional. Romanowski-Giemsa stain. Photographical lens  $\times 40$

A significant difference between study groups was found when evaluating the dynamics of cell composition of Pap smears on the 5<sup>th</sup> day after surgery. From variance analysis with iterative measurements, it was proved that there are statistically significant changes in the cell composition of cytograms in both groups on the 5<sup>th</sup> day after surgery ( $p < 0.001$ ). A statistically significant interaction has been proved between factors of time and group ( $p < 0.001$ ).

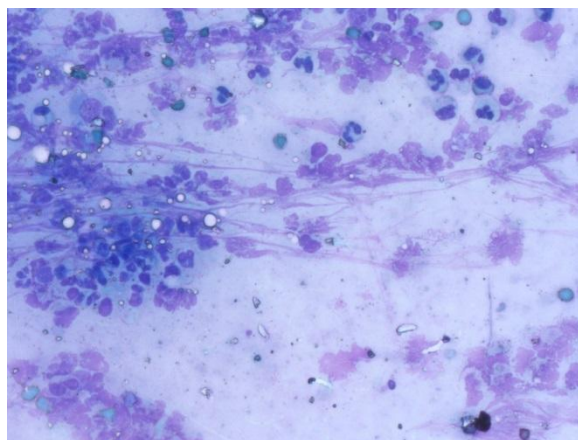


On the 9<sup>th</sup> day after surgery, in intervention group, a statistically significant decrease in DN ( $3.8 \pm 0.5\%$ ) was seen, intact neutrophils predominated – SNN ( $28.2 \pm 1.4\%$ ), BN –  $2.4 \pm 0.4\%$  ( $p < 0.001$ ). Of note was a statistically significant increase in RDI values –  $8.1 \pm 0.4$ , in the number of macrophages –  $15.8 \pm 1.6\%$ , and fibroblasts –  $8.4 \pm 0.8\%$  ( $p < 0.001$ ). Young elements of connective tissue, polyblasts predominated over neutrophils and located among fibrous structures of intermediate substance. Epithelium was represented in smears as layers of cells. There was no microflora. A cytologic pattern corresponded to regenerative inflammatory or regenerative type of cell-mediated response.

By the 9<sup>th</sup> day, a cytologic pattern in the control group started to take the features, inherent in regenerative processes. There was a statistically significant decrease in the number of DN –  $12.4 \pm 0.5\%$ , and more intact forms appeared: SNN –  $24.2 \pm 1.4\%$ , BN –  $6.2 \pm 0.4\%$  ( $p < 0.05$ ). RDI consistently exceeded 1:  $2.5 \pm 0.4$ . Few intracellular microbes were identified in the phase of complete phagocytosis. The number of mononuclear cells substantially declined, and their derivative forms came to be regularly found while differentiating: the number of polyblasts rose, with more fibroblasts –  $3.2 \pm 0.5\%$ ; the number of macrophages increased  $6.7 \pm 0.8\%$ . Delicate fibers of intermediate substance were observed along with cell elements. A cytologic pattern of smears corresponded to regenerative inflammatory type of cytograms. Figures 4 and 5 present the fragments of Pap smears from the wound surface on the 9<sup>th</sup> day in study groups.



**Fig.4.** Cytogram fragment of smear from the wound surface on the 9<sup>th</sup> day, intervention group. Young elements of connective tissue, fibroblasts, polyblasts, macrophages are among fibrous structures of intermediate substance. Epithelium is represented as layers of cells. Romanowski-Giemsa stain. Photographic lens  $\times 40$



**Fig.5.** Cytogram fragment of smear from the wound surface on the 9<sup>th</sup> day, control group. Number of mononuclear cells decreased, amount of polyblasts, fibroblasts, macrophages increased. Delicate fibrous structures of intermediate substance were observed. Romanowski-Giemsa stain. Photographic lens  $\times 40$

Cell composition of Pap smears in patients with soft tissue phlegmons from study groups is presented in Table 4.

**Table 4.** Cell composition of Pap smears in patients with soft tissue phlegmons from study groups ( $M \pm \sigma$ ), in % per 100 cells

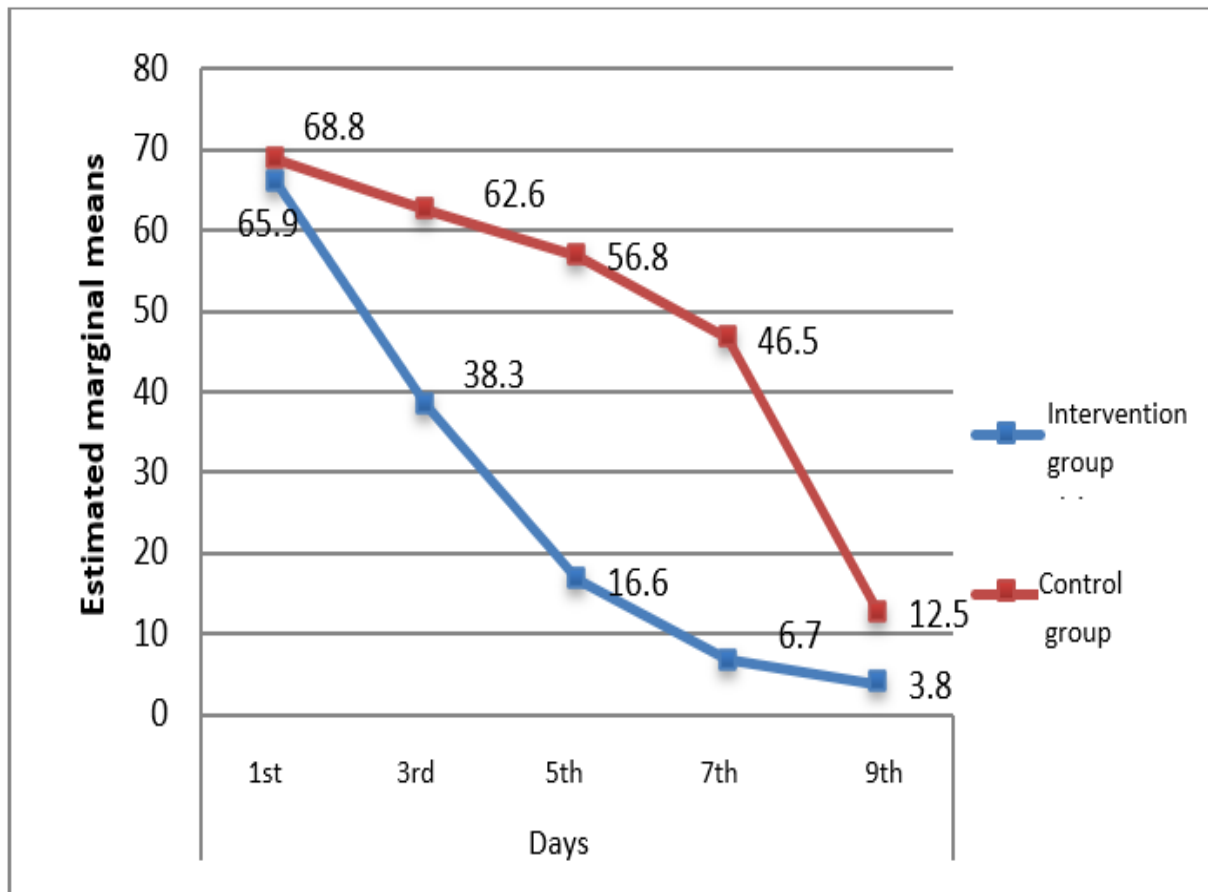
Types of cells	Intervention group		Control group	
	5 <sup>th</sup> day	9 <sup>th</sup> day	5 <sup>th</sup> day	9 <sup>th</sup> day
DN	$16.58 \pm 1.32$	$3.79 \pm 0.29$	$56.76 \pm 1.24$	$12.52 \pm 0.43$
BN	$6.26 \pm 0.49$	$2.44 \pm 0.25$	$6.28 \pm 0.49$	$6.16 \pm 0.19$
SNN	$41.94 \pm 2.28$	$28.25 \pm 0.83$	$42.38 \pm 2.39$	$24.18 \pm 0.92$
RDI	$2.94 \pm 0.29$	$8.15 \pm 0.11$	$0.86 \pm 0.05$	$2.43 \pm 0.11$
L	$5.86 \pm 0.39$	$7.60 \pm 0.59$	$2.76 \pm 0.23$	$4.33 \pm 0.70$
MP	$4.62 \pm 0.36$	$16.06 \pm 0.82$	$2.21 \pm 0.19$	$6.70 \pm 0.48$
F	$4.62 \pm 0.36$	$16.06 \pm 0.82$	$2.21 \pm 0.19$	$6.70 \pm 0.48$

Note 1. DN - degenerate neutrophils, BN - banded neutrophils, SNN - segmentonuclearneutrophils, RDI - regeneration and degeneration index, L – lymphocytes, MP – macrophages, F–fibroblasts.

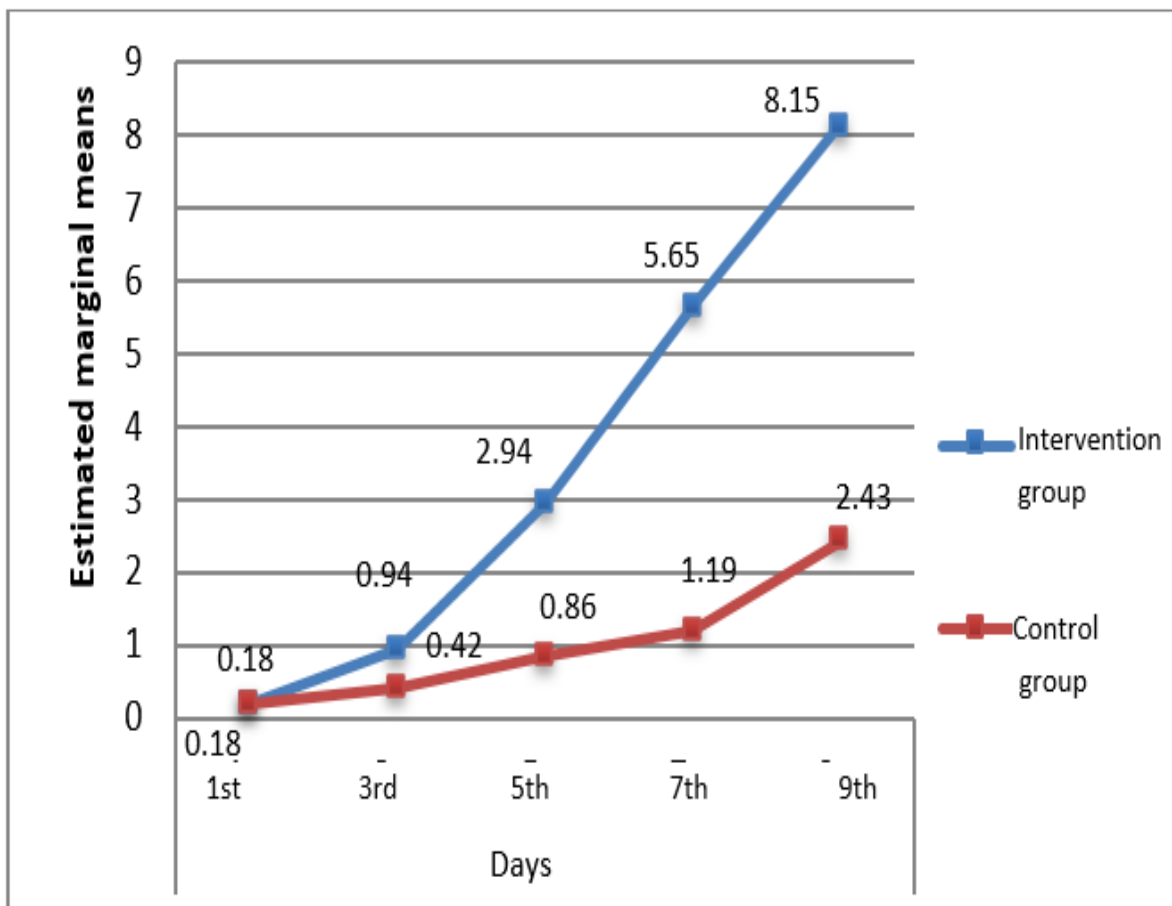
For both groups, statistically significant changes in cell composition in cytogram on the 1<sup>st</sup> and 9<sup>th</sup> day after surgery have been proved: a decrease in the number of DN in intervention group ( $M \pm \sigma$ ) from  $64.5 \pm 9.2\%$  to  $3.8 \pm 0.3\%$ , in control group from  $68.8 \pm 6.2\%$  to  $12.5 \pm 0.4\%$  ( $p < 0.001$ ); an increase in SNN in intervention group ( $M \pm \sigma$ ) from  $15.2 \pm 0.6\%$  to  $28.3 \pm 0.8\%$ , in control group from  $16.2 \pm 0.4\%$  to  $24.2 \pm 0.9\%$  ( $p < 0.001$ ); an increase in RDI value - in intervention group ( $M \pm \sigma$ ) from  $0.2 \pm 0.1\%$  to  $8.2 \pm 0.1\%$ , in control group from  $0.2 \pm 0.1\%$  to  $2.4 \pm 0.1\%$  ( $p < 0.001$ ).

In intervention group, where programmed rehabilitation technologies were employed, the number of degenerate neutrophils had decreased more rapidly, there appeared more intact neutrophils, RDI increased more quickly, and the differences between groups were generally statistically significant throughout the entire follow-up period ( $p < 0.001$ ).

A significant interaction between factors of time and group ( $p < 0.001$ ) was also identified; by the 9<sup>th</sup> day, in intervention group the number of degenerate forms was substantially lower:  $3.8 \pm 0.3\%$  as opposed to control group ( $12.5 \pm 0.4\%$ ); there were more intact neutrophils:  $28.3 \pm 0.8\%$  and  $24.2 \pm 0.9\%$ , respectively. A quicker increase in RDI values in intervention group on the 9<sup>th</sup> day ( $8.2 \pm 0.1$ ) as compared with control group ( $2.4 \pm 0.1$ ) was observed. It demonstrated more active phagocytosis, rapid cleansing of purulent cavity. The dynamics of mean values for degenerate neutrophils and values of regeneration and degeneration index in Pap smears of patients with soft tissue phlegmons from both study groups is presented in Figures 6 and 7.



**Fig.6.** Dynamics of mean values of degenerate neutrophils in cytograms of patients with soft tissue phlegmons from both study groups



**Fig.7.**Dynamics of mean values of regeneration and degeneration index (RDI) in cytograms of patients with soft tissue phlegmons from both study groups

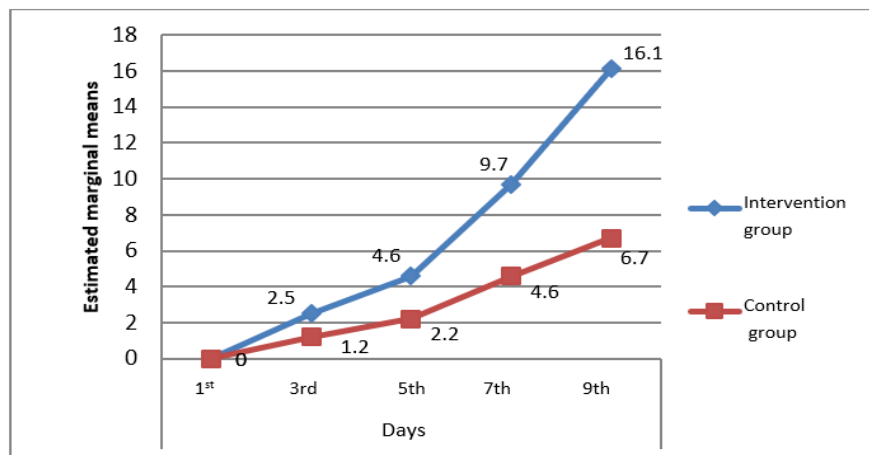
To evaluate reparative capacity of purulent wounds, a cytologic assessment was made of quantitative composition of lymphocytes, macrophages, and fibroblasts in the study groups on the 1<sup>st</sup> and 9<sup>th</sup> day after surgery. For both groups, there have been proved a statistically significant increase in the number of lymphocytes: in intervention group ( $M \pm \sigma$ ) from  $0.4 \pm 0.2\%$  to  $7.6 \pm 0.6\%$ , in control group from  $0.2 \pm 0.1\%$  to  $4.3 \pm 0.7\%$  ( $p < 0.001$ ); and statistically significant increase in the number of active macrophages: in intervention group ( $M \pm \sigma$ ) to  $16.1 \pm 0.8\%$ , in control group to  $6.7 \pm 0.5\%$  ( $p < 0.001$ ). On the 9<sup>th</sup> day, a statistically significant increase in the number of fibroblasts: in intervention group ( $M \pm \sigma$ ) to  $16.1 \pm 0.8\%$ , in control group to  $6.7 \pm 0.5\%$  ( $p < 0.001$ ) has also been seen.

In intervention group, where programmed rehabilitation technologies were employed, the number of lymphocytes increased more rapidly, earlier occurrence of macrophages and cells of young connective tissue in the form of fibrocytes, fibroblasts, and differences between the groups were generally statistically significant throughout the entire follow-up period ( $p < 0.001$ ).

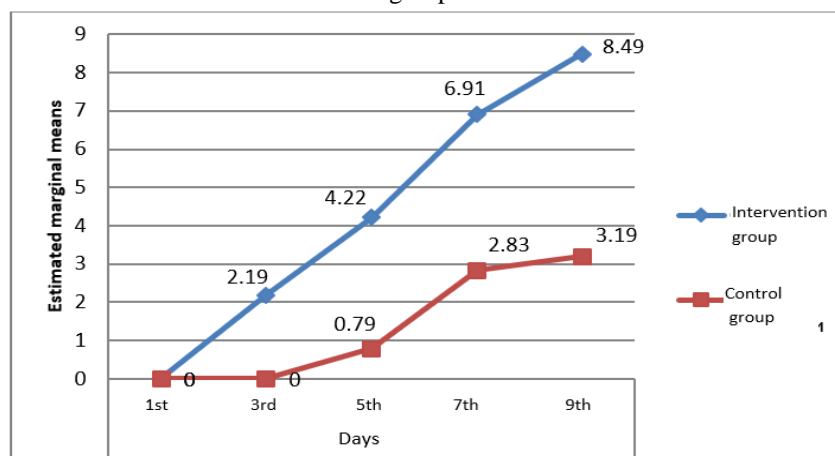
A significant interaction between factors of time and group ( $p < 0.001$ ) was also identified; in intervention group by the 9<sup>th</sup> day, the number of lymphocytes was considerably higher:  $7.5 \pm 0.6\%$  as distinguished from control group ( $2.5 \pm 0.6\%$ ), the number of macrophages was higher:  $12.17 \pm 0.68\%$  and  $2.21 \pm 0.19\%$ , respectively. In intervention group, there was noted an earlier occurrence of young connective tissue cells in the form of fibrocytes, fibroblasts, and an increase in their number by the 9<sup>th</sup> day to  $6.44 \pm 0.38\%$ , as opposed to the control group  $-1.39 \pm 0.13\%$ . It demonstrated active regeneration processes in the wound in the intervention group of patients, and the structure of



cytograms was regenerative. The dynamics of mean values for macrophages and fibroblasts in Pap smears of patients with soft tissue phlegmons from both study groups is presented in Figures 8 and 9.



**Fig.8.**Dynamics of mean macrophage values in cytograms of patients with soft tissue phlegmons from both study groups



**Fig.9.**Dynamics of mean fibroblast values in cytograms of patients with soft tissue phlegmons from both study groups

## Discussion

The analysis of the dynamics of cytologic pattern in patients with soft tissue phlegmons in the study groups has shown that, in the control group, a low intensity of cell-mediated responses in the wound and prolonged inflammation phases were identified with conventional treatment, and inflammatory type of cytograms was observed only 9 days after surgery. Sluggish reparative processes in the wound were also seen in the control group, defining a very prolonged regeneration phase and later onset of scar reorganization phase. It resulted in longer healing time.

The use of programmed rehabilitation technologies allowed creating conditions for enhanced rehabilitation of suppurative focus, resulted in shortening of all wound process phases. Surgical debridement of suppurative focus, prolonged postoperative lavage of wound cavity, drain process software made it possible to promptly remove devitalized tissues, toxins, and proteolytic enzymes from the wound, having decreased microbial contamination therein. It extremely decreased the duration of necrotic tissue rejection stage. Early closure of the wound with sutures, employing active drainage in conditions of minor inflammatory response in the wound, greatly accelerated reparative processes, facilitating development and completion of regeneration phase.

## Conclusion

A high-speed of cell-mediated responses in the wound was identified during the cytologic study of smears in patients with soft tissue phlegmons using programmed rehabilitation technologies. A statistically significant more rapid decrease in the number of degenerative forms of neutrophils, positive redistribution of banded and segmented nuclear neutrophils together with the increased regeneration and degeneration index were therewith noted, which are indicative of a quicker reversal of inflammatory process. Also observed with certainty in earlier periods was an occurrence of macrophages and cells of young connective tissue in the form of fibrocytes, fibroblasts, fibrous fibers, what demonstrated active regeneration processes in the wound.

The use of programmed rehabilitation technologies will make it possible to optimise the management of patients with purulent inflammatory diseases of various origin and at different locations, to enhance treatment results and quality of patients' life.

## References

- [1] Sartelli, M., Guirao, X., Hardcastle, T.C. (2018). WSES/SIS-E consensus conference: recommendations for the management of skin and soft-tissue infections. *World Journal of Emergency Surgery*, 13, 58. <https://doi.org/10.1186/s13017-018-0219-9>
- [2] May, A.K. (2009). Skin and soft tissue infections. *Surgical Clinics of North America*, 89(2), 403-420. <https://doi.org/10.1016/j.suc.2008.09.006>
- [3] Ustin, J.S., & Malangoni, M.A. (2011). Necrotizing soft-tissue infections. *Critical care medicine*, 39(9), 2156-2162. <https://doi.org/10.1097/CCM.0b013e31821cb246>.
- [4] Tret'yakov, A.A., Petrov, S.V., Neverov, A.N., & Shchetinin, A.F. (2015). Treatment of purulent wounds. *Novosti khirurgii*, 6(23), 680-687.
- [5] Kuzin, M.I., & Kostyuchenok, B.M. (1990). *Wounds and wound infections: A guide for physicians*. Moscow: Medicine, 592.
- [6] May, L., Klein, E.Y., Martinez, E.M., Mojica, N., & Miller, L.G. (2017). Incidence and factors associated with emergency department visits for recurrent skin and soft tissue infections in patients in California, 2005–2011. *Epidemiology & Infection*, 145(4), 746-754. <https://doi.org/10.1017/S0950268816002855>
- [7] Stevens, D.L., Bisno, A.L., Chambers, H.F., Dellinger, E.P., Goldstein, E.J.C., Gorbach, Sh.L., Hirschmann, J.V., Kaplan, Sh.L., Montoya, J.G., & Wade, J.C. (2014). Practice Guidelines for the Diagnosis and Management of Skin and Soft Tissue Infections: 2014 Update by the Infectious Diseases Society of America. *Clinical Infectious Diseases*, 59(2):e10–e52. <https://doi.org/10.1093/cid/ciu296>
- [8] *Statistical Digest 2018. Resources and activity of healthcare facilities. Key healthcare indicators. Part VI: stat. digest / M.*, 2019. – 170p.
- [9] Stadelmann, W.K. (1998). Physiology and healing dynamics of chronic cutaneous wounds / W.K. Stadelmann. *American Journal of Surgery*, 176(2), 26S–38S.
- [10] Midwood, K.S. (2004). Tissue repair and the dynamics of the extracellular matrix / K.S. Midwood. *The International Journal of Biochemistry & Cell Biology*, 36(2), 1031-1037.
- [11] Deodhar, A.K., & Rana, R.E. (1997). Surgical physiology of wound healing: a review. *Journal of Postgraduate Medicine*, 43(2), 52-56.
- [12] Eskes, A.M., Gerbens, L.A., Van Der Horst, C.M., Vermeulen, H., & Ubbink, D.T. (2011). Is the red-yellow-black scheme suitable to classify donor site wounds? An inter-observer analysis. *Burns*, 37(5), 823-827. <https://doi.org/10.1016/j.burns.2010.12.019>.
- [13] Zemskov, M.A., Chorochilov, A.A., Iljina, E.M., & Domnich, O.A. (2011). Peculiarities of changes of immune status in chronic inflammatory diseases. *Journal of experimental and clinical surgery*, 4(3), 468-472.

- [14] Lacci, K., &Dardik, A. (2010). Platelet-rich plasma: support for its use in wound healing. *Yale Journal of Biology and Medicine*, 83(1), 1-9.
- [15] Han, T., Wang, H., &Zang, Y.Q. (2012). Combining platelet-rich plasma and extracellular matrix-derived peptides promote impaired cutaneous wound healing in vivo. *Journal of Craniofacial Surgery*, 23(2), 439-447.
- [16] Larichev, A.B., Shishlo, V.K., Lisovsky, A.V., Chistyakov, A.L., &Vasiliev, A.A. (2011). Wound infection prevention and morphological aspects of aseptic wound healing. *Journal of Experimental and Clinical Surgery*, 4(4), 728-733.
- [17] Titova, M.I., Svetukhin, A.M., Kurochkina, A.I., Astasheva, N.G., Doroshina, T.I., Krylova, N.N., &Agofonov, V.A. (2000). Current methods of morphological and hemostasiological analysis of reparative process in wounds making use of information programs. *Klinicheskaiia laboratornaia diagnostika*, (7), 24-33.
- [18] Kocjan, G. (2017). *Cytopathology of the Head and Neck: Ultrasound Guided FNAC*. 2nd ed. -Wiley-Blackwell, 212.
- [19] Field, A.S. (ed.) (2017). *Practical Cytopathology. A Diagnostic Approach to Fine Needle Aspiration Biopsy*. Elsevier, 563.
- [20] Ivanusa, S.Y., Risman, B.V., &Ivanov, G.G. (2016). Modern ideas about methods of assessment the course of the wound process in patients with purulo-necrotic complications of the diabetic foot syndrome. *Herald of the Russian Military Medical Academy*, 54, 190–194. <http://elibrary.ru/item.asp?id=26280216>
- [21] Larichev, A.B., Chistyakov, A.L., &Komlev, V.L. (2016). Comparative assessment of wound healing by using a local flap and full-thickness skin graft in reconstructive head and neck surgery. *Wounds and wound infections*, 3(2), 37-46. <https://doi.org/10.17650/2408-9613-2016-3-2-37-46>
- [22] Kamaev, M.F. (1954). *Types of cytograms in a superficial biopsy of the wound*. Collection of works of the Odessa medical Institute named after N. I. Pirogov. Kiev, 267-276.
- [23] IuA, D., Larichev, A.B., &AIu, A. (1990). Substantiation of using forced early secondary suture in the treatment of suppurative wounds by the method of vacuum therapy. *Vestnik Khirurgii Imeni II Grekova*, 144(3), 126-128.